Intersections between semantic cognition and affective processing: Insights from neuropsychology and neuroimaging

Nicholas Souter

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Abstract

Semantic cognition, the basis for our understanding of the world, is supported by both the storage of semantic representations and the ability to flexibly retrieve them – semantic control. Semantic control dictates our ability to parse ambiguous information, and is supported by a distributed semantic control network (SCN). Patients with semantic aphasia (SA) experience multimodal semantic control deficits following left hemisphere stroke. Using cognitive neuropsychology and neuroimaging, this thesis further explores the neural bases of semantic retrieval and tests the relevance of semantic control to emotion, valence, and reward. Key findings were: (i) SA patients experience diffuse disconnection beyond lesion site. Lesion and structural disconnection of left-lateralised SCN nodes predict semantic impairment, while domain-general control impairment is predicted by lesion to adjacent fronto-parietal regions and by interhemispheric structural disconnection. (ii) SA patients present with impaired categorisation of facial emotion portrayals, susceptible to effects of cues and miscues. (iii) Valence congruency between words facilitates semantic matching, while semantic relatedness facilitates valence matching. SA patients present with impaired valence matching, exacerbated by semantic distractors. (iv) Impairments in the retrieval of weak associations can be facilitated in SA using cued extrinsic rewards. (v) The retrieval of both contextual and emotional associations is associated with activation in SCN, with these tasks being dissociated by default mode subnetworks. Effects of retrieval demands on the default mode network run orthogonally to effects of task. This thesis provides novel insight into the complex neural basis of retrieving meaning and emotion. It also contributes to our understanding of the impairments in SA, as well as how they can be ameliorated. Finally, this thesis supplements conceptually-focused models of emotion processing, stressing a role of semantic control. This work contributes to an increasingly clear understanding of controlled semantic retrieval and its contribution to cognition across domains.

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Author's declaration

I, Nick Souter, declare that this thesis is a presentation of original work and I am the sole author, under the supervision of Professor Beth Jefferies. This work has not previously been presented for an award at this, or any other, University. All sources are acknowledged as References.

The following empirical chapters included in this thesis have been published in peer-reviewed journals:

Chapter 2

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Chapter 3

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Chapter 5

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The following chapter has been submitted for publication and is currently under review, and is also available as a pre-print:

Chapter 4

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Supervisor's declaration

As the primary supervisor of Nicholas Souter, I confirm that this thesis is the work of the candidate. Where I am named as co-author, this is due to my role in editing and supervising. The role of other collaborators have been detailed in the acknowledgements section for each empirical chapter.

Chapter 1: Literature review

1.1. Overview

The ways in which we process conceptual information affects how we make sense of the world. When encountering a dog, for instance, we rely on several sources of information. This includes visual features, such as four legs and a wagging tail; auditory features, such as barking or yapping; praxis features, relating to the manner appropriate to pet or stroke them; and valence features, with dogs being, for many, positive entities who evoke joy. These features interact with an abstract representation of what a dog is – free of any one modality (Lambon Ralph et al., 2017). Finally, it is important that we flexibly use context to understand how to interact with this concept. The ways in which we use all of this information will likely be very different when encountering a familiar family pet, versus a sniffer dog in airport security (Jefferies, 2013; Noonan et al., 2013). Research into 'semantic cognition' helps us understand how all this information is integrated and controlled. Evidence from cognitive neuropsychology and neuroscience has provided important insights into the structure of semantic cognition (e.g., Jefferies et al., 2019; Lambon Ralph et al., 2017). Evidence suggests the importance of dissociable systems supporting the storage of semantic representations, and controlled retrieval mechanisms needed to bring to the fore non-dominant aspects of our knowledge when this is required by the context or when relevant to our goals (Jefferies et al., 2019). These dissociable systems rely on different regions and networks in the brain. Semantic control ability appears to share features with, but be separable from, more domain-general cognitive control resources (Gao et al., 2021). Importantly, it appears that all these interacting mechanisms might be implicated in domains that are ostensibly separable from semantic cognition, including episodic memory (Vatansever et al., 2021), social cognition (Diveica et al., 2021), and emotion recognition (Lindquist, 2017).

Many neuropsychological investigations have focused on patients with semantic aphasia (SA) – characterised by impairment in semantic control typically following left hemisphere stroke (e.g., Jefferies & Lambon Ralph, 2006; Thompson et al., 2017). Study of these patients has provided insight into the neural basis of semantic control and to the abilities and behaviours which rely on this process being intact (e.g., Stampacchia et al., 2018; Thompson et al., 2018; 2022). Relatively little is known about how focal lesions in this

group may impact diffuse structural and functional connections in the brain. Developing our understanding in this area could provide insight into how distributed functional networks support controlled semantic retrieval, as well as the extent to which impairments in domain-general and semantic control dissociate. Research into SA patients also allows us to appreciate the diverse functions which rely on semantic control and can therefore be affected by its impairment (e.g., Stampacchia et al., 2018). This thesis will test for effects of semantic control impairments on the processing of hedonic valence and discrete emotion categories. The relevance of semantic control to this domain has rarely been considered in previous work. The thesis will also investigate whether semantic retrieval in SA patients is susceptible to modulation by intrinsic and extrinsic reward, as has been demonstrated for cognitive control more generally (e.g., Yee et al., 2019): performance in SA may benefit from the provision of rewards, or this effect may be disrupted by alterations in valence processing. Finally, neuroimaging with neurologically healthy adults may allow us to better understand how diverse functional networks contribute to tasks which rely on retrieval of both associative and emotional features of concepts. To advance knowledge of the neurocognitive basis of semantic and emotional processing, the empirical chapters in this thesis employ a combination of cognitive neuropsychology with SA patients and task-based functional magnetic resonance imaging (fMRI) with healthy young adults.

1.2. The structure of meaning

1.2.1. A spectrum of semantic representation from embodied to abstract

In navigating and interpreting the external world, we are forced to make sense of a jumble of complex and ambiguous input. Theories of semantic cognition attempt to define how this information is integrated and processed. Theories have varied in terms of how they explain this processing. Some models stress an important role of sensorimotor features, providing an 'embodied' basis for semantic knowledge. For example, the processing of action words such as 'lick', 'pick', and 'kick' appears to recruit brain regions typically associated with the respective motor action (Pulvermüller, 2005). This suggests a degree of reliance on sensorimotor regions, supporting the notion that meaning is grounded in action and perception (Binder & Desai, 2011). This view is also supported by evidence that patient groups can present with seemingly category-specific semantic impairments, for instance with dissociated impairments in the processing of verbal and visual stimuli (Warrington &

Shallice, 1984). Others have argued against this view, suggesting instead that semantic knowledge is supported by an amodal and symbolic system, rooted in language. Under this framework, the meaning of a word is defined not by its sensorimotor referents, but by its relation to other words (Landauer & Dumais, 1997). There is an increasing acceptance within the field that semantic representation can likely not be supported by a system that is either fully embodied or fully symbolic. The fully symbolic account is challenged by aforementioned neuroimaging evidence implicating sensorimotor regions in semantic processing, while the fully embodied account is challenged by our ability to process abstract concepts (e.g., 'love', 'justice', 'time') that lack sensorimotor features (Vigliocco et al., 2009). Accordingly, Meteyard et al. (2012) argue that effective semantic cognition likely relies on both sources of information, with modality-specific input that is processed in amodal convergence zones.

1.2.2. The 'hub and spoke' model of semantic cognition

The 'hub and spoke' framework of semantic cognition similarly suggests the importance of both modality-specific and amodal processing. This account argues that representations of concepts are stored in a heteromodal "hub" (Lambon Ralph et al., 2017). These concepts are heteromodal in so far as they are not grounded in or restricted to any one sensory modality. It has been argued that this hub is located in the anterior temporal lobes (ATLs; Lambon Ralph et al., 2010). This is consistent with evidence that patients with semantic dementia (SD) experience loss of conceptual knowledge following relatively focal atrophy of the ATLs (Patterson et al., 2007). SD patients are particularly impaired when retrieving names for low-frequency or low-familiarity pictures, suggesting progressive loss of weakly-encoded knowledge (Jefferies et al., 2009; Rogers et al., 2015). This is further supported by task-based neuroimaging evidence; ATL specifically activates to semantic tasks across a range of modalities (Binney et al., 2010; Visser & Lambon Ralph, 2011), and deactivates to non-semantic tasks (Humphreys et al., 2015). This activation is seen across stimuli and tasks, supporting the heteromodal nature of this hub (Visser et al., 2010). Furthermore, neuroimaging evidence shows that processing of combinatory semantics relating to conceptually coherent information evokes a stronger response in ATL (Pylkkänen, 2019; Teige et al., 2019). SD patients also experience behavioural symptoms beyond the semantic domain. This includes affective abnormalities such as apathy, emotional withdrawal, and diminished empathy (Bozeat, Gregory, et al., 2000; Hodges & Patterson, 2007). These behavioural effects could reflect some degree of atrophy in orbitofrontal

regions, given that SD is thought to be a temporal lobe variant of frontotemporal dementia (Hodges & Patterson, 2007), in which atrophy to this region is common (Perry et al., 2006). These effects might also reflect a role of semantic cognition in affective processing, and/or commonalities between the brain mechanisms that support semantic and affective aspects of cognition.

The heteromodal hub interacts with modality-specific "spokes" distributed throughout the cortex (Lambon Ralph et al., 2010). These spokes allow for coherent semantic representations by providing input from diverse modalities including vision, sound, speech, praxis, function, and valence (Lambon Ralph et al., 2017). The concept of a hammer, for instance, will rely not only on its visual features but also on the noise it makes when colliding with wood, and the arching motion needed to swing it. Abstraction of all of these sensory-motor features to form a coherent heteromodal concept of "hammer" is supported by the ATL hub (Binney et al., 2012; Lambon Ralph et al., 2010). This framework challenges more distributed models of semantic cognition, wherein communication between modality-specific regions may be sufficient for coherent representations (e.g., Mahon & Caramazza, 2011). Increasingly, theory and evidence support the need for integrative hubs or convergence zones in semantic representation (Meteyard et al., 2012; Pulvermüller, 2013). The benefits of a heteromodal hub becomes clearer when considering the need for the semantic system to go beyond sensory-motor features alone in order to aid judgements of overall higher-order conceptual similarity (Patterson et al., 2007). Indeed, modelling of semantic representation has demonstrated the benefits of distributional semantics which factor in patterns of overall semantic similarity between words (Rotaru et al., 2018).

The hub and spoke architecture is supported by neuroimaging evidence. fMRI evidence suggests that ATL is specifically implicated in the decoding of object identity and integration of features (Coutanche & Thompson-Schill, 2015). Ventral portions of ATL, in particular, represent the meaning of stimuli, independent of presentation modality (Murphy et al., 2017). Furthermore, white matter tracts connecting temporo-occipital sensory cortices to the ATLs are associated with a shift from perceptual to conceptual processing (Chiou et al., 2018), supporting an abstraction from featural to heteromodal representations. Using fMRI, Chiou and Lambon Ralph (2019) probed the mechanics of the interaction between the hub and spokes. Left ATL was consistently engaged across tasks probing action and place knowledge. Responses in spoke regions specialised for either action or place knowledge were found to be task-specific. Importantly, a bidirectional relationship was found, with activation

both in the hub and in the spokes modulating activation in the other. Modulation from ATL was dominant in this relationship, suggesting an ability of ATL to tailor retrieval to focus on specific features according to task requirements. Studies employing computational modelling have successfully simulated effective semantic cognition using a single multi-modal hub in conjunction with modality-specific spokes (Hoffman et al., 2018; Jackson et al., 2021). Finally, the severity of semantic impairment in SD is predicted not only by direct atrophy of ATL, but also diminished connectivity between ATL and spoke regions (Guo et al., 2013). These findings paint a picture in which effective interpretation of conceptual input is driven by a dynamic interplay between a heteromodal hub and modality-specific spokes.

1.2.3. Alternative accounts of semantic hubs

Alternative accounts have challenged core assumptions of the hub and spoke framework. The position of ATL as a heteromodal semantic hub has been disputed – some researchers have instead argued for a more important role of the angular gyrus (AG). The bilateral AG has been shown to activate during the process of combining concepts into coherent semantic representations, and atrophy to this region predicts semantic impairment in dementia (Price et al., 2015). Furthermore, excitation of left AG using transcranial direct current stimulation selectively facilitates judgements about meaningful word pairs (Price et al., 2016). This region has high resting-state connectivity with ATL and responds during the retrieval of easy global associations (Davey et al., 2016). Such findings have resulted in AG being proposed as an integrative and heteromodal hub (Bonner et al., 2013) or multimodal convergence zone (Kuhnke et al., 2022). These investigations have not found such evidence for the involvement of ATL. This may be attributable to methodological challenges in effectively scanning this region. fMRI signal in ATL is frequently distorted due to its proximity to air-filled cavities – the resulting drop-out in signal is referred to as the susceptibility artifact (Visser et al., 2010). Recent advances in fMRI, such as the implementation of dual gradient-echo echo planar imaging, have been shown to be promising in increasing signal in this area (Halai et al., 2014).

Others have challenged the notion of a single hub. The ‘dual hub’ account argues that dissociable hubs store taxonomic and thematic information. While taxonomic information reflects categories into which concepts can be sorted (DOG - ANIMAL), thematic information reflects relationships between concepts which frequently co-occur (DOG – BALL). Schwartz et al. (2011), for instance, provide evidence that while damage to left ATL is associated with taxonomic errors in picture naming, damage to the left temporoparietal

junction (including aspects of AG) is associated with thematic errors. It has been argued that AG may be positioned to support thematic associations due to its connectivity to the hippocampus, relating to processing of event structures which would be beneficial for this purpose, while ATL is connected to the perirhinal cortex, important for visual discrimination and therefore taxonomic categorisation (Davis & Yee, 2019). The dynamic multilevel reactivation framework (Reilly et al., 2016) argues for the existence of low-order hubs in the AG and posterior middle temporal gyrus which support connectivity with sensorimotor regions, and high-order hubs in ATL which support symbolic transformation of input. Using an 'embodied' framework, Fernandino et al. (2016) similarly found evidence of five separate multimodal convergence zones during the processing of words, including the left parahippocampal gyrus, left retrosplenial cortex, posterior cingulate cortex/precuneus, medial prefrontal cortex (PFC), and AG, using fMRI. These convergence zones were specialised for particular modalities/features (e.g., colour, shape, motion). These findings are consistent with the embodied notion that semantic processing is supported by modality-specific information, rather than symbolic and amodal representation. Such evidence is challenged by studies which support the existence of a single heteromodal hub in ATL. For instance, using fMRI Chiou and Lambon Ralph (2019) observed that the ATL is engaged by semantic tasks regardless of modality, in a domain-general fashion, in conjunction with activation in modality-specific spokes. Using reverse-engineered computational modelling, Jackson et al. (2021) similarly demonstrated that processing of concepts is most efficiently achieved when a single amodal hub operates in concert with spokes. Functional similarities between ATL and AG may be due in part to their shared alliance with the default mode network (DMN). Both regions are partially overlapping with this network (Humphreys et al., 2015). DMN supports heteromodal representation across domains (Smallwood et al., 2021), consistent with the hub and spoke account of how concepts are computed.

1.2.4. The CSC Framework: Insights from neuropsychology

The hub and spoke framework provides an account of how coherent concepts are produced, but the storage of such representations is not sufficient for effective semantic cognition. Semantic retrieval also needs to be controlled while disregarding unhelpful information (Hoffman, 2018; Jefferies, 2013). The Controlled Semantic Cognition (CSC) framework distinguishes between semantic storage and retrieval as two distinct but inextricably linked processes (Lambon Ralph et al., 2017). Evidence for this framework comes from neuropsychological studies with semantically impaired patients. Jefferies and

Lambon Ralph (2006) compared SD patients to communication-impaired stroke survivors with aphasia. Semantic impairment was found in both groups, with important qualitative differences. SD patients showed the expected amodal loss of conceptual information, with high item-consistency across tests suggesting degradation of specific concepts. In contrast, aphasia patients showed low item-consistency across tests, and were more negatively affected in contexts requiring a high degree of cognitive control. These results suggest a double dissociation between the storage of amodal semantic representations, and the ability to control their retrieval in a flexible manner, known as semantic control. Considering the hub-and-spoke model in the context of the CSC framework, effective semantic cognition relies on 'triangulation' of unimodal concepts, modality-specific spokes, and executive semantic retrieval (Chiou et al., 2018). Evidence from computational modelling of cortical architecture suggests that controlled semantic cognition works best in conjunction with a single multimodal hub (Jackson et al., 2021). Research in cognitive neuroscience and neuropsychology has allowed us to conceptualise the function of semantic control, and the conditions under which it is required.

1.2.5. Deficits of semantic control

Impaired multimodal semantic control following stroke is referred to as semantic aphasia (SA; Jefferies, 2013). This follows from the original use of SA as a label by Head (1926), who described impaired manipulation of verbal and non-verbal information for symbolic processing. Semantic impairment in SA has frequently been studied using thematic association tasks. Such tasks rely on manipulation of contextual information, and SA patients accordingly present with marked impairment (Thompson et al., 2017). Performance is impaired further when retrieving non-dominant meanings of words (Noonan et al., 2010) or low-relevance conceptual features (Montefinese et al., 2020), reflecting increased control demands when accessing weakly-encoded concepts. Furthermore, SA patients show impaired ability to supress irrelevant information, demonstrated through impaired synonym judgement when presented with thematic distractors (Noonan et al., 2010; Samson et al., 2007). These impairments give rise to difficulty in maintaining the global coherence of speech in SA (Hoffman et al., 2020). Semantic control deficits extend to non-verbal behaviours. SA patients show impairment when selecting objects that are appropriate for completing actions, particularly when target objects would not canonically be used for this purpose (e.g., cracking a nut with a hammer; Corbett et al., 2011). These non-verbal deficits manifest as disorganised performance of naturalistic actions (Corbett et al., 2009).

The profile of impairment in SA presents opportunities for facilitation of retrieval and communication. Jefferies et al. (2008) demonstrated that presenting SA patients with phonemic cues during a picture naming task resulted in near ceiling-level accuracy. These effects were not as strong in SD patients, who still presented with severe anomia following cueing. Such cueing techniques can facilitate access to representations and allow patients to disregard irrelevant alternatives. Noonan et al. (2010) studied the effect of contextual cues on SA patients' ability to perform thematic associations between a probe and target word, presented alongside three foils. Each probe had both a 'dominant' and 'non-dominant' interpretation (e.g., 'pen'; predominantly a writing utensil, subordinately a structure for housing pigs). Providing sentences with contextual cues (alluding to the correct interpretation of the probe word relative to the target) improved SA patients' accuracy, even for non-dominant relationships. When patients were presented with contextual miscues (cueing the incorrect interpretation of the probe word), accuracy declined. Lanzoni et al. (2019) observed similar cueing and miscueing effects when providing SA patients with contextually-relevant visuospatial and emotionally valenced picture cues. Together these results demonstrate the potential to facilitate semantic retrieval in SA through external cues. Recent evidence suggests that retrieval in SA can be facilitated by providing training on a task that involves retrieving diverse associations, with feedback concerning ways in which given concepts can be linked, with some evidence of generalization to untrained items (Stampacchia et al., 2021).

Evidence from SA patients also suggests that impairments in semantic control may extend to domains which are ostensibly separate from semantic cognition. Stampacchia et al. (2018) demonstrated that SA patients have deficits in episodic recall which are akin to their semantic deficits, and that performance on both domains is similarly impacted by interference from strongly-encoded but irrelevant information. These impairments in episodic control affect both word and picture tasks, mirroring the multi-modal nature of pure semantic control impairments, and are similarly sensitive to external cueing (Stampacchia et al., 2019). Such findings suggest that there are common representation and control mechanisms underlying these two dissociable processes (Cogdell-Brooke et al., 2020; Vatansever et al., 2021). More generally, these findings support the notion that impairments in the controlled retrieval of conceptual information may have wide reaching impacts across multiple domains, including social cognition (Binney & Ramsey, 2020; Diveica et al., 2021).

1.2.6. The neural substrates of semantic control

Research into semantic control has revealed neural substrates that are dissociable from those involved in semantic long-term memory. This has led to an understanding that semantic control is not supported by modular regions, but by a distributed 'semantic control network' (SCN; Hallam et al., 2016). Two meta-analyses have attempted to define this network through the synthesis of neuroimaging data, contrasting tasks with high semantic control demands to those with low demands. The first such endeavour, by Noonan et al. (2013), implicated a number of regions including the left and right ventral PFC including the inferior frontal gyrus (IFG), left posterior middle temporal gyrus (pMTG), left dorsal AG bordering intraparietal sulcus, and dorsomedial frontal lobe. Although right frontal clusters were identified, this map was largely left-lateralised. An updated meta-analysis of semantic control demands by Jackson (2021) implicated five clusters, including (1) left frontal (IFG, insula, orbitofrontal cortex, and precentral gyrus), (2) left temporal (pMTG, posterior inferior temporal gyrus, and posterior fusiform gyrus), (3) bilateral dorsomedial PFC (dmPFC), (4) right IFG (pars orbitalis) and insula, and (5) right IFG (pars triangularis). The AG was implicated here in semantic cognition overall, but not in semantic control. Jackson (2021) argues that the prior implication in the Noonan et al. (2013) meta-analysis may be due in part to this region's role in domain-general cognitive control (Fedorenko et al., 2013).

Individual investigations of the basis of semantic control have most frequently implicated left IFG and pMTG. Neuroimaging investigations have revealed the importance of both regions in semantic judgement tasks (e.g., Zhang et al., 2019). Specifically, it has been argued that left IFG may constrain semantic retrieval in line with current goals by modulating visual processing regions (Zhang et al., 2021). pMTG may contribute to this process by constraining semantic retrieval in a top-down and goal-directed fashion (Davey et al., 2016). Studies of patients with SA frequently report left IFG as the site of peak lesion overlap (e.g., Hallam et al., 2018; Lanzoni et al., 2019; Stampacchia et al., 2018), although widespread damage to other frontal, temporal, and parietal regions is also common (e.g., Chapman et al., 2020; Jefferies et al., 2008; Rogers et al., 2015; Thompson et al., 2018). Indeed, temporoparietal damage is sufficient to produce deficits in semantic control that are comparable to those in patients with frontal damage (Thompson et al., 2022). Evidence from lesion-symptom mapping in left hemisphere stroke by Vigliocco et al. (2020) provides further insight. In a task requiring integration of speech and gestures from actors in video clips, beneficial effects of congruency in meaning were associated with lesions to IFG and sparing

of posterior temporal regions in a speech task, while the opposite pattern was observed in a gesture task. Behavioural costs from incongruent stimuli were associated with lesions to both aspects, and to more anterior temporal components. Both IFG and posterior temporal regions are argued to play a role in extracting meaning from input, while ATL plays a specialised role in integration. Given these findings, it may be that IFG and pMTG both support controlled semantic retrieval, while also being biased towards different input modalities.

Research employing transcranial magnetic stimulation (TMS) has provided evidence that inhibition of both left IFG and pMTG interferes with picture naming in the context of high retrieval demands (Krieger-Redwood & Jefferies, 2014), judgements of semantic relatedness (Davey et al., 2015; Whitney et al., 2011), and integration of gesture and speech input (Zhao et al., 2021). Furthermore, using both fMRI and TMS, Hallam et al. (2016) demonstrated that disrupting left IFG during a semantic judgement task increased activation in left pMTG, and other regions including right IFG and pre-supplementary motor area. This pattern might reflect compensatory activation within the broader SCN, with these regions becoming more important for controlled retrieval and comprehension when left IFG is suppressed. Similarly, neuroimaging with SA patients with left IFG lesions provided evidence of compensatory activation in both pMTG and ATL during the performance of a semantic task (Hallam et al., 2018).

Overall, evidence from neuropsychology and neuroimaging supports the existence of a distributed but largely left-lateralised functional network which underpins controlled semantic retrieval.

1.2.7. Contributions of the multiple demand network

The multiple demand network (MDN) is a large-scale network argued to support domain-general cognitive control (Duncan, 2001; 2010; Fedorenko et al., 2013). Cognitive control involves distinct processes including inhibition, cognitive flexibility, and working memory – effective control of these processes allows us to use context and internal goals to guide top-down processing of external information (Braem & Egner, 2018). MDN comprises a set of widely distributed and bilateral fronto-parietal regions, including the precentral gyrus, middle frontal gyrus, intraparietal sulcus, and anterior cingulate cortex. Temporal and occipital regions are also implicated, including the lateral occipital cortex (Fedorenko et al., 2013). Other studies have provided evidence that MDN regions divide into subnetworks, depending on the current task demands (Camilleri et al., 2018). SCN and MDN recruit

adjacent regions, particularly in lateral and medial frontal and lateral temporal cortices (Davey et al., 2016; Gao et al., 2021; Wang et al., 2020). In places, these functionally-defined networks are not only adjacent, but overlapping (Noonan et al., 2013). Evidence further suggests that MDN regions support the performance of tasks with high semantic control demands (Krieger-Redwood et al., 2015; Wang et al., 2020).

Given this convergence, one could question whether these networks are distinct constructs. However, these networks do diverge in their degrees of lateralisation – while elements of SCN are in the right hemisphere, this network is predominantly left lateralised (Gonzalez Alam et al., 2019; 2022; Jackson, 2021). In contrast, MDN is largely bilateral (Fedorenko et al., 2013). It could be argued that evidence of a left lateralised SCN is due to the fact that semantic control tasks rely primarily on verbal input (Jackson, 2021; Rice et al., 2015). However, evidence from Humphreys and Lambon Ralph (2017) comparing semantic, visuospatial, and resting-state fMRI data demonstrates that aspects of left IFG and pMTG respond specifically to semantic, but not domain-general, control demands. Similarly, evidence from Gao et al. (2021) suggests no shared neural coding of cognitive demands of working memory and semantic tasks within SCN, despite common coding within MDN. These findings suggest a degree of specialisation in SCN, dissociable from MDN.

Neuropsychological research suggests that in both SA patients and patients with dysexecutive symptoms, impairments in executive dysfunction frequently covary with semantic control impairment (Thompson et al., 2018). Evidence of impairment in domain-general cognitive control in some, but not all, SA cases has been reported in subsequent studies (Hoffman et al., 2020; Lanzoni et al., 2019; Montefinese et al., 2020). Domain-general cognitive control may play a foundational role in guiding semantic retrieval. Alternatively, it has been argued that executive deficits in SA are a spurious consequence of poor test comprehension (Chapman et al., 2020). Indeed, the true relationship between semantic impairment and executive impairment remains unclear (Gainotti, 2014). A third possibility is that the proximity of SCN and MDN means that these networks are frequently lesioned together following left hemisphere stroke, yet remain dissociable more broadly. Further work is needed to disambiguate the neural bases of these impairments in SA.

1.2.8. The separation between long term semantic representation and control processes

There is still debate concerning the extent to which effective semantic cognition truly relies on a separation between representation and control mechanisms. This theoretical

separation is based on the premise that weakly encoded information and associations have a disadvantage in the retrieval process, meaning a mechanism is needed to use them effectively (Lambon Ralph et al., 2017). As covered, the separation between representation and control has been supported by studies testing the CSC framework, with conclusions converging across neuropsychology (e.g., Jefferies & Lambon Ralph, 2006) and computational modelling (Hoffman et al., 2018; Jackson et al., 2021). Together, these findings suggest that the most efficient semantic system is one in which semantic representations interact with a dissociable control mechanism. Convergent findings from neuropsychology (e.g., Jefferies & Lambon Ralph, 2006), neuroimaging (e.g., Teige et al., 2019), and TMS (e.g., Davey et al., 2016) also suggest a neural dissociation with the semantic network, with regions including left IFG and pMTG supporting tasks with high control demands, while others such as ATL and AG do not. The separation between semantic representation and control has received relatively little attention outside of studies adopting the CSC framework. Despite this, studies and reviews observing memory retrieval increasingly acknowledge the need for semantic control, or context sensitivity more generally, to facilitate effective interpretation (e.g., Faber et al., 2019; Gilboa & Moscovitch, 2021; Hanson & Chrysikou, 2018).

The notion of semantic control can be broadly compatible with both embodied and symbolic frameworks of semantics, given that this process reflects how representations are retrieved in a context-appropriate manner, regardless of the systems in which they are encoded and grounded. Despite this, some embodied models of semantics have argued against the relevance of external information altogether (e.g., Varela et al., 1991), given that representations rely instead on previously encoded information which is tied to internal sensory-motor referents. As noted by Meteyard et al. (2012), however, a degree of context independence is likely necessary in order to fit existing representations to novel environments and experiences. Symbolic approaches to semantics rely on the assumption that meaning is given to words by their relationship to other words (Landauer & Dumais, 1997). As such, the meaning of a word can be modulated according to the context of the sentence in which it is encountered (Barsalou, 1999). For example, it would be necessary to contextually modulate interpretation of the word ‘ball’ between scenarios where it is encountered alongside the words either ‘gown’ or ‘sport’. In such a scenario, a mechanism specialised to control access to inhibit strongly encoded information and facilitate weakly encoded information relating to a given concept (e.g., that a ‘ball’ can refer to a formal event as well as a spherical object) would be beneficial. As argued in Section 1.2.1, effective semantic representation likely

relies on elements of both embodiment and abstract symbolism, suggesting that a degree of context-sensitivity is required.

Overall, studies interrogating the CSC framework appear to support the existence of semantic control. The existence of this mechanism is also theoretically compatible with the need for context-sensitivity, the primary function of semantic control. Neuroimaging research explicitly investigating the substrates underlying semantic control provides further insight into this dissociation.

1.3. Interacting systems supporting semantic cognition

Research into the neural basis of semantic cognition may benefit from considering the ways in which distinct networks interact to facilitate effective retrieval, as well as the role of macro-level cortical organisation.

1.3.1. Semantic control and representation substrates

As described by the CSC framework (Lambon Ralph et al., 2017), effective semantic cognition is supported by interactions between long-term conceptual representations and controlled retrieval processes, associated with bilateral ATL and left IFG, respectively. These regions also broadly correspond to separate networks; ATL is allied with and partially overlapping with DMN and limbic networks, including core DMN regions such as left AG, while IFG shows stronger connections with other SCN and MDN regions, and with the frontoparietal network defined using resting-state fMRI (Davey et al., 2016). Intrinsic connectivity between left IFG and pMTG is stronger than connectivity between these sites and ATL or AG, supporting the view that SCN is distinct from semantic regions that are not implicated in controlled retrieval (Gonzalez Alam et al., 2019). While patterns of intrinsic connectivity with ATL are relatively symmetrical, connectivity between IFG and pMTG is stronger in the left hemisphere than in the right hemisphere, supporting the left-lateralised nature of SCN (Gonzalez Alam et al., 2019). In contrast, core representation in the ATLs appears largely bilateral, despite some graded hemispheric specialisations for the processing of specific features (Gonzalez Alam et al., 2021; Rice et al., 2015; 2017; 2018). These networks underpinning semantic cognition can be understood as separate, but intrinsically linked. Ventral ATL has been shown to be functionally connected to a number of sites implicated in semantic control, including IFG, pMTG, and medial PFC, both at rest and

during semantic task performance (Jackson et al., 2016). Studies of the 'language network' while at rest have similarly implicated left ATL as being functionally connected to the ipsilateral IFG and pMTG (Hurley et al., 2015). When contrasting a featural task to a less effortful semantic task, Chiou et al. (2018) did not observe direct modulation of ATL-IFG functional connectivity, but did observe increased connectivity between IFG and an occipitotemporal 'spoke' region. This supports the notion of task-induced modulation of the semantic network.

1.3.2. White matter tracts linked to semantic cognition

The coherent network behaviour seen across distributed nodes of the semantic control network and other large-scale distributed networks is thought to be underpinned by long-range white matter tracts. Several different tracts are associated with semantic cognition, including the inferior longitudinal fasciculus (ILF), uncinate fasciculus (UF), and inferior fronto-occipital fasciculus (IFOF; Almairac et al., 2015; Han et al., 2013; Sierpowska et al., 2019). The anatomical structure of these tracts may account for their implication in semantic cognition. The ILF connects temporo-occipital regions to ATL, and as such may serve a semantic ventral stream by connecting this ATL hub to spoke regions (Herbert et al., 2018). The UF may similarly contribute to semantic knowledge, by connecting ATL to frontal regions (although this does not include IFG; Von Der Heide et al., 2013). The IFOF may serve a role in accessing meaning from visual input given that it connects both prefrontal and posterior temporal regions to the occipital cortex (Almairac et al., 2015). These tracts are therefore well placed to support elements of semantic cognition.

Recent investigations have explicitly investigated the white matter basis of semantic control. Nugiel et al. (2016) demonstrated that macrostructure in the left ILF and IFOF predicts performance on a latent semantic knowledge task drawing on semantic control resources. Similarly, in a task manipulating the strength of forced choice semantic associations, Marino Dávolos et al. (2020) implicated the left ILF in controlled semantic retrieval. The seeming importance of left hemisphere tracts for this function is consistent with the largely left lateralised grey matter network underlying semantic control. Conversely, evidence suggests the white matter basis of domain-general cognitive control may be bilateral, consistent with the bilateral nature of MDN; decline in executive function has been associated with comprised integrity of the corpus callosum (Bodini et al., 2013; Johnson et al., 2017; Jokinen et al., 2007; Voineskos et al., 2012).

Neuropsychological research has raised the question of whether disruption to specific tracts may contribute to semantic deficits in SD via disruption of connections to the ATLs (Fang et al., 2018). Ding et al. (2020) explicitly dissociated deficits in SA and SD on the basis of white matter damage. While impairments in SA were predicted by damage to left fronto-subcortical and fronto-temporal/occipital networks, those in SD were associated with factional anisotropy of a left medial temporal white matter network. This provides further evidence of dissociable substrates underlying semantic representation and control. Regions in a functional network can suffer both structural and functional disconnection as a result of a lesion, giving rise to behavioural impairments beyond those explained by the lesion itself. Structural disconnection can be conceptualised as cases where a given white matter tract is physically and directly impacted by lesion, which may sever connectivity to other regions. Functional disconnection instead reflects abnormalities to typical functional connectivity between regions (Salvalaggio et al., 2020). Measures of such disconnection have been used to map post-stroke impairments in diverse functions (Salvalaggio et al., 2020; Thiebaut de Schotten et al., 2020). For instance, structural disconnection has been shown to predict post-stroke executive impairment (Langen et al., 2018) and apraxia (Garcea et al., 2020), while functional disconnection can predict post-stroke depression (Padmanabhan et al., 2019) and amnesia (Ferguson et al., 2019). This approach has not yet been applied to impaired semantic control but could provide novel insight into the patterns of impairment seen in SA, and the neurocognitive structure of semantic cognition. This will be explored in Chapter 2.

1.3.3. Contributions of the default mode network

SCN overlaps not only with MDN regions but also with aspects of DMN: it is spatially interposed between these two networks (Chiou et al., 2022). Traditional accounts have conceptualised DMN as showing task-related deactivation; this pattern is frequently observed in demanding decision-making tasks (Raichle, 2015). More recent research, however, has conceptualised DMN as supporting various aspects of higher-order cognition. In particular, DMN appears important for heteromodal, abstract, memory-guided and internally-focused processing (Gordon et al., 2020; Murphy et al., 2018; Smallwood et al., 2021) and for integrating information across the cortex (Lanzoni et al., 2020). Accordingly, DMN has been implicated in diverse functional domains including emotional processing, episodic memory, social cognition, and semantic retrieval (Mancuso et al., 2022). Similarly, SCN is recruited beyond the semantic domain, contributing to episodic retrieval (Stampacchia et al., 2018) and social cognition (Diveica et al., 2021). Broadly, both SCN and

DMN appear to support internally-focused but demanding processes, including the processing of conceptual information.

Patterns of intrinsic connectivity within DMN reveal a medial temporal (MT) subnetwork and a lateral fronto-temporal (FT) subnetwork (Andrews-Hanna and Grilli, 2021; Andrews-Hanna et al., 2014; Chiou et al., 2020; Gurguryan & Sheldon, 2019; Sheldon et al., 2019). The MT subnetwork contains aspects of the hippocampus and parahippocampal gyrus, implicated in mental scene construction and episodic memory (Sheldon & Levine, 2016). Conversely, the FT subnetwork is allied to ATL, thought to provide a multimodal hub for the abstraction of conceptual information (Chiou & Lambon Ralph, 2019; Lambon Ralph et al., 2017) and involved in the processing of valence (Juran et al., 2016; Spiers et al., 2017; Wang et al., 2019). In this way, these subnetworks may be associated with different forms of memory. A 'core' DMN subnetwork sits at points where the MT and FT subnetworks are spatially interdigitated (Braga & Buckner, 2017; Yeo et al., 2011), and may assist in the integration of spatial, semantic, and valence information to form coherent representations (Lanzoni et al., 2020). The structure of DMN subnetworks may account for the broad range of functions subserved by DMN.

A distinct resting-state frontoparietal control network (FPCN), referred to here as 'control B'[1], sits in distributed frontal, parietal, and temporal regions. The control B network functionally couples with DMN, and has been proposed as important for tasks which require controlled processing of internally-focused tasks (Dixon et al., 2018; Yin et al., 2022). The control B network partly overlaps with DMN, as defined by the Yeo et al. (2011) 7-network parcellation, but largely sites outside of it. It has been argued that, by virtue of its connectivity to DMN semantic processing regions, control B may aid in the regulation of conceptual information (Faber et al., 2019). Control B dissociates from another adjacent resting state network, 'control A', which functionally couples with the dorsal attention network, associated with externally-focused control processes (Dixon et al., 2018; Yin et al., 2022).

It is becoming increasingly clear that DMN supports a diverse range of functions and relies on interactions with other systems to function effectively. However, much is still

[1] The control B and control A networks are often referred to in the literature as FPCNa and FPCNb, respectively. The terminology used for these resting-state networks throughout this thesis is consistent with the labels frequently given to the Yeo et al. (2011) and Schaefer et al. (2018) 17-network solution, based on parcellations of 1,000 and 1,489 brains, respectively.

unknown about the structure of DMN and its allied systems. For instance, it is unclear how subnetwork functions may dissociate for the performance of two semantic tasks which require a focus on different features. It may be that both MT DMN and FT DMN support semantic cognition, with functional dissociations reflecting the representations needed for a given task. Alternatively, there may be dissociations in the types of memory tasks they support, with the MT DMN specialised more for episodic recall and the FT DMN for semantic retrieval. As mentioned above, there is evidence of common control mechanisms in key SCN nodes supporting both semantic and episodic retrieval (Barredo et al., 2015; Stampacchia et al., 2018; Vatansever et al., 2021). Functional contributions of DMN subnetworks may similarly cut across memory types. Furthermore, it is unclear how DMN activation may be modulated by changing retrieval demands. These questions will be addressed in Chapter 6.

1.3.4. The position of the SCN

It has been argued that, by virtue of its position between MDN and DMN, SCN may serve as a functional nexus between these two networks. Chiou et al. (2022) attempted to characterise the topographical location of SCN as a whole. Both at the individual- and group-level, SCN was found to be 'sandwiched' between DMN and MDN. Beyond this, the observed function of SCN was characterised as a hybrid of these two networks, in so far as it supports both executively demanding tasks and those which require conceptual representation (see also Wang et al., 2021). Elements of SCN such as left IFG and pMTG have been shown to uniquely present with high functional connectivity to both heteromodal DMN regions and cognitive control sites within MDN (Davey et al., 2016; Gonzalez Alam et al., 2022). In particular, the degree of connectivity between the left ventrolateral PFC (including IFG) and sites in DMN and ventral attention network predicts successful retrieval of strong and weak semantic associations, respectively (Zhang, Nathaniel, et al., 2022). This connectivity may contribute to the integration of control processes with semantic knowledge, allowing the regulation of spreading activation in the semantic system in line with current goals. Both MDN and DMN have been shown to represent semantic goal information, regardless of specific semantic category, findings which challenge the notion of invariable functional dissimilarities across these two networks (Wang et al., 2021). Such findings support the dynamic and interconnected nature of SCN, with a particular importance of the surrounding MDN and DMN in orchestrating effective semantic cognition. The relative positions of these three networks can be seen in Figure 1.1. Evidence of graded transitions from blue, to green,

to yellow, to orange, to red in this figure reflect areas where SCN is intermediary between DMN and MDN. This is particularly evident in the left temporal lobe and in medial PFC.

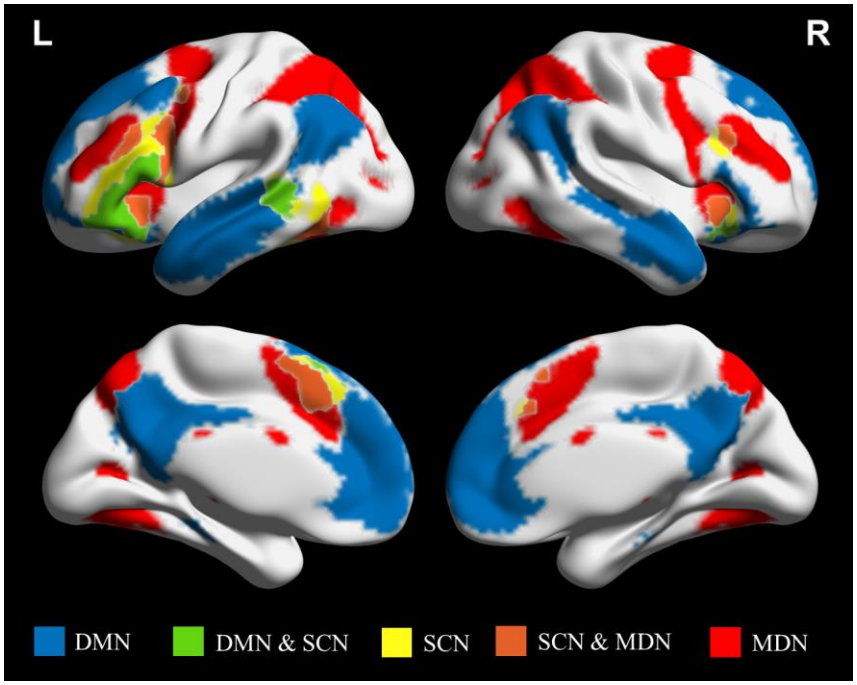


Figure 1.1. The relative positions of SCN, DMN, and MDN, including their overlap. SCN map taken from Jackson (2021) meta-analysis. MDN map taken from Fedorenko et al. (2013), with threshold of t > 1.5. DMN taken from Yeo et al. (2011) 7-network parcellation. SCN = semantic control network, DMN = default mode network, MDN = multiple demand network. Data visualised with the BrainNet Viewer (Xia et al., 2013; https://www.nitrc.org/projects/bnv/).

It should be noted that these networks each overlap with regions implicated in language processing. To quantify this, maps of SCN, MDN, and DMN were compared to a map of the language network taken from a Neurosynth term-based meta-analysis (Yarkoni et al., 2011), using 1101 studies, and a threshold of Z > 3.1. The observed overlap discussed below is largely left-lateralised. SCN implicates key language processing regions including the IFG, MFG, fontal pole, and pMTG. Tasks manipulating semantic control demands frequently use verbal stimuli (Rice et al., 2015), and language regions may therefore be overrepresented in meta-analytic maps of SCN (e.g., Jackson, 2021). Beyond this, however, semantic retrieval is central to language due to its importance in bringing meaning to our verbal experiences in a context-dependent manner (Jefferies, 2013), likely accounting for the presence of SCN regions in the language network. MDN implicates language regions in the precentral gyrus, insula, lateral occipital cortex, and inferior temporal gyrus. Accordingly, it

has been argued that language does not exist in isolation from control mechanisms. These mechanisms may be particularly useful during demanding comprehension tasks (Fedorenko, 2014), although evidence has demonstrated that language and thought do functionally dissociate (Fedorenko & Varley, 2016). Finally, DMN intersects with language regions in the temporal pole, superior temporal gyrus, and IFG. The temporal pole overlaps with the ventral ATL, the proposed site of a semantic hub (Lambon Ralph et al., 2010). As discussed above, the central role of the semantic system in language may therefore account for this overlap. In this thesis, I discus semantic retrieval as a multimodal process encompassing both language and nonverbal actions, in line with the hub and spoke model (Lambon Ralph et al., 2017). As such, when functional networks are interrogated in Chapter 2 and Chapter 6, explicit focus is not given to the language network as its own entity. Rather, I focus on lesion to and activation in SCN and to the adjacent core semantic regions, DMN, and MDN, as well as their areas of overlap.

1.3.5. Hierarchical cortical gradients

DMN, SCN and MDN can also be understood in terms of large-scale cortical organisation. Functional 'gradients' are continuous hierarchies in the brain, organised according to the similarity in functional connectivity across the cortical surface (Huntenburg et al., 2018; Margulies et al., 2016). They are recovered by performing a decomposition of cortex-wide intrinsic connectivity patterns, with each gradient reflecting a particular dimension of variation in connectivity.

The principal gradient is the dimension of connectivity that explains the most variance in the human and macaque brain (Margulies et al., 2016). It is organised such that unimodal sensorimotor regions lie at one end, and heteromodal regions, including those in DMN, at the other (Margulies et al., 2016). Control networks including MDN lie towards the middle. SCN sits between MDN and DMN on this gradient in terms of intrinsic connectivity (Wang et al., 2021), with regions implicated in semantic control found to recruit different portions of the gradient from those implicated in visuospatial control (Chiou et al., 2022). The principal gradient benefits a number of diverse tasks which rely on the integration of sensory features and abstract heteromodal processing; including semantic cognition, episodic memory, and social cognition (Irish & Vatansever, 2020; Margulies et al., 2016). It may therefore be possible to gain a better understanding of such functions by further researching the relationship between distinct functional networks on this gradient.

Other gradients also explain variance in cortical organisation. Gradient 2 reflects the distinction between motor and visual regions, while Gradient 3 reflects differences between core DMN and frontoparietal control regions. The structure of these three gradients predicts individual variability in behaviour, in terms of both ongoing patterns of self-reported thought (Mckeown et al., 2020) and the performance of semantic and non-semantic tasks (Shao et al., 2022). The principal gradient has also been shown to predict functional differences across hemispheres. Gonzalez Alam et al. (2022) studied differences in intrinsic connectivity between the left and right hemisphere. Left hemisphere parcels were closer to the heteromodal end of the principal gradient than those in the right hemisphere, consistent with the heteromodal functions supported by the left hemisphere. Beyond this, participants for whom control B sat closer to the heteromodal end of the gradient in the left compared to the right hemisphere presented with more efficient semantic retrieval, consistent with the importance of control B in internally-oriented control (Dixon et al., 2018). This study demonstrates the utility of gradients in elucidating the contributions of functional networks.

1.4. Emotion processing and valence

1.4.1. The structure of emotion

As for semantic cognition, emotion processing relies on sensory motor features, such as facial, bodily, and physiological signals associated feeling ‘fear’, as well as abstract aspects, such one’s personal account of the category of ‘fear’ (Satpute & Lindquist, 2019). Like semantic cognition, the retrieval of emotional information may also need to be flexibly controlled, given that contextual factors may influence one’s interpretation of input in order to parse their emotional state. Emotions may fall into a unique category of which the typical mechanisms involved in semantic processing are not applicable. Alternatively, it may be that the same representation and control mechanisms implicated in the CSC framework (Lambon Ralph et al., 2017) overlap with those involved in emotion processing. As of yet, it is unclear how semantic control might relate to the processing of affective stimuli.

Emotion is typically understood as comprised of two dimensions; valence and arousal. Valence refers to whether an entity can be considered positive or negative, whereas arousal reflects the degree of stimulation caused by an emotional item (Lang et al., 1993). A number of cortical and subcortical regions have been implicated in the processing of emotional

stimuli, including the bilateral amygdala, medial PFC, and orbitofrontal cortex (Lindquist, Satpute, et al., 2016; Sabatinelli et al., 2011). However, valence and arousal features of stimuli have also been shown to have dissociable effects on brain activation (Citron et al., 2014). For example, Kensinger and Schacter (2006) demonstrated that aspects of amygdala and PFC respond to stimulus arousal regardless of valence, while processing of positive and negative valence is supported by a dissociation in the medial and lateral PFC, respectively. Valence and arousal features also have measurable effects on cognition. The emotion-enhanced memory effect, for instance, reflects that emotionally arousing stimuli are more readily remembered than neutral stimuli (Talmi & McGarry, 2012). Kang et al. (2014) demonstrated that this effect is subject to dual-task demands, and therefore relies on controlled processing, for positive but not negative arousing stimuli. Overall, it is clear that valence comprises an important element of a stimulus.

1.4.2. Valence as a semantic feature

As mentioned, the "hub and spoke" framework argues for a role of basic sensory "spokes" in the formation of amodal concepts, but also acknowledges the role of hedonic valence (Lambon Ralph et al., 2017). Concepts may be distilled from valence as from action and sensory features (Martin, 2016). This may be particularly true for abstract semantic concepts (Kousta et al., 2011; Vigliocco et al., 2009), with the emotion system playing a specialised role in providing these words with a basis in internal processes such as one's experience of emotional states (Vinson et al., 2014). This has been demonstrated using fMRI; the anterior cingulate cortex is particularly important for the processing of abstract words, with activation modulated by concept valence (Vigliocco et al., 2014). Emotional valence also benefits the learning of abstract words, both in multimodal semantic language models (Rotaru & Vigliocco, 2019) and in children (Ponari et al., 2018; 2020). Specialised emotion processing regions, including the amygdala and orbitofrontal cortex, may act as spokes in generating emotional aspects of concepts, via connections to the ATLs (Riberto et al., 2019). As such, valence becomes a core component of heteromodal representations. Indeed, overall similarity in (positive) valence correlates with similarity in associative semantic similarity in ATL (Meersmans et al., 2020). Of relevance here is a proposed dissociation between affective valence and semantic valence (Itkes et al., 2017; 2019). While the former reflects experiential aspects of valenced stimuli (e.g., deriving joy from a flower), the latter reflects knowledge about stimulus valence (e.g., that we know flowers are positively valenced entities). Itkes and Kron (2019) argue that it is possible to retrieve the semantic valence of a

stimulus without the experiential and embodied components associated with affective valence. Relationships between valence and meaning in the semantic domain will not necessarily extend to the affective domain.

If valence does serve as a core aspect of semantic representations, it may be that access to relevant valence cues can facilitate semantic retrieval under ambiguous conditions. Prior study of SA patients suggests that emotionally valenced pictures can facilitate thematic associations (Lanzoni et al., 2019). In healthy adults, Marino Dávolos et al. (2020) similarly demonstrated that valence congruency between target and probe words aids the retrieval of weakly encoded associations. Such findings are comparable to observations that contextual information can be used to cue semantic retrieval (Noonan et al., 2010), and suggest that valence in itself may be inherently semantic. It may also be the case that effective semantic control is needed to interpret the valence of concepts. If so, this process may be impaired in SA, and susceptible to semantic cues and miscues. Chapter 4 will further explore the relationship between access to valence and meaning in both healthy adults and SA.

1.4.3. Early models of emotion processing

Discrete emotion categories, such as happiness and anger, should be viewed as distinct from valence. Emotion states can be considered a superordinate category containing discrete concepts (e.g., anger, sadness, and happiness), while valence is an inherent quality possessed by concepts on a continuous dimension from positive to negative. As for semantic concepts more generally, each emotion category may itself be characterised by valence (e.g., ‘anger’ is a strongly negatively valenced concept). Indeed, emotion categories may be particularly reliant on valence and arousal information, given that they are intrinsically associated with subjective feelings. Early models of emotion argued that access to discrete emotion categories may be innate and universally shared by all humans (Izard, 1994). Such accounts take a ‘basic’ or ‘universal’ view of emotion. This view is supported in part by evidence that emotion states (e.g., anger) seem to be experienced cross-culturally, without shared language or experience across cultures (Ekman, 1994). Indeed, access to these innate constructs may be an adaptive trait, in allowing humans to effectively communicate basic needs and emotional states (Darwin, 1872). As such, emotions are biologically primitive, and invariant access to them serves an essential social function (Izard, 1992). This model assumes, given that basic emotion states are innate, that each discrete state should recruit specific neural substrates (Ortony & Turner, 1990). Evidence for this supposition from neuroimaging and lesion studies does present some support for neurobiological signatures of

basic emotions (Celeghin et al., 2017). However, such studies have largely ruled out the possibility of one-to-one mappings between discrete emotion states and specific regions (Hamann, 2012). Other early models similarly stress the importance of the physiological bases of emotion. Under the James-Lange theory, for instance, conscious perception of emotion is secondary to the perception of somatic changes that occur in response to external stimuli (James, 1884; Lang, 1994). Schacter and Singer (1962) instead argued that perception of emotional experience is determined by physiological arousal, but in conjunction with cognitive interpretation based on the context at hand.

These early models therefore consider a range of possible determinants of emotion perception but neglect the role of language and conceptual processing. Indeed, under the basic emotion framework, interpretation of emotion states operates entirely independently from language (Ekman & Cordaro, 2011). More recent theories have argued that the ways in which emotion categories are learned, perceived, and experienced, may rely on conceptual representations that are formed over time, rather than being innate.

1.4.4. Conceptually based models of emotion processing

There may be several ways in which meaning and conceptual knowledge inform the processing of emotion states. The perception of discrete emotions may rely on heteromodal representation of the respective emotion state (e.g., 'ANGER'), to the same extent as concepts such as 'HAMMER' or 'DOG' (Lambon Ralph et al., 2017). Beyond representation, control processes may allow us to retrieve emotion concept knowledge in a flexible manner. Alternatively, the perception of emotion may be automatic and instantaneous, without the scope for controlled processing. Effective emotion processing may also rely on the integration of features across domains and modalities. Core assumptions of and evidence for theories in this field are outlined below.

The constructionist account of emotion processing argues that language and conceptual knowledge play a foundational role in our ability to perceive discrete emotions (Lindquist et al., 2015). Accordingly, semantic satiation, disrupting access to verbal emotion labels (e.g., "sad") through verbal repetition, can impair categorical perception of respective facial emotion portrayals (Gendron et al., 2012; Lindquist et al., 2006). This suggests that emotion labels may facilitate processing of emotion states even when not task-relevant. Beyond language, ratings of perceived conceptual similarity between two emotion categories predicts behavioural markers of perceived perceptual similarity between respective facial

portrayals of emotion (Brooks & Freeman, 2018). This suggests that emotion perception has a basis in conceptual knowledge, not confined to the verbal domain. Developmental accounts have argued that exposure to emotion labels facilitates the formation of emotion concept knowledge, which in turn facilitates categorical emotion perception (Hoemann et al., 2019). While the constructionist account of emotion has suggested involvement of language and conceptual knowledge in both emotion perception and experience (Barret, 2006), this is contentious. In this context, the experience of emotion would relate to one's ability to subjectively feel anger. This is dissociable from knowledge of what anger is, and therefore ability to perceive it in the world. Critics claim that language-based theories may rely too heavily on the assumption that findings pertaining to emotion perception generalise to emotional experience (Sauter, 2018).

Other models have also acknowledged the importance of conceptual knowledge in emotion. The perception-action model (PAM) of empathy argues that the ability to perceive and understand emotion in others is reliant on rapid access to representations of emotion states (Preston, 2007). Research using an 'Emostroop' paradigm has provided evidence that presenting incongruent facial expressions behind emotion labels during a semantic categorisation task interferes with performance, implying rapid activation of emotion concept knowledge upon perceiving facial portrayals (Preston & Stansfield, 2008). Such effects have been shown to persist in the context of impaired cognitive functioning (Osborne-Crowley et al., 2019). Other researchers have considered the importance of multimodal input in emotion perception, arguing that cohesive emotion categories are constructed through the integration of physiological changes, language, and concept knowledge (Kajić et al., 2019; Zhou et al., 2021). These emotion models share similarities with models of conceptual representation, in so far as they rely on automatic spreading activation, heteromodal representation, and the integration of features and knowledge (Jefferies, 2013; Lambon Ralph et al., 2017; Vatansever, Bzdok, et al., 2017).

If conceptual knowledge is foundational for emotion processing, semantic impairment should also manifest as impaired emotion processing. As mentioned, SD patients frequently present with affective behavioural abnormalities (Bozeat, Gregory, et al., 2000). To observe direct effects of semantic impairment on emotion perception, Lindquist et al. (2014) assessed the ability of three SD patients to sort pictures displaying facial portrayals of emotion into six categories. Relative to controls, SD patients produced fewer piles, and frequently made within-valence sorting errors. Broadly, these patients presented with preserved ability to

distinguish the valence (positive, negative, or neutral) of faces, but impaired ability to distinguish the specific emotion state within valence categories (e.g., “anger” versus “fear”). Patients’ accuracy improved when sorting in the presence of exemplar portrayals of the six emotion categories, but not in the presence of verbal labels of each emotion state. Similarly, Kumfor et al. (2018) demonstrated that SD patients present with impaired ability to decode facial or bodily portrayals of emotion. Such deficits in SD are partially explained by performance on verbal semantic tests (Miller et al., 2012). This impairment may be attributable to strong connectivity between the ATLs, atrophied in SD, and key emotion processing sites including the amygdala (Rosen et al., 2002). Interestingly, prior work by Martin and Fedio (1983) demonstrated that patients with Alzheimer’s disease show relative preservation of judgements of affective meaning (relating to emotion categories), despite presenting with otherwise impaired single-word comprehension. Later research by Catricalà et al. (2014) replicated this effect. Together, these studies therefore suggest that emotion concept knowledge can be lost, while also suggesting that emotion categories may form a special category of abstract concepts that may be protected from degradation in certain pathologies.

Comparable investigations observing discrete emotion categories have not been conducted with SA patients. Effects of semantic control impairments on emotion processing may be similar to those observed following the loss of amodal concepts (Lindquist et al., 2014) or following temporary disruption of access to emotion labels (Gendron et al., 2012). Alternatively, if semantic processing of stimuli reflecting discrete emotion states is automatic upon perception (Preston, 2007), the need for semantic control may be bypassed. While not focusing on semantic processing explicitly, Jastorff et al. (2016) provide evidence for a dissociation in the functions of left ATL and IFG in emotion processing, using a paradigm in which participants were required to both identify and categorise emotion in animated emotionally expressive gaits. In patients with behavioural variant of frontotemporal dementia, grey matter density in left ATL and IFG were positively associated with the ability to detect and categorise emotion, respectively. An fMRI experiment with healthy participants similarly implicated left IFG as a classifier for participants’ ability to discriminate discrete emotion states. Jastorff et al. (2016) acknowledge that left IFG’s involvement in semantic retrieval may account for its ability to generate cohesive representations of emotion based on sensorimotor input.

Neuropsychological investigations focusing on the role of semantic control in emotion processing would further test conceptually-based models and provide additional characterisation of impairments in SA. This will be investigated in Chapter 3. Addressing this question may also have clinical implications, allowing us to understand and respond to emotional difficulties frequently observed in post-stroke aphasia, such as depression and anxiety (Døli et al., 2017). The current discussion may be particularly relevant to symptoms of alexithymia after stroke; difficulties recognising and communicating one's own emotions (Hobson et al., 2020). As mentioned, SD patients also present with affective abnormalities in the context of semantic impairment (Hodges & Patterson, 2007). There may be a shared basis to these behavioural phenomena, attributable in part to difficulties in processing and categorising emotional information.

1.4.5. Controlled processing of emotion

It may be that SCN supports the control of emotion, as it does for conceptual retrieval more generally (Jackson, 2021). Like semantic retrieval (Wang et al., 2020), the internally-focused control of emotion may also rely on MDN and domain-general control. Meta-analysis of emotion-specific response inhibition tasks has revealed substrates which highly overlap with those implicated in domain-general interference tasks, including the dorsal anterior cingulate cortex, anterior insula, and IFG (Chen et al., 2018). A recent investigation of response inhibition demonstrated that manipulation of stimulus valence selectively increased activation in the anterior insula and reduced activation in the medial orbitofrontal cortex and ventral striatum, suggesting an emotion-specific mechanism beyond domain-general control alone (Zhuang et al., 2021).

Emotion regulation, the process of modulating emotional responses to stimuli and events, has also been considered in the context of controlled processing. Regulation strategies which may depend on control resources can be broadly split into those requiring suppression of an emotional response and altering of attention, and those which involve cognitive reframing of an emotional response (Braunstein et al., 2017; Engen & Anderson, 2018; Saragosa-Harris & Silvers, 2022). These latter strategies may be more likely to implicate SCN regions, given this network's role in accessing alternative conceptual information (Jackson, 2021). Reappraisal is characterised by attempts to consciously change one's emotional evaluation or appraisal of an affective stimulus (Buhle et al., 2014). Investigations into the neural mechanisms underlying reappraisal have frequently implicated substrates that are similar to those implicated in semantic retrieval, including bilateral IFG, AG, and

dmPFC, and left pMTG (Buhle et al., 2014; Kohn et al., 2014; Messina et al., 2015; Morawetz et al., 2017). These regions have all been implicated in SCN (Noonan et al., 2013; Jackson, 2021). Messina et al. (2015) speculate that both executive function and a specific semantic attentional system may be recruited when switching between alternative representations of emotional stimuli. The overlap between the emotion reappraisal meta-analytic map from Messina et al. (2015) and both SCN and MDN is displayed in Figure 1.2.

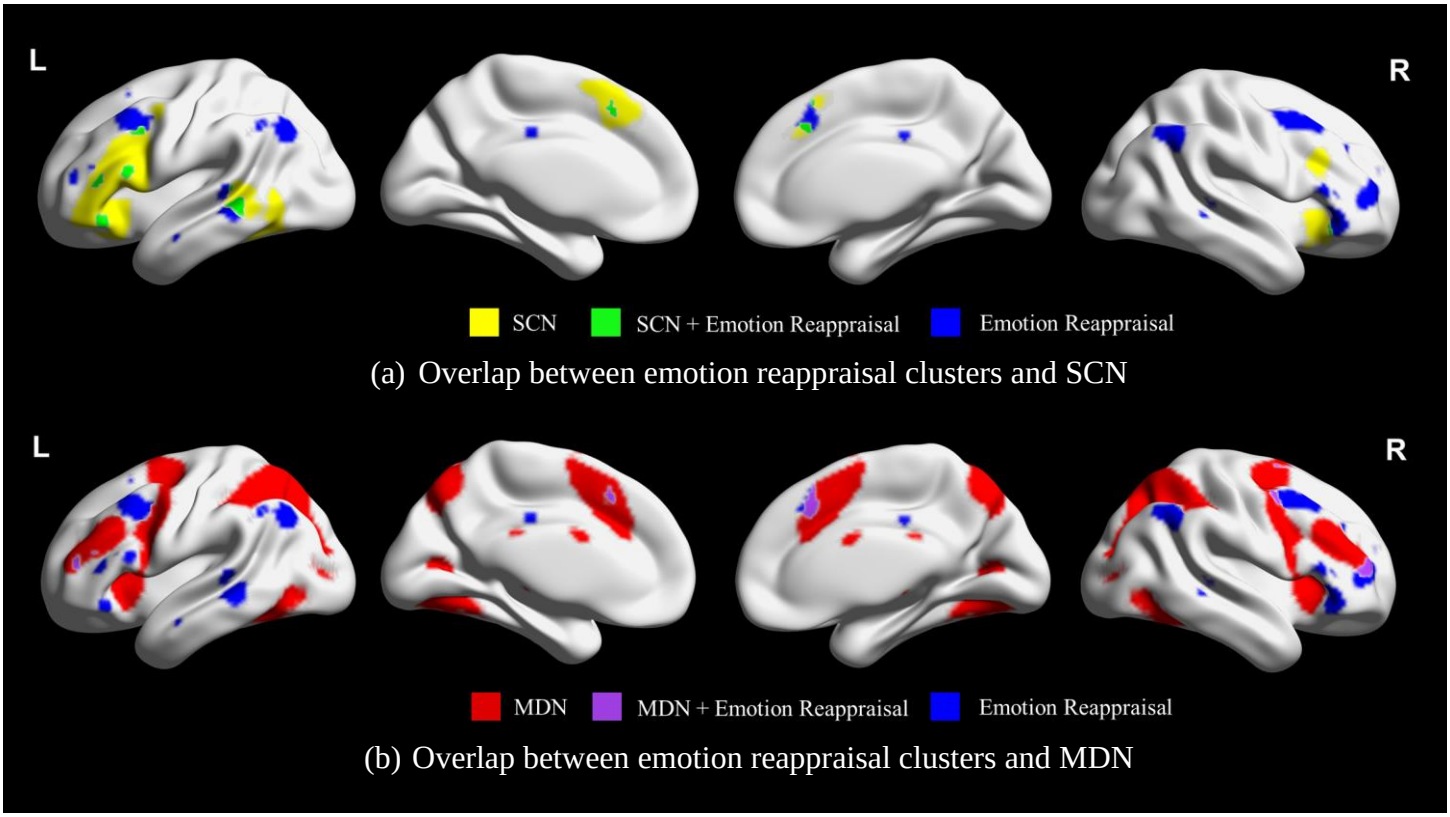


Figure 1.2. A meta-analytic map of clusters significantly activated during emotion reappraisal from Messina et al. (2015), overlaid with (a) the meta-analytic SCN from Jackson (2021) and (b) a map of MDN associated with demanding tasks from Fedorenko et al. (2013). Data for the Messina et al. (2015) map provided by the first author. SCN = semantic control network, MDN = multiple demand network. Data visualised with the BrainNet Viewer (Xia et al., 2013; https://www.nitrc.org/projects/bnv/).

Overlap with SCN is observed in the left frontal regions (including IFG), left pMTG, bilateral dmPFC, and right orbitofrontal cortex. Overlap with MDN is observed in bilateral frontal regions, bilateral dmPFC, and right AG and insula. It should be noted that reappraisal activation is not largely left lateralised, as SCN is. While temporal clusters are mostly restricted to the left hemisphere, frontal and parietal clusters are more bilateral. Overall,

17.5% of the reappraisal mask falls within MDN, and 19.2% within SCN (networks are not mutually exclusive)[2]. It may be that both domain-general and semantic control play a role in tasks which require an evaluation of the affective nature of stimuli. SCN may be particularly important by facilitating the retrieval of less dominant or automatic emotional responses. Functional neuroimaging could test whether SCN is implicated in the ability to generate and switch emotional responses to probes. This will be explored in Chapter 6.

1.5. Reward and motivation

1.5.1. Extrinsic and intrinsic reward

While the study of valence and emotion processing may aid in characterising the nature of impairments in SA, study of motivation and reward may provide insight into how impairments might be ameliorated. Prior work has demonstrated that semantic retrieval in SA can be aided by external prompts including phonemic cues (Jefferies et al., 2008), contextual sentences (Noonan et al., 2010), and emotional and visuospatial pictures (Lanzoni et al., 2019). This is consistent with the notion that semantic representations are not lost in SA; their retrieval is disrupted but subject to facilitation (Jefferies & Lambon Ralph, 2006). Manipulations of reward may prove effective in modulating the demands of the semantic retrieval process itself, without relying on item-specific cues. This is based on evidence, as summarised below, that reward can bolster domain-general cognitive control by strengthening task representation (e.g., Swirsky & Spaniol, 2019). It may be possible to influence semantic control demands in a similar fashion. Indeed, there is behavioural overlap in semantic and domain-general control, with impairments in these domains correlating in patient groups (Thompson et al., 2018), and neural overlap between the networks subserving these functions; SCN and MDN (Noonan et al., 2013). The sections below characterise extrinsic and intrinsic reward before reviewing evidence of their effects on cognition.

Extrinsic rewards are incentives from the external environment which motivate behaviours in accordance with goals (Ryan & Deci, 2000). Extrinsic rewards may be (a) social, such as positive facial expressions, (b) token 'points', such as those allocated on a leader board in a game, or (c) monetary incentives. Extrinsic reward has been associated with increased activation in the ventromedial PFC and subcortical areas including the caudate and

[2] Conversely, 8.9% of SCN fell within the reappraisal mask, compared to 1.8% of MDN

putamen (Lin et al., 2012), in which cumulative reward value and reward prediction errors are represented (Juechems et al., 2017; Mas-Herrero et al., 2019). The functional relationship between these cortical and subcortical regions, characterised by dopaminergic transmission, allows for the use of reward value to overcome physical and mental costs (Soutschek & Tobler, 2018). A task can be said to be intrinsically motivating if one experiences enjoyment or interest during it (Mori et al., 2018). Intrinsic motivation is therefore not reflective of the qualities of a task, but of one's subjective experience. Evidence suggests that the neural substrates of extrinsic and intrinsic motivation overlap (Di Domenico & Ryan, 2017).

1.5.2. Effects of reward on cognition

Cognitive control is effortful because it draws on a system of limited resources (Yee & Braver, 2018). Tasks requiring high levels of control are therefore aversive, resulting in decreased engagement (Botvinick & Braver, 2015). The appetite for attaining a reward may supersede this aversion, and aid in overcoming cognitive costs by strengthening task representations, shielding goal-directed action from interference, and magnifying the potential benefits of an action (Goschke & Bolte, 2014; Westbrook et al., 2020). These are all functions that are likely to be taxed during tasks with high semantic control demands, which often require inhibiting interference from task-irrelevant information (Hoffman, 2019). Extrinsic reward benefits control due to its ability to increase both cognitive stability and flexibility, dependent on task demands (Fröber et al., 2019; Notebaert & Braem, 2015). Performance-contingent monetary rewards have been shown to improve top-down control of visuo-spatial attention (Small et al., 2005) and performance on demanding task-switching paradigms (Capa et al., 2013). It has also been observed that imbuing words with higher token value leads to improved recognition sensitivity (Hennessee et al., 2017). These effects are context-sensitive; benefits of reward rely on relative difference between high- and low-reward allocations, rather than absolute value (Otto & Vassena, 2021).

Effects of reward may ameliorate deficits in cognitive control. Healthy ageing is associated with cognitive decline, in both semantic control (Hoffman, 2018; 2019) and domain-general cognitive control (Swirsky & Spaniol, 2019). Yee et al. (2019) studied the effect of extrinsic reward on performance on a cued task-switching paradigm in young and older adults. Incentives improved older adult performance up to the level of young adult baseline performance. This may provide implications for motivation-based intervention for age-related cognitive decline. Such effects are likely observed due to preserved structural and functional substrates associated with motivation (Swirsky & Spaniol, 2019) and

compensatory increased connectivity between reward processing and frontal regions (Bowen et al., 2020). It may be possible to harness this same effect for impaired semantic control.

Task-based neuroimaging has explored the substrates of the interaction between reward and control. Research using multi-voxel pattern analysis with fMRI demonstrated that reward-induced improvements in task-switching performance were associated with increased task representation across MDN (Shashidhara & Erez, 2019). Reward may improve the ability of MDN to employ effective control. Indeed, a set of MDN-allied regions are consistently recruited in motivated cognitive control, including the intraparietal sulcus and dorsolateral PFC (Parro et al., 2018). Using TMS, Hippmann et al. (2019) studied the functional nexus which allows for this modulation of MDN. Disruption of the left inferior frontal junction (IFJ) increased beneficial effects of reward on task-switching, suggesting an inhibitory role of this region in modulating the effect of reward on cognitive control. Regions implicated in motivated cognitive control are believed to be largely intact in SA, while the inhibitory left IFJ is often damaged (e.g., Thompson et al., 2022). Findings pertaining to extrinsic reward may therefore have implications for addressing deficits in semantic control. While prior work has studied post-stroke changes in reward sensitivity (e.g., Rochat et al., 2013), studies of modulatory effects of reward in post-stroke aphasia are lacking.

Relatively little is known about effects of intrinsic motivation on cognitive control, due in part to difficulty in experimentally manipulating task enjoyment. Huskey et al. (2018) provided evidence that intrinsic motivation can be manipulated by providing an appropriate balance between task difficulty and individual competency. Increased states of motivation were associated with increased attentional engagement, likely reflecting bolstered cognitive control. Such designs involve a degree of sacrifice in experimental control relative to studies manipulating extrinsic reward value. Quantifying the effect of intrinsic motivation on control may be simpler through the use of easily manipulatable proxies.

1.5.3. Self-reference

Self-reference may be one such proxy for intrinsic motivation. Self-referential processing refers to the processing of stimuli associated with or belonging to oneself. Disclosing information about the self with others has been shown to be rewarding, with participants willing to forgo monetary rewards for this purpose (Tamir & Mitchell, 2012). There are overlapping neural substrates underlying reward processing and self-reference, including the pregenual anterior cingulate cortex and the right ventrolateral PFC (Enzi et al.,

2009). Like intrinsic motivation, self-reference recruits the left anterior insula, not seen for extrinsic reward (Enzi et al., 2009). Northoff and Hayes (2011) argue that motivation and self-reference may interact, with items with self-relevance having inherently high value assignment. Alternatively, self-reference may be located on the lower end of a reward continuum, acting as a prerequisite for value assignment. Accordingly, Sui and Humphreys (2015a) argue that self-referential encoding may bias attention in the same way as reward; increasing stimulus salience by invoking a positive emotional reaction. In this way, self-referential processing can be viewed as a subset of motivated cognition (Madan, 2017).

Evidence suggests that self-reference can affect cognition. This has been frequently studied in relation to memory (Hou et al., 2019; Klein, 2012; Sui & Humphreys, 2015b). For instance, classifying adjectives as relating or not relating to oneself leads to better recognition of these words than if processed through semantic or structural encoding (Glisky & Marquine, 2009). Benefits of self-reference for memory have been shown to persist in SA (Stampacchia et al., 2019), despite episodic memory deficits (Cogdell-Brooke et al., 2020; Stampacchia et al., 2018). This is consistent with prior evidence of preserved self-reference effects in amnesic patients (Sui & Humphreys, 2013). Benefits of self-reference have also been observed in attention (Sui & Humphreys, 2015b), perception (Sui et al., 2012), and working memory (Röer et al., 2013). It may be that, by virtue of its motivational status, self-reference can also be harnessed to benefit semantic retrieval in SA.

1.5.4. Gamification

Potentially beneficial effects of reward and self-reference are relevant to the principle of ‘gamification’ – using elements of games, such as points, badges, and leaderboards, to promote a target behaviour (Landers, 2014). This is most frequently used in education, where it tends to be effective in increasing motivation and engagement, but has also been applied to industries including health, organisation, and data gathering (Hamari et al., 2014). The possible use of gamification strategies for post-stroke aphasia rehabilitation has received little research attention. Such applications may be limited by the heterogeneity of aphasia, making a catch-all gamified strategy elusive (Hymes et al., 2021). Preliminary evidence from Romani et al. (2019) suggests that gamified elements, including a point system, can be used to benefit word production in people with aphasia. These benefits generalised to assessments outside the game context, suggesting improvements in functional communication. Evidence that extrinsic rewards and/or self-reference benefit post-stroke semantic impairments could have implications for the gamification of aphasia rehabilitation. This will be explored in Chapter 5.

1.6. Thesis aims

Effective semantic cognition relies on a number of dissociable but interacting processes. Mechanisms involved in controlled semantic retrieval may serve functions beyond those that are ostensibly semantic, such as the control of episodic retrieval and social cognition. Little has been done to assess the relationship between semantic control and the processing of affective stimuli. This thesis will address several open questions. First, this thesis will aim to better characterise the functional networks implicated in semantic retrieval, and to understand how local damage and network disconnection following left-hemisphere stroke predicts semantic impairments in SA. Second, this thesis will extend constructionist models of emotion processing by investigating effects of impaired semantic control on the categorisation of discrete emotions. Third, this thesis will characterise the role of hedonic valence in semantic retrieval, and of semantic relatedness in valence processing, in both SA patients and neurologically healthy adults. Fourth, this thesis will extend existing literature on domain-general cognitive control to investigate modulatory effects of extrinsic and intrinsic motivation on semantic retrieval in SA. Finally, this thesis will characterise the contribution of DMN and functional control networks to the retrieval of both emotional and semantic associations to pictures, using task-based fMRI. An overview of the methods used for these purposes is presented below, followed by a description of each empirical chapter.

1.7. Overview of methods

1.7.1. Behavioural testing

Empirical chapters of this thesis rely on behavioural testing with human subjects. This was most frequently done in relation to patients with SA and controls (in Chapters 2, 3, 4, and 5). These investigations tested for impairments in specific neuropsychological domains (see section 1.7.2) and on experimental tasks. Behavioural testing with neurologically healthy young adults was conducted in Chapter 4 and Chapter 6. Behavioural data was typically analysed with ANOVAs and tests of correlation, with mixed effects models used in cases where small sample size made it advantageous to control for random variation attributable to participant identity. Sample size for neuropsychological chapters was dictated by practical constraints, as explained in section 1.8. Efforts were made to recruit and test as many patients with SA as was possible. For Chapter 6, recruitment of participants was limited by funding available to support the fMRI scanning of participants, at a maximum of 33. For young adult

data in Chapter 4, a sample size of 60 was judged as being of suitable size to uncover behavioural effects, while also being feasible to recruit without participant payment funds available.

1.7.2. Cognitive neuropsychology

Cognitive neuropsychology aims to provide insight into cognitive functions using patient populations as a model. This is based on the idea that observing effects of specific lesions on selective functions allows for inferences about the organisation of the mind and brain (Caramazza & McCloskey, 1988). This is reliant on the assumption of normality – that the organisation of a given cognitive system is homogeneous across healthy brains (Caramazza & McCloskey, 1988). While early researchers argued the importance of single case studies, groups of patients with shared aetiology and cognitive profiles can be effective in revealing functional associations and dissociations (Robertson et al., 1993), particularly when a case-series is reported (with a detailed breakdown of performance available for each individual case to establish group homogeneity). A dissociation refers to a case where a patient is identified as having impairment of one function, but preservation of another. A 'double dissociation' occurs when a second patient shows the opposite dissociation, and this implies that separable systems underpin these functions (Shallice, 1988). Conversely, an association is observed when different routes to broad impairments for the same domain (e.g., semantic cognition) produce common effects on a given outcome (Garrido et al., 2018).

Chapter 3 of this thesis tests for evidence of association or dissociation for impairments in a facial emotion categorisation task between patients with SD (previously collected data) and SA. These patients show impairments in semantic representation and control, respectively (Jefferies & Lambon Ralph, 2006). Chapters 2, 4, and 5 relied exclusively on patients with SA, and as such could not test for association or dissociation. SA patients do not present with purely semantic deficits – they frequently present with marked executive dysfunction (Thompson et al., 2018). While it therefore cannot be concluded that any deficits observed here are a direct result of impaired semantic control specifically, these studies show the impairments that co-occur with impaired semantic control, and help us to better understand the conditions under which this impairment is most marked.

1.7.3. Symptom mapping

1.7.3.1. Lesion symptom mapping

Chapter 2 aimed to characterise the neural bases of impairments in semantic control and domain-general cognitive control in SA. Symptom mapping was used in conjunction with three measures of damage: locally-lesioned tissue, white-matter disconnection predicted from lesion, and intrinsic functional connectivity changes predicted from lesion. Permutation testing was used to identify damaged voxels related to poorer behavioural performance across the sample. Lesion symptom mapping has been used to study the relationship between brain and behaviour for myriad cognitive functions and has regularly been applied to post-stroke aphasia (Bates et al., 2003). This same technique was used to examine dissociations between semantic impairment and non-verbal cognitive control deficits in SA.

1.7.3.2. Structural disconnection symptom mapping

Stroke can have diffuse effects on the brain beyond focal damage from lesion (Fornito et al., 2015). Beyond grey matter functional networks, cognitive functions can be supported by connectivity along white matter tracts. Stroke often affects white matter and leads to 'structural disconnection', disrupting functional networks (Salvalaggio et al., 2020). This is likely to affect neurocognitive functions that are supported by highly distributed networks, including semantic cognition which draws on the IFOF to link posterior and anterior semantic regions within the left hemisphere (Nugiel et al., 2016) and executive control which might draw on the corpus callosum to link left and right hemisphere frontal and parietal components (Bodini et al., 2013). These network-level effects can be estimated probabilistically, using patients' lesion locations relative to tractography data from a sample of healthy volunteers (Foulon et al., 2018). As with site of lesion, patterns of structural disconnection across a sample can be used to map symptoms (Thiebaut de Schotten et al., 2020).

1.7.3.3. Functional disconnection symptom mapping

Functional connectivity refers to covariance in activation between brain regions. Resting-state fMRI data (see Section 1.7.5) from a sufficiently large sample of neurologically healthy participants can be used to extract regions that exhibit particularly high functional connectivity with a given region of interest (Rogers et al., 2007; van den Heuvel & Pol, 2010). Functional networks are often characterised by high functional connectivity between their nodes. As such, focal brain damage can cause network-level disruption to typical patterns of functional connectivity, resulting in 'functional disconnection' (Salvalaggio et al., 2020). Such disruption may prevent regions beyond the lesion site from working in concert to

effectively support a cognitive function. The techniques most appropriate for measuring functional disconnection are contentious (Boes, 2021; Bowren et al., 2022; Pini et al., 2021). However, broadly speaking, this measure relies on extracting a map of functional connectivity to a given patient's lesion site. It follows logically that any patterns of functional connectivity to this damaged tissue will now be disrupted. Patterns of functional disconnection across a sample can then be mapped onto specific symptoms. This measure is 'indirect', in so far as it is estimated from on data reflecting typical functional connectivity in healthy adults. While this measure may not be as representative as directly measuring functional connectivity in patient groups with resting-state fMRI (Salvalaggio et al., 2020), it does provide an accessible proxy that does not rely on additional patient scanning.

1.7.4. Task-based fMRI

Chapter 5 used task-based fMRI in healthy young participants. fMRI is a non-invasive method which provides a proxy of metabolic activity in the brain through the imaging of deoxygenated haemoglobin. This is based on the premise that the displacement of deoxygenated haemoglobin, imageable due to its paramagnetic properties, is reflective of increased oxygenated blood flow to a region (Ogawa et al., 1993). This is taken to reflect increased metabolic demand and therefore increased activation. Through the measurement of deoxygenated haemoglobin, blood oxygen level-dependent (BOLD) signal can be extracted in order to quantify neuronal activity (Arthurs & Boniface, 2002; Toronov et al., 2003). BOLD signal is modelled using a haemodynamic impulse response function (HRF), reflective of the haemodynamic response to a given event in a given voxel (Stephan et al., 2004). Through such modelling, time-series across the brain can be extracted and compared between conditions, allowing for characterisation of the neural bases of a function or behaviour.

1.7.4.1. Whole-brain analysis

Chapter 6 uses whole-brain univariate analysis of task-based fMRI data. This analysis first relies on modelling the BOLD response in each voxel in each period of time in each experimental conditions of interest. Statistical thresholding can then be used to highlight clusters of voxels that are significantly active in a given condition over implicit baseline, or relative to another condition. Since there are many voxels in the brain, these thresholding approaches are often based on the size of contiguous clusters, and use randomised field theory to establish the cluster size that would be expected by chance, given the number of voxels reaching a particular threshold of activation.

1.7.4.2. ROI analysis

As well as examining whole-brain responses under a given condition, it can be useful to interrogate the extent to which a given region of interest (ROI) – normally identified by previous literature – is activated by each experimental condition (Poldrack, 2007). This approach was used in Chapter 6 when characterising the contribution of functional and resting-state networks. Mean percent signal change was extracted across all the voxels in each network defined by earlier studies. Interactions between network and task condition were then analysed using analysis of variance.

1.7.4.3. Parametric analysis

Rather than binary classifications of condition, parametric analysis relies on relative differences in variables of experimental interest. Signal is modelled relative to how it parametrically varies, relative to such a variable (Cohen, 1997). In doing so, one can extract clusters of voxels in which increases in activation are proportional to increases in this variable. This method was used in supplementary analysis of Chapter 6, when measuring the parametric relationship between BOLD activation and self-reported ratings of task difficulty.

1.7.5. Resting-state fMRI

As well as employing tasks with explicit instructions during fMRI, it is possible to measure spontaneous low-frequency variation in BOLD signal while a participant is at rest (Lee et al., 2013). This is known as resting-state fMRI, and can be used to capture the covariance of activation between regions (Lowe et al., 2000). This may reveal patterns of meaningful intrinsic connectivity which in turn can provide insight into the functional architecture of the brain. This can be used to characterise the degree of functional connectivity between a given region and the rest of the brain. Resting-state fMRI data was not collected for the current thesis. Nonetheless, chapters relied on networks and gradients defined using resting-state data.

1.7.5.1. Resting-state networks

Resting-state data can be used to parcellate networks based on functionally coupled regions as measured by their intrinsic connectivity. In order to do so, time-series correlations are run between all pairs of parcels across the cortex. A clustering algorithm is then used to group voxels together with others that present with the most similar patterns (Cohen et al., 2008). Yeo et al. (2011) used resting-state data from 1,000 participants in this fashion, producing a 7- and 17-network parcellation of the human cortex. Both parcellations provide

insight into functionally segregated networks, including DMN (in its entirety in the 7-network parcellation, and comprising distinct subnetworks in the 17-network parcellation) and frontoparietal control regions. These parcellations were used in Chapter 6 when parsing functional contributions of DMN and its components.

1.7.5.2. Cortical gradients

Resting-state fMRI data can be used to construct spatial gradients that reflect similarity in connectivity patterns across the cortex. Extraction of gradients relies on diffusion embedding, a nonlinear approach to dimensionality reduction which captures patterns of connectivity over space (Coifman et al., 2005). Using group-level connectivity matrices that explain maximal variance in connectivity, gradients are extracted and plotted on the cortical surface (Shao et al., 2022). The end result is a cortical hierarchy, separating regions maximally associated with one functional profile from those associated with another. Using resting-state data from 820 participants from the Human Connectome Project (Van Essen et al., 2013), Margulies et al. (2016) defined the 'principal gradient' as the hierarchy that explained the largest amount of variation. This gradient was anchored by sensorimotor processing regions at one end, and by heteromodal regions implicated in DMN at the other. Gradients found to explain the second and third highest amount of variance reflected a separation between visual and motor sensory regions, and DMN frontoparietal control regions, respectively (Margulies et al., 2016; Shao et al., 2022). Maps of these three gradients were used to situate clusters identified in fMRI task activation in Chapter 6.

While resting-state networks uncover binary and discrete parcellations, gradient analysis looks for dimensions of connectivity change. As such, gradients consider the full spectrum of connectivity similarity between voxels, with every part of the brain falling somewhere on this dimension rather than belonging to a discrete category. These two measures are therefore opposed in their methods, but provide complementary insight. While networks allow for broad statements concerning differential functions, gradients characterise meta-organisation of the brain. The organisation of discrete networks can be reflected by gradients. Margulies et al. (2016) located each of the 7- and 17-network solutions (Yeo et al., 2011) on the principal gradient, demonstrating meaningful organisation with DMN at the maximally heteromodal end and visual and somatosensory networks at the unimodal end. Analysis of both resting-state networks and cortical gradients in Chapter 6 should provide distinct but complementary insight into the functional characterisation of task activation.

1.8. Summary of empirical chapters

Chapter 2 of this thesis focuses on conceptualising the patterns of damage associated with impairments in semantic control and domain-general control in SA. Using 23 existing structural MRI scans, damage was quantified using three techniques. First, lesions were manually traced, allowing for quantification of the sites maximally damaged in this group. Diffuse damage from lesion was then measured using both 'structural disconnection' and 'functional disconnection', as described in section 1.7.3. above. This chapter then observed the extent of damage to systems key to semantic retrieval, including core semantic regions, SCN, MDN, and DMN. Finally, using maps of lesion, structural disconnection, and functional disconnection, symptom mapping was used to shed further light on the dissociable substrates responsible for semantic-specific and domain-general control impairments in this group. These results provide further insight into the specialisation of neural systems in semantic retrieval and cognitive control, as well as providing novel characterisation of SA.

Widespread damage beyond lesion site in SA may be partly responsible for the diverse range of impairments in SA. In Chapter 3, two studies were used to observe a domain not yet investigated in relation to semantic retrieval – emotion perception. This was inspired by evidence from Lindquist et al. (2014) that semantic storage deficits in SD are associated with difficulty categorising pictures of facial portrayals, with frequent within-valence errors. This paradigm was repeated with seven SA patients. A novel prosody cueing forced-choice paradigm was also used, which also required patients to sort faces by emotion category. In doing so, this chapter aimed to elucidate the role that semantic control may play in emotion categorisation, and test for benefits from contextually-relevant cues. It was predicted that impairments in semantic control would lead to comparable emotion processing impairments as seen in SD, and that patients would benefit from cues. Such findings could supplement the constructionist account of emotion, which stresses the importance of conceptual information in emotion processing. Data was collected remotely during the COVID-19 pandemic, limiting the sample to the seven patients in the patient database willing and able to engage with online testing. This small sample size is acknowledged in the limitations section of this chapter.

Rather than focusing on discrete emotion categories, Chapter 4 investigated whether hedonic valence acts as an intrinsic aspect of concepts. Valence congruency between words may aid thematic matching between them, as has been previously shown (Marino Dávolos et

al., 2020). Conversely, semantic relatedness may benefit the ability to match words by valence, while semantically related but valence-incongruent distractors may impair performance. For a sensitive measure of response time, Experiment 4.1 tested these predictions in 60 healthy young adults. In Experiment 4.2 these same tasks were used with five SA patients and 15 age-matched controls. It was predicted that semantic relatedness would have marked effects on valence matching, while valence congruency would benefit semantic matching. These effects were predicted to be exaggerated in SA, with patients also showing baseline valence matching impairments, due to greater difficulties in inhibiting task-irrelevant information. These experiments should address predictions of embodied and hub-and-spoke accounts that semantic concepts are grounded in valence. Furthermore, they may provide insight into the role of semantic control in valence processing. As for Chapter 3, data were collected remotely during COVID-19 restrictions, limiting our patient sample size.

Chapter 5 studied another aspect of affective cognition in SA – motivation. Studies have demonstrated that extrinsic reward can be used to improve performance on domain-general cognitive control tasks, and to ameliorate age-related control deficits (e.g., Yee et al., 2019). This chapter tested whether these effects generalise to semantic control in a sample of SA patients and healthy controls. Experiment 5.1 observed the effect of high and low levels of extrinsic reward, in the form of token points, on the retrieval of strong and weak semantic associations. The same design was used in Experiment 5.2, but with a manipulation of self-reference to increase intrinsic motivation. Both extrinsic reward and self-reference were predicted to ameliorate semantic control impairments in SA during the retrieval of weak associations, given that these confer greater semantic control demands than strong association trials. This study may provide insight into whether affective properties of stimuli can be harnessed to bolster controlled semantic retrieval, despite evidence of any deficits in the processing of affective stimuli. If so, these findings may have implications for the gamification of treating post-stroke semantic impairment. Data for this chapter were collected in-person prior to the COVID-19 pandemic, allowing access to a larger sample of 16 patients.

Chapter 6 utilised fMRI in order to better understand the neural systems underlying the retrieval of both semantic contextual and emotional responses to pictures. The contributions of SCN were investigated, which should contribute to internally-focused controlled processing, and MDN, which may be engaged if sufficient domain-general control is required. DMN was of particular interest here. In a sample of 32 young adults, participants were required to generate semantic contextual or emotional associations to pictures, first by

providing an automatic and dominant association in the ‘generate’ phase, followed by a weaker subordinate association in the ‘switch’ phase. This chapter looked for functional dissociations in the contributions of DMN subnetworks, including FT and MT DMN, to either semantic context or emotional associations. This chapter then assessed whether activation within subnetworks was modulated by changing retrieval demands across the generate and switch phases. Alternatively, processing of retrieval demands in DMN may be supported by other control regions allied to DMN, independent of task. It was further predicted that SCN may play a general-purpose role across association types and phases, due to its specialisation in the controlled processing of internal information. As well as providing novel insight into the shared neural bases of contextual and emotional associations, this project may better characterise the functional contributions of DMN to semantic cognition.

A general discussion in Chapter 7 will draw findings from these studies together, considering implications for (1) multiple domains of impairment in semantic aphasia, (2) the relationships between emotion, meaning, and control, (3) neural systems supporting aspects of cognitive control, and (4) the role of the default mode network in semantic retrieval.

Chapter 2: Mapping lesion, structural disconnection, and functional disconnection to symptoms in semantic aphasia

This chapter is adapted from a published article:

Souter, N., Wang, X., Thompson, H., Krieger-Redwood, K., Halai, A. D., Lambon Ralph, M. A., Thiebaut de Schotten, M., & Jefferies, E. (2022). Mapping lesion, structural disconnection, and functional disconnection to symptoms in semantic aphasia. *Brain Structure and Function, 227,* 3043-3061. https://doi.org/10.1007/s00429-022-02526-6.

Data for this chapter are publicly available on the Open Science Framework (https://osf.io/6psqj/) and on Neurovault (https://neurovault.org/collections/KGXBJXSX/).

Acknowledgements and author's contribution

This project was conceptualised by Nick Souter along with co-authors Elizabeth Jefferies and Michel Thiebaut de Schotten. This project was run on previously collected patient data and MRI scans, to which both Nick Souter and Hannah Thompson had contributed. Hannah Thompson, Ajay D. Halai, and Matthew Lambon Ralph assisted with the procurement of resources for this project. Curation and analysis of data was managed and conducted by Nick Souter under the supervision of Elizabeth Jefferies and Michel Thiebaut do Schotten, with assistance in the setup and interpretation of analysis from Xiuyi Wang and Katya Krieger-Redwood. Zhiyao Gao aided in the procurement of functional network maps, and Lucy Cogdell-Brooke provided advice for manual lesion tracing. Nick Souter wrote the full original draft of this paper. Elizabeth Jefferies edited manuscript drafts, and all other co-authors provided feedback on the final draft.

2.1. Abstract

Patients with semantic aphasia have impaired control of semantic retrieval, often accompanied by executive dysfunction following left hemisphere stroke. Many but not all of these patients have damage to the left inferior frontal gyrus, important for semantic and cognitive control. Yet semantic and cognitive control networks are highly distributed, including posterior as well as anterior components. Accordingly, semantic aphasia might not only reflect local damage but also white matter structural and functional disconnection. Here we characterise the lesions and predicted patterns of structural and functional disconnection in individuals with semantic aphasia and relate these effects to semantic and executive impairment. Impaired semantic cognition was associated with infarction in distributed left-hemisphere regions, including in the left anterior inferior frontal and posterior temporal cortex. Lesions were associated with executive dysfunction within a set of adjacent but distinct left frontoparietal clusters. Performance on executive tasks was also associated with interhemispheric structural disconnection across the corpus callosum. In contrast, poor semantic cognition was associated with small left-lateralized structurally disconnected clusters, including in the left posterior temporal cortex. Little insight was gained from functional disconnection symptom mapping. These results demonstrate that while left-lateralized semantic and executive control regions are often damaged together in stroke aphasia, these deficits are associated with distinct patterns of structural disconnection, consistent with the bilateral nature of executive control and the left-lateralized yet distributed semantic control network.

2.2. Introduction

To understand the world around us, we draw on two connected but dissociable components; a store of long-term semantic knowledge (e.g., Patterson et al., 2007) and control processes that shape retrieval to suit current circumstances (Lambon Ralph et al., 2017; Rogers et al., 2015). This distinction is highlighted by comparing semantic dementia (SD) and semantic aphasia (SA).

SD patients show conceptual degradation associated with atrophy of the ventral anterior temporal lobes (vATL) and highly consistent semantic deficits across tasks that probe the same items (Bozeat, Lambon Ralph, et al., 2000; Mummery et al., 2000), in line with the view this site acts as a 'semantic hub' for heteromodal concepts (Lambon Ralph et al., 2017; Patterson et al., 2007). According to the hub-and-spoke model of semantic cognition, the vATL 'hub' works in concert with modality-specific 'spokes' in order to generate generalisable and coherent representations (Rogers et al., 2021). In contrast to those with SD, patients with SA have intact conceptual representations but an impaired ability to retrieve information in a flexible and context-appropriate manner, following left inferior frontal and/or temporoparietal stroke (Jefferies, 2013; Jefferies & Lambon Ralph, 2006)[3]. Such deficits are multi-modal, such that these patients experience impairments in non-verbal attribution of appropriate object use (Corbett et al., 2011), as well as in verbal semantic matching between words (Noonan et al., 2010). SA patients show stronger-than-normal effects of cues and miscues designed to help or hinder conceptual retrieval (Jefferies et al., 2008; Lanzoni et al., 2019; Noonan et al., 2010). These effects are accompanied by poor retrieval of weak associations and the subordinate meanings of ambiguous words and objects, as well as more significant impairment when targets are presented alongside strong distractors (Noonan et al., 2010). Consequently, the study of these patients can provide insights into the neurocognitive mechanisms that allow us to use our conceptual knowledge in a controlled way.

Semantic deficits in SA are thought to reflect damage to a distributed but largely left-lateralised semantic control network (SCN), but evidence demonstrating the functional relevance of connectivity between key SCN nodes is lacking. While the peak lesion overlap

[3] vATL is typically spared in SA, since the anterior temporal cortical artery branches below the main trifurcation of the middle cerebral artery and because this watershed region has a dual blood supply from the middle and posterior cerebral arteries (Borden, 2006; Conn, 2003).

in SA is in the left posterior inferior frontal gyrus (IFG), not every case shows damage here. Lesions are also highly variable within the left parietal and posterior temporal cortex (Chapman et al., 2020; Hallam et al., 2018; Lanzoni et al., 2019; Stampacchia et al., 2018). This lesion heterogeneity is anticipated by neuroimaging meta-analyses of healthy participants (Jackson, 2021; Noonan et al., 2013), which highlight reliable activation of posterior components of SCN, most notably the left posterior middle temporal gyrus (pMTG), along with IFG in tasks with high semantic control demands (e.g., Becker et al., 2020; Krieger-Redwood et al., 2015; Zhang et al., 2021). Studies employing inhibitory stimulation suggest that both left IFG and pMTG play a critical role in semantic control (Davey et al., 2015; Whitney et al., 2011). Moreover, damage or inhibitory stimulation of left IFG elicits increased activation in left pMTG (Hallam et al., 2016; 2018), as would be expected within a distributed functional network. While this work suggests that both anterior and posterior sites support semantic control, the structural and functional disconnection that is anticipated from the diverse lesions in SA has not been clearly delineated. We might expect similar and overlapping disconnection patterns across cases with different lesions (affecting anterior and posterior components of SCN, for example), given the same network is thought to be damaged in patients with semantic deficits.

Another unresolved issue concerns the extent to which SCN is distinct from the multiple-demand network (MDN), which supports executive control across domains (Fedorenko et al., 2013). Like SCN, MDN includes highly distributed anterior and posterior components and neuroimaging studies of healthy participants suggest these networks are adjacent in lateral temporal and lateral and medial frontal cortex (Davey et al., 2016; Gao et al., 2021; Wang et al., 2020). This proximity of SCN and MDN in the left hemisphere may explain why SA patients, selected to show heteromodal semantic deficits, frequently also present with non-semantic executive impairment (Thompson et al., 2018). Since MDN regions support the performance of semantic tasks with high control demands (Krieger-Redwood et al., 2015; Wang et al., 2020), damage to these regions will contribute to difficulties regulating semantic cognition. Nevertheless, SCN and MDN diverge in their degrees of lateralisation. While SCN is largely left-lateralised, MDN comprises distributed bilateral regions (Camilleri et al., 2018; Gao et al., 2021; Gonzalez Alam et al., 2019). As such, effective semantic control should involve connectivity within the left-hemisphere, while domain-general control should rely more on interhemispheric connectivity (Gonzalez Alam et al., 2022), allowing the integration of information across right-hemisphere regions dominant

in the control of visuospatial processing with contralateral frontal regions (Wu et al., 2016). As a result, structural or functional disconnection-symptom mapping may separate semantic control impairment from general executive deficits in a way that cannot be achieved by lesion-symptom mapping in patients with left-hemisphere stroke.

Unlike MDN, SCN also overlaps with regions of the default-mode network (DMN) – indeed, nodes of SCN fall in between MDN and DMN in the left hemisphere (Davey et al., 2016; Gao et al., 2021; Wang et al., 2020). Posterior aspects of left IFG, bordering the inferior frontal sulcus, overlap with MDN and are implicated in executive control, while anterior aspects of left IFG that fall within DMN are thought to be engaged more specifically in controlled semantic retrieval (Badre & Wagner, 2007; Krieger-Redwood et al., 2015; Zhang et al., 2021). DMN also extends beyond semantically relevant regions; this large bilateral network is associated with task-related deactivation (Raichle, 2015), the coordination of information across the cortex (Lanzoni et al., 2020), and multiple forms of abstract, internal and heteromodal cognition (Gordon et al., 2020; Murphy et al., 2018; Smallwood et al., 2021). In addition to overlapping with SCN in left lateral posterior temporal and ventral and dorsomedial prefrontal cortex (Davey et al., 2016; Gao et al., 2021; Wang et al., 2020), DMN overlaps with key heteromodal sites relevant for semantic cognition irrespective of control demands, including semantic regions in ATL (Smallwood et al., 2021) and angular gyrus (Vatansever, Manktelow, et al., 2017).

Given the above evidence, we might expect semantic and executive deficits in SA following left-hemisphere stroke to be associated with similar lesion profiles but distinct patterns of disconnection. Structural and functional disconnection within the left-lateralised components of SCN may underpin semantic deficits. At the same time, broader executive impairment across domains may relate to disconnection between left and right control regions. Studies already show that white matter connections between anterior temporal and occipital/middle temporal regions predict semantic impairment beyond the contribution of grey matter damage alone (Fang et al., 2018). Tracts implicated in semantic cognition in the left hemisphere include the inferior fronto-occipital fasciculus (IFOF), anterior thalamic radiation (ATR), uncinate fasciculus (UF) and inferior longitudinal fasciculus (ILF; Almairac et al., 2015; Han et al., 2013; Sierpowska et al., 2019). The left ILF and left IFOF have been associated with semantic control specifically (Marino Dávolos et al., 2020; Nugiel et al., 2016). Moreover, distinct changes in structural connectivity are associated with semantic impairment in SD and SA patients: SA is related to changes in left frontal-subcortical and left

frontal-temporal/occipital networks, while symptoms in SD are associated with fractional anisotropy of a left medial temporal white matter network (Ding et al., 2020). Conversely, a decline in executive function occurs with compromised integrity of the corpus callosum, in both healthy ageing (Johnson et al., 2017; Jokinen et al., 2007; Voineskos et al., 2012) and patient groups (Bodini et al., 2013), consistent with the theory that demanding tasks rely on cross-hemispheric integration (Gazzaniga, 2005; Schulte & Müller-Oehring, 2010). Accordingly, impairments in semantic control and executive function may be predicted by left-lateralised and bilateral disconnection, respectively.

This study aimed to characterise typical patterns of infarct, plus structural and functional disconnection, in a sample of 23 SA patients. The use of such 'connectomic' data may help to elucidate the relationship between diffuse networks and impairments following cerebral insult (Fornito et al., 2015). We assessed the impact of lesion on functional networks including SCN, MDN and DMN, given all these networks are implicated in semantic cognition. Individual patterns of structural disconnection were predicted by tracking white matter fibres likely to pass through a patient's lesion based on diffusion-weighted imaging data from neurologically healthy participants (Foulon et al., 2018). Structural disconnection in stroke patients assessed in this way has been shown to reflect functional activation better than lesion location alone (Thiebaut de Schotten et al., 2020), and to predict post-stroke symptoms including apraxia (Garcea et al., 2020) and executive impairment (Langen et al., 2018). Similarly, measures of functional disconnection were derived by assessing patterns of intrinsic functional connectivity with the lesion site, using resting-state scans from neurologically healthy participants and seed-based functional connectivity analysis (Salvalaggio et al., 2020). Although this functional disconnection metric has been shown to be less predictive of cognitive deficits than structural disconnection (Salvalaggio et al., 2020), here we implemented a method thought to have higher sensitivity, which involved performing principal components analysis of resting-state data from a sample of healthy adults from each patient's lesion and seeding the first component of this functional connectivity pattern. Evidence from Pini et al. (2021) suggests that this approach provides better anatomical specificity and behavioural prediction than seeding the entire lesion.

We explored associations between measures of lesion location, structural disconnection, and functional disconnection and performance on semantic cognition and non-semantic executive function tests. We would expect adjacent or similar lesions to predict deficits of semantic cognition and executive control, given that the networks supporting these

functions in the left hemisphere are thought to have a similar topological organisation. Moreover, we would expect *peak* lesion location to fall within SCN, given that SA patients show deregulated conceptual retrieval. We may also predict some lesion extension into adjacent DMN, MDN, and core semantic regions, given their spatial proximity to SCN and potential contributions to semantic cognition. These lesions should be accompanied by widespread structural and functional disconnection that is again maximal within SCN. However, since executive control is thought to draw on the bilateral MDN, while semantic control is strongly left-lateralised, the broader patterns of disconnection that predict performance within these domains may be more distinct. Accordingly, poor semantic cognition should be associated with left-lateralised patterns of structural and functional disconnection (across left-hemisphere components of DMN, SCN and MDN). Executive dysfunction on non-semantic tasks might be related to more bilateral patterns of disconnection specifically within MDN.

2.3. Method

Ethics approval for this study was granted by the York Neuroimaging Centre at the University of York (date: 24/10/2019, project ID: P1363).

2.3.1. Participants

Participants were 23 SA patients with impaired multimodal semantic control following left hemisphere stroke. Patients were recruited from communication support groups across Yorkshire, Surrey, and Manchester in the UK. Patients were all right-handed and native English speakers, had a mean age of 62.2 (SD = 11.9) and a mean age of leaving education of 16.3 (SD = 1.5)[4]. Participants underwent structural MRI and cognitive testing at least six months post-stroke, with a mean of 6.7 years (SD = 5.5) since the infarct, such that patients were in the chronic phase and changes in brain function would have been relatively gradual and subtle. Scans were obtained close in time to the behavioural testing. Volunteers were excluded if they reported participating in ongoing rehabilitation at the time of testing. All patients reported no history of traumatic brain injury or suspected or confirmed neurodegenerative disorders. Patients were selected to show impairment on at least one

[4] Age of leaving education missing for one participant (P19).

verbal and one nonverbal measure of semantic control, in line with Head's (1926) definition of SA as multimodal impairment in the manipulation of knowledge for symbolic processing.

2.3.2. Background neuropsychological testing

Patients completed a series of tests probing language, memory, executive function, visuospatial processing, and semantic cognition. A description of all tasks can be seen in the Background Neuropsychology Supplementary Materials section *Description of Assessments*, and a summary of the sample's performance in the Chapter 2 Supplementary Materials section *Background Neuropsychology Sample Summary*.[5] Patients' individual performance on tests of background neuropsychology and semantic cognition can be seen in Supplementary Table 2.1 and Supplementary Table 2.2, respectively. Patients had variable impairment of word repetition and commonly showed impaired category fluency, letter fluency and verbal working memory. Fourteen patients were impaired on at least one test of executive function. Most patients had relatively good visuospatial processing.

All patients were impaired on at least one verbal and one nonverbal measure of semantic cognition, in line with our inclusion criteria. We found 78% of patients were impaired on the word version of Camel and Cactus Test (CCT) of semantic associations, while 52% were impaired on the picture version. Most patients showed near-ceiling performance on a simple test of word-picture matching, as has previously been shown (e.g., Lanzoni et al., 2019; Thompson et al., 2018). The majority of cases (80%) showed impaired picture naming. All patients who were tested with phonemic cueing showed evidence of improved accuracy as a result, except for patients performing at floor level. Similarly, when the relevant data was available, patients showed strong effects of semantic control manipulations across a series of assessments, including difficulty retrieving subordinate conceptual information, susceptibility to contextual cues and miscues, and deleterious effects of semantic distractors on synonym judgement.

Principal components analysis (PCA) with oblique rotation was used to extract a composite score for semantic tasks that were maximally available across the sample: namely word and picture CCT, and overall performance on the no cue version of the 'ambiguity'

[5] While neuropsychology data from chapters 3, 4, and 5 include different patients from within the same sample, Chapter 2 used a larger pool of patients from three separate samples. As such, while background neuropsychology data for other chapters is reported together in the Background Neuropsychology Supplementary Materials, data for the Chapter 2 sample is presented separately within the Chapter 2 Supplementary Materials. Pseudonymised patient identifiers are consistent across Chapters 3, 4, and 5, but not for Chapter 2.

assessment (Noonan et al., 2010). In doing so, we aimed to obtain a single score to reflect semantic performance across tasks for each participant. PCA was performed with data from the 21 patients who completed all three tests. This analysis revealed that all three tests loaded strongly on a single component with an eigenvalue of 2.6 (loadings: CCT words = .95; CCT pictures = .92; ambiguity = .92) that explained 87% of variance in performance. We extracted a 'semantic cognition composite score' from this component, with lower values reflecting greater impairment of semantic cognition. Patients' individual composite scores are presented in Supplementary Table 2.2. Performance on the Brixton Spatial Anticipation Test (Burgess & Shallice, 1997) was taken to reflect patients' degree of impairment in cognitive control beyond the semantic domain[6], for the 20 patients for whom data were available. This task involved anticipating the locations where a dot would move to, given past patterns, and shifting these predictions when the pattern changed. Performance on the Brixton test correlated positively with patients' semantic composite scores ($r(18) = .61$, $p = .005$), providing evidence that poorer semantic performance was accompanied by poorer executive control on a non-verbal task.

In summary, while SA patients were screened in on the basis of verbal and nonverbal semantic impairment, they were not excluded on the basis of impairment in other domains. Many SA patients in this sample presented with multi-domain impairment beyond semantic cognition, in common with earlier studies (e.g., Thompson et al., 2018). The symptom mapping employed in the current investigation can therefore test for dissociable substrates underlying semantic and domain-general cognitive control impairments.

2.3.3. MRI acquisition

Structural T1 images were obtained for all patients. Patients in York (N = 13) were scanned using a 3T GE HDx Excite MRI scanner on a T1-weighted 3D fast spoiled gradient echo sequence (TR = 7.8ms, TE = minimum full, flip-angle = 20^o, matrix size = 256 x 256, 176 slices, voxel size = 1.13 x 1.13 x 1mm). Patients in Manchester (N = 8) were scanned using a 3T Philips Achieva MRI scanner using a T1-weighted 3D inversion recovery sequence (TR = 9.0ms, TE = 3.93ms, flip-angle = 8^o, matrix size = 256 x 256, 150 slices, voxel size = 1 x 1 x 1mm). Scanning parameters for patients scanned in Surrey (N = 2) are not available.

[6] This measure was selected as it is a sensitive measure of executive impairment and was widely-available in our sample.

For analysis of functional disconnection, we used resting state scans from an independent sample of 207 neurologically healthy volunteers recruited from the University of York. Data were collected from the whole brain on a 3T GE HDx Excite MRI scanner using single-shot 2D gradient-echo-planar imaging (TR = 3s, TE = minimum full, flip-angle = 90^{o}, matrix size = 64 x 64, 60 slices, voxel size = 3 x 3 x 3mm, 180 volumes). We excluded sixteen participants: nine due to missing behavioural data, one due to missing MRI data, one due to incorrect TR in MRI acquisition, and four during pre-processing because they exceeded our motion cut-off of .3 mm, had more than 20% invalid scans and/or mean global signal change of z > 2. The final sample size, therefore, consisted of 191 participants. Estimates of structural disconnection were based on diffusion-weighted data from healthy controls, collected on a 3T GE Signa HDx TwinSpeed system (TR = 20/30 R-R intervals, TE = 93.4ms, matrix size = 128 x 128, 60 slices, voxel size = 2.4 x 2.4 x 2.4mm).

2.3.4. Lesion segmentation

Patients' T1 scans underwent brain extraction in ANTs using a template from the OASIS Brain Project (https://www.oasis-brains.org/; Marcus et al., 2010). Registration to MNI152 space was also performed using ANTs linear registration (version 2.1.0; Avants et al., 2011; 2014), which utilises a symmetric normalisation model. Default parameters were used including aligning centres and orientations, accounting for scaling factors, ending with affine transformation, and including optimisation for cost function (Avants et al., 2011). Patients' lesions were then manually drawn in MRICron, using a combination of the 3D fill tool feature and subsequent validation of each slice. Care was taken to avoid implicating enlarged sulci or ventricles in the lesion: cases where sulci or ventricles have been implicated by the 3D tool are typically observable through visual inspection by cross-referencing axial, sagittal, and coronal views of a given slice, and in such cases the respective highlighting was removed from the lesion drawing.

2.3.5. Structural disconnection

The BCBtoolkit (Foulon et al., 2018; http://www.toolkit.bcblab.com) was used to generate probabilistic maps of spreading structural disconnection. This approach uses a set of ten healthy controls' DWI datasets (Rojkova et al., 2016) to track fibers passing through each patient's lesion. This makes it possible to estimate likely structural disconnection from a lesion even when no diffusion-weighted imaging is acquired. The control sample used here is independent of the sample used to estimate functional disconnection (see Section 2.3.3). Patients' lesions in the MNI152 are used as seeds for tractography in Trackvis (Wang et al.,

2007). Tractographies from the lesions were transformed in visitation maps (Thiebaut de Schotten et al., 2011) and binarised. Finally, a percentage overlap map was produced by summing the normalized visitation map of each healthy subject at each point in MNI space. In the resulting disconnectome map for each patient, the value of each voxel reflects the interindividual variability of tract reconstructions in controls, resulting in a value between 0 and 1 reflecting the probability of disconnection (Thiebaut de Schotten et al., 2015). Disconnectome maps for each patient were thresholded at 0.5, such that the disconnectome maps corresponded to the exact white matter anatomy of more than 50% of the healthy controls (Foulon et al., 2018). While 50% is the default threshold in the BCBtoolkit, disconnectome maps were also generated at thresholds of 40% and 60% to test the stability of our analysis. Symptom mapping at these alternative thresholds (using the same procedure outlined in Section 2.3.8) produced similar clusters to those identified at the 50% threshold, as seen in Supplementary Figure 2.1.

In order to assess the effect of structural disconnection on specific white matter tracts, probabilistic tracts included in the BCBtoolkit (Foulon et al., 2018) were extracted, thresholded at a value of 0.95, and used to visualise the tracts of interest. We were specifically interested in tracts implicated in semantic cognition, language, domain-general cognitive control, or the confluence of these functions (Agosta et al., 2010; Almairac et al., 2015; Bodini et al., 213; Dick et al., 2019; Ding et al., 2020; Han et al., 2013; Huang et al., 2015; Johnson et al., 2017; Marino Dávolos et al., 2020; Nugiel et al., 2016; Rizio & Diaz, 2016; Sierpowska et al., 2019; Spitz et al., 2013), including the uncinate fasciculus (UF), anterior thalamic radiation (ATR), inferior longitudinal fasciculus (ILF), inferior fronto-occipital fasciculus (IFOF), frontal aslant tract (FAT), arcuate fasciculus (AF), superior longitudinal fasciculus (SLF), and corpus callosum. We quantitatively assessed the effect of structural disconnection on these tracts using the Tractotron function of the BCBtoolkit (Foulon et al., 2018). Tractotron maps the lesion from each patient onto tractography reconstructions of specific white matter pathways obtained from a group of healthy controls (Rojkova et al., 2016), and quantifies both the probability of a given tract being disconnected, and the proportion of this tract that is likely to be disconnected (Thiebaut de Schotten et al., 2014).

2.3.6. Functional disconnection

We generated maps of functional connectivity to each patient's lesion location, to provide an indirect measure of functional disconnection. Typically, functional disconnection has been estimated by using patients' entire binarised lesion in seed-based functional connectivity analysis (e.g., Salvalaggio et al., 2020). However, this approach can be problematic when seeding large lesions, which contain multiple functionally distinct regions that couple to different networks (Boes, 2021; Bowren et al., 2022). We therefore adopted a method proposed by Pini et al. (2021), whereby PCA is first conducted on the connectivity of all voxels within each lesion in a sample of neurologically healthy adults (here, the same 191 participants described in Section 2.3.3). Forty components were extracted for each lesion. Given that the first principal component extracted explains the largest amount of variance, this component was taken as the main within-lesion connectivity axis. The first component for each patient was thresholded such that only voxels within the lesion with an absolute coefficient above the 20th percentile were retained. This threshold has been shown to provide higher functional specificity than higher and lower percentile thresholds (Pini et al., 2021). The resulting thresholded map was then binarised and seeded in functional connectivity analysis using an independent sample of resting-state fMRI scans from neurologically healthy participants (as described in Section 2.3.3). Compared with seeding the entire lesion, this approach has been shown to improve behavioural prediction and anatomical specificity of estimates of functional disconnection (Pini et al., 2021). All PCAs and functional connectivity analyses were conducted using the CONN functional connectivity toolbox V.20.b (Whitfield-Gabrieli & Nieto-Castanon, 2012; www.nitrc.org/projects/conn) in MATLAB.

Functional resting-state volumes were skull-stripped, slice-time (interleaved) and motion-corrected, and co-registered to the high-resolution structural image, spatially normalised to MNI space using the unified-segmentation algorithm, smoothed with a 6 mm FWHM Gaussian kernel, and band-passed filtered (.008-.09 Hz) to reduce low-frequency drift and noise effects. A pre-processing pipeline of nuisance regression included motion (twelve parameters: the six translation and rotation parameters and their temporal derivatives) and scrubbing (all outlier volumes were identified through the artifact detection algorithm included in CONN with conservative settings: scans for each participant were flagged as outliers based on scan-by-scan change in global signal above $z > 3$, subject motion threshold above 5 mm, differential motion and composite motion exceeding 95% percentile in the

normative sample). We used the anatomical CompCor approach, a PCA-based approach which attempts to isolate aspects of images caused by artefacts (Satterthwaite et al., 2019), and removes these nuisance variables in a single linear regression step in order to provide a clear signal (Behzadi et al., 2007). CompCor also includes a linear detrending term, eliminating the need for global signal normalisation. A covariate containing quality assurance parameters flagged average subject motion as outliers for scrubbing at a threshold of .5 mm based on framewise displacement. Group-level analyses in CONN were cluster-size FWE corrected and controlled for the number of seeds (Bonferroni, $p < .002$), and used a height threshold of $p < .001$. The resulting output files were thresholded such that only positively associated voxels remained and were taken to reflect patients' maps of functional disconnection.

2.3.7. Functional networks

We assessed the effect of patients' lesions on networks of interest. To identify SCN, we used the map from Jackson (2021), derived from a meta-analysis of studies that manipulated semantic control demands. To identify semantic regions outside SCN, we used a map from the meta-analytic tool Neurosynth (Yarkoni et al., 2011) for the term 'Semantic'. MDN was defined using a map from Fedorenko et al. (2013) reflecting activation associated with global effects of difficulty across seven diverse tasks, thresholded at $t > 1.5$. We also identified areas common to both SCN and MDN, using voxels overlapping between the respective maps described above. Finally, DMN was defined using the 7-network parcellation from Yeo et al. (2011). All maps were mutually exclusive such that (1) any voxels contained within MDN, SCN, or Neurosynth semantic network were removed from DMN (i.e. this map focussed on domain-general responses, excluding regions specifically implicated in semantic cognition); (2) any voxels contained within SCN or MDN were removed from the Neurosynth semantic network (i.e., this map excluded both DMN and control regions and as such focussed on those involved in semantic representation or more automatic aspects of retrieval and not more controlled patterns of retrieval); and (3) any voxels contained within both SCN and MDN were removed from each individual map and placed in the conjunctive 'MDN + SCN' map (such that SCN-only regions were not implicated in domain-general control). Visualisations of each mutually exclusive network can be seen in Figure 2.2 when results of the network damage analysis are reported.

As discussed in Section 1.3.4, elements of all functional networks studied here overlap with regions implicated in language processing. Given that we were interested in

controlled semantic retrieval as a multimodal process, the 'language network' it not explicitly investigated. This network should be largely captured in the intersection of DMN, core semantic, and SCN regions.

We assessed the mean percentage of each network that was lesioned across the sample. As all lesions were restricted to the left hemisphere, each network was confined to the left hemisphere for this analysis. All network maps were binarized prior to analysis. We identified for a given patient, the number of voxels implicated in both their binary lesion file and a given functional network, computed as a percentage of the total number of voxels implicated in this network. This process was also conducted for patients' functional disconnection maps (Supplementary Figure 2.2). We did not assess overlap with the structural disconnection maps since these were confined to white matter.

The SCN map (Jackson, 2021) spans five distinct clusters including (1) left frontal regions (left IFG, insula, orbitofrontal cortex, and precentral gyrus), (2) left posterior temporal regions (left pMTG, posterior inferior temporal gyrus, and posterior fusiform gyrus), (3) the bilateral dmPFC, (4) the right IFG (pars orbitalis) and insula, and (5) the right IFG (pars triangularis). SCN was split into these separate clusters in order to observe spreading disconnection within SCN beyond lesion site. We extracted the mean percentage of each cluster that overlapped with each patient's lesion map; we then identified whether patients' structural and functional disconnection maps showed any overlap with each SCN cluster that fell outside the respective patient's lesion.

2.3.8. Symptom mapping

We assessed the patterns of lesion, structural disconnection, and functional disconnection associated with the semantic composite score and executive function performance. Patients' binary lesion segmentations, continuous structural disconnection maps, and continuous functional disconnection maps were separately entered into nonparametric 2-sample t-tests in Randomise (Winkler et al., 2014; https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Randomise/UserGuide), using 5,000 permutations. Threshold-free cluster enhancement was implemented to identify clusters (Smith & Nichols, 2009). This analysis was restricted to the 20 patients for whom both the semantic cognition composite and Brixton test scores were available. Each model was set up such that the input was a 4D file containing all patient maps. In each case simultaneous regressors included the size of a given patient's respective input file size (i.e., the overall size of the binary lesion

map or disconnection map), their semantic composite, and their Brixton performance. Within each model, clusters implicated for a given behavioural measure therefore regressed out the size of the input file as well as performance on the other behavioural measure. A binary mask containing the addition of all patient input files was used. Contrasts were specified such that the resulting output revealed (i) clusters associated with better semantic performance, (ii) clusters associated with poorer semantic performance, (iii) clusters associated with better Brixton performance, and (iv) clusters associated with poorer Brixton performance. All resulting t-value maps were thresholded at a value of 2.6 for interpretation.
Lesioned/disconnected clusters associated with better behavioural performance reflect better performance relative to the sample mean, rather than absolute improvements in performance as a result of damage. Such clusters were not of explicit interest in the current analysis, so are reported in Supplementary Figure 2.3.

2.4. Results

Data for this project are available on the Open Science Framework (https://osf.io/6psqj/). Unthresholded group-level NIFTI files corresponding to the results presented here can be seen on Neurovault (https://neurovault.org/collections/10333/).

2.4.1. Lesion profile

We first characterised the regions most typically lesioned across the sample. The lesion group map reflecting maximum overlap is provided in Figure 2.1a. An unthresholded view is provided in Supplementary Figure 2.4a. Due to the relative heterogeneity of the lesions (see Figure 2.1d), this image has a minimum threshold of four cases, while a higher minimum threshold of 19 cases is used for the structural and functional disconnection overlap maps. Lesions encompassed a range of left frontoparietal regions; for each anatomical region extracted from the Harvard-Oxford atlas[7], we calculated the percentage of the sample (N = 23) that showed some evidence of damage. These regions included left IFG (pars triangularis, 56.5%, and pars opercularis, 69.6%), frontal pole (52.2%, with this region including pars orbitalis), middle frontal gyrus (MFG; 60.9%), insular cortex (60.9%), precentral gyrus (82.6%), postcentral gyrus (73.9%), supramarginal gyrus (SG; 65.2%), and angular gyrus (AG; 65.2%). In some cases, lesions extended to temporal and occipital regions, including

[7] These anatomical regions were thresholded at a value of 30 such that they were mutually exclusive.

pMTG (34.8%), temporo-occipital part of MTG (39.1%), superior temporal gyrus (STG; 47.8%), inferior temporal gyrus (ITG; 34.8%), planum temporale (52.2%), temporal pole (43.5%), lateral occipital cortex (LOC; 69.6%), and occipital pole (30.4%). Damage to the temporal pole spared vATL in every case. Some of the damage described here is not visible in Figure 2.1a due to the heterogeneity of lesion location. For example, while eight patients show damage to some aspect of pMTG, this damage does not always fall in the same voxels, meaning this region does not appear to be impacted to this extent in the thresholded overlap.

2.4.2. Structural disconnection

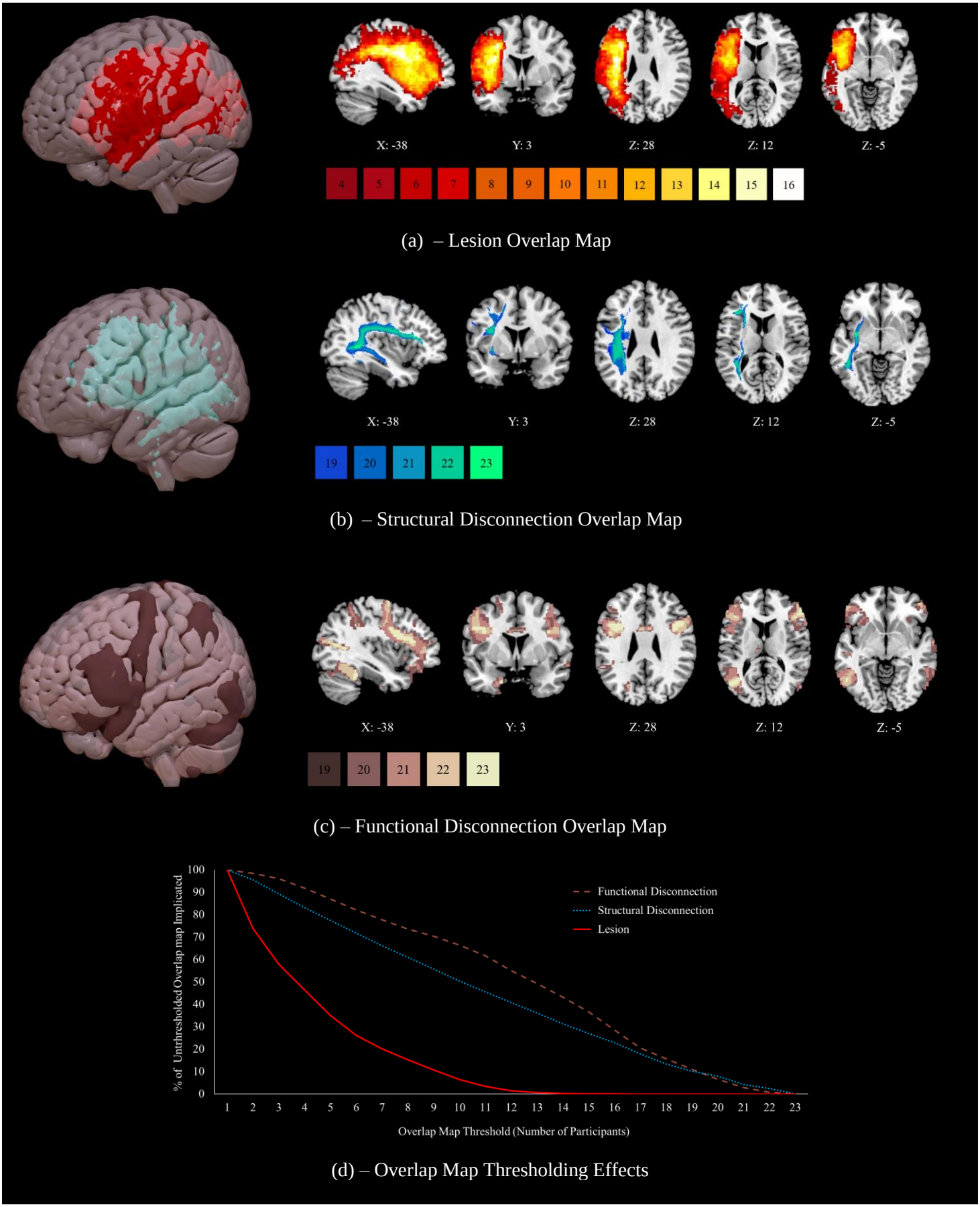
Using patients' lesions in conjunction with the disconnectome function of the BCB Toolkit, we extracted maps of probabilistic spreading white matter structural disconnection for each patient in order to characterise typical patterns of diffuse damage beyond lesion site. The structural disconnection group map reflecting maximum overlap can be seen in Figure 2.1b. An unthresholded view provided in Supplementary Figure 2.4b. Extensive structural disconnection was found to be likely throughout the left hemisphere. Twenty-one patients showed some evidence of right hemisphere structural disconnection. While disconnection in the left hemisphere was convergent, right hemisphere disconnection was relatively heterogenous, meaning it cannot be observed in Figure 2.1b at the selected threshold of 19 cases (observable at threshold of 17, see Supplementary Figure 2.4b). Supplementary Figure 2.5 shows the mean probability of each tract being disconnected (Supplementary Figure 2.5a), as well as estimates of the mean proportion of each tract that was disconnected across the sample (Supplementary Figure 2.5b), both estimated using Tractotron (see Section 2.3.5). This figure also provides visualisations of the structural disconnection overlap map (Supplementary Figure 2.5c) and each tract of interest (Supplementary Figure 2.5d-k). The mean probability of disconnection was above 60% for all tracts that were examined. The mean proportion of disconnection was highest for ILF, SLF III and anterior AF. Figure 2.1d suggests that patterns of structural disconnection seen in this sample were relatively homogeneous and highly overlapping, despite heterogenous lesions. Applying a threshold of ten patients reduces the size (in voxels) of the overall lesion overlap map by 93.5%, while this same threshold reduces the structural disconnection overlap map by only 49.7%.

2.4.3. Functional disconnection

In order to assess the intrinsic functional architecture associated with structural disconnection, we subjected each patient's lesion to PCA, and treated the first component as the main within-lesion connectivity axis, which was then used a seed in a resting-state

analysis of an independent sample of healthy individuals in CONN to provide maps of functional disconnection. Figure 2.1c provides the functional disconnection group map reflecting maximum overlap. An unthresholded view is provided in Supplementary Figure 2.4c. The resting-state maps associated with all 23 patients' lesions showed functional disconnection bilaterally of the frontal pole (including pars orbitalis), IFG (pars opercularis and pars triangularis), insular cortex, MFG, precentral gyrus, postcentral gyrus, and posterior SG, and of right AG, left posterior ITG, left inferior LOC, right superior LOC, and left temporooccipital parts of MTG and ITG. In most cases, patients' functional disconnection maps predicted disconnection of the superior frontal gyrus (SFG; 95.7%)[8], pMTG (95.7%), aMTG (left = 73.9%, right = 65.2%), anterior ITG (left = 73.9%, right = 82.6%), anterior STG (left = 87.0%, right = 91.3%), posterior STG (left = 91.3%, right = 95.7%), anterior SG (left = 95.7%, right = 91.3%), occipital pole (91.3%), and planum temporale (73.9%), and of the left AG (95.7%), right inferior LOC (95.7%), left superior LOC (95.7%), right posterior ITG (95.7%), and right temporooccipital parts of ITG and MTG (95.7%). These patterns of functional disconnection were relatively homogeneous, with a threshold of ten patients reducing the overall size of the functional disconnection overlap map by only 33.6% (see Figure 2.1d).

[8] Numbers in this section reflect the percentage of the sample showing functional disconnection to the respective region.



(a) – Lesion Overlap Map

(b) – Structural Disconnection Overlap Map

(c) – Functional Disconnection Overlap Map

(d) – Overlap Map Thresholding Effects

Figure 2.1. (a) Lesion overlap between 4 and 16 cases. Lesions are confined to the left hemisphere and are frontoparietal, peaking in the precentral and middle frontal gyri. (b) Structural disconnection overlap between 19 and 23 cases, generated using the BCB Toolkit. Structural disconnection is left lateralised at this threshold and shows maximal overlap with the superior longitudinal fasciculus and inferior fronto-occipital fasciculus. (c) Functional disconnection overlap between 19 and 23 cases, generated using CONN. Functional disconnection is bilateral and extensive, peaking in the temporooccipital part of the left inferior temporal gyrus and the right inferior frontal gyrus pars triangularis. 3D renderings generated in SurfIce. (d) A line graph reflecting the homogeneity of structural and functional disconnection relative to lesion location, with increasing thresholds reducing the overall size of the lesion overlap map at a much higher rate than for either disconnection measure. N = 23

2.4.4. Damage and disconnection within functional networks

2.4.4.1. Mean percent lesioned

We observed the extent of lesion to each functional network of interest. The mean percentage of voxels lesioned in left hemisphere aspects of DMN, semantic non-control, SCN, SCN+MDN and MDN networks is shown in Figure 2.2a[9]. The greatest damage was seen in SCN regions (Figure 2.2d), followed by SCN+MDN (Figure 2.2e). MDN (Figure 2.2f) and non-control semantic regions (Figure 2.2c) showed more modest damage, and damage to DMN was minimal (Figure 2.2b). An equivalent analysis of functional disconnection is provided in Supplementary Figure 2.2. Most (≥ 57.8%) of SCN, MDN, SCN+MDN and core semantic regions were functionally disconnected across the sample. DMN was also affected but across less than half of the network (30.8%). As seen in Supplementary Table 2.3, a significantly smaller percentage of DMN was lesioned than other functional networks, excluding core semantic regions. The extent of lesion did not differ significantly between other networks of interest. A significantly smaller percentage of DMN was also functionally disconnected when compared to all other networks. Furthermore, a greater percentage of voxels in SCN and shared between SCN and MDN were functionally disconnected than in core semantic regions. A greater percentage of voxels shared between SCN and MDN were functionally disconnected when compared to MDN alone (see Supplementary Table 2.3).

[9] Note that these average percentages will be impacted by differences in the relative size of each network. The average number of voxels lesioned over the total size of the respective number of voxels in each network is: DMN: 772/13,618, Semantic: 479/3,549, SCN: 934/3,538, MDN & SCN: 409/1,777, MDN: 1,817/12,731.

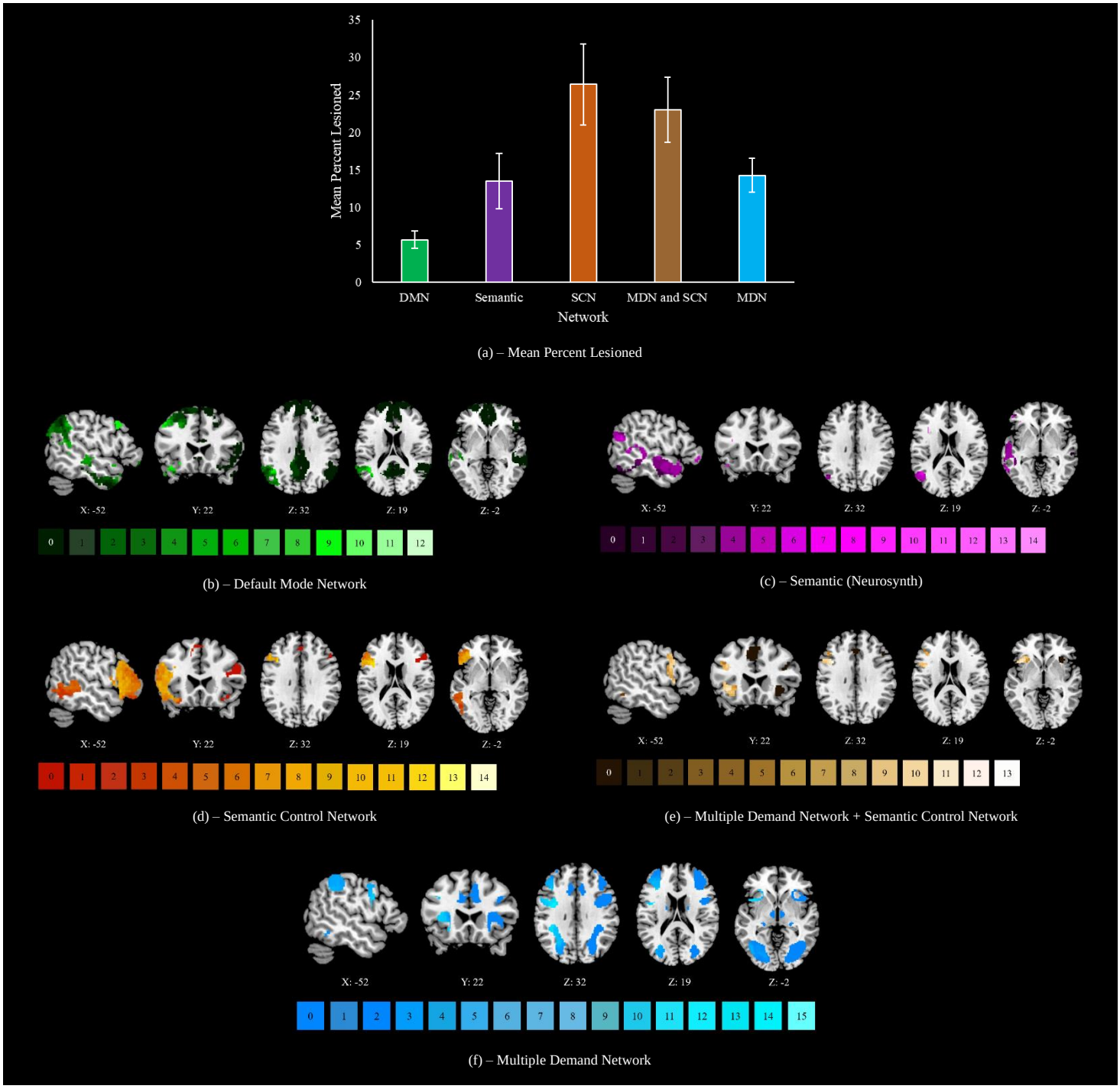


Figure 2.2. (a) Mean percentage lesioned for each network of interest (confined to the left hemisphere). DMN = default mode network, SCN = semantic control network, MDN = multiple demand network. This peaks in SCN at 26%, followed by areas shared by MDN and SCN at 23%, core semantic regions and regions exclusive to MDN both at 14%, and DMN at 6%. Locations of most frequent damage are displayed for each network. Any right hemisphere aspects of each network are visualised but were never impacted by lesion. (b) DMN, lesion peaks in the angular gyrus and insular cortex at 12 cases. (c) Core semantic regions, lesion peaks in the inferior frontal gyrus pars opercularis at 14 cases. (d) SCN, lesion peaks in the inferior frontal gyrus pars opercularis at 14 cases. (e) Regions shared by SCN and MDN, lesion peaks in the middle frontal and precentral gyri at 13 cases. (f) MDN, lesion peaks in the precentral gyrus at 15 cases. Keys under each map reflect the number of patients with lesion to a given voxel. N = 23

2.4.4.2. Spreading SCN disconnection

In order to understand typical damage to key semantic control regions in SA, we next identified SCN components most likely to be lesioned across the sample and looked for evidence of spreading structural and functional disconnection to SCN regions beyond the lesion site. The SCN map was split into its distinct clusters (see Section 2.3.7). Table 2.1 presents the percentage of each cluster lesioned for each patient, as well as a binary measure of whether this cluster showed evidence of structural or functional disconnection. Most cases had lesions in the left frontal cluster (16/23). All patients had structural and functional disconnection to this cluster, including when this cluster was not itself lesioned. A smaller number of cases had a lesion encompassing a left posterior temporal cluster (10/23) but again, all patients showed evidence of its structural and functional disconnection. A majority of cases showed evidence of structural (19/23) and functional disconnection (22/23) to the bilateral dmPFC cluster, despite only two cases showing direct lesion to this site. Four patients did not show direct lesion to any of the three left hemisphere SCN nodes. Even in these cases, diffuse connection was still frequently observed across the network. The two right hemisphere frontal clusters were spared in terms of lesion and structural disconnection but were both functionally disconnected in all but one patient.

Overall, these results suggest maximum impact to areas implicated in semantic control in SA patients, with some damage to core semantic and domain-general control regions and relative sparing of DMN. Patients reliably show evidence of spreading structural and functional disconnection to left hemisphere sites in SCN that are not directly lesioned.

Table 2.1. Lesion, structural disconnection (SDC), and functional disconnection (FDC) to semantic control network clusters.

	Left IFG, insula, OFC, & precentral gyrus			Left pMTG, pITG, & pFG			Bilateral dmPFC			Right IFG (pars orbitalis)			Right IFG (pars triangularis)		
Patient	Lesion	SDC	FDC	Lesion	SDC	FDC	Lesion	SDC	FDC	Lesion	SDC	FDC	Lesion	SDC	FDC
P01	×	✓	✓	46%	✓	✓	×	×	✓	×	×	✓	×	×	✓
P02	29%	✓	✓	39%	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P03	×	✓	✓	×	✓	✓	×	×	✓	×	×	✓	×	×	✓
P04	45%	✓	✓	20%	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P05	×	✓	✓	9%	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P06	48%	✓	✓	×	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P07	×	✓	✓	3%	✓	✓	×	×	✓	×	×	✓	×	×	✓
P08	80%	✓	✓	25%	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P09	8%	✓	✓	×	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P10	72%	✓	✓	38%	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P11	48%	✓	✓	1%	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P12	63%	✓	✓	×	✓	✓	3%	✓	✓	×	×	✓	×	×	✓
P13	19%	✓	✓	×	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P14	×	✓	✓	×	✓	✓	×	✓	×	×	×	×	×	×	✓
P15	5%	✓	✓	×	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P16	24%	✓	✓	54%	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P17	×	✓	✓	×	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P18	35%	✓	✓	×	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P19	64%	✓	✓	×	✓	✓	4%	✓	✓	×	×	✓	×	×	✓
P20	20%	✓	✓	×	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P21	×	✓	✓	×	✓	✓	×	×	✓	×	×	✓	×	×	✓
P22	82%	✓	✓	46%	✓	✓	×	✓	✓	×	×	✓	×	×	✓
P23	93%	✓	✓	×	✓	✓	×	✓	✓	×	×	✓	×	×	✓
Group Mean	34%	N/A	N/A	9%	N/A	N/A	0.3%	N/A	N/A	0%	N/A	N/A	0%	N/A	N/A
Patients Impacted	16	23	23	10	23	23	2	19	22	0	0	22	0	0	23

Note: Semantic control network clusters taken from Jackson (2021). Lesion columns reflect the percentage of each cluster impacted by a given patient's lesion. In SDC and FDC columns, ticks reflect cases where these was any overlap with a cluster and patients' structural disconnection and functional disconnection maps, respectively. Crosses occur when a given cluster was not lesioned/disconnected. Patients Impacted reflects the number of patients for whom the given cluster was lesioned/disconnected. IFG = inferior frontal gyrus, OFC = orbitofrontal cortex, pMTG = posterior middle temporal gyrus, pITG = posterior inferior temporal gyrus, pFG = posterior fusiform gyrus, dmPFC = dorsomedial prefrontal cortex, SDC = structural disconnection, FDC = functional disconnection.

2.4.5. Symptom mapping

Next, we identified lesioned and disconnected voxels associated with poorer behavioural performance. Damage or disconnection was used to predict lower scores on the semantic cognition composite (comprising word and picture semantic associations and comprehension of ambiguous words) and the Brixton Spatial Anticipation Test, which probes non-verbal cognitive control, with results thresholded at $t > 2.6$. At this threshold, clusters associated with semantic and executive performance were mutually exclusive with no overlapping voxels within each analysis. We also examined the extent to which the clusters found in lesion-symptom mapping were implicated in our functional networks of interest, visual representations of which can be seen in Figure 2.2.

2.4.5.1. Lesion-symptom mapping

Lesioned clusters associated with lower semantic cognition composite and Brixton scores can be seen in Figure 2.3a. Clusters implicated in semantic cognition showed overlap with SCN, particularly in anterior IFG, MFG, frontal pole, pMTG, and temporo-occipital part of MTG. Overlap with MDN was observed in posterior IFG/inferior frontal sulcus, MFG, frontal pole, inferior LOC, intraparietal sulcus, and superior parietal lobule. Overlap with both DMN and core semantic regions was observed in the frontal pole, pMTG, temporo-occipital part of MTG, and temporo-occipital part of ITG. Outside of these networks, clusters were observed in the precentral gyrus, postcentral gyrus, and occipital pole. Clusters associated with poorer performance on the Brixton test showed overlap with SCN in posterior IFG, MFG, SFG, and precentral gyrus. Overlap with MDN was observed in intraparietal sulcus, SG and postcentral gyrus. Overlap with DMN occurred in SFG, while core semantic regions were not implicated. The percentage of each network of interest (restricted to the left hemisphere) implicated in these lesion-symptom maps is shown in Supplementary Figure 2.6.

2.4.5.2. Structural disconnection-symptom mapping

The results of the structural disconnection analysis can be seen in Figure 2.3b. Structurally disconnected clusters associated with lower semantic cognition composite scores were minimal but were confined to the left hemisphere in regions including the frontal pole, precentral and postcentral gyri, pMTG, and occipital pole. These clusters were proximal to the regions identified in the lesion analysis but were not large enough to implicate specific white matter tracts and may not have clinical significance. There were no structurally disconnected clusters associated with poor semantic cognition in the right hemisphere. In contrast, poorer Brixton performance was associated with a pattern of interhemispheric

structural disconnection across the corpus callosum, consistent with a role of interhemispheric connectivity in executive control in this visuo-spatial task.

2.4.5.3. Functional disconnection-symptom mapping

The results of the functional disconnection analysis are shown in Figure 2.3c. Lower semantic cognition composite scores and poorer Brixton performance were both predicted by small functionally disconnected clusters in the brainstem, bilateral cerebellum, right parahippocampal gyrus, and right temporal fusiform cortex. Poorer Brixton performance was also associated with functional disconnection of the right temporal pole and of white matter proximal to the right precentral gyrus. In both cases, these clusters were sparse and too small to implicate functional networks; consequently, they may not have clinical significance.

In summary, left hemisphere lesion sites associated with poorer semantic cognition are mutually exclusive from but adjacent to those implicated in executive function (in line with previous studies showing that the semantic control network lies between DMN and MDN regions on the cortical surface; Davey et al., 2016; Wang et al., 2020). In contrast, the substrates for structural disconnection are more divergent across semantic and executive tasks, since the small clusters associated with poor semantic cognition are left-lateralised, while executive dysfunction is associated with cross-hemispheric disconnection. Clusters identified from functional disconnection symptom mapping were small and did little to distinguish between semantic and executive performance.

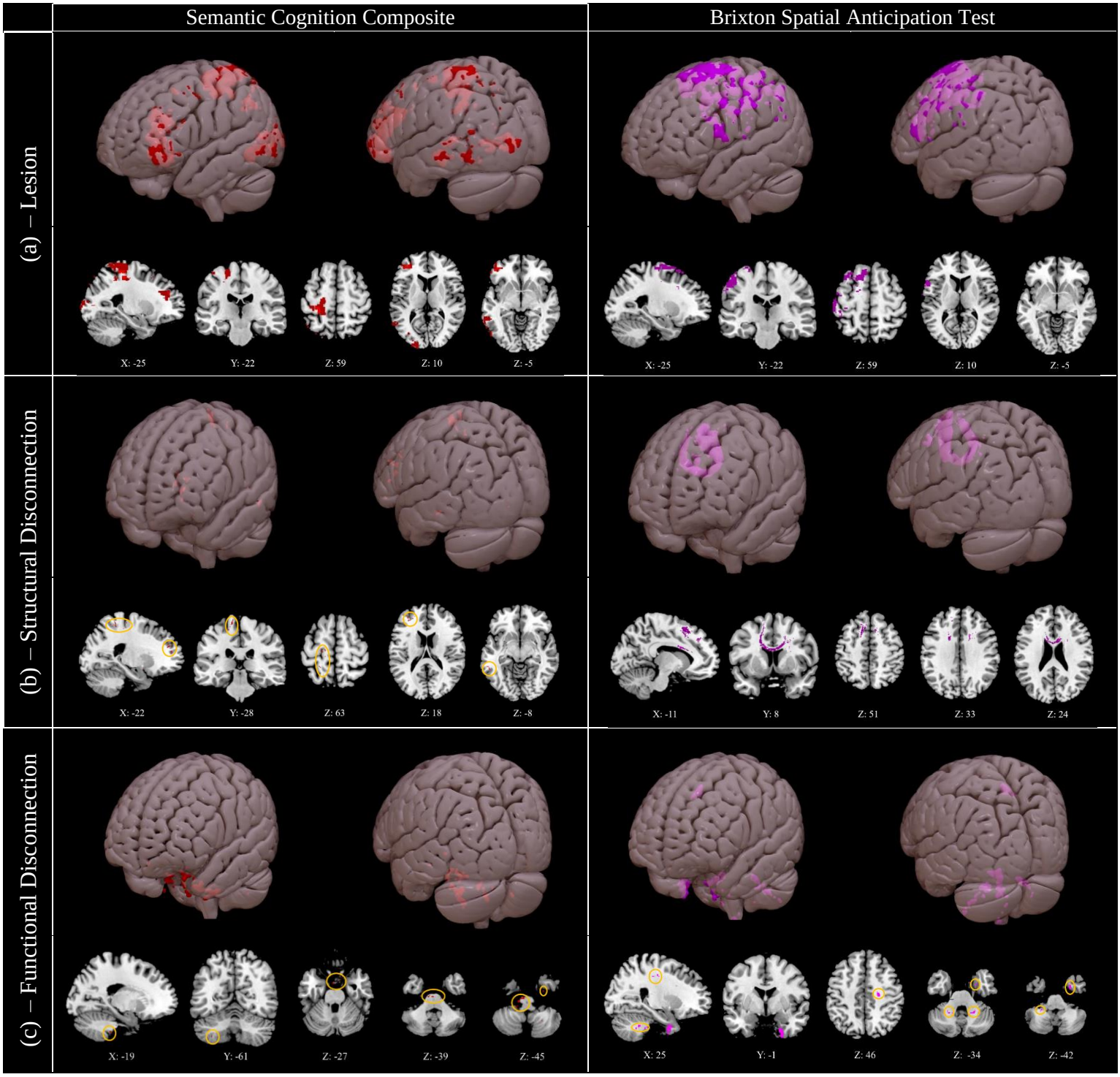


Figure 2.3. Clusters identified in symptom mapping as associated with poorer performance. This is done for both the semantic composite score (left) and Brixton Spatial Anticipation Test (right), for (a) lesion, (b) structural disconnection, and (c) functional disconnection. Generated using non-parametric permutation tests in Randomise with threshold-free cluster enhancement. Highlighted voxels have a t-value of 2.6 or higher. Small clusters are highlighted in orange circles. 3D rendering generated in SurfIce. Lesioned clusters associated with poorer semantic and Brixton performance are left lateralised, and reflect the regions listed in Section 2.4.5.1. Structurally disconnected clusters are small and left lateralised for semantic cognition, reflecting regions listed in Section 2.4.5.2, while for Brixton performance one large cluster is observed across the corpus callosum. Functionally disconnected clusters are small for both measures, reflecting regions listed in Section 2.4.5.3. N = 20

2.5. Discussion

This study characterised lesion location, structural disconnection, and functional disconnection in semantic aphasia (SA) patients who have impaired semantic control following left hemisphere stroke. Lesions were most common within the semantic control network (SCN), and areas commonly responsive to semantic control and executive function (the multiple demand network [MDN]; Duncan, 2010). Lesions were heterogenous as is typical of this population (e.g., Chapman et al., 2020; Hallam et al., 2018), with many but not all cases having frontal damage. Measures of structural and functional disconnection, anticipated from lesion location, showed extensive effects spreading beyond the lesion, frequently affecting structurally-intact SCN regions. This may account for the similarity of control deficits seen in SA patients despite divergent lesion profiles.

When mapping behavioural performance to lesion site, more severe deficits of semantic cognition and non-semantic cognitive control were associated with lesions in adjacent areas of the left frontoparietal cortex – consistent with studies from healthy participants suggesting that semantic and domain-general executive regions are supported by adjacent left hemisphere regions (Davey et al., 2016; Gao et al., 2021). Associations between functional disconnection and cognitive performance were limited and did not identify distinct patterns for semantic and executive deficits. In contrast, semantic and executive deficits had different associations with structural disconnection. While insight into semantic performance from structural disconnection was limited, with small frontal, parietal, and posterior temporal clusters in the left hemisphere, proximal to lesioned substrates, being highlighted, executive dysfunction was predicted by interhemispheric structural disconnection across the corpus callosum. These different patterns are consistent with previous studies showing that SCN is largely left-lateralised, while domain-general executive function is supported by the bilateral MDN (Fedorenko et al., 2013; Gonzalez Alam et al., 2019). In this way, we can explain why similar left hemisphere clusters are associated with poor semantic cognition and cognitive control and provide an account of the hemispheric differences in structural disconnection associated with these deficits.

Previous descriptions of SCN have highlighted left IFG and pMTG as key structures (Jackson, 2021; Jefferies, 2013; Jefferies et al., 2019; Lambon Ralph et al., 2017; Noonan et al., 2013). Patients in the current sample frequently presented with direct damage to these SCN sites, and invariably had some degree of structural and functional disconnection within

this network. This pattern was observed even in four patients who showed no direct SCN damage; in these cases, semantic impairment may be attributable to SCN disconnection (although direct effects of other areas of lesion might also be relevant in regions involved in semantic cognition yet omitted from prior meta-analyses of semantic control). This damage and disconnection of SCN regions in SA is consistent with neuroimaging evidence implicating left IFG and pMTG in semantic control (Jackson, 2021; Noonan et al., 2013). Topographically, SCN lies between DMN and MDN in the left hemisphere (Davey et al., 2016; Wang et al., 2020), and this network has been proposed as a functional nexus between core semantic and domain-general control regions (Davey et al., 2016). Accordingly, the current results revealed that adjacent but distinct frontoparietal lesions resulted in poorer semantic cognition and executive function, consistent with prior evidence of adjacent neural substrates for these functions (Wang et al., 2018). This may account for why some SA patients present with executive dysfunction while others do not (Thompson et al., 2018). Indeed, 14 of the current 23 patients presented with some degree of executive dysfunction, with performance on the Brixton Spatial Anticipation Test positively correlating with semantic performance. It may be that impaired semantic control does not necessitate executive impairment (Chapman et al., 2020), but that the proximity of these substrates means that these functions are frequently impaired together. Frequent damage to substrates underlying semantic or domain-general control or both in SA may give rise to broad deficits in constraining internal aspects of cognition (Souter et al., 2021 [Chapter 3 of this thesis]; Stampacchia et al., 2018), reflected in heightened susceptibility to external cues and miscues in semantic retrieval (Jefferies et al., 2008; Noonan et al., 2010), along with strong effects of distractors in semantic decision-making (Corbett et al., 2011; Noonan et al., 2010).

While the lesioned substrates associated with semantic cognition included SCN regions as expected, areas outside this network were also implicated, including LOC and postcentral gyrus. It is worth noting that the semantic composite score derived here reflects general semantic cognition (albeit performance on highly demanding heteromodal tasks) rather than semantic control specifically, and this may account for the inclusion of regions not typically associated with controlled processing. Evidence has suggested the involvement of LOC in processing visual features of concepts (Coutanche & Thompson-Schill, 2015), while the postcentral gyrus has been implicated in sensorimotor representation (Kropf et al., 2019). Furthermore, LOC has been shown to decode category- and task-related semantic information (Wang et al., 2021). Similarly, the postcentral gyrus has been implicated in the

performance of divergent thinking tasks, which require the generation of alternative uses of objects (Cogdell-Brooke et al., 2020). Such a process is comparable to semantic control in requiring focus on subordinate conceptual information. Finally, LOC and postcentral gyrus are adjacent to pMTG and dorsal AG, respectively; two nodes that have been implicated in semantic control (Hodgson et al., 2021; Noonan et al., 2013). Ultimately, while the functional contribution of LOC and postcentral gyrus are not fully understood, these regions may support conceptual retrieval by either representing features of concepts or by supporting semantic decision-making.

In previous studies, several white matter tracts have been associated with semantic cognition, including the IFOF, ATR, UF, and ILF (Almairac et al., 2015; Han et al., 2013; Sierpowska et al., 2019). These tracts were reliably disconnected across the sample, as were others including the SLF, AF, and FAT. The SLF and AF have both been implicated in language processing (Catani & Mesulam, 2008; Han et al., 2013), and the FAT in both language and executive function (Dick et al., 2019). However, the clusters we identified in the semantic cognition structural disconnection symptom mapping were too small to implicate any specific tracts. This may in part be because the pattern of structural disconnection across the sample was diffuse and widespread; multiple tracts underpin semantic cognition and damage to any one of them may be sufficient to produce an impairment of semantic cognition. This analysis may have also been hampered by insufficient statistical power, due to our relatively small sample size. Despite this, our findings are consistent with emerging accounts of the lateralisation of control functions. Clusters associated with demanding semantic tasks were small and left-lateralised, intersecting with SCN. Contrasts of hard over easy semantic judgements in studies of healthy participants also reveal a highly left-lateralised network (Gonzalez Alam et al., 2019; Jackson, 2021; Noonan et al., 2013). In contrast, vATL's role in long-term semantic representation is highly bilateral (Gonzalez Alam et al., 2019; Rice et al., 2015). Conversely, executive performance on a demanding visual-spatial task was predicted by interhemispheric structural disconnection across the corpus callosum, indicating that this task may be supported by a more bilateral network, in line with prior work (e.g., Bodini et al., 2013; Johnson et al., 2017; Schulte & Müller-Oehring, 2010). Neuroimaging studies show that bilateral activation underlies executive function (Camilleri et al., 2018; Fedorenko et al., 2013) and (especially in visual-spatial tasks), the most robust responses are often right-lateralised (Dick et al., 2019; Gonzalez Alam et al., 2018). Moreover, a recent study found

that control networks show different patterns of connectivity across the hemispheres, with left-lateralised control regions showing stronger connectivity with heteromodal regions of DMN (Gonzalez Alam et al., 2022). In this way, the left lateralised nature of the semantic control network may be adaptive, allowing control regions to separate from visuospatial responses when internal aspects of cognition are constrained.

Prior studies investigating the predictive value of indirect measures of structural disconnection (inferred from lesion location, as in the current study) have yielded inconsistent results. Salvalaggio et al. (2020) provided evidence that structural disconnection is comparable to lesion location in its ability to predict post-stroke deficits across domains. Halai et al. (2020) directly measured structural disconnection using diffusion weighted imaging data, and conversely found no added benefit relative to direct observations of abnormal tissue when predicting post-stroke aphasia, citing tight coupling between lesion and disconnection as a possible cause. This is consistent with our observation that the small clusters of structural disconnection associated with deficits in semantic cognition largely followed lesioned substrates, although a different pattern was found for executive dysfunction. Hope et al. (2018) similarly found limited predictive value of indirectly measured structural disconnection beyond lesion location for predicting aphasia severity, while other studies have suggested unique contributions from such measures (Del Gaizo et al., 2017; Kristinsson et al., 2021). It may be that structural disconnection is unlikely to explain unique variation in behavioural performance beyond lesion location when patients have been selected to show particular deficits associated with areas of cortex that are lesioned, as was the case for semantic deficits in our sample. However, since stroke lesions are typically unilateral, structural disconnection may be more likely to explain unique variance in other domains associated with bilateral networks, including executive dysfunction. This is consistent with prior evidence demonstrating the utility of structural disconnection in reflecting inter-hemispheric networks (Thiebaut de Schotten et al., 2020).

Clusters highlighted by functional disconnection were limited in the current study, but included the bilateral cerebellum, brainstem, and right ventral temporal regions across both semantic and executive measures. Unlike structural disconnection, patterns of functional disconnection did not distinguish between our two behavioural domains. While the cerebellum is reliably activated in neuroimaging studies (Buckner, 2013; Stoodley & Schmahmann, 2009), other sites such as medial temporal cortex have relatively low signal-to-noise (e.g., Olman et al., 2009) and the validity of these observed clusters is therefore

unclear. The appropriateness of using indirect estimates of functional disconnection to predict behavioural deficits, and the methods that can be used to determine these estimates, also remains contentious (Boes, 2021; Bowren et al., 2022; Salvalaggio et al., 2021a; Umarova & Thomalla, 2020). Some studies have found that indirect measures of functional disconnection have relatively poor utility for predicting behavioural deficits post-stroke compared with measures of structural disconnection (Salvalaggio et al., 2020); our findings do not challenge this view, although other studies report more success (Cohen et al., 2021; Ferguson et al., 2019; Padmanabhan et al., 2019). Discrepancies between studies may reflect differences in data pre-processing or the methods used to estimate the accuracy of behavioural predictions (Salvalaggio et al., 2021b). Therefore, our lack of meaningful results might reflect methodological limitations, even though we employed recent recommendations for estimating functional disconnection, using PCA to identify connectivity patterns within each patients' lesion, rather than seeding the entire lesion. This approach has been reported to increase functional specificity and support behavioural prediction (Pini et al., 2021).

2.5.1. Limitations

There are some important limitations of this study. First, the current sample size was relatively small, due to practical barriers in recruiting, testing, and scanning patients who fit the criteria for SA. Secondly, as data were collated across three samples of SA patients, there were a limited number of tests on which all patients had been assessed. Our analysis of executive function was confined to the Brixton Spatial Anticipation Test. While performance on Raven's Coloured Progressive Matrices (Raven, 1962) was available for each patient, scores across these two tests did not meet the necessary assumptions of PCA, and so a composite score was not derived. While the Brixton test is a sensitive measure of executive impairment (van den Berg et al., 2009), the use of a broader set of tests would be helpful in establishing the relationship between damage and general deficits of cognitive control. Third, measures used to examine impaired semantic cognition were not specific to semantic control. Prior investigations have consistently concluded that SA patients present with preserved semantic storage and impaired controlled retrieval (e.g., Jefferies & Lambon Ralph, 2006; but see Chapman et al., 2020 for an alternative view). However, in the absence of a comparison group we cannot rule out the possibility that aspects of our results reflect impaired semantic processing more generally. A comparison of disconnection in SA and SD may provide additional insights into how these conditions differentially impact networks associated with controlled retrieval and core semantic representation. SD patients show disrupted functional

connectivity between the left anterior hippocampus, ATL/insula and MTG (Chen et al., 2017), but a group comparison of SD and SA cases is not yet available. A study directly comparing structural connectivity in SD and SA cases found semantic performance is predicted by fractional anisotropy of the left medial temporal network in SD, as opposed to left fronto-subcortical and fronto-temporal/occipital networks in SA (Ding et al., 2020); however, network differences linked to conceptual representation and control may be confounded by differences in aetiology between these groups, since stroke frequently damages white-matter tracks, while the knife-edge atrophy in SD primarily affects grey matter. Indeed, Andreottia et al. (2017) provide evidence that that structural network disruption in SD is localised to regions directly affected by atrophy, suggesting that symptom mapping from such a measure may provide limited additional insight. A final limitation is that our measures of functional and structural disconnection were indirect. Direct measures of resting-state functional connectivity have been shown to predict post-stroke symptoms to a greater extent than indirectly measured functional disconnection (Salvalaggio et al., 2020).

2.5.2. Conclusion

We assessed patterns of spreading structural and functional disconnection in left hemisphere stroke patients with semantic aphasia. These results highlight damage to SCN in this group, both as a direct result of lesions and following spreading disconnection. We show that semantic and domain-general executive control are supported by adjacent substrates in the left hemisphere and yet associated with distinct patterns of structural disconnection that are left-lateralised and bilateral, respectively.

2.6. Link to Chapter 3

Chapter 2 added to existing knowledge concerning the neural profiles of patients with semantic aphasia (SA). Prior research has extensively mapped the neuropsychological deficits of this group, including impaired semantic retrieval in the context of ambiguous input reflecting semantic control deficits (Noonan et al., 2010), and domain-general executive dysfunction (Thompson et al., 2018). Here, distinct but adjacent lesioned substrates were associated with poorer semantic cognition and executive function. These measures were linked to left lateralised and bilateral substrates, respectively, as measured by structural disconnection. This chapter therefore provided novel insights into the similarities and differences in the neural basis of semantic-specific and domain-general cognitive control. Recent evidence also suggests that the relevance of the semantic control network extends beyond the semantic domain. For example, SA patients present with impairments in the controlled retrieval of episodic information, comparable to those observed in the semantic domain (Stampacchia et al., 2018). Similarly, the semantic control network has been shown to be sensitive to the executive demands of social cognitive tasks (Diveica et al., 2021). Such patterns may emerge because semantic control plays a foundational role in tasks that require an internally-oriented focus on heteromodal information. In SA, these processes may be disrupted both by local effects of left-lateralised lesions and spreading disconnection.

Emotion processing is another domain in which the relevance of semantic cognition has been a focus of recent research. In particular, constructionist accounts of emotion processing (Lindquist et al., 2015) argue that our ability to discriminate discrete emotion categories is reliant on appropriate concept knowledge of a given emotion state. As such, perception of facial portrayals of emotion can be interrupted in healthy participants using semantic satiation methods – momentarily disrupting access to emotion representations as concepts become inaccessible (Gendron et al., 2012; Lindquist et al., 2006). Patients with semantic storage deficits in semantic dementia also show impairments in these tasks (Lindquist et al., 2014). Despite such language- and conceptually-based models of emotion processing, the relevance of semantic control mechanisms has not been explicitly investigated. Chapter 3 aims to bridge this gap, by observing effects of semantic control impairments in SA on discrete emotion discrimination in the context of varying task demands. In doing so, this chapter adds to the conclusions of Chapter 2 by providing insight into the wide reaching implications of control impairments in this group.

Chapter 3: Impaired emotion perception and categorization in semantic aphasia

This chapter is adapted from a published article:

Souter, N. E., Lindquist, K. A., & Jefferies, E. (2021). Impaired emotion perception and categorization in semantic aphasia. *Neuropsychologia, 162,* 108052. https://doi.org/10.1016/j.neuropsychologia.2021.108052.

Data for this chapter are publicly available on Mendeley Data (https://data.mendeley.com/datasets/zwxxscny6x/3).

Acknowledgements and author's contribution

This project was conceptualised by Nick Souter along with co-authors Elizabeth Jefferies and Kristen Lindquist. Study 3.1 of this project used a procedure adapted from a 2014 paper by Kristen Lindquist. Nick Souter oversaw the design, adaptation, and creation of the tasks, coding of experimental scripts in Python, data collection, data analysis, and data curation. Research assistants Marcus Glennon and Anna Clegg assisted with data collection. Sarah Knight provided advice on the appropriate use of mixed models. Nick Souter wrote the full original draft of this paper. Elizabeth Jefferies edited manuscript drafts, and Kristen Lindquist provided feedback on the final draft.

3.1. Abstract

According to a constructionist model of emotion, conceptual knowledge plays a foundational role in emotion perception; reduced availability of relevant conceptual knowledge should therefore impair emotion perception. Conceptual deficits can follow both degradation of semantic knowledge (e.g., semantic 'storage' deficits in semantic dementia) and deregulation of retrieval (e.g., semantic 'access' deficits in semantic aphasia). While emotion recognition deficits are known to accompany degraded conceptual knowledge, less is known about the impact of semantic access deficits. Here, we examined emotion perception and categorization tasks in patients with semantic aphasia, who have difficulty accessing semantic information in a flexible and controlled fashion following left hemisphere stroke. In Study 3.1, participants were asked to sort faces according to the emotion they portrayed – with numbers, written labels and picture examples each provided as category anchors across tasks. Semantic aphasia patients made more errors and showed a larger benefit from word anchors that reduced the need to internally constrain categorization than comparison participants. They successfully sorted portrayals that differed in valence (positive vs. negative) but had difficulty categorizing different negative emotions. They were unimpaired on a control task that involved sorting faces by identity. In Study 3.2, participants matched facial emotion portrayals to written labels following vocal emotion prosody cues, miscues, or no cues. Patients presented with overall poorer performance and benefited from cue trials relative to within-valence miscue trials. This same effect was seen in comparison participants, who also showed deleterious effects of within-valence miscue relative to no cue trials. Overall, we found that patients with deregulated semantic retrieval have deficits in emotional perception but that word anchors and cue conditions can facilitate emotion perception by increasing access to relevant emotion concepts and reducing reliance on semantic control. Semantic control may be of particular importance in emotion perception when it is necessary to interpret ambiguous inputs, or when there is interference between conceptually similar emotional states. These findings extend constructionist accounts of emotion to encompass difficulties in controlled semantic retrieval.

3.2. Introduction

Semantic cognition underpins our ability to acquire, store and retrieve conceptual information. An outstanding question in this field concerns the nature of the relationship between semantic cognition and emotion. Within the semantic memory literature, the 'hub and spoke' framework proposes that conceptual representations are reliant on interactions between a transmodal hub and modality-specific spokes, resulting in rich heteromodal representations of concepts (Patterson et al., 2007). The anterior temporal lobes (ATL) have been implicated as the site of this hub, while the spokes in this system provide input from sensory modalities including sound and vision, as well as from hedonic valence (Lambon Ralph et al., 2017) – reflecting how positive or negative a given concept is on a continuous scale. Riberto et al. (2019) argues that regions connected to ATL, including the amygdala and orbitofrontal cortex, may act as spokes by generating emotional aspects of heteromodal representations. Under this framework, valence information is therefore an important feature of concepts.

The constructionist model of emotion considers the inverse of this relationship; namely the contribution that language and conceptual knowledge make to the perception of emotion (Lindquist et al., 2015). Rather than focusing on valence as an inherent quality of stimuli, this theory corresponds to the processing of discrete emotion categories, such as anger, happiness, and sadness. Perceiving facial muscle portrayals of these emotion results in rapid and automatic activation of emotion concepts (Osborne-Crowley et al., 2019; Preston, 2007). Moreover, temporarily disrupting access to emotion labels (e.g., "angry") using semantic satiation impairs the perception of facial emotion portrayals (Gendron et al., 2012; Lindquist et al., 2006), indicating an involvement of language in emotion processing even when not explicitly necessary. Beyond language, Brooks and Freeman (2018) found that ratings of conceptual similarity between pairs of emotion categories (e.g., "fear" and "anger") predicted perceived perceptual similarity of faces corresponding to these categories. Similarly, exposure to emotion labels is thought to aid children's formation of emotion concepts, which expedites their perception of discrete facial emotions (Hoemann et al., 2019). Interoceptive models similarly argue that physiological valenced feelings and conceptual information interact to construct our interpretation of emotion categories (Zhou et al., 2021). These models and studies all suggest that accessing knowledge about emotional states facilitates the perception of discrete emotional portrayals.

This account implies that impairments in semantic cognition should also manifest as impairments in emotion perception. Patients with semantic dementia (SD) experience a progressive loss of heteromodal conceptual knowledge following atrophy focussed on bilateral ATL (Bozeat, Lambon Ralph, et al., 2000; Mummery et al., 2000), often accompanied by emotional difficulties including apathy, diminished empathy, and emotional withdrawal (Bozeat, Gregory, et al., 2000; Hodges & Patterson, 2007). To test predictions of the constructionist model, Lindquist et al. (2014) studied the ability of SD patients with left ATL atrophy to categorize pictures of facial emotion portrayals. Participants were asked to sort photographs of faces portraying six English language categories of emotion (anger, disgust, fear, happiness, sadness, and neutral) into as many piles as meaningful. SD patients spontaneously created three to four piles reflecting the valence of the facial portrayals (i.e., pleasant, unpleasant, and neutral), whereas healthy age-matched controls created on average seven to eight categories reflecting specific emotions. Providing patients with exemplar facial portrayals improved their ability to sort by emotion, whereas the presence of written emotion category labels did not. Notably, SD patients were able to sort the faces into six categories by identity, suggesting that their errors did not reflect general cognitive impairment. Kumfor et al. (2018) similarly demonstrated impaired ability to decode facial or bodily portrayals of emotion in SD, regardless of task demands. The failure of conceptual anchors to boost categorization performance is consistent with SD patients' highly predictable semantic deficits when the same concepts are probed using different tasks (Bozeat, Lambon Ralph, et al., 2000; Jefferies & Lambon Ralph, 2006) and the weak impact of cues on semantic retrieval (Jefferies et al., 2008). Evidence suggests that emotion processing deficits in SD are partially explained by performance on verbal semantic tests (Miller et al., 2012), supporting the view that these deficits are attributable to semantic impairment. It has also been argued that this impairment arises in part due to strong connectivity of ATL with key emotion processing regions such as the amygdala (Rosen et al., 2002). Together, these studies suggest a loss of conceptual knowledge following semantic storage deficits in SD impairs the ability to perceive specific emotional states.

While SD patients show highly consistent semantic storage deficits across tasks, patients with semantic aphasia (SA) have semantic access deficits that result in deregulated conceptual retrieval across verbal and non-verbal tasks following infarcts in left inferior lateral prefrontal and/or temporoparietal cortices (Corbett et al., 2011; Jefferies, 2013; Jefferies & Lambon Ralph, 2006). Moreover, whereas SD patients show relatively good

performance on tests of non-verbal reasoning, semantic deficits in SA often co-occur with executive dysfunction (Thompson et al., 2018). SA patients' access to specific concepts is dependent on task demands (Jefferies & Lambon Ralph, 2006): they can show near-normal performance when the control demands of semantic tasks are minimised and have more severe deficits when meanings are ambiguous or strong distracters are presented (e.g., Montefinese et al., 2020; Noonan et al., 2010; Thompson et al., 2017). The impairment in SA can also be ameliorated by providing cues which constrain the meaning of target concepts, reducing the need for controlled retrieval. For instance, phonemic cues facilitate picture naming (Jefferies et al., 2008) and sentence contexts support semantic decisions (Noonan et al., 2010). Lanzoni et al. (2019) found facial emotion portrayals also influence semantic access in SA: positive interpretations of ambiguous words are more accessible following smiling faces, while negative interpretations become less accessible. SA patients can therefore be cued to access concepts that they often fail to retrieve, suggesting that, unlike in SD, the concepts themselves are not degraded. This qualitative difference is thought to reflect differences in the distribution of atrophy and infarcts in SD and SA: ATL is a watershed region with a dual blood supply (Phan et al., 2007) and consequently heteromodal conceptual knowledge may be relatively invulnerable to damage from stroke.

In line with this dissociation between SD and SA, the controlled semantic cognition (CSC) framework (Jefferies, 2013; Lambon Ralph et al., 2017; Rogers et al., 2015) proposes that semantic control processes interact with conceptual representations to support the flexible retrieval of appropriate knowledge. Converging neuroimaging and neurostimulation studies of healthy participants implicate the left inferior frontal gyrus (IFG) and posterior middle temporal gyrus (pMTG), often damaged in SA, in controlled semantic retrieval (Badre et al., 2005; Davey et al., 2016; Hallam et al., 2016; Thompson-Schill et al., 1997). This left-lateralised network is thought to constrain the retrieval of both verbal and nonverbal information (Krieger-Redwood et al., 2015) and can bias the interaction of sensory-motor spokes with the hub in accordance with the information required (Chiou et al., 2018; Jefferies et al., 2019; Zhang et al., 2021). Neuroscientific studies show that the semantic control network is partially distinct from both multiple demand cortex, which supports domain-general cognitive control (Davey et al., 2016; Diachek et al., 2020; Gao et al., 2021; Jackson, 2021; Noonan et al., 2013), and default mode network regions that underpin more integrative or automatic aspects of conceptual retrieval (e.g., ATL and AG; Humphreys et al., 2015; Lanzoni et al., 2020; Vatansever, Bzdok, et al., 2017).

The relevance of this distinction between conceptual representation and semantic control processes for emotion perception has not been investigated to date, although Robertson et al. (1999) observed impaired emotion categorization in a single aphasia patient and cited conceptual difficulties as a possible cause. More generally, evidence from healthy adults has suggested involvement of top-down processes in the perception of discrete emotions, as demonstrated by tasks implementing categorical emotion primes (Carroll & Young, 2005; Doyle et al., 2021; Zemack-Rugar et al., 2007) and those manipulating the context in which emotional facial portrayals appear (Aviezer et al., 2008). In the current study, we investigated the effects of deregulated semantic retrieval in SA patients on perception of emotion from facial portrayals. If activation of discrete emotion concepts (e.g., anger, sadness) is automatic upon perceiving certain configurations of facial muscle movements in others (Osborne-Crowley et al., 2019; Preston, 2007), controlled semantic retrieval may not be required for this process. Consequently, the perception of emotion may be unimpaired in SA. Alternatively, if perceptual processing of emotion is influenced by the accessibility of conceptual knowledge (Gendron et al., 2012; Lindquist et al., 2006), impaired retrieval may interfere with the activation of relevant emotional states, particularly when in the presence of competing and conceptually similar portrayals. This hypothesis is supported by evidence that left IFG, a key semantic control region (Jackson, 2021), is implicated in the discrimination of emotional states (Jastorff et al., 2016).

In Study 3.1, we adopted the procedures used by Lindquist et al. (2014) with SD patients, and collected a comparative sample of SA cases. This paradigm allowed us to assess the effects of impaired semantic control on emotion categorization with minimal constraints, and in the presence of numbers, written words, and exemplar faces, provided as sorting anchors. In the unconstrained free sort, the need to categorise faces according to emotion (e.g., ‘angry’) as distinct from related distractors (e.g., sad or disgusted faces) is expected to tax semantic control. The need to internally constrain categorisation was expected to be reduced by sorting anchors, and consequently SA patients might benefit more from their availability than healthy comparison participants. Study 3.2 examined the effects of emotional prosody on the categorisation of facial emotion portrayal in an alternative forced choice design. Prosody was either consistent with the portrayed facial emotion (cue condition) or inconsistent (miscue condition). Within-valence miscues (e.g., sad prosody preceding an angry face) were expected to impair performance, since they required the suppression of information that was irrelevant but conceptually similar to the target concept.

SA patients were expected to be impaired relative to comparison participants, especially following miscues. Overall, these studies (i) provide further evidence that semantically-impaired participants are impaired at discriminating portrayals of distinct emotional categories yet are not impaired at recognising positive and negative valence and (ii) show that, in both SA patients and comparison participants, emotion recognition is sensitive to the requirement to control conceptual processing.

3.3. Method

Ethics approval for this study was granted by the York Neuroimaging Centre at the University of York (date: 24/10/2019, project ID: P1363).

3.3.1. Participants

The overall sample consisted of seven patients, and 33 healthy comparison participants. Patients were recruited from communication support groups across Yorkshire. All patients had aphasia following left hemisphere stroke and showed semantic impairment across verbal and non-verbal tasks (see Section 3.3.3.). These inclusion criteria were adopted since heteromodal semantic impairment following left hemisphere stroke has been shown to be associated with deregulated access to conceptual information, as opposed to a degraded store of conceptual knowledge (Jefferies, 2013). Comparison participants were healthy adults broadly similar to the patients for age and level of education, with no history of psychiatric or neurological disorder. As a subset of participants from Study 3.1 participated in Study 3.2, respective demographics are reported separately in Sections 3.4.1.1. and 3.5.1.1.

3.3.2. Lesion Analyses

Three patients (P4, P6, and P10) had structural MRI scans at the York Neuroimaging Centre. These scans underwent brain extraction and registration to MNI space in ANTs (Avants et al., 2011) using a template from the OASIS Brain Project (https://www.oasis-brains.org/; Marcus et al., 2010). Each patient's lesion was manually traced in MRICron. Care was taken to avoid implicating enlarged ventricles or sulci. Manually segmented lesion locations for these three patients are presented in Figure 3.1. It was not possible to obtain structural scans for the remaining four patients, due to contraindications for scanning and/or closure of scanning facilities during the COVID-19 pandemic. Clinical acute-stage scans were obtained for P16 (MRI) which showed evidence of a left frontal lesion, and for P12

(CT) which showed evidence of a left fronto parietal lesion. These data suggest that at least five out of seven patients had damage to left lateral prefrontal cortex, known to be important for semantic control.

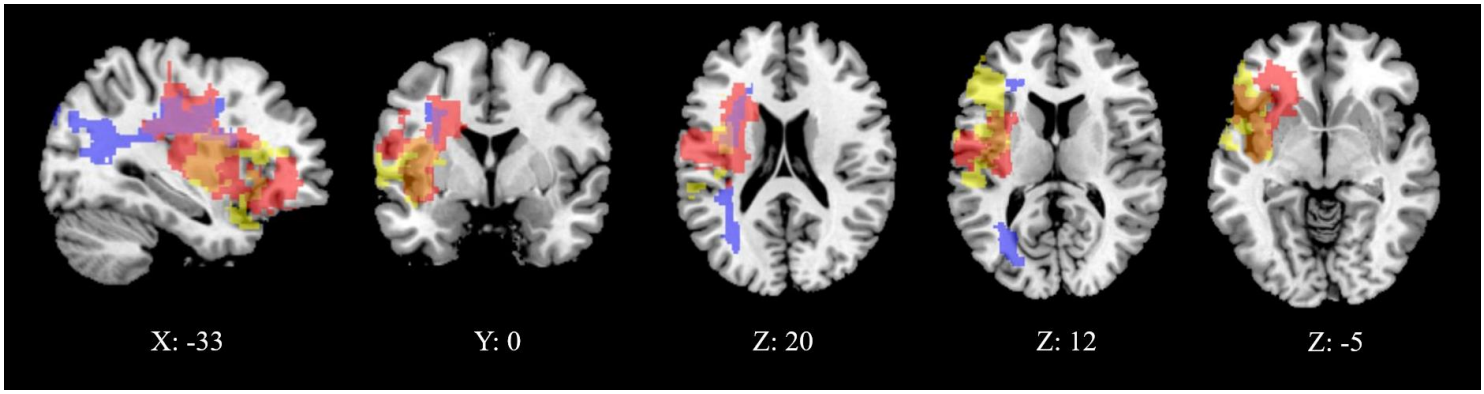


Figure 3.1. Manually segmented lesion location for P4 in red, P6 in blue, and P10 in yellow. Overlap of P4 and P6 can be seen in purple, P4 and P10 in orange, and overlap of all three in dark pink. There is no exclusive overlap of P6 and P10 here. The lesions for all three patients impact left IFG. P4's lesion extends to left pMTG. Voxel coordinates are displayed under each slice.

3.3.3. Background neuropsychological testing

Patients completed a series of neuropsychological assessments, testing language, memory, visuospatial function, executive function, and semantic cognition. The protocol used here was similar to that described in Stampacchia et al. (2018). Each patient's performance on the background neuropsychology measures is shown in Supplementary Table BN.1, while Supplementary Table BN.2 provides data on tests of semantic cognition. Background Neuropsychology Supplementary Materials also provide task descriptions (see Section '*Description of Assessments'*) and an interpretation of the sample's performance on these measures (see Section *'Chapter 3 Sample Summary'*). Patients presented with largely preserved word repetition, but impairments in verbal fluency and working memory. Visuospatial processing was largely preserved across the sample. Across a series of executive function tests, three patients showed some evidence of impairment. While the extent of executive dysfunction in SA is debated (see Thompson et al., 2018, and Chapman et al., 2020, for alternative viewpoints), the current sample may be less impaired than previous studies from our group, due to the need for patients to meet the constraints associated with remote testing (e.g., self-directed computer use) during the COVID-19 pandemic.

Patients showed a variable degree of impairment on core tests of semantic cognition. As expected, impairment was highest on tests that had larger semantic control demands, with patients showing effects of cues and miscues, competition from strong thematic distractors, and difficultly retrieving subordinate conceptual information in both the verbal and non-verbal domains. Each patient showed impairment on at least one verbal and one non-verbal test of semantic control. This is consistent with the view that patients with SA have multi-modal impairment in the manipulation of knowledge for the purpose of symbolic processing, as first outlined by Head (1926). The degree of impairment for each patient was derived from a semantic control composite score, extracted from a larger sample of SA patients (Souter, Stampacchia, et al., 2022 [Chapter 5 of this thesis]; N = 17, including the current sample) using principal components analysis (PCA) with oblique rotation. This component reflects performance on tasks with high semantic control demands, including word and picture versions of the Camel & Cactus Test (Bozeat, Lambon Ralph, et al., 2000), the ambiguity task (Noonan et al., 2010), the synonym judgement task (Samson et al., 2007), and the object use task (Corbett et al., 2011). For each patient, regression scores for this component were extracted, with lower scores indicating greater impairment. Each patient's composite scores are in Supplementary Table BN.2, and the full results of this PCA are presented in Table 5.1.

3.4. Study 3.1: Emotion portrayal categorization

3.4.1. Method

3.4.1.1. Participants

The Study 3.1 sample included seven patients (four female) with a mean age of 57.0 (SD = 9.2), a mean age of leaving education of 18.4 (SD = 3.8) and a mean of 11.5 years (SD = 5.4) since stroke. We also collected data from 33 healthy comparison participants (20 female) with a mean age of 67.7 (SD = 9.5), and a mean age of leaving education of 20.8 (SD = 3.0). Patients and comparison participants did not significantly differ on age when leaving education: $t(38) = -1.8$, $p = .078$. The comparison participants were significantly older than the patients: $t(38) = -2.7$, $p = .010$ (this difference should underestimate impairment in the patients). In the original study on SD (Lindquist et al., 2014), patients were compared to comparison participants in the emotion free sort task only, while we collected control data for

all sorting tasks to establish how word and face anchors aid SA patients, relative to comparison participants. Informed consent was obtained for all participants.

3.4.1.2. Design

This study used a mixed design, with patients and comparison participants completing four tasks with varying levels of constraint; free sort, number anchored sort, word anchored sort, and face anchored sort. These tasks were completed over the course of a single session. No limits were put on timing, but administration typically lasted between 40 and 60 minutes.

3.4.1.3. Stimuli

As in the original paradigm (Lindquist et al., 2014), stimuli were taken from the IASLab Face Set[10] (https://www.affective-science.org/face-set.shtml). A full list of stimuli (by identity code) is provided in Supplementary Table 3.1. We replicated the short version of the sorting tasks used in the original publication, with six identities (half male, half female) all portraying facial muscle configurations associated with the six English language emotion categories of anger, sadness, disgust, fear, happiness, and neutral. This resulted in 36 stimuli overall. One male identity from the original paradigm was substituted for a novel identity, as perceptual similarity between two identities was found to cause confusion in the free sort task (see Section 3.4.1.4.2.). Two patients (P10, P11) and three comparison participants who had completed the full study with the male identity used in the original paradigm, were retested on the identity free sort task with the updated stimuli. These participants were not retested on the remaining conditions, as practice effects (i.e., knowledge of the number and contents of the emotion categories) in the emotion free sort condition would have been unavoidable.

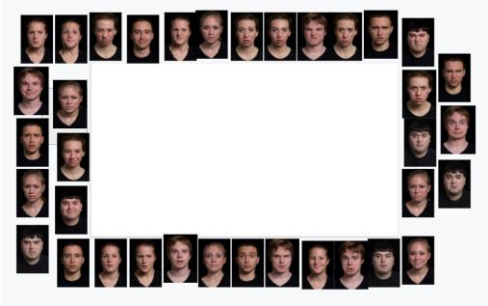
3.4.1.4. Procedure

Due to COVID-19 social distancing measures, the procedure from Lindquist et al. (2014) was adapted for online remote testing. Stimuli were presented online using Google Slides, while the researcher and participant conversed on the video conferencing software Zoom (Zoom Video Communications Inc., 2016). Both the participant's and researcher's video were turned off, to prevent them obscuring the stimuli. By default, the researcher shared their screen to show the stimuli on Google Slides, and gave the participant remote control of their cursor. This allowed participants to click and drag the stimuli around the screen. If technical issues arose, participants were sent a direct link to the Google Slides

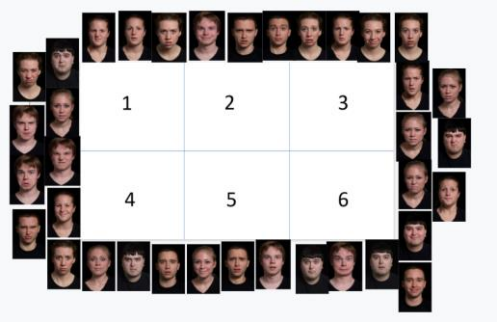
[10] Development of the Interdisciplinary Affective Science Laboratory (IASLab) Face Set was supported by the National Institutes of Health Director's Pioneer Award (DP1OD003312) to Lisa Feldman Barrett.

document, allowing them to move the stimuli around themselves while the researcher viewed the same document, still speaking to the participant on Zoom or by telephone. One patient (P6) was unable to engage with online testing. In this case, physical stimuli were printed, laminated, and sent to P6, who then completed the study while on a Zoom call with the researcher. Figure 3.2 provides a summary of the Study 3.1 stimuli and procedure.

(a) – Example Study 3.1 stimuli

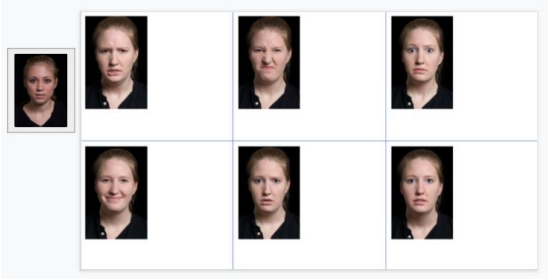


(b) – Emotion/identity free sort

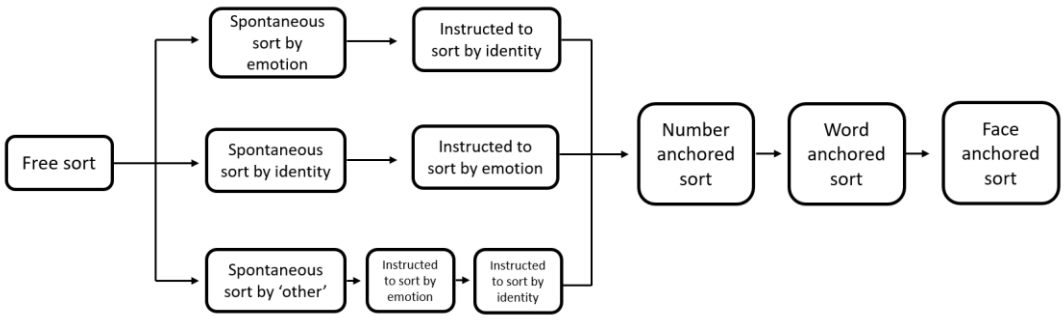


(c) – Number anchored sort

(d) – Word anchored sort



(e) – Face anchored sort



(f) – Order of Study 3.2 tasks

Figure 3.2. A summary of the Study 3.1 stimuli and procedure, including (a) examples of stimuli, layout of stimuli during (b) free sort (including emotion and identity free sort), (c) number anchored sort, (d) word anchored sort, and (e) face anchored sort tasks, and (f) the order these tasks were completed in.

3.4.1.4.1. Emotion free sort

The stimuli were distributed randomly around the outside of the screen, with the center of the screen left clear to allow room for creating piles (see Figure 3.2b). Participants

were told: *"On this slide there are a series of pictures spread out. What I want you to do is organize them into groups that are meaningful to you. You can create as many piles as you need to. At the end, each pile should be sorted so that one type of picture only is included in there. It is sometimes helpful to look through the set of pictures first before you begin sorting. This is not timed, so feel free to take as long as you need. You can also change the piles while you are sorting or at the end—it is up to you. Do you have any questions?"*. Participants were told that the researcher was unable to give further instructions, but that there were no wrong approaches. After sorting had finished, participants were asked "*Can you tell me about how you sorted the pictures?*". Of the patients, four sorted spontaneously by emotion, two by identity, and one by gender. Of the comparison participants, 22 sorted spontaneously by emotion, nine by identity, one by gender, and one by attempting to organise faces symmetrically across the screen. Participants who had not initially sorted by emotion were then told; "*The people on this slide are all feeling something. Some of them feel the same way and some of the people feel differently. What I want you to do now is to sort the faces in the pile based on how the people feel. You should create piles where each person feels exactly the same way. At the end, each pile you've made should have pictures of only people who feel the same way. Are these instructions clear?*". Participants who spontaneously sorted by gender or using other irrelevant factors were explicitly instructed to sort by emotion (as above) and then to sort by identity (as below). Once participants had sorted by emotion they were asked, for each pile; "*What are the people in this pile feeling?*". Participants were prompted to provide a specific emotion adjective to each pile. At the end of each sorting task, participants were advised to check over their piles and move any stimuli they believed they had sorted incorrectly. There was no difference in overall emotion free sort accuracy between participants who first sorted by emotion, and those who first sorted by identity/other categories [patients: U = 2.0, p = .154, comparison participants: U = 103.0, p = .491], suggesting that performance was not affected by increased exposure or explicit instructions.

3.4.1.4.2. Identity free sort

As noted above, some participants spontaneously sorted the faces according to identity. In cases where they had not, following the emotion free sort task, they were shown the screen described above (Figure 3.2b) and were told; "*On this slide there are pictures of a bunch of people. There are several pictures of each person in the pile. What I would like you to do is to sort the people in this pile into new piles based on their identity. You can create as many new piles as you need to. At the end, each pile you've made should have pictures of*

only one person in it. Please go as slowly as you need to. This will not be timed. Feel free to examine the images before you begin sorting. Do you have any questions before you begin?". This was intended to act as a control task, to identify cognitive or visual difficulties that could affect emotion categorization.

3.4.1.4.3. Number anchored sort

Following the free sort task, participants were explicitly told to sort stimuli by emotion into six distinct piles. The layout was the same as used for the free sort tasks, with the exception that boxes numbered one to six were included in the middle of the screen to serve as anchors (see Figure 3.2c). Participants were instructed; "*Now I want you to again sort these pictures based on feeling, but this time I am going to ask you to make 6 piles. I have 6 different numbers that I have laid out for you so that you can keep track of how many piles you create. Again, I want you to sort based on feeling. In each pile, there should be only people who feel the same way. At the end, each pile you've made should have pictures of only people who feel the same way. Please go as slowly as you need to. This will not be timed. Feel free to examine the images before you begin sorting. Do you have any questions before you begin?*". All participants followed the instructions and made six piles, except for one patient (P10) who indicated they were unable to perceive a sixth emotional state and finished with five piles.

3.4.1.4.4. Word anchored sort

Participants were then again explicitly asked to sort the faces by emotion, this time with the aid of word anchors which labelled what the faces in each pile should feel. In this case, stimuli were not spread around the screen but appeared one at a time in an area on the left of the screen, in a randomised order (see Figure 3.2d). This was done as participants were now sorting the stimuli to specific anchors rather than to each other, which was anticipated to be easier to perform when stimuli appeared one at a time. Each stimulus remained on screen after it had been initially sorted and, as with prior conditions, participants were free to change their categorization of a given stimulus at any point during the condition. Participants were instructed; "*Now I want you again sort these pictures based on feeling, but this time I am going tell you what should be in each of the 6 piles. There are 6 words laid out here so that you can keep track of the piles. Again, I want you to sort based on feeling. In each pile, there should be only people who feel the same way. I want you to sort into this pile, people who feel angry. In this pile, I want you to sort people who feel disgusted. In this pile, I want you to sort people who feel fearful. In this pile, I want you to sort people who feel happy. In this pile, I*

want you to sort people who feel sad. In this pile, I want you to sort people who feel neutral. At the end of your sorting, each pile you've made should have pictures of only people who feel the same way. Please go as slowly as you need to. This will not be timed. Feel free to examine the images before you begin sorting. Do you have any questions before you begin?".

3.4.1.4.5. Face anchored sort

In the final task, participants were again explicitly asked to sort stimuli by emotion, this time matching them to exemplar facial portrayals of each of the six English language emotion categories. Example pictures were of a female actor taken from the IASLab Face Set who was posing facial muscle movements prototypically associated with the six emotion categories. These six anchors were presented on the slide's background and were made slightly larger than the stimuli to be sorted, to help participants keep track of the reference picture. Again, stimuli appearing one at a time on the left of the screen in a randomised order (see Figure 3.2e). Participants were instructed; "*Now I want you to again sort these pictures based on feeling, but this time I am going to start the piles for you. Here are six different pictures of the same woman. The woman feels differently in each of the pictures. Again, I want you to sort the pile of pictures into these already started piles based on feeling. In each pile, there should be only people who feel the same way. At the end of your sorting, each pile you've made should have pictures of only people who feel the same way. Please go as slowly as you need to. This will not be timed. Feel free to examine the images before you begin sorting. Do you have any questions before you begin?*".

3.4.1.5. Data Analysis

For each participant, the number of piles created in the emotion free sort task was recorded, reflecting categorization of emotional portrayals with minimal explicit instruction. We also computed accuracy for each participant in each sorting task. For the emotion free sort and number anchored sort tasks, errors were classified as cases where a face was sorted into a pile where the dominant portrayal was of a different emotion, or into piles with no one dominant portrayal. A pile was classified as having a dominant portrayal when at least 50% of its faces corresponded to one emotion category. In the word anchored sort and face anchored sort tasks, errors were defined as cases where a stimulus was not placed in the pile of its conceptual or perceptual equivalent, regardless of the dominant portrayal of faces placed in that pile. Error types were classified in terms of whether they were within-valence (e.g., both involving negatively-valenced states, such as mistaking a sad portrayal as angry) or across-valence (e.g., mistaking a neutral portrayal as sad, or a happy portrayal as fearful).

Full error classification data is provided in Supplementary Table 3.2. Accuracy in the identity sort control task was also assessed. Errors were classified as cases where a face was sorted into a pile of pictures with a different dominant identity, or a pile with no dominant identity. A pile was classified as having a dominant portrayal when at least 50% of its faces corresponded to one identity. While in the original paradigm (Lindquist et al., 2014) accuracy was graphically presented in terms of '% total errors', for the sake of consistency with Study 3.2 we present '% correct' for each task.

Each patient was classified as being either impaired or not impaired in terms of their overall accuracy in each emotion sorting task. This was done using Singlims (Crawford et al., 2010), which compares individual patient scores to the respective mean and standard deviation of a comparison sample to estimate degree of impairment. Singlims was also used for each individual error type for each patient in each task (e.g., to reflect whether an individual patient made an abnormally high number of negative within-valence errors in each task; reflected in Supplementary Table 3.2). In each case, one-tailed *p*-values were interpreted against a significance threshold of .05.

Finally, to compare performance in the free sort task with each type of anchor across the two groups, mixed effects logistic regressions were used. Three models were created in R (R Core Team, 2020), comparing the initial emotion free sort task with performance following each anchor type (numbers, words, and faces). We used separate models for each task comparison rather than an omnibus model due to the fact that this study was comprised of four distinct tasks, tested separately with varying instructions (in contrast, Study 3.2 below presented multiple conditions within one experiment). For each model, group and task were entered as categorical fixed factors, and participant identity as a random factor. Introducing this random intercept allows for these models to systematically account for variability attributable to participant identity, and therefore to better isolate variability caused by the fixed factors of interest (Bell et al., 2019). We modelled each individual stimulus in each task, coded as having been sorted either correctly or incorrectly. All models were fit by maximum likelihood, based on Gaussian Hermite approximation. Models were run using the lme4 package (version 1.1-25; Bates et al., 2015). As these are logistic models, estimate coefficients reflect log transformation of odds ratios (Larsen et al., 2000). Likelihood ratio tests were used to look for significant main effects or interactions of task by group for each model. These tests compared two nested models using the chi-square distribution, to determine whether removing a predictor (e.g., group) significantly changed the overall

model. Using this same procedure, we modelled accuracy on the identity sort control task, including group and emotion category as fixed effects, and participant identity as a random factor. All data for Study 3.1 are publicly available on Mendeley Data (https://data.mendeley.com/datasets/zwxxscny6x/3).

3.4.2. Results

3.4.2.1. Sorting based on identity

Three of the seven patients (P6, P12, P15), and five of the 33 comparison participants made some mistakes on the identity sort control task, even though all participants in the original paradigm (Lindquist et all., 2014) performed this task perfectly (under different viewing conditions). However, there was no difference in accuracy in emotion free sort for participants who had and had not made errors in the identity free sort task [patients: U = 2.5, p = .212, comparison participants: U = 34.5, p = .074]. Furthermore, mixed effects logistic regression found no effect of group on identity sorting accuracy (see Supplementary Table 3.4), showing that the SA group did not present with domain-general deficits in sorting in a control task that did not involve accessing categorical representations of emotion.

3.4.2.2. Sorting based on emotion portrayal

On average, comparison participants created 5.7 (SD = 1.4) piles in the emotion free sort task, with 58% producing six or seven piles. This is similar to Lindquist et al. (2014), where 61% of older adults produced six or seven piles. Of the SA patients, three created four piles, two created five, one created six, and one created seven. In Lindquist et al. (2014), the three SD patients all produced either three or four piles reflecting hedonic valence of the portrayals (pleasant, unpleasant, neutral). Therefore, while some SA patients appeared similar to SD patients in terms of perceiving limited discrete emotion states, others identified more categories (although this did not always correspond with greater accuracy, see Supplementary Table 3.2).

Next, we considered the emotion labels provided by SA patients for all piles in the emotion free sort task. Of the piles which were represented by one dominant emotion, 70% were attributed the correct emotion label or a largely appropriate alternative to it (e.g., a happy pile labelled as ‘pleasure’, or a neutral pile labelled as ‘normal’). The majority of correct labels were for piles of happy or neutral faces, when within-valence discrimination

was not necessary. Within-valence labelling errors (e.g., an angry pile labelled as ‘fear’) occurred in 25% of cases, and there was only one case of across valence error (a fearful pile labelled as ‘happy’ by P16). SD patients in the original sample from Lindquist et al. (2014) were similarly accurate in labelling piles as happy or neutral but were sometimes vague in their labelling of negative piles, using labels such as “rough” or “not up”. Such vague descriptions were rare in the current sample.

Each patient’s overall accuracy (percent correct) for each sorting task, as well as group averages, can be seen in Figure 3.3. Due to the small patient sample size, it was not possible to calculate correlations between task performance and degree of semantic impairment. Instead, patients in Figure 3.3 are ordered from most to least impaired (from left to right), allowing for the visualisation of effects of semantic impairment on performance. As determined by Singlims analysis, six of the seven patients were impaired in at least one task, as determined by a significantly lower accuracy when compared to comparison participants. The only patient not to show evidence of emotion discrimination impairment was the one with the mildest semantic impairment (on the basis of the semantic control composite score, see Section 3.3.3.).

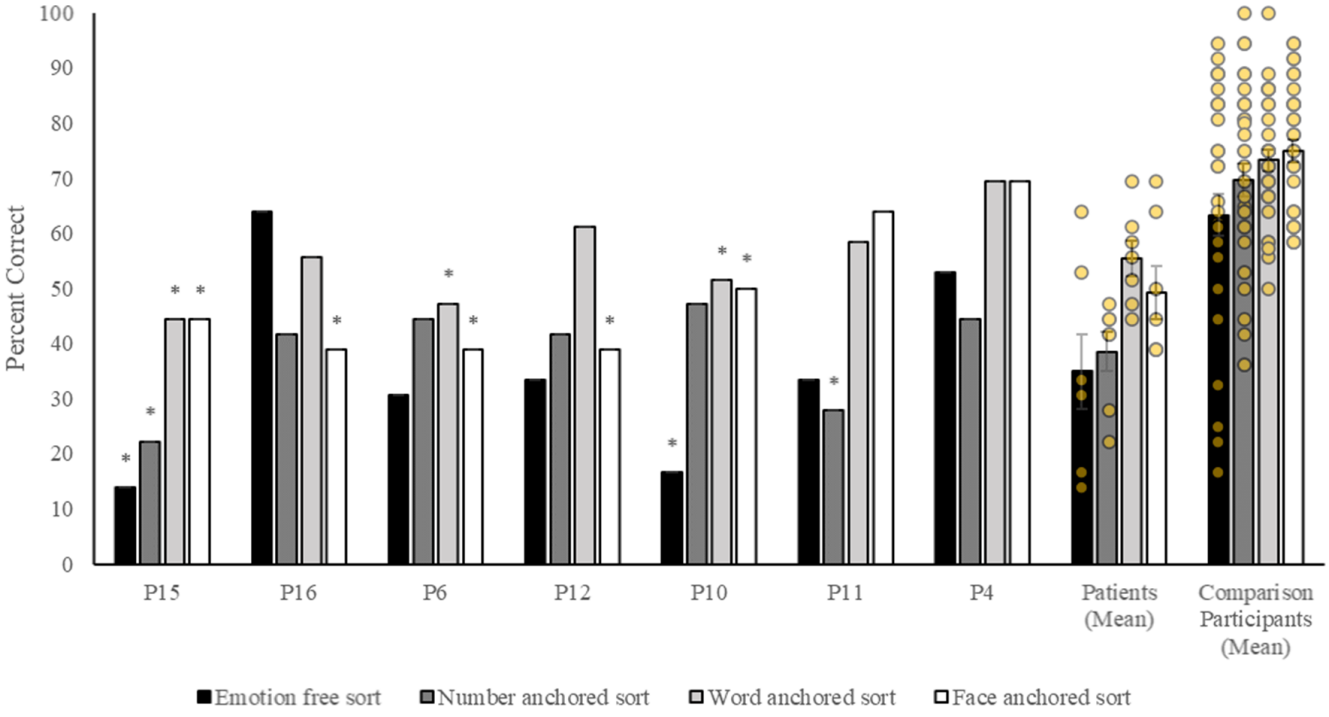


*Figure 3.3. Total percent correct in the Study 3.1 emotion free sort, number anchored sort, word anchored sort, and face anchored sort tasks, for each individual patient, and the mean percent correct of patients and comparison participants. Patients are ordered (left to right) from the most to least semantically impaired, based on their semantic control composite score. Error bars reflect one standard error of the mean. Individual data points for both patients and controls for each task are represented by yellow circles. * = impaired performance based on Singlims analysis.*

Patients not only showed lower overall accuracy but were more likely to make certain types of errors than comparison participants. As seen in Supplementary Table 3.2, SA patients were most likely to make an abnormal number of negative within-valence errors, relative to comparison participants. This resembled the SD patients in Lindquist et al. (2014; see Supplementary Table 3.3) and follows from the constructionist hypothesis that semantic knowledge is especially useful for disambiguating between same-valence faces (Lindquist et al., 2014). The SA patients also frequently showed abnormally high rates of neutral faces sorted into negative piles, and other across-valence mistakes. They appeared to be at least as impaired as the SD patients on emotion sorting: in the free sort task, although there was substantial variation in performance, SA patients had an average accuracy of 35%, ranging between 14% and 64% (while the three SD patients in Lindquist et al., 2014, presented with 38%, 56%, and 61% accuracy on this task).

Mixed effects logistic regressions for the accuracy data are reported in Table 3.1. For each of the three models, examining the impact of a type of constraining information (numbers, word labels, emotional faces) relative to performance in the free sort task, likelihood ratio tests revealed a significant contribution of group, with comparison participants more likely to produce a correct response than patients. A significant contribution of task was found for both the number and word anchored models, suggesting that these more constrained tasks increased the likelihood of correct responses, relative to free sort, while the task effect for the face anchored model approached significance. A significant interaction between task and group was observed for the word anchored model. As seen in Figure 3.3, this reflected greater facilitation of performance in SA patients than comparison participants from the provision of word anchors, compared with free sort, reflected by mean differences in accuracy between these tasks (patients: 20.4%, comparison participants: 9.9%).

Table 3.1. Output for Study 3.1 mixed effects logistic regressions used to observe effects of group and task on the odds of sorting a given stimulus correctly.

Variable	Estimate	Lower 95% CI	Upper 95% CI	Likelihood Ratio Test
Free sort vs number anchored sort				
Intercept	-0.15	-0.59	0.29	-
Task	**-0.33**	**-0.63**	**-0.04**	**$\chi(1) = 4.90$, $p = .027$ ***
Group	**1.08**	**0.60**	**1.57**	**$\chi(1) = 15.58$, $p < .001$ ***
Task*Group	0.27	-0.06	0.60	$\chi(1) = 2.61$, $p = .106$
Free sort vs word anchored sort				
Intercept	-.38	-0.82	0.06	-
Task	**0.58**	**0.29**	**0.88**	**$\chi(1) = 15.54$, $p < .001$ ***
Group	**1.25**	**0.76**	**1.74**	**$\chi(1) = 19.44$, $p < .001$ ***
Task*Group	**-0.37**	**-0.70**	**-0.04**	**$\chi(1) = 4.89$, $p = .027$ ***
Free sort vs face anchored sort				
Intercept	-0.30	-0.74	0.14	-
Task	0.27	-0.02	0.56	$\chi(1) = 3.24$, $p = .072$
Group	**1.14**	**0.65**	**1.63**	**$\chi(1) = 16.75$, $p < .001$ ***
Task*Group	0.07	-0.26	0.40	$\chi(1) = 0.18$, $p = .669$

Note: * reflects significance at the .05 threshold. CI = confidence interval. Models run in R using lme4 package (version 1.1-25; Bates et al., 2015). As these are logistic models, estimate coefficients reflect log transformation of odds ratios (Larsen et al., 2000).

In summary, Study 3.1 found that SA patients, who presented with the hallmarks of deregulated retrieval, were at least as impaired as SD patients (with degraded semantic knowledge) at sorting emotional facial emotion portrayals. Patients made similar errors to those reported previously in SD, in which different within-valence emotions are confused. Patients with SA also benefitted to a greater extent than healthy comparison participants from emotion word anchors relative to free sort – presumably because these labels increased the accessibility of semantic information about different emotions in the context of deregulated retrieval.

3.5. Study 3.2: Emotion cueing

Study 3.1 provided evidence that impairments in semantic control can interfere with emotion categorization in patients with SA. Discrimination of facial portrayals of emotion may require inhibition of conceptually-similar emotional categories, particularly for states with prototypically high conceptual and perceptual similarity, such as anger and sadness. This conflict may result in misidentification of emotional portrayals in SA patients with deregulated semantic retrieval, as accuracy is impeded both by competition from superficial visual similarities and overgeneralisation of an overarching category (e.g., negative affect). These difficulties could be ameliorated in SA patients by providing conceptual cues which make the target information more accessible, consistent with evidence that multimodal cues facilitate access to conceptual information in SA (Jefferies et al., 2008; Lanzoni et al., 2019; Noonan et al., 2010). Equally, miscueing irrelevant information may increase selection demands, and therefore impede accurate emotion categorization (Noonan et al., 2010). Study 3.2 established whether the retrieval of emotional categories in SA was influenced by auditory cues and miscues to emotion categories (i.e., prosody), in an alternative forced-choice design. Cues were predicted to reduce semantic control demands by constraining interpretation of the subsequent portrayal. Within-valence miscues were predicted to increase semantic control demands by requiring participants to inhibit irrelevant but conceptually similar information. Across-valence miscues were not predicted to affect semantic control demands, as the miscued information is conceptually dissimilar to the target emotion category.

3.5.1. Method

3.5.1.1. Participants

A subset of the participants from Study 3.1 participated in Study 3.2. This included six patients (three female) with a mean age of 60.0 (SD = 6.3), a mean age of leaving education of 18.8 (SD = 4.0) and a mean of 11.6 years (SD = 6.0) since their most recent stroke. The sample also included 15 healthy comparison participants (11 female) with a mean age of 65.1 (SD = 7.1), and a mean age of leaving education of 20.5 (SD = 2.2). Patients and comparison participants did not significantly differ on age: $t(19) = -1.5$, $p = .140$, or on age when leaving education: $t(19) = -1.3$, $p = .223$.

3.5.1.2. Design

Study 3.2 required participants to match individually presented facial portrayals to one of three emotion labels: 'angry', 'happy', and 'sad'. Trials were preceded by either a 'cue'/'miscue' period or a 'no cue' period. A repeated measures design was used, with all participants completing the task across the four conditions of cue, no cue, miscue within-valence, and miscue across-valence. Facial stimuli and prosody cues were restricted to the emotions of anger, happiness, and sadness. On cue trials, facial stimuli were preceded by an auditory cue which was congruent in emotion with the face displayed (e.g., a happy voice preceding a happy face). On miscue within-valence trials, facial stimuli were preceded by an incongruent prosody cue of the same valence, but of a different emotion (e.g., an angry voice preceding a sad face). On miscue across-valence trials, facial stimuli were preceded by an incongruent prosody cue of the opposite valence (e.g., a happy voice preceding an angry face). Prosody cues were recordings of "babbling" (ba-ba-ba, without semantic content), spoken in different tones of voice associated with specific emotions. The study was conducted over two sessions, with 66 trials in each session, and 132 trials overall. Session order was counterbalanced across participants. Trials were split over 36 cue, 36 no cue, 36 miscue across-valence, and 24 miscue within-valence trials. Fewer miscue within-valence trials were included as it was not possible to provide within-valence miscues for happy portrayals. Each condition and probe emotion were equally represented across sessions.

3.5.1.3. Stimuli

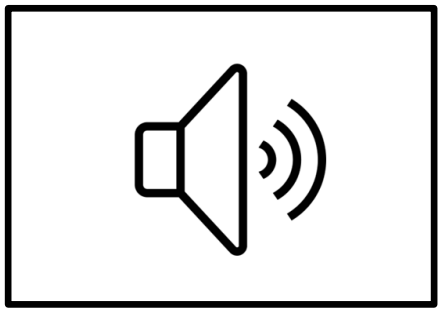
As with Study 3.1, stimuli were taken from the IASLab Face Set (https://www.affective-science.org/face-set.shtml). A full list of stimuli used (by identity code) can be seen in Supplementary Table 3.1. Facial muscle portrayals of the English

language emotion categories anger, happiness, and sadness were obtained for 12 identities (half male, half female), resulting in 36 stimuli overall. Prosody cues were taken from the Aprosodia Battery (Ross et al., 1997). These were recordings of actors saying "ba-ba-ba-ba-ba" with either angry, happy, or sad prosody. These cues were seven, eight, and six syllables long, respectively. The same single angry, happy, and sad prosody cues were used throughout the experiment.

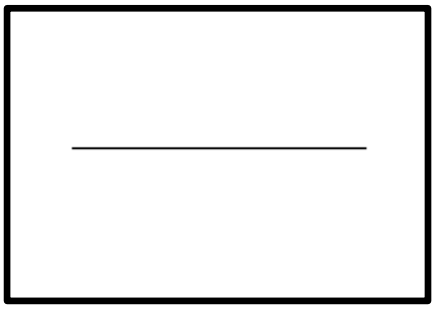
3.5.1.4. Procedure

Study 3.2 was administered online due to COVID-19 social distancing restrictions. Stimuli were presented using PsychoPy3 (Peirce et al., 2019). Before beginning, the researcher called the participant over Zoom (Zoom Video Communications Inc., 2016). Both the participant's and researcher's video were turned off, to prevent them obscuring the stimuli. The researcher shared their screen and computer sound with the participant and gave them remote control of their cursor, which remained visible on the screen. Figure 3.4 provides a summary of the Study 3.2 stimuli and procedure, including examples of stimuli.

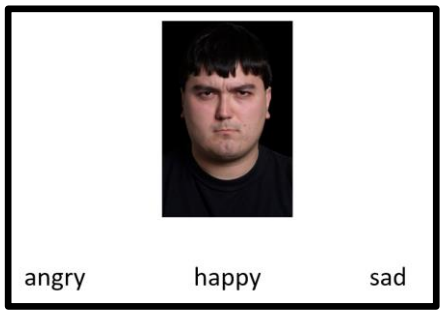
(a) – Examples of Study 3.2 stimuli



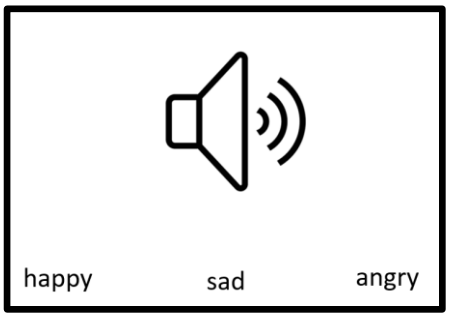
(b) – Cue or miscue graphic



(c) – No cue graphic



(d) – Experimental decision phase



(e) – Prosody identification trials

Figure 3.4. A summary of the Study 3.2 stimuli and procedure, including (a) examples of stimuli, graphics used during the (b) 'cue' or 'miscue' phase and the (c) 'no cue' phase, and presentation of stimuli and response options during (d) the experimental decision phase and (e) the 'prosody identification' trials which followed completion of the study.

Participants were told: "*On each trial, you will be presented with one picture, with three words underneath it. Each word will correspond with an emotion that the person in the picture could be feeling. It will be your job to indicate which emotion you think the person in the photo is feeling. To do this, move the cursor over the word you want to select."*. Prior to each session, participants were presented with five practice trials, which included feedback. Each participant demonstrated an understanding of the task instructions and verified that they could clearly hear the audio cues during these trials.

Each trial was preceded by either a cue/miscue or a no cue phase. For cue/miscue trials, a graphic of a loudspeaker appeared on the screen while the audio played for

approximately 3.5 seconds (see Figure 3.4b). In no cue trials, a horizontal black line appeared in place of the loudspeaker, for a silent period of 3.5 seconds (see Figure 3.4c). In the decision phase of the task, a face appeared in the middle of the screen with three emotion labels beneath it: 'angry', 'happy', and 'sad' (see Figure 3.4d). The position of these labels, and of the target label, was counterbalanced across trials. Due to impaired reading ability in some patients, these labels were read aloud from left to right on each trial for patients, but not for comparison participants. To indicate their response, the participants moved the cursor over the word they wished to choose, and the researcher keyed in their response. This was viewed as the closest analogue to participants pointing at the screen (the typical method employed in our in-person testing). Each trial was followed by a 1.5 second fixation cross. All trials were presented in a randomised order. The position of the response options was moved by 150 pixels in the horizontal direction for each alternating trial, to ensure that the participant always needed to move the cursor to respond, even in cases where the position of the correct response was the same over subsequent trials. Participants were offered a break at the half-way point of each session. After the completion of the second session, participants completed a 'prosody identification' task, in which they were presented with the three audio cues in isolation and asked to match them to their respective emotion label (see Figure 3.4e).

3.5.1.5. Data Analysis

For each participant, mean accuracy (percentage correct) and response time (seconds) in each condition were recorded. Each patient was classified as being either impaired or not impaired in their overall accuracy for each condition. As in Study 3.1, this was done using Singlims (Crawford et al., 2010). Again, one-tailed p-values were interpreted against a significance threshold of .05. As in Study 3.1, a mixed effects logistic regression was performed in R (R Core Team, 2020), to compare accuracy across groups and on each of the cue conditions (cues, across-valence miscues, within-valence miscues) relative to the no cue condition. While Study 3.1 employed serially presented discrete tasks, the current analysis compared performance across conditions within a single experiment within one omnibus model. Group and condition were entered as dichotomous fixed factors, and participant identity as a random factor. These factors were used to predict the likelihood of a correct response for each individual trial, coded as either correct or incorrect. The model was fitted using maximum likelihood, based on Gaussian Hermite approximation. The model was run using the lme4 package (version 1.1-25; Bates et al., 2015). As this is a logistic model, estimate coefficients reflect log transformation of odds ratios (Larsen et al., 2000).

Likelihood ratio tests were used to test for the significance of effects or interactions of group and condition, by statistically comparing the overall model to nested versions with specific effects removed. Participants' mean response time across conditions is presented in a bar graph in Supplementary Figure 3.1 and analysed using a mixed effects linear regression in Supplementary Table 3.5, followed by pairwise contrasts in Supplementary Table 3.6. Due to the data collection occurring over Zoom, this response time analysis should be interpreted cautiously. All data for Study 3.2 are publicly available on Mendeley Data (https://data.mendeley.com/datasets/zwxxscny6x/3).

3.5.2. Results

Each patient's percentage accuracy for each condition, as well as group averages for patients and comparison participants, can be seen in Figure 3.5. As in Study 3.1, patients in Figure 3.5 are ordered from most to least impaired (left to right). As determined by Singlims, four of the six patients were impaired for at least one condition, relative to comparison participants (with normal performance overall for the least and third least semantically impaired patients). All participants performed with 100% accuracy when categorizing happy portrayals, regardless of condition, and angry and sad faces were never erroneously labelled as happy. All errors were within-valence, involving confusion of angry and sad portrayals.

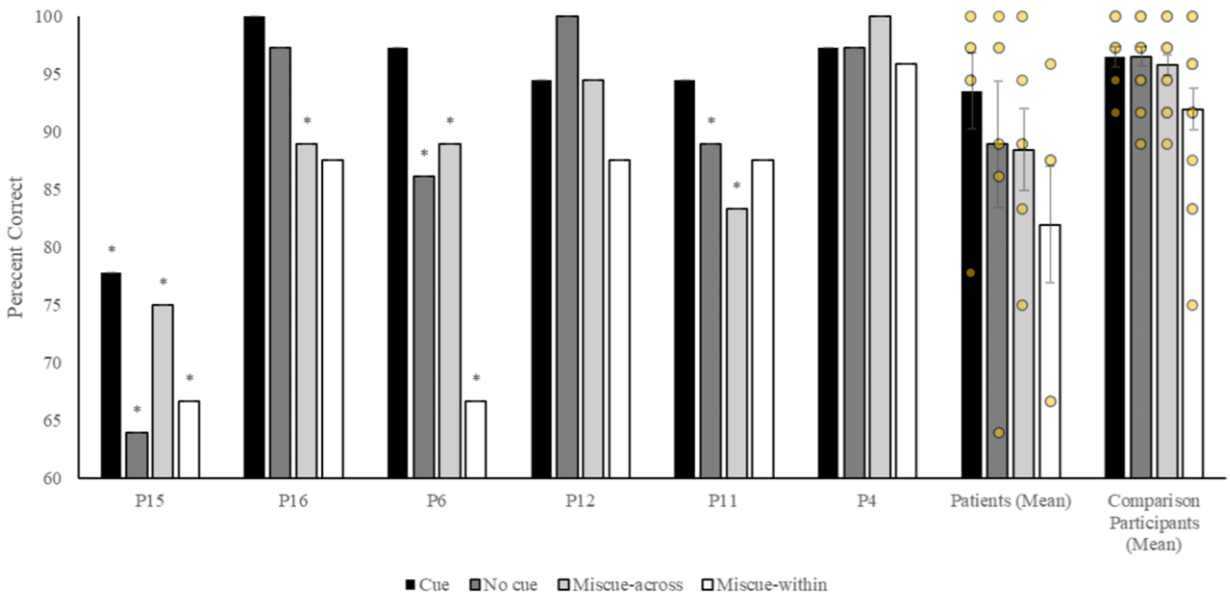


*Figure 3.5. Total percent correct in the cue, no cue, miscue across-valence, and miscue within-valence conditions, for each individual patient and group means. Patients are ordered (left to right) from the most to least semantically impaired, based on their semantic control composite score. Errors bars reflect standard error of the mean. Individual data points for both patients and controls for each condition are represented by yellow circles. * = impaired performance based on Singlims analysis.*

The results of the mixed effects logistic regression for accuracy are reported in Table 3.2. The model revealed a significant contribution of group, with comparison participants more likely to produce a correct response than patients. A significant effect of condition was found. The group by condition interaction was non-significant. To parse the observed condition main effect, we observed pairwise post-hoc comparisons using the emmeans package (Lenth, 2020) in R, with the Tukey HSD method for multiple comparisons applied. We observed the difference between each combination of conditions, reported in Table 3.3. Contrasts were split by group as we were specifically interested in effects of cueing in SA. Patients had a significantly higher probability of a correct response during cue than miscue within-valence trials. This suggests a difference in performance between the trials with the highest and lowest semantic control demands. Comparison participants showed this same effect, but also demonstrated diminished probability of a correct response in miscue within-valence trials relative to the no cue baseline. Neither group showed significant difference between cue and no cue trials.

Table 3.2. Output for the Study 3.2 mixed effects logistic regression observing effects of group and condition on the odds of responding correctly to a given trial.

Variable	Estimate	Lower 95% CI	Upper 95% CI	Likelihood Ratio Test
Intercept	2.33	1.57	3.09	-
Group	**1.21**	**0.24**	**2.18**	**$\chi(1) = 5.57$, $p = .018$***
Condition	**-**	**-**	**-**	**$\chi(3) = 12.3$, $p = .006$***
Group by Condition	-	-	-	$\chi(3) = 1.75$, $p = .626$

Note: * reflects significance at the .05 threshold. CI = confidence interval. Model was run in R using lme4 package (version 1.1-25; Bates et al., 2015). As this is a logistic model, estimate coefficients reflect log transformation of odds ratios (Larsen et al., 2000). Overall condition effect and group by condition interaction do not include an estimate value, as these effects are not provided by the overall model. The respective likelihood ratio test results were obtained by comparing the full model to nested versions in which all condition main effects or interactions were removed.

Table 3.3. Post-hoc pairwise contrasts of the Study 3.2 accuracy mixed effects logistic regression, comparing the likelihood of a correct response across conditions within the patient and comparison groups.

Contrast	Patients	Comparison Participants
No cue – cue	OR = 0.54, $p = .308$	OR = 1, p = 1
No cue – miscue across-valence	OR = 1.05, $p = .999$	OR = 1.22, $p = .921$
No cue – miscue within-valence	OR = 1.85, $p = .216$	**OR = 2.46, $p = .018$***
Cue – miscue across-valence	OR = 1.96, $p = .237$	OR = 1.22, $p = .921$
Cue – miscue within-valence	**OR = 3.46, $p = .004$***	**OR = 2.46, $p = .018$***
Miscue across-valence – miscue within-valence	OR = 1.76, $p = .279$	OR = 2.01, $p = .080$

Note: * reflects significance at the .05 threshold. P-values were corrected using the Tukey HSD method for multiple comparisons. Contrasts were run using the emmeans package (Lenth, 2020) in R. OR = odds ratio.

When tested on prosody identification, all comparison participants accurately labelled each cue. Three patients made mistakes, with P16 labelling the happy cue as “angry”, P6 labelling the angry cue as “sad”, and P15 switching the labels for angry and sad cues. This may suggest diminished ability to accurately perceive emotion from prosody cues (i.e., impaired emotion perception across modalities), as suggested by prior studies of left hemisphere stroke patients (Leung et al., 2017). Despite this, all three of these patients performed better on trials with cues than on no cue and miscue trials (in two cases, by a margin of over 10%, see Figure 3.5). This implicit sensitivity to emotion cues, even when not explicitly identified, is consistent with deregulated semantic access in SA.

3.6. Discussion

The current study assessed the ability to perceive and categorize discrete facial emotion portrayals in SA patients with multimodal impairment in controlled semantic retrieval following left hemisphere stroke. Constructionist models of emotion argue for a necessary role of conceptual knowledge in guiding emotion perception, insofar as conceptual knowledge helps to transform otherwise ambiguous facial muscle movements into perceptions of discrete emotion categories (Barrett et al., 2007; Lindquist et al., 2015; Lindquist, Gendron, et al., 2016). In this way, judgements of similarity in facial portrayals of emotion may be grounded in judgements of semantic similarity. Accordingly, there is evidence of impaired facial emotion perception when access to emotion concepts is temporarily impaired in healthy comparison participants due to semantic satiation (Gendron et al., 2012; Lindquist et al., 2006). Progressive loss of heteromodal concepts in semantic dementia similarly results in impaired facial emotion perception (Lindquist et al., 2014). This study builds on these findings to demonstrate that deficits of controlled semantic retrieval in patients with SA are similarly associated with impaired emotion perception.

In Study 3.1, we adapted a paradigm from Lindquist et al. (2014), previously used with SD patients. This task required patients to sort pictures of facial emotion portrayals into piles corresponding to discrete emotional states, with minimal task instruction, and with numbered, word, and face anchors. As predicted, comparison participants consistently outperformed SA patients, with all but one patient being impaired on at least one sorting task. Impairments in this group were at least as severe as those previously observed in SD. Moreover, the SA group did not show impairment on a control task in which they sorted faces according to identity, suggesting that general deficits in sorting behaviour are unlikely to explain their difficulties in sorting portrayals of categorical emotional states. Constraining the intended number of discrete emotion portrayals with number anchors improved accuracy across the sample. Benefits of face anchors were marginal but did not reach significance. While both groups benefited from word anchors, these benefits were larger for SA patients than comparison participants. These results are consistent with the view that semantic control is needed to resolve competition between conceptually similar emotion categories, and to access categorical information in the face of ambiguous input. Introducing relevant conceptual information (word anchors) may have ameliorated patients' deficits by reducing this ambiguity.

Study 3.2 required participants to match facial emotion portrayals to emotion labels in a three alternative forced choice design. Trials were preceded by affective prosody cues or miscues, presented auditorily, alluding to the correct or incorrect interpretation of the subsequent portrayal of emotion. These cues were compared to a no cue control condition. In line with our hypotheses, SA patients were consistently impaired relative to the comparison group. Patients presented with significantly higher accuracy on cue trials when compared to the most challenging within-valence miscue trials. Comparison participants showed this same pattern, but also presented with lower accuracy on within-valence miscue trials when compared to the no cue baseline. As previously observed for other modalities (e.g., Lanzoni et al., 2019), semantically-related miscues may have resulted in more errors overall because they increased the competition from conceptually-related distractor emotions. The lack of a difference between no cue and miscue-within valence trials in SA might reflect the way that some patients (e.g., P15, P11) performed poorly on both conditions, while comparison participants frequently performed near ceiling-level in the absence of cues, but made errors following within-valence miscues. This null result might also reflect high variability across conditions in patients, relative to the more homogeneous performance seen in the comparison participants. No effect of the less challenging across-valence miscues was observed in either group. The lack of a condition by group interaction suggests that effects of miscuing were equivalent for patients and comparison participants. Again, this study implicates controlled semantic retrieval in emotion processing.

Overall, these results are consistent with the constructionist claim that emotion perception is reliant on conceptual representations of emotional states (Lindquist et al., 2015). Semantic storage deficits (i.e., in SD) are already known to impair emotion discrimination and categorization (Kumfor et al., 2018; Lindquist et al., 2014; Miller et al., 2012; Rosen et al., 2002); this study extends these observations to SA patients thought to have deregulated semantic cognition following left hemisphere stroke. If perception of emotion from facial portrayals is non-verbal and automatic (Tracy & Robins, 2008) or if activation of emotion concepts is automatic upon perceiving relevant emotion portrayals (Preston, 2007), semantic control impairments, which affect the retrieval of concepts under ambiguous conditions, might not be expected to interfere with emotion categorization. Our results do not support this account, since SA patients have deficits of emotion perception which are at least equivalent to those seen following storage deficits. This finding builds on the constructionist account of emotion, in suggesting that, as well as intact representations, semantic control is

required for effective emotion discrimination. Emotion categorization may not be entirely automatic and can be disrupted when there is ambiguity or competition. It should be noted that access to the valence of faces or concepts may be relatively automatic, accounting for the observation that across-valence discrimination was relatively spared in SA patients. If semantic control is important for the retrieval of discrete emotion states, emotion processing could be viewed as reliant on the successful resolution of ambiguity and selection among competing conceptual representations, as has been observed for semantic decisions in other domains (Noonan et al., 2010).

A comparison of the SA patients in this study with the SD sample in Lindquist et al. (2014) supports the hypothesis, stemming from the CSC framework, that SA patients show greater impairment when task demands are high (Jefferies, 2013). Errors in the original sample of SD patients were largely constrained to within-valence mistakes. In the current SA sample, within-valence errors were still the most common, but patients also produced across-valence errors, often confusing negative and neutral faces. Across the four tasks, 10% of piles made by patients were found to include faces with one predominant identity (i.e., 50%+ pictures in a pile had the same identity). This suggests that some errors in the SA group may have been driven by the perceptual similarities between faces with the same identity, which may have interfered with judgements about emotion. The relative preservation of across-valence discrimination is likely also attributable to higher semantic similarity between emotion states that fall within the category of negative expressions, for instance. Of the two SD patients from Lindquist et al. (2014) who had completed the constrained conditions, both appeared to benefit considerably from the presence of face anchors, but not word anchors. The inverse relationship was found in the current sample, with SA patients benefiting from word anchors but not face anchors, perhaps because the words were stronger cues to distinct categories of emotion. While both picture and word cues have been effective in earlier studies of semantic cognition in SA (e.g., Corbett et al., 2011; Jefferies et al., 2008) the face anchors provided similar information to the target pictures, as opposed to an explicit guide to the way these stimuli could be categorised. These findings conceptually replicate evidence that individuals with alexithymia, a subclinical trait associated with difficulty labelling and describing emotions, benefited more from the presence of word primes than face primes in a repetition priming task (Nook et al., 2015).

Contrary to prior research (e.g., Lanzoni et al., 2019; Noonan et al., 2010), Study 3.2 provides limited evidence of the effectiveness of cues in facilitating access to relevant

information. Patients' accuracy significantly increased in the cue relative to the within-valence miscue trials, suggesting a difference across manipulations which maximally vary in their semantic control demands, but there was no effect of cues on accuracy relative to the no cue baseline. This may in part be due to the limited patient sample size in the current study, or due to the fact that several patients performed near ceiling-level in the baseline no cue condition, leaving limited opportunities for cue-induced improvement. Deleterious effects of within-valence miscues across the sample are consistent with prior evidence that task-irrelevant miscues impair semantic judgements in SA by increasing the need to internally constrain retrieval (Noonan et al., 2010). These miscues required participants to inhibit emotion concepts which were irrelevant but conceptually similar to the target emotion. The inhibition of competing conceptual information is a key feature of semantic control (Gray, 2020; Hoffman, 2018), and lower accuracy under this condition was therefore anticipated. In comparison, across-valence miscues that were less conceptually similar, did not affect participants' accuracy. We observed equivalent effects of within-valence miscues for SA patients and control participants, consistent with evidence that priming irrelevant emotion labels can interfere with healthy adults' identification of discrete facial emotion portrayals (Fugate et al., 2018; Lindquist et al., 2006). This effect was expected to be larger in patients than in healthy controls; subsequent work employing a larger sample of SA patients is needed to establish if the effect size is equivalent for these two groups.

3.6.1. *Limitations*

There are some limitations stemming from the remote testing that we employed as a result of the COVID-19 pandemic. Under these restrictions it was not possible to obtain full structural scans of four patients in the current sample, limiting our ability to associate impaired emotion perception with lesion site and therefore to make precise neuroanatomical conclusions. Furthermore, remote testing directly led to the exclusion of more severely-impaired SA patients who were unable to engage with the technological demands of the tasks. Communication was also more challenging under these conditions, and the instructions of Study 3.1 were complex – yet the patient group showed no impairment in the control task which involved sorting by identity. They were similarly impaired in Study 3.2, which probed emotion categorization with far simpler task demands. Viewing conditions during online testing were also more challenging than in face-to-face testing. Controls showed similar performance on the emotion free sort condition here (63.3% correct) and in the original paradigm (70.0% correct; Lindquist et al., 2014). However, there was a difference on the

identity sort task: all SD patients and controls in Lindquist et al. performed perfectly, while in our Study 3.1, three patients and five controls made errors. Participants who made errors on this task did not show poorer performance on the emotion sort task (see Section 3.4.2.1); consequently, these errors may have reflected suboptimal viewing conditions and the challenges of computer-assisted testing.

In common with other studies of SA, the patients in the current sample were not solely impaired on background tests of semantic control and did present with some non-verbal and non-semantic deficits in executive function and visuospatial processing (Thompson et al., 2018). This is unsurprising given that the semantic control network is adjacent to left hemisphere components of the bilateral multiple-demand network, which supports executive control across domains (Gao et al., 2021; Wang et al., 2020). As a result, the two networks are often damaged together by stroke (Souter, Wang et al., 2022 [Chapter 2 of this thesis]), although deficits of semantic control are likely to be more severe following left-hemisphere stroke (Thompson et al., 2016), since this network is strongly left-lateralised (Gao et al., 2021; Gonzalez Alam et al., 2019). A more general cognitive impairment was particularly marked in background neuropsychological testing for P15, who also presented with the poorest overall performance in both Studies 3.1 and 3.2. It is worth noting that P15 did present with preserved performance on some demanding non-semantic tasks, including the Test of Everyday Attention, and the Trail Making Test B. Furthermore, some of the easier tasks that P15 was below the official cut-off for (e.g., Trail Making Test A, word-picture matching) nevertheless elicited very few errors. Regardless, we cannot provide definitive evidence that non-semantic impairments in the sample did not contribute to poor emotion categorization, even though the SA group were not impaired on a control identity sort task, relative to the comparison group.

Comparisons between the current SA patients and the SD patients of Lindquist et al. (2014) should be made cautiously given the disparities in the testing environment. The current findings allow only for qualitative comparison between these groups. A recent study of 16 SD patients provided evidence of correlations between category fluency performance, facial emotion recognition ability, and conceptual and taxonomic knowledge about emotion (Bertoux et al., 2020). Future research with a similarly large sample of both SD and SA patients could be helpful in understanding the effects of both the nature and severity of semantic impairment on emotion categorization deficits. It would also be interesting to relate deficits of emotional recognition in SA to emotional difficulties commonly seen following

stroke, including depression and anxiety (Døli et al., 2017) and alexithymia (Hobson et al., 2020). However, the paradigms employed here probed semantic valence (i.e., knowledge about affective qualities, e.g., knowing that flowers are positively valenced), rather than experiential affect (e.g., feeling delight; Itkes et al., 2019; Itkes & Kron, 2019), and as such do not address this issue directly.

Recently, Sauter (2018) argued that language-based models of emotion processing may place too much weight on the assumption of a direct link between lexical, conceptual, and perceptual processing of emotion, and that "inferences cannot be drawn directly from findings in one domain (e.g., emotion words) to another (e.g., emotion perception, emotion production, or emotion experience)" (p. 112). While the current studies used verbal and auditory prompts to facilitate access to emotion concepts, our analysis was confined to the knowledge of and perception of facial emotion portrayals. These findings therefore cannot be directly applied, for example, to the ability to sort words by emotion, or to the ability to appropriately experience subjective feelings of anger. As semantic control impairments in SA are multimodal (Jefferies, 2013), future research could test the prediction that emotion processing impairments extend across modalities (see Osborne-Crowley et al., 2020 for an example from patients with traumatic brain injury).

3.6.2. *Conclusion*

The current study provides evidence that impaired controlled semantic retrieval in SA disrupts the perception of discrete emotion categories for portrayals of facial emotion, and that manipulating access to relevant conceptual information can affect emotion perception, even in the absence of impaired semantic or language processing. These findings lend support to the constructionist model of emotion in suggesting a foundational role of conceptual knowledge in supporting emotion perception. Access to emotion category representations appears to involve semantic control processes, which are required to resolve ambiguity and to select representations among competing distractors.

3.7. Link to Chapter 4

Adding to existing knowledge concerning the constructionist model of emotion processing (Lindquist et al., 2015), Chapter 3 of this thesis provided evidence that impairments in controlled semantic retrieval in semantic aphasia (SA) can impair categorical emotion perception, as has previously been demonstrated following loss of amodal concepts in semantic dementia (Lindquist et al., 2014). These findings add weight to the claim that discrete emotion perception is not innate and universal, but relies on existing knowledge of the world, and the ability to access it in a context-appropriate manner. Discrete emotion states can be considered a superordinate category, containing states such as disgust, happiness, and anger. A distinction should be drawn between this categorisation and the representation of hedonic valence. Valence is a core dimension of affect, reflecting whether a stimulus can be considered to be negative or positive in nature, on a continuous scale. Valence interacts with the independent dimension of arousal to constitute the emotional content of a stimulus (Lang et al., 1993).

Separate from the representation of discrete emotion states, there may be interactions between semantic representation and the processing of hedonic valence. The hub-and-spoke model of semantic cognition considers that heteromodal semantic representations (stored in the ventral anterior temporal lobes) rely on input from modality-specific 'spokes' across the cortex, including valence (Lambon Ralph et al., 2017). Indeed, concepts have been argued to have a basis in valence, as they do in action and perceptual features (Martin, 2016; Zhou et al., 2021). Valence has been shown to play an important role in the learning and representation of words, particularly those that are abstract in nature (Ponari et al., 2020; Vigliocco et al., 2014). Evidence from Marino Dávolos et al. (2020) suggests that valence congruency between words can facilitate semantic matching, particularly for weak semantic associations. This has not yet been studied in the context of impaired semantic control. In Chapter 4 of this thesis, we investigated how access to valence information affects judgements of global semantic relatedness, as well as how global semantic relatedness impacts ability to match words according to valence. This was assessed both in healthy adults and with SA patients. In doing so, we aimed to investigate the relationship between conceptual knowledge and the core affective dimension of valence, as well as any exacerbating effects of semantic control impairments.

Chapter 4: How do valence and meaning interact? The contribution of semantic control

This chapter is publicly available as a preprint:

Souter, N. E., Reddy, A., Walker, J., Marino Dávolos, J., & Jefferies, E. (2022). How do valence and meaning interact? The contribution of semantic control. *PsyArXiv*. https://doi.org/10.31234/osf.io/vte82.

Data for this chapter are publicly available on the Open Science Framework (https://osf.io/fgjcs/).

Acknowledgements and author's contribution

This project was conceptualised by Nick Souter along with co-authors Elizabeth Jefferies and Julián Marino Dávolos. Nick Souter oversaw the creation of stimuli, experimental design, coding of experimental scripts in Python, data analysis, and data curation. Data for both experiments was collected by Nick Souter along with co-authors Ariyana Reddy and Jake Walker, for whom this project served as the basis for their MSci research project. Ariyana Reddy and Jake Walker also assisted in the creation of stimuli. Zhiyao Gao provided advice for the process of obtaining Word2Vec scores for stimuli. Nick Souter wrote the full original draft of this paper. Elizabeth Jefferies edited manuscript drafts, and Ariyana Reddy, Jake Walker, and Julián Marino Dávolos provided feedback on the final draft.

4.1. Abstract

The hub-and-spoke model of semantic cognition proposes that conceptual representations in a heteromodal 'hub' interact with and emerge from modality-specific features or 'spokes', including valence (whether a concept is positive or negative), along with visual and auditory features. As a result, valence congruency might facilitate our ability to link words conceptually. Semantic relatedness may similarly affect explicit judgements about valence. Moreover, conflict between meaning and valence may recruit semantic control processes. Here we tested these predictions using two-alternative forced-choice tasks, in which participants matched a probe word to one of two possible target words, based on either global meaning or valence. Experiment 4.1 examined timed responses in healthy young adults, while Experiment 4.2 examined decision accuracy in semantic aphasia patients with impaired controlled semantic retrieval following left hemisphere stroke. Across both experiments, semantically-related targets facilitated valence matching, while related distractors impaired performance. Valence congruency was also found to facilitate semantic decision-making. People with semantic aphasia showed impaired valence matching and had particular difficulty when semantically-related distractors were presented, suggesting that the selective retrieval of valence information relies on semantic control processes. Taken together, the results are consistent with the hypothesis that automatic access to the global meaning of written words affects the processing of valence, and that the valence of words is also retrieved even when this feature is task-irrelevant, affecting the efficiency of global semantic judgements.

4.2. Introduction

A representation of PUPPY may rely on knowledge concerning typical visual features, characteristic yapping noises, and that puppies are positive entities who evoke joy. It can be argued that valence (whether items are pleasant or unpleasant) is a core feature of heteromodal concepts. The 'hub-and-spoke' framework suggests that semantic representation relies on interactions between a transmodal hub in the anterior temporal lobes (ATL) and modality-specific spokes; including perceptual and motor features along with valence (Lambon Ralph et al., 2017). Amygdala and orbitofrontal cortex may support the integration of emotion-based features through connections with ATL (Riberto et al., 2019). Patients with semantic dementia (SD), following ATL atrophy, show degradation of conceptual knowledge across tasks that probe the same concepts (Jefferies & Lambon Ralph, 2006), and experience difficulty categorising facial emotions (Lindquist et al., 2014). This suggests that the ability to make sense of discrete emotions relies on conceptual representations (Lindquist et al., 2015). While discrete emotion categories are dissociable from hedonic valence as a fundamental property of stimuli, it may be that these emotion states rely particularly on valence as a feature, given that they correspond to subjective states of feeling. Concepts are grounded in valence as well as action and perception (Martin, 2016). Indeed, valence information benefits abstract word learning (Ponari et al., 2018) and modulates activation in the anterior cingulate cortex, important for abstract word processing (Vigliocco et al., 2014). In this way, valence can be considered a semantic feature. Conceptual information should therefore modulate the accessibility of valence features and vice versa.

Semantic cognition relies not only on heteromodal representations, but also on the ability to flexibly shape their retrieval; 'semantic control' (Lambon Ralph et al., 2017). Semantic control demands are maximised when meaning is ambiguous and/or there is competition from task-irrelevant aspects of meaning (Jefferies et al., 2019). Neuropsychological studies reveal a double dissociation between degraded conceptual knowledge in SD, and disordered multi-modal semantic control in semantic aphasia (SA) following left frontal-temporal-parietal stroke (Jefferies & Lambon Ralph, 2006). SA patients are sensitive to executive demands of semantic tasks (Jefferies, 2013): they have difficulty retrieving non-dominant conceptual information and are susceptible to semantic distractors (Noonan et al., 2010). This frequently co-occurs with domain-general executive dysfunction (Thompson et al., 2018). SA patients are highly sensitive to cues that reduce the need to

internally constrain retrieval (Noonan et al., 2010). Facial emotions can cue appropriate interpretation of ambiguous words that have both positive and negative meanings in SA (Lanzoni et al., 2019). Emotional features may modulate semantic control demands by constraining retrieval. SA patients also show deficits in accessing emotions from facial portrayals; common processes may constrain the retrieval of meaning and emotion (Souter et al., 2021 [Chapter 3 of this thesis]).

Neuroimaging research implicates a distributed but largely left-lateralised 'semantic control network' (SCN) in semantic retrieval, which includes anterior left inferior frontal gyrus (IFG) and posterior middle temporal gyrus (pMTG; Jackson, 2021). These regions are adjacent to domain-general control regions (Gao et al., 2021). Lesion to and structural disconnection between these left-hemisphere regions predicts semantic control deficits in SA, while domain-general executive deficits are associated with cross-hemispheric disconnection (Souter, Wang, et al., 2022 [Chapter 2 of this thesis]). Regions of SCN are also implicated in tasks involving valence – including comparisons of lexical decision for valenced versus neutral words (Pauligk et al., 2019) and the resolution of conflict from valence incongruency (Gao et al., 2020). SCN may play a role in controlling the retrieval of emotion along with other aspects of meaning.

Semantic control may be required to match words by valence when they do not share other features (PUPPY and CAKE both have positive valence but no semantic link), since a single task-relevant feature must compete with many irrelevant features. This has been reported for colour (Thompson-Schill et al., 1997). Global semantic similarity facilitates feature matching, reducing SCN activation (Wang et al., 2020). Global similarity refers to the overall similarity of contexts in which words are used, and should be sensitive to shared features and strength of association. If access to valence irrespective of global similarity requires semantic control, patients with SA should be impaired at valence matching. Furthermore, a mismatch in valence may make it harder to identify global links between words. This effect, based on a single task-irrelevant feature, should be smaller than the effect of global semantic similarity on valence matching. Valence congruency between words facilitates healthy adults' detection of global semantic relationships, particularly for weak associations (Marino Dávolos et al., 2020). This may be magnified in SA due to difficulty resolving competition from valence. Here, we investigated effects of (i) semantic relatedness on the ability to match words by valence and (ii) valence congruency on the ability to match words by semantic relatedness. In Experiment 4.1, we studied healthy young adults, asked to

respond as fast and accurately as possible. In Experiment 4.2, we observed SA patients and age-matched controls to establish if these effects are magnified by semantic control deficits.

4.3. Experimental Paradigm

4.3.1. Stimuli

Stimuli were nouns taken from a database (Warriner et al., 2013) which reports mean valence, arousal, and dominance of words on a scale from 1 to 9, based on participant ratings. We classified words above 6 as positively valenced, between 4 and 6 as neutral, and below 4 as negative[11]. We excluded words with a standard deviation of valence ratings above 2, which may have ambiguous meaning (e.g., 'jam') or diverse emotional reactions (e.g., 'religion'). We assessed the strength of association between each probe-target and probe-foil pair using word2vec (Mikolov et al., 2013), a measure of semantic distance between words based on co-occurrence in text and an effective proxy for semantic relatedness (Pereira et al., 2016). Other approaches are available, such as asking participants to self-generate associations. Co-occurrence was the most practical way of measuring semantic relatedness while balancing psycholinguistic properties. An association was considered 'strong' if word2vec was above 0.2, 'weak' if between 0.1 and 0.2, and negligible if below 0.1. Stimuli were controlled for valence, strength of association, word frequency, and psycholinguistic factors (see Chapter 4 Supplementary Materials section '*Stimulus Properties*'). Negative words were significantly higher in arousal than positive words – a result of attempting to source appropriate valenced stimuli while balancing other factors. To observe for potential effects of this confound, each mixed effects model used in this study was re-run with arousal congruency between probe and target word as a predictor (see Supplementary Table 4.2). Across the majority of models, no effect of arousal was observed. The only exceptions were for response time models in Experiment 4.1, where an effect of arousal was observed for both the binary valence matching and task comparison models. In these cases, higher arousal was associated with faster responses. The inclusion of arousal did not attenuate significant effects in any model. It is therefore likely that observed effects of valence congruency can be largely attributed to valence itself, rather than arousal.

[11] Valenced words included largely emotion-laden terms with acquired affective connotation (e.g., war, rainbow). 9.5% of stimuli could be considered emotion-label, representing affective states (e.g., hope, terror).

4.3.2. Valence Matching Task

The valence matching task required participants to match one of two words to a probe word by valence. The target was always the same valence as the probe, while the foil was the opposite valence. Participants were told: "*your task is to indicate which of the two words on the bottom has the same emotional valence (positive or negative) as the word on the top*". We manipulated strength of semantic association. In the *associated target* condition, the probe had a strong association with the target and no association with the foil. In the *no association* condition, the probe had no association with either response option. In the *associated distractor* condition, the probe had no association with the target but a strong association with the foil. It was predicted that the *associated target* condition would facilitate valence matching through semantic cueing, while the *associated distractor* condition would impair matching by requiring inhibition of the distractor. Example trials can be seen in Figure 4.1a.

4.3.3. Semantic Matching Task

The semantic matching task required participants to match one of two words to a probe by semantic relatedness. Participants were told: "*your task is to indicate which of the two words on the bottom has the strongest connection to the word on top*". Two conditions manipulated valence congruency, a third manipulated association strength. In the *congruent target* condition, the target had a strong association to the probe and was congruent in valence, while the foil had no association and was incongruent. In the *congruent distractor* condition, the target had a strong association to the probe but was incongruent in valence, while the foil had no association but was congruent. In the *weak association* condition, the target had a weak association to the probe, while the foil had no association. Valence congruency was not manipulated here due to challenges sourcing weakly associated targets while manipulating valence. The valence of the foil was congruent with the probe in half of the trials, and incongruent in the remainder. Example trials can be seen in Figure 4.1b.

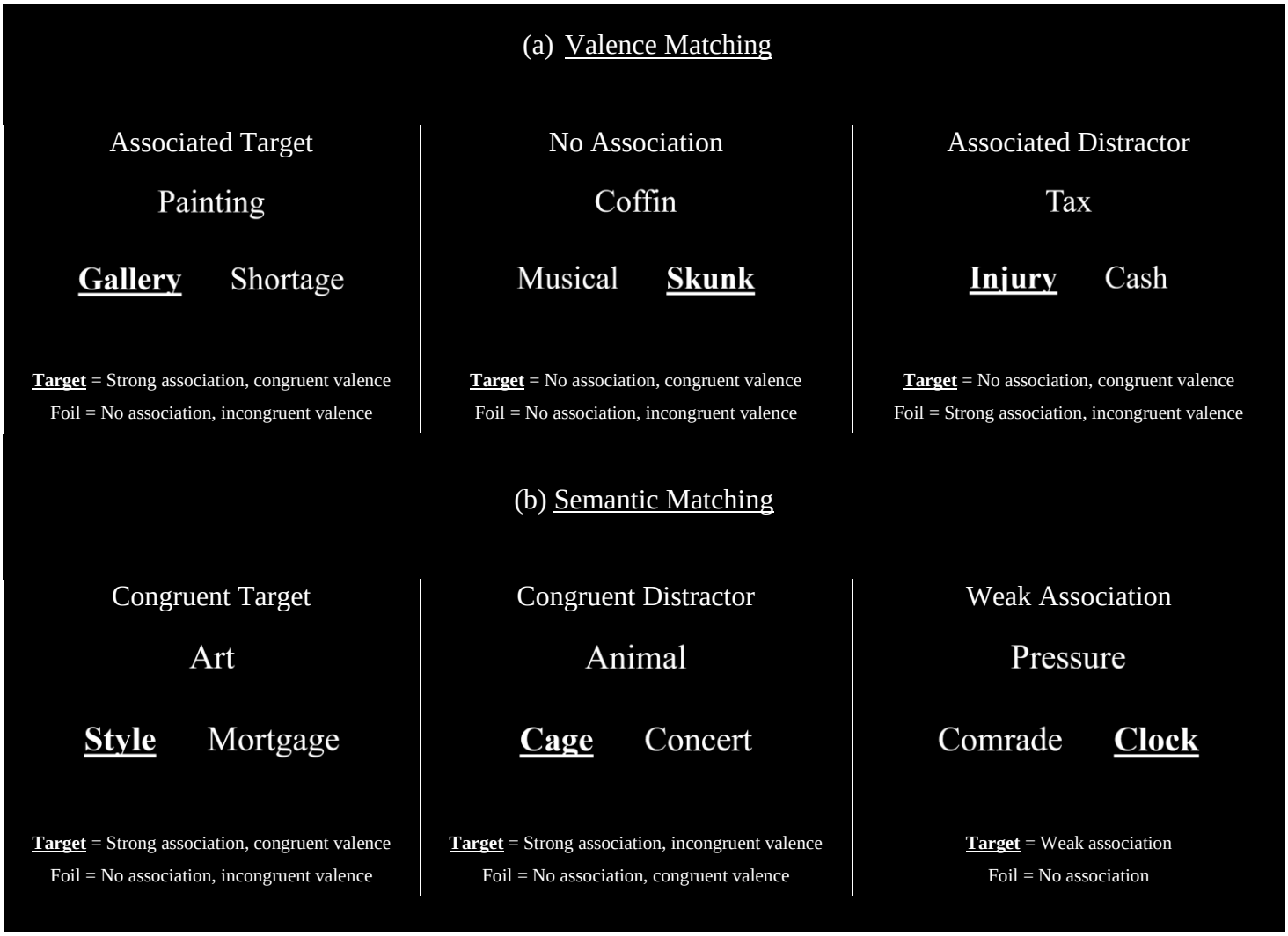


Figure 4.1. Examples of trials in each condition in the (a) valence matching and (b) semantic matching tasks. The relationship to the probe word for both the target and foil is explained for each example. Target words are underlined and in bold.

4.3.4. Trial Structure

The experiment was split across two sessions separated by at least a week, each containing a block of valence matching and of semantic matching. Trial order was randomised within blocks. The same response triads were used across (i) '*valence – associated target*' and '*semantic – congruent target*' and (ii) '*valence – associated distractor*' and '*semantic – congruent distractor*' (target response switched). Triads in the '*valence – no association*' condition were re-used in the '*semantic – weak association*' condition, with one response option replaced with a weakly-associated target. Presentation order was counterbalanced, such that if a given triad appeared in valence matching in session 1, it appeared in semantic matching in session 2. The target response appeared on the left in half

of the trials, and on the right in the remainder. Each condition contained 27 trials, resulting in 81 trials per task, and 162 trials overall.

4.4. Experiment 4.1: Young adults

4.4.1. Method

Ethics approval for both Experiment 4.1 and 4.2 was granted by the York Neuroimaging Centre at the University of York (date: 24/10/2019, project ID: P1363).

4.4.1.1. Participants

Participants were neurologically healthy adults tested on the online platform Gorilla (www.gorilla.sc; Anwyl-Irvine et al., 2020). Eighty-six participants were recruited opportunistically. Participants automatically received an email one week after the first session, prompting them to complete the second. Participants were excluded if they did not complete the second session (N = 11), if they scored below chance (50% accuracy) on any condition (N = 14), or if their median response time for any condition was an outlier (N = 3), as determined in SPSS (version 27.0; IBM Cop, 2020). The final sample consisted of 60 adults (38 female) between the ages of 19 and 41 [Mean (SD) = 25.1 (5.6)].

4.4.1.2. Design

A within-subjects design was used; all participants completed both the valence matching and semantic matching tasks.

4.4.1.3. Procedure

Block order (valence/semantic) was randomised within each session. At the start of each block participants saw instructions explaining the matching strategy and an example trial with explanation of the correct answer. The valence matching instructions did not disclose that association strength would be manipulated, and semantic matching instructions did not disclose that valence congruency or association strength would be manipulated. Participants were instructed to press the '1' key on their keyboard to select the left response option, and '2' to select the right option. Before each block, participants completed six practice trials including feedback. Between blocks, participants saw a screen warning them of the change in task instructions. No time limit was applied.

4.4.1.4. Data Analysis

For each condition we extracted each participant's accuracy (percent correct) and response time (RT; seconds) for correct responses. Median RT, rather than mean RT, was extracted for each condition at the individual-level to reduce effects of outliers. At the group-level, the mean of median RTs for each condition was assessed. We entered accuracy and RT on all conditions into separate principal components analyses (PCA) with varimax rotation, to assess the extent to which performance on conditions load onto common components.

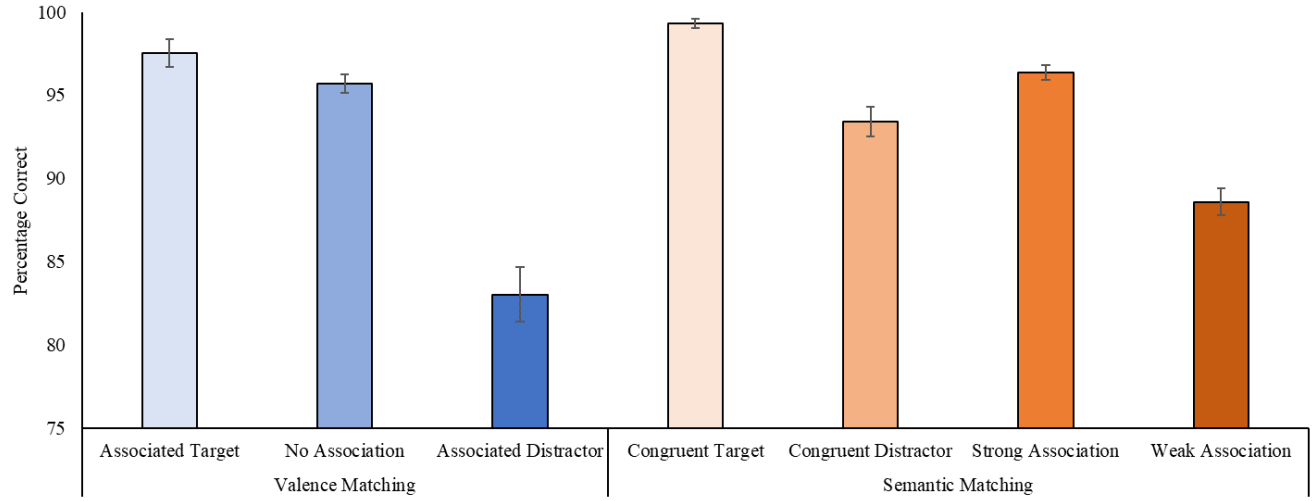
For statistical comparisons of tasks and conditions, we used mixed effects regressions in R (R Core Team, 2020). Models observing accuracy were logistic models, predicting the likelihood of a correct response for a given trial under varying conditions. Those observing RT were linear models. For each RT model, outliers were addressed by removing RTs larger than either 10 seconds or 3 standard deviations above a given participant's mean RT in each condition. RTs were log transformed such that residuals were approximately normally distributed. Each model included participant identity and item (trial) as crossed random factors. Likelihood ratio tests determined the contribution of specific effects and interactions, by statistically comparing full models to nested versions with the respective effect removed, using the chi-square distribution.

Four models were created, for both accuracy and RT data. (1) a '*valence matching'* model restricted to the valence matching task included condition (*associated targe*t vs. *no association* vs. *associated distractor*) as a fixed effect, reflecting the effect of semantic relatedness. (2) A '*semantic matching (binary)'* model included binary association strength (*strong association* vs. *weak association*) as a fixed effect. This *strong association* score was derived by averaging across the *congruent target* and *congruent distractor* conditions. This score should control for valence, as trials are equally split across congruent targets and foils. While target valence congruency was not manipulated for *weak association* trials, the foil was congruent in half trials. (3) This was followed by a '*semantic matching (parametric)*' model, given evidence that valence congruency effects depend on association strength (Marino Dávolos et al., 2020). This allowed us to consider the interaction between valence congruency (*congruent target* vs. *congruent distractor*) and parametric probe-target association strength (using word2vec scores) as fixed factors. We used the same method to assess effects of association strength on valence matching – restricted to the *no association* and *associated distractor* conditions, given that target strength was matched across them. This observes effects of semantically-associated distractors on valence matching as a function

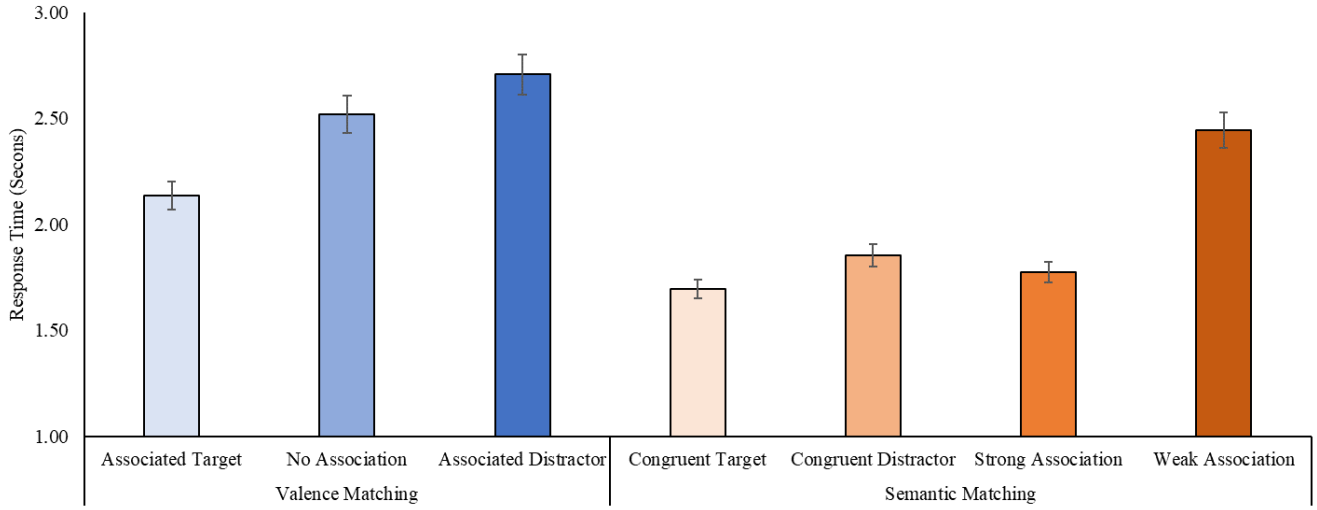
of association strength but does not provide insight into the relationship between valence congruency and processing of meaning. This analysis is reported in the Chapter 4 Supplementary Materials section '*Valence Congruency Mixed Effects Models – Experiment 4.1*'. (4) Finally, a '*task comparison*' model included task (valence vs. semantic) and difficulty (easy ['*valence – associated target*' and '*semantic – congruent target*'] vs. hard ['*valence – associated distractor*' and '*semantic – congruent distractor*']) as fixed effects, as well as their interaction. This allowed us to compare performance across tasks and assess whether either difficulty manipulation was more influential than the other. When necessary, significant effects were followed by post-hoc contrasts in emmeans (Lenth, 2020), which quantify differences based on odds ratios (OR), with Bonferroni correction applied.

4.4.2. Results

Participants' mean accuracy and RT in each condition can be seen in Figure 4.2.



(a) – Accuracy



(b) – Response Time

Figure 4.2. Participants' (a) mean accuracy (percentage correct) and (b) mean response time (seconds) for each task and condition in Experiment 4.1. Error bars reflect one standard error of the mean. The 'Strong Association' bars reflect the average of performance on the 'Congruent Target' and 'Congruent Distractor' conditions.

4.4.2.1. Principal components analysis

PCA revealed two components for accuracy and one for RT (see Table 4.1).

Table 4.1. Rotated component matrices for principal components analysis of Experiment 4.1 with varimax rotation, examining accuracy and response time across conditions.

		Accuracy		Response Time
		Component 1	Component 2	Component 1
Matching Task	Condition	(Eigenvalue = 1.83)	(Eigenvalue = 1.73)	(Eigenvalue = 4.65)
Valence	Associated target	**.772**	-.206	**.845**
	No association	**.806**	.099	**.871**
	Associated distractor	.149	**.701**	**.836**
Semantic	Congruent target	**.705**	.122	**.903**
	Congruent distractor	-.129	**.716**	**.913**
	Weak association	.032	**.841**	**.908**

Note: Strong loadings for each component in bold.

The first accuracy component appears to reflect conditions which should be automatic; valence matching without semantically-associated distractors and semantic matching with valence-congruent targets. The second component appears to reflect conditions which should require controlled processing; valence matching with associated distractors, semantic matching with valence-incongruent targets, and weak associations. The RT factor suggests that faster responses on a given condition are associated with faster responses on all other conditions. Our interpretation is based on the nature of the conditions that load on each component. Alternative interpretations are possible.

4.4.2.2. Mixed effects models

Results of Experiment 4.1 mixed effects models, for both accuracy and RT, can be seen in Table 4.2.

Table 4.2. Output of Experiment 4.1 mixed effects models.

Model	Measure	Variable	Estimate	Lower 95% CI	Upper 95% CI	Likelihood Ratio Test
Valence Matching	Accuracy	Intercept	3.87	3.50	4.25	-
		Condition	**-**	**-**	**-**	**$\chi(2) = 41.5$, $p < .001$***
	Response Time	Intercept	0.75	0.69	0.82	-
		Condition	**-**	**-**	**-**	**$\chi(2) = 29.3$, $p < .001$***
Semantic Matching (Binary)	Accuracy	Intercept	4.73	4.07	5.39	-
		Association strength	**-1.74**	**-2.65**	**-0.82**	**$\chi(1) = 13.3$, $p < .001$***
	Response Time	Intercept	0.60	0.54	0.66	-
		Association strength	**0.30**	**0.24**	**0.37**	**$\chi(1) = 58.4$, $p < .001$***
Semantic Matching (Parametric)	Accuracy	Intercept	2.49	2.04	2.94	-
		Valence congruency	1.28	-0.51	3.08	$\chi(1) = 1.94$, $p = .163$
		Association strength	**6.07**	**4.16**	**7.99**	**$\chi(1) = 37.69$, $p < .001$***
		Valence by strength	**-6.54**	**-11.6**	**-1.43**	**$\chi(1) = 6.10$, $p = .014$***
	Response Time	Intercept	0.97	0.91	1.04	-
		Valence congruency	**-0.37**	**-0.54**	**-0.20**	**$\chi(1) = 17.39$, $p < .001$***
		Association strength	**-0.77**	**-0.93**	**-0.61**	**$\chi(1) = 71.23$, $p < .001$***
		Valence by strength	**0.88**	**0.40**	**1.36**	**$\chi(1) = 12.62$, $p < .001$***
Task Comparison	Accuracy	Intercept	3.97	3.47	4.48	-
		Task	**0.19**	**-0.45**	**0.83**	$\chi(1) = 0.33$, p = .563
		Difficulty	-0.36	-1.12	0.39	$\chi(1) = 0.89$, p = .346
		Task by difficulty	**-1.89**	**-2.92**	**-0.86**	**$\chi(1) = 12.3$, p < .001***
	Response Time	Intercept	0.73	0.66	0.80	-
		Task	**0.14**	**0.07**	**0.20**	**$\chi(1) = 16.1$, p < .001***
		Difficulty	**-0.09**	**-0.17**	**-0.01**	**$\chi(1) = 4.74$, p = .030***
		Task by difficulty	**0.14**	**0.03**	**0.25**	**$\chi(1) = 5.77$, p = .016***

Note: * reflects a significant result. Accuracy models were run in R using lme4 package (version 1.1-25; Bates et al., 2015). As these are logistic models, estimate coefficients reflect log transformation of odds ratios (Larsen et al., 2000). The response time models were run in R using lmerTest package (version 3.1-3; Kuznetsova et al., 2017), response time values are log transformed. The valence matching condition effects do not include estimate values, as these effects are not provided by the overall models. The respective likelihood ratio test results were obtained by comparing the full models to nested versions in which condition effects were removed. CI = confidence interval.

4.4.2.2.1. Valence matching

The binary valence matching model revealed a significant effect of condition for both accuracy and RT, suggesting effects of semantic relatedness on valence matching. To parse this effect, contrasts in emmeans were used to compare both the *associated target* and the *associated distractor* condition to the *no association* baseline (each corrected for four comparisons). For accuracy, this revealed better performance in the *no association* relative to the *associated distractor* condition [OR = 5.3, $p < .001$] but no difference between *no association* and *associated target* [Z = -1.0, $p > 1$]. This is likely the case because accuracy was near ceiling in both *no association* and *associated target*, with associated distractors notably impairing performance. Conversely, for RT, faster responses were observed for *associated target* relative to *no association* [Z = 4.5, $p < .001$], while no difference was observed between *no association* and *associated distractor* [Z = -1.6, $p = .433$]. RTs may be particularly fast during *associated target* given that the semantic associations facilitate automatic responses, reducing the need for deliberation on valence. Despite different patterns across accuracy and RT, these results suggest that semantically-related targets facilitated valence matching, while distractors impaired performance.

4.4.2.2.2. Semantic matching (binary)

The first semantic matching model observed for binary effects of association strength. For both accuracy and RT there was a significant effect of association strength, reflecting higher accuracy on *strong association* than *weak association* trials.

4.4.2.2.3. Semantic matching (parametric)

The semantic task involved separate manipulations of valence congruency and association strength. To establish if these factors interact, a second semantic model was run with a parametric fixed effect of association strength. Stronger associations between probe and target predicted more accurate and faster responses, while valence congruency predicted faster responses. Valence congruency did not affect accuracy. For both measures, a significant interaction was found. These interactions were parsed using the emtrends function of the emmeans package (Lenth, 2020), and visualised using the ggpredict function of the ggeffects package (Lüdecke, 2018); see Figure 4.3[12]. For the *congruent target* condition, greater association strength was associated with a higher probability of a correct response and

[12] Although RT was estimated using a linear mixed effects model, trends visualised are curved as RT values were log-transformed. Similarly, accuracy was estimated using log transformation of odds ratios.

faster responses [accuracy: association = 6.07, LCL[13] = 4.16, UCL = 7.99, RT: association = -0.77, LCL = -0.93, UCL = -0.61]. For the *congruent distractor* condition, no effect of association strength was observed [accuracy: association = -0.47, LCL = -5.20, UCL = 4.27, RT: association = 0.11, LCL = -0.34, UCL = 0.56]. This suggests that benefits of association strength may not occur when participants must resolve inconsistency between valence and meaning. Stronger associations appear more advantageous under less challenging conditions when incongruency is not present.

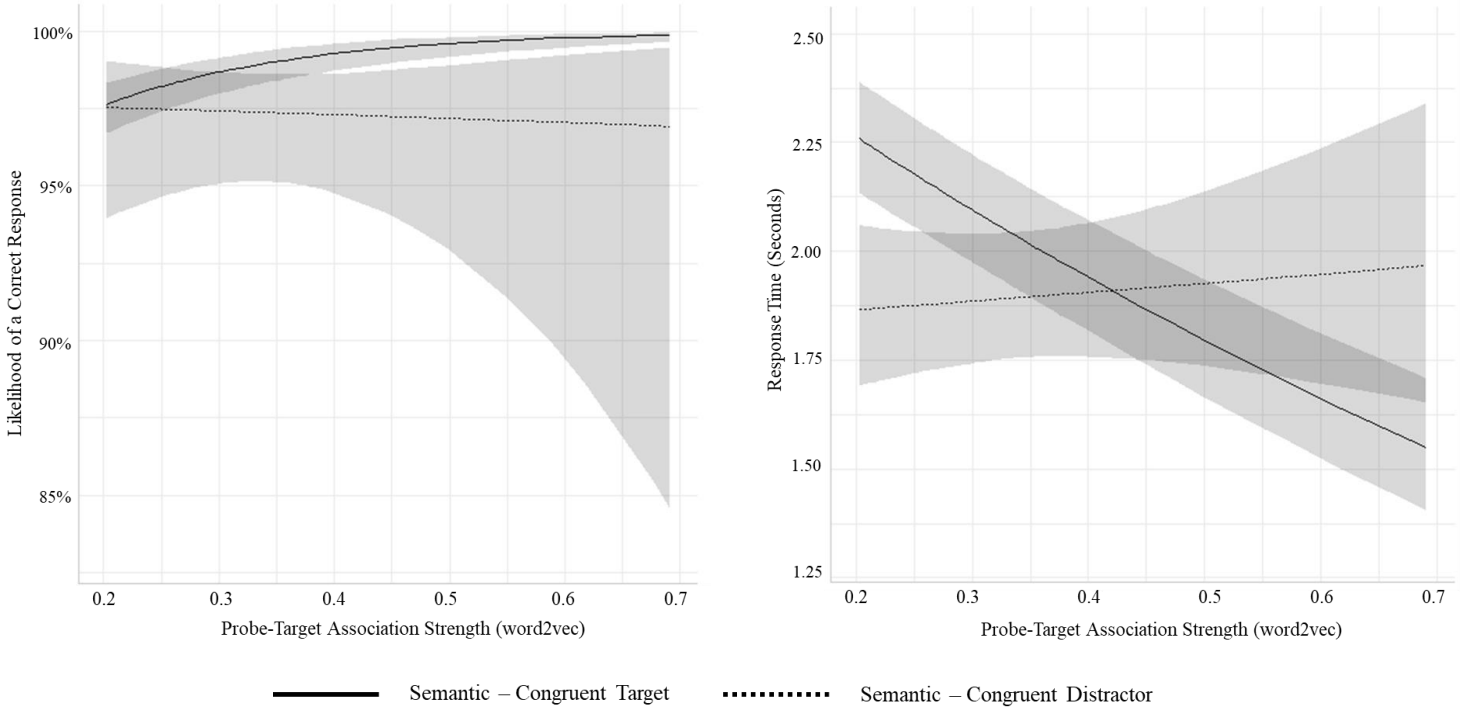


Figure 4.3. Associations between probe-target association strength and both the likelihood of a correct response (left) and response time (right) for the Experiment 4.1 semantic matching task. Grey shaded areas reflect confidence intervals based on the standard errors.

4.4.2.2.4. Task comparison

Finally, we compared the effect of congruency/relatedness across tasks. For RT, we observed a significant effect of task and difficulty, as well as a significant interaction of the two. As reflected in Figure 4.2, this reflects faster responses for easier conditions in each task, and faster responses overall for the semantic matching task relative to the valence matching task. The observed interaction reflects larger effects of semantic relatedness on

[13] LCL = lower confidence limit, UCL = upper confidence limit.

valence matching than of valence congruency on semantic matching (see Figure 4.2), as expected as valence is only one of many semantic features. For accuracy, this same interaction was observed, but no significant main effect of either task or difficulty.

4.5. Experiment 4.2: Semantic aphasia patients

Experiment 4.2 employed the same tasks, with SA patients and age-matched controls.

4.5.1. Method

4.5.1.1. Participants

Participants included five patients and 15 neurologically-healthy controls. All patients had left hemisphere stroke. They had an average age of 61.5 (SD = 6.3), average age of leaving education of 19.8 (SD = 3.6), and an average of 13.6 years (SD = 5.0) since stroke. Controls had an average age of 65.0 (SD = 6.7) and average age of leaving education of 21.2 (SD = 3.0). Patients were selected from a database of SA patients who were recruited from communication support groups across Yorkshire. Patients in the current sample were those able to engage with remote testing due to restrictions during the COVID-19 pandemic. Information on lesion location, when available, is reported in the Chapter 4 Supplementary Materials section '*Lesion Analysis'* and displayed in Supplementary Figure 4.3.

4.5.1.2. Background neuropsychological testing

Patients were tested on language, memory, visuospatial processing, executive function, and semantic cognition. Each patient's performance on the background neuropsychology measures is shown in Supplementary Table BN.1, while Supplementary Table BN.2 provides data on tests of semantic cognition. Background Neuropsychology Supplementary Materials also provide task descriptions (see Section '*Description of Assessments'*) and an interpretation of the sample's performance on these measures (see Section '*Chapter 4 Sample Summary'*). Patients showed minimal impairment in word repetition, but all showed impaired verbal fluency. Four had impaired verbal working memory. All had preserved visuospatial processing. Two were impaired on at least one test of executive function.

On the Cambridge Semantic Battery (Bozeat, Lambon Ralph, et al., 2000), patients showed variable performance on picture naming, but invariably improved following phonemic cueing. Patients performed near ceiling on word-picture matching and showed at least some impairment on picture and word versions of the associative Camel and Cactus

Test. All showed impairment on assessments which manipulated semantic control: including difficulty retrieving subordinate thematic associations, deleterious effects of semantic distractors, and benefits of contextual cueing. Given relatively preserved performance on aspects of the Cambridge Semantic Battery, patients should be conceptualised as presenting with impairments in semantic control, rather than deficits in semantic representation as seen in SD (Jefferies & Lambon Ralph, 2006). All patients were impaired on at least one verbal and non-verbal measure of semantic control, consistent with the approach taken by Jefferies and Lambon Ralph (2006), although the current sample may have relatively mild impairment due to the use of demanding semantic tasks. Our sample is also consistent with the original definition of SA as impairment in the flexible manipulation of information for abstract and symbolic processing (Head, 1926). Patients' deficits extend beyond those reported by Head (1926), with added evidence of impaired language, working memory, and executive function. Patients were not excluded based on impairments beyond the semantic domain. Patients were grouped based on the presence of shared semantic control impairments, as in prior studies (e.g., Stampacchia et al., 2018). Using this group, we can ask whether semantic control impairments in SA extend to valence matching, but cannot rule out the contribution of non-semantic impairments.

Patients' degree of semantic control impairment was quantified using the results of PCA previously conducted on a larger sample (N = 17, including the current five; Souter, Stampacchia, et al., 2022 [Chapter 5 of this thesis]). Regression scores were taken as patients' semantic control composite scores. These can be seen in Supplementary Table BN.2. Loadings for this component are in Table 5.1.

4.5.1.3. Design

We used a mixed design, with patients and controls completing both the valence matching and semantic matching tasks.

4.5.1.4. Procedure

The paradigm was coded in PsychoPy3 (Peirce et al., 2019) and run remotely over Zoom (Zoom Video Communications Inc., 2016). The researcher shared their screen such that the participant could see the experiment, and gave them remote control of the cursor. At the start of each session, participants were shown instructions and practice trials as in Experiment 4.1 (see Section 4.4.1.3). To respond, participants moved the cursor over the response they wished to select. The researcher then recorded their choice by pressing a button

– an analogue to pointing at the screen, the method typically employed during our in-person testing.

4.5.1.5. Data Analysis

Accuracy (percent correct) was the dependent measure. Each patient was classified as either impaired or not impaired on each condition using Singlims (Crawford et al., 2010), which compares an individual score to the respective control mean and standard deviation. One-tailed p-values below .05 were taken as reflecting impairment.

As in Experiment 4.1, we used mixed effects logistic regressions in R (R Core Team, 2020). All models were fit by maximum likelihood, based on Gaussian Hermite approximation, and run using the lme4 package (version 1.1-25; Bates et al., 2015). Models predicted the likelihood of a correct response for a given trial under varying conditions and included participant identity and item as random factors. Likelihood ratio tests determined the contribution of specific effects and interactions, by statistically comparing full models to nested versions with the respective effect removed, using the chi-square distribution. These models replicated the design used for Experiment 4.1, with the addition of effects and interactions of group.

Four models were created. (1) A '*valence matching*' model restricted to the valence matching task used group (patients vs. controls), condition (*associated target* vs. *no association* vs. *associated distractor*), and their interaction as fixed effects. (2) A '*semantic matching (binary)*' model restricted to the semantic matching task used group (patients vs. controls), binary association strength (*strong association* vs. *weak association*) and their interaction as fixed effects. As in Experiment 4.1, *strong association* trials were comprised of both *congruent target* and *congruent distractor* trials. (3) This was followed by a '*semantic matching (parametric)'* model, which allowed us to consider the interaction between valence congruency (*congruent target* vs. *congruent distractor*) and parametric probe-target association strength (using word2vec scores), across groups (patients vs. controls)[14]. (4) Finally, a '*task comparison*' model included group (patients vs. controls), task (valence vs. semantic), and difficulty (easy ['*valence – associated target*' and '*semantic – congruent target*'] vs. hard ['*valence – associated distractor*' and '*semantic – congruent distractor*']) as

[14] As in Experiment 4.1, we used the same method to assess the effect of association strength on valence matching – restricted to the *no association* and *associated distractor* conditions. This analysis is reported in the Chapter 4 Supplementary Materials section '*Valence Congruency Mixed Effects Models – Experiment 4.2*'.

fixed effects. Each possible interaction was included. When necessary, interactions were followed by post-hoc contrasts in emmeans (Lenth, 2020), which quantify differences based on odds ratios (OR), with Bonferroni correction applied.

4.5.2. Results

4.5.2.1. Impairment of individual patients assessed with Singlims

Each patient's percentage accuracy for each condition, and average accuracy for patients and controls, can be seen in Figure 4.4. Conditions on which patients were impaired, determined in Singlims, are reflected by asterisks. In the valence matching task, patients performed near ceiling on the *associated target* condition, with none impaired. Two patients were impaired on the *no association* condition. Three were impaired on the *associated distractor* condition, performing at or below chance-level. In the semantic matching task, patients generally performed near ceiling on the *congruent target* condition, with only one impaired. None were impaired on the *congruent distractor* condition. Only one was impaired on *strong association* trials (the confluence of *congruent target* and *congruent distractor*). Three patients were impaired on the *weak association* condition, with one performing close to chance.

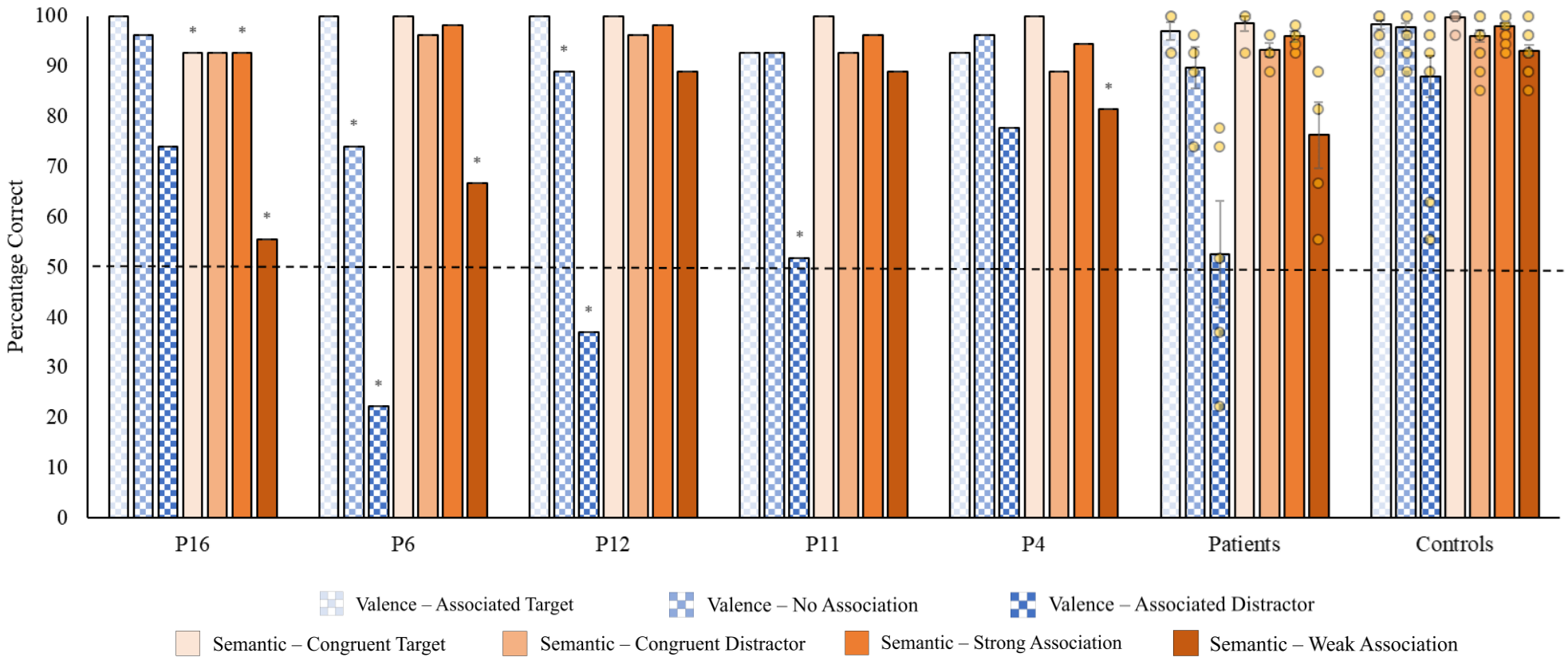


*Figure 4.4. Percentage correct for each condition in the valence and semantic matching tasks for each patient and for the average of the patient and controls groups. * reflects impairment relative to controls based on Singlims analysis. The dotted line reflects chance level performance (50%). Individual data points for both patients and controls for each condition are represented by yellow circles. Error bars reflect one standard error of the mean. Patients are ordered left to right in descending order of semantic control impairment, on the basis of their semantic control composite score.*

4.5.2.2. Group comparison mixed effects models

Experiment 4.2 mixed effects logistic regressions are in Table 4.3.

Table 4.3. Output of Experiment 4.2 mixed effects logistic regressions.

Model	Variable	Estimate	Lower 95% CI	Upper 95% CI	Likelihood Ratio Test
Valence Matching	Intercept	3.08	2.27	3.88	-
	Group	**1.64**	**0.80**	**2.49**	**$\chi(1) = 11.9$, $p = .001$***
	Condition	**-**	**-**	**-**	**$\chi(2) = 57.0$, $p < .001$***
	Group by condition	**-**	**-**	**-**	**$\chi(2) = 9.60$, $p = .008$***
Semantic Matching (Binary)	Intercept	3.91	3.04	4.78	-
	Group	**1.32**	**0.41**	**2.24**	**$\chi(1) = 7.44$, $p = .006$***
	Association strength	**-3.07**	**-3.84**	**-2.31**	**$\chi(1) = 69.5$, $p < .001$***
	Group by association strength	**0.90**	**0.21**	**1.58**	**$\chi(1) = 6.53$, $p = .011$***
Semantic Matching (Parametric)	Intercept	0.80	-0.05	1.66	-
	Group	**2.38**	**1.49**	**3.26**	**$\chi(1) = 19.2$, $p < .001$***
	Valence congruency	**4.15**	**1.07**	**7.23**	**$\chi(1) = 7.09$, $p = .008$***
	Probe-Target association	**10.12**	**6.70**	**13.54**	**$\chi(1) = 42.9$, $p < .001$***
	Group by congruency	-1.27	-4.05	1.50	$\chi(1) = 0.79$, $p = .374$
	Group by association	-2.93	-6.36	0.51	$\chi(1) = 2.79$, $p = .095$
	Valence congruency by association	**-13.22**	**-21.73**	**-4.71**	**$\chi(1) = 8.33$, $p = .004$***
	Group by association by congruency	2.18	-5.50	9.86	$\chi(1) = 0.30$, $p = .584$
Task Comparison	Intercept	2.81	1.91	3.72	-
	Group	**1.80**	**0.87**	**2.73**	**$\chi(1) = 12.4$, $p < .001$***
	Task	0.80	-0.14	1.74	$\chi(1) = 2.82$, $p = .093$
	Difficulty	0.98	-0.22	2.18	$\chi(1) = 2.65$, $p = .104$
	Group by task	-0.20	-1.15	0.75	$\chi(1) = 0.17$, $p = .682$
	Group by difficulty	-0.98	-2.10	0.14	$\chi(1) = 3.00$, $p = .083$
	Task by difficulty	**-4.44**	**-6.03**	**-2.85**	**$\chi(1) = 32.1$, $p < .001$***
	Group by task by difficulty	**1.89**	**0.44**	**3.34**	**$\chi(1) = 6.58$, $p = .010$***

Note: * reflects significance at the .05 threshold. Models were run in R using lme4 package (version 1.1-25; Bates et al., 2015). As these are logistic models, estimate coefficients reflect log transformation of odds ratios (Larsen et al., 2000). The valence matching condition effect and group by condition interaction do not include an estimate value, as these effects are not provided by the overall model. The respective likelihood ratio test results were obtained by comparing the full model to nested versions in which all condition main effects or interactions were removed. CI = confidence interval.

4.5.2.2.1. Valence matching

The valence matching model revealed significant effects of group and condition, and a group by condition interaction. The effect of group reflected higher accuracy in controls than patients. To parse the interaction, contrasts in emmeans compared performance on each

condition between groups. While no difference was found for the *associated target* condition (OR = .48, $p > 1$), controls were more likely than patients to produce a correct response in the *no association* (OR = .13, $p = .002$) and *associated distractor* (OR = .08, $p < .001$) conditions. This suggests impaired valence matching in patients, most notable in the presence of related distractors, that is ameliorated by related targets. When running within-group contrasts (Supplementary Table 4.5), both groups show reduced accuracy following associated distractors, relative to baseline. Neither sees a significant improvement from associated targets. While patients do not benefit from related targets in absolute terms, this is the only condition on which they do not present with impairment relative to controls.

4.5.2.2.2. Semantic matching (binary)

The first semantic matching model observed for binary effects of association strength. Again, controls were more likely to produce a correct response than patients. There was also a significant effect of association strength, reflecting higher accuracy on *strong association* than *weak association* trials. Finally, a significant group by association strength interaction reflects that patients were disproportionately impaired by weak associations (see Figure 4.4).

4.5.2.2.3. Semantic matching (parametric)

The second semantic matching model looked for parametric effects of association strength, and interactions with group and valence congruency. Controls were more likely to produce a correct response than patients. We observed an effect of valence congruency, reflecting higher accuracy in the *congruent target* than *congruent distractor* condition (see Figure 4.4). We observed a significant effect of probe-target association strength, and an interaction between strength and valence congruency. This interaction was parsed using the emtrends function of the emmeans package (Lenth, 2020), and visualised using the ggpredict function of the ggeffects package (Lüdecke, 2018; Figure 4.5). Across groups, a positive effect of association strength on accuracy was found for the *congruent target* condition (association = 8.66, LCL = 5.79, UCL = 11.52). In the *congruent distractor* condition, no effect was observed (association = -3.48, LCL = -9.89, UCL = 2.94).

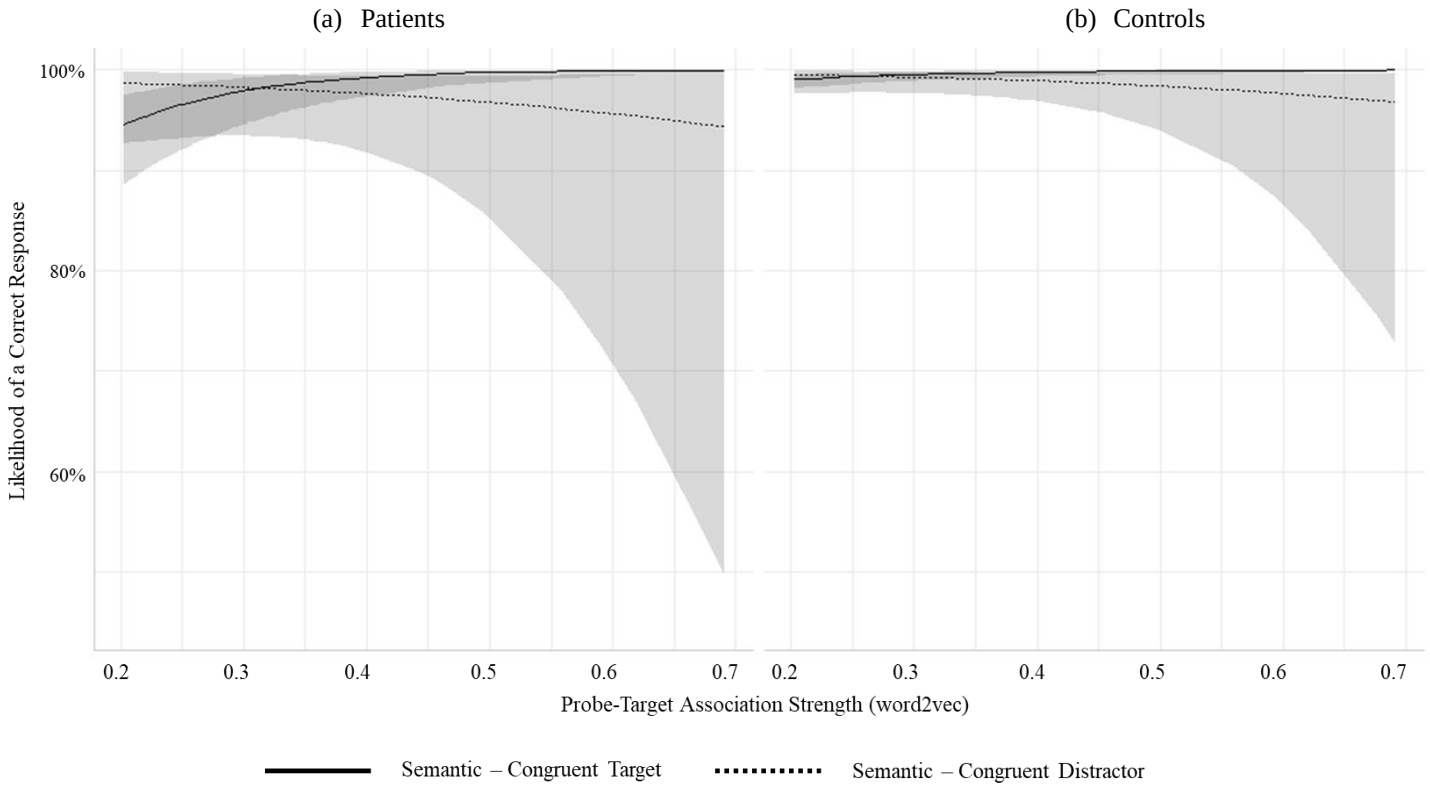


Figure 4.5. Associations between probe-target association strength and the likelihood of a correct response for the Experiment 4.2 semantic matching task in (a) semantic aphasia patients and (b) control participants. Grey shaded areas reflect confidence intervals based on the standard errors.

4.5.2.2.4. Task comparison

A significant effect of group reflected that controls were more likely to provide correct responses than patients. There was a task by difficulty interaction, and a group by task by difficulty interaction. As reported in Section 4.2.2.1, patients were less likely to produce a correct response than controls for *valence – associated distractor* trials but not for *valence – associated target* trials. No group differences were observed for *semantic – congruent target* (OR = .13, p = .469), or *semantic – congruent distractor* trials (OR = .45, p = .746). Effects of semantic relatedness on valence matching were larger than effects of valence congruency on semantic matching, particularly for patients (see Figure 4.4). This might reflect difficulty selecting goal-relevant features when semantic control demands are high.

4.6. Discussion

The hub-and-spoke model implicates valence as a feature of semantic concepts (Lambon Ralph et al., 2017), supported by research into abstract word processing (Ponari et al., 2018; Vigliocco et al., 2014). Accordingly, valence may influence judgements of semantic relatedness. Due to modulation of semantic control demands, global semantic similarity may influence ability to match words by valence. Such effects may be exaggerated in SA patients with impairments in constraining internal information. In young adults with a sensitive measure of RT (Experiment 4.1) and in five left-hemisphere stroke patients with SA and age-matched controls (Experiment 4.2), we found evidence that (i) accessing word valence is vulnerable to interference from overall meaning; (ii) valence congruency can facilitate access to word meaning, (iii) effects of semantic relatedness on valence matching are larger than effects of valence congruency on semantic matching, and (iv) effects of semantic distractors on valence matching are increased in SA. We further demonstrated that in the context of strong semantic associations, parametric increases in probe-target association strength facilitate responses only when words are congruent in valence. Finally, participants were more accurate and faster when retrieving strong than weak semantic associations – heightened in SA.

Valence can be considered a semantic feature, as concepts are grounded in valence as they are for action and perception (Martin, 2016). A distinction can be made between 'affective' valence; experiencing something as negative – and 'semantic' valence; knowing something is negative (Itkes & Kron, 2019). One may understand that a flower is a positive entity without deriving joy. This distinction may be reflected in the separation between emotion-laden words that are imbued with affective connotations, and emotion-label words that convey affective states (Zhang et al., 2017). Only 9.5% of words across conditions were emotion-label, meaning terms were largely emotion-laden. The intersection of valence and meaning is consistent with theory that perception of discrete emotions, which themselves are inherently valenced, relies on semantic knowledge (Lindquist et al., 2015). Indeed, this ability is impaired following deficits in semantic storage (Lindquist et al., 2014) and control (Souter et al., 2021 [Chapter 3 of this thesis]). Matching words by valence may require participants to focus on a specific feature while disregarding others that together determine global similarity. This may account for why valence matching was impaired by related distractors; this requires inhibition of task-irrelevant features. Accordingly, SA patients were

disproportionately affected by this manipulation. SA patients were frequently impaired on valence matching even in the absence of distractors. Patients were not impaired relative to controls in the context of semantically-related targets, suggesting facilitatory effects of global relatedness in accessing concept valence. The observed effects of cueing and miscueing in SA are consistent with prior evidence (Noonan et al., 2010). The current findings suggest an important role of valence in the lexicon; it may facilitate access to other featural and contextual aspects of concepts.

Due to dominance of global relatedness over specific features (Thompson-Schill et al., 1997), effects of valence on semantic judgements were predicted to be modest. Nevertheless, we saw improved semantic matching in the context of valence-congruency. This is consistent with prior evidence of facilitatory effects of valence congruency on semantic matching (Marino Dávolos et al., 2020). Due to the design employed, we could not replicate previous analysis from Marino Dávolos et al. (2020), demonstrating that valence congruency is particularly helpful for retrieving weak associations. Valence congruency was only manipulated for strongly-associated word pairs. We instead looked for effects of parametric probe-target association strength under conditions of valence-congruency and incongruency. Greater association strength facilitated semantic matching when the probe and target were congruent in valence, but not when they were incongruent. Benefits of stronger associations were reduced when participants needed to resolve valence incongruency between the probe and target, while disregarding valence-congruent distractors. Given the results of Marino Dávolos et al. (2020), we might expect this interaction to take a different form when weaker associations are presented, reflecting the changing contribution of decisional uncertainty and controlled retrieval demands as task parameters vary.

Current findings suggest that access to valence is susceptible to control demands. Indeed, PCA in Experiment 4.1 suggests that accuracy on conditions that were more automatic or control-demanding loaded onto separate factors, regardless of task (semantic vs. valence). The involvement of control in valence processing is highlighted by evidence that divided attention can disrupt emotion-enhanced memory effects of valenced stimuli (Kang et al., 2014). Specific neural substrates may support controlled valence processing. Zhuang et al. (2021) compared neural activation during tasks requiring domain-general response inhibition to those involving manipulation of emotional context. Lateral frontal regions were engaged regardless, while ventral striatum and medial orbitofrontal cortex were sensitive to emotional context. SCN regions including bilateral IFG and left pMTG (Jackson, 2021) are

reliably activated for tasks requiring reappraisal of valenced stimuli (Messina et al., 2015). Messina et al. (2015) argue for contributions of semantic processing and executive control to emotion reappraisal, due to the need to access alternative representations of affective stimuli. SCN has been argued to allow for the integration of long-term abstract memory representations with goals (Wang et al., 2020). This network, damaged in SA (Souter, Wang, et al., 2022 [Chapter 2 of this thesis]), may support the control of both meaning and emotion.

4.6.1. Limitations

Due to restrictions during the COVID-19 pandemic, Experiment 4.2 was conducted remotely. The demands of this method (e.g., self-directed computer use) led to the exclusion of more impaired patients from our database, reducing our sample size. For the same reason, it was not possible to obtain neuroanatomical scans for all patients, preventing us from relating behavioural impairment with lesion profile. We saw evidence of individual-level task impairments, determined by Singlims. These impairments were not consistent across all patients. Further work with larger groups may be helpful in confirming our observations. We saw group-level differences in mixed effects models while controlling for random variation attributable to participant identity, suggesting meaningful group differences. Despite this, this sample size limits out ability to predict whether effects would generalise to other patients with this symptom profile. Second, it should be noted that valence judgements are subjective. 'Gallery', for instance, may be positive for some participants but negative for others. Despite this, participants without semantic control impairment performed at ceiling even in the *no association* condition (Experiment 4.1 = 95.7%, Experiment 4.2 controls = 97.8%), suggesting consensus on categorical valence. Finally, it has been argued that valence is more important in the representation of abstract concepts which lack physical properties (Kousta et al., 2011). Evidence suggests interactions between valence and word concreteness in the recruitment of semantic control regions (Pauligk et al., 2019). In the current investigation, we did not manipulate concreteness; future research may benefit from considering this factor. Finally, while we observed that effects of semantic relatedness on valence matching were greater than effects of valence congruency on semantic matching, it should be noted that metrics of semantic relatedness and valence congruency were obtained using different methods (valence by participant ratings, and relatedness by word embeddings). This could be viewed as limiting to the ability to directly compare the numerical impact of these two variables.

4.6.2. Conclusion

This study suggests that access to valence information during an explicit matching may not be entirely automatic; task-irrelevant semantic information can impact retrieval. Such effects are particularly prominent in patients with impaired semantic control, likely due to difficulty in constraining internal information. Similarly, valence congruency facilitates judgements of global semantic relatedness, suggesting that valence constitutes an important feature of heteromodal concepts. These results provide novel insights into the relationship between semantic retrieval and valence processing.

4.7. Link to Chapter 5

Chapter 4 of this thesis provided further insight into the role of conceptual knowledge in affective processing, and of the importance of valence in facilitating access to concepts. Combined with findings from Chapter 3, this thesis has so far provided evidence for baseline impairments in the categorisation of discrete emotions and of the classification of word valence, in patients with semantic aphasia (SA). These findings are in line with evidence of widespread and diverse impairments in this group, co-occurring with general executive dysfunction (Thompson et al., 2018) and affecting domains beyond semantic cognition, such as episodic memory (Stampacchia et al., 2018). Both Chapters 3 and 4 are also consistent with prior evidence (Jefferies et al., 2008; Noonan et al., 2010) that semantic control impairments in SA can be ameliorated through the provision of cues and contextual information which allude to concept meaning. Indeed, a recent investigation provided evidence that training SA patients to make conceptual links between concepts can ameliorate impairments, with effects extending beyond trained items (Stampacchia et al., 2021).

Chapter 5 studied another affective domain that may have implications for the amelioration of semantic control impairments – motivation. This was based on evidence that cued extrinsic rewards can bolster cognitive control (Swirsky & Spaniol, 2019), and ameliorate age-related impairments (Yee et al., 2019). Such effects have not been investigated in relation to semantic control, although in many ways this process can be considered analogous to domain-general control (Thompson et al., 2018). We studied effects of both cued extrinsic reward and self-reference on the ability of SA patients to make semantic associations. Self-reference may serve as a proxy for intrinsic motivation (Madan, 2017), and typical benefits of self-reference for recognition memory have been shown to persist in SA (Stampacchia et al., 2019). Evidence of facilitatory effects of cues and task constraints in Chapters 3 and 4 are consistent with prior evidence that semantic retrieval can be assisted by alluding to properties of the target stimulus. If effects of motivation are found to be effective for this same purpose, this study would provide evidence that retrieval can be assisted even without having received item-specific cues. Such a finding may have implications for rehabilitation of post-stroke semantic impairments, particularly in the employment of ‘gamified’ strategies which may utilise typical elements of games, including performance-contingent token points. Alternatively, affective abnormalities identified in SA in Chapters 3 and 4 may preclude motivational factors from having a facilitatory effect.

Chapter 5: Motivated semantic control: Exploring the effects of extrinsic reward and self-reference on semantic retrieval in semantic aphasia

This chapter is adapted from a published article:

Souter, N. E., Stampacchia, S., Hallam, G., Thompson, H., Smallwood, J., & Jefferies, E. (2022). Motivated semantic control: Exploring the effects of extrinsic reward and self-reference on semantic retrieval in semantic aphasia. *Journal of Neuropsychology, 16*(2), 407-433. https://doi.org/10.1111/jnp.12272.

Data sharing via a public repository is not possible for the current study, due to insufficient consent. Researchers who wish to access the data should contact the Research Ethics Committee of the York Neuroimaging Centre, or the corresponding author.

Acknowledgements and author's contribution

This article was conceptualised together by Nick Souter and Elizabeth Jefferies as part of a PhD proposal, following conversations between Elizabeth Jefferies and co-authors Glyn Hallam, Hannah Thompson, and Jonathan Smallwood. Experiment 5.1 was created by Sara Stampacchia prior to the start of Nick Souter's PhD, who also oversaw data collection for this experiment. During this time, data was also collected by undergraduate project students Emma Parker, Ellicia Swindells, and Annabelle Harding. Nick Souter finished Experiment 5.1 data collection upon starting at the University of York. Experiment 5.2 was created and coded by Nick Souter, who also oversaw data collection. Data collection and stimulus validation was aided by research assistants Dominika Varga, Chloe Orme, Cate Correia, Amelia Shelton, and Marcus Glennon. Lucilla Lanzoni provided advice in generating a lesion overlap map. Nick Souter oversaw all formal data curation and analysis, and wrote the full original draft of this paper. Elizabeth Jefferies edited manuscript drafts, and all other co-authors provided feedback on the final draft.

5.1. Abstract

Recent insights show increased motivation can benefit executive control, but this effect has not been explored in relation to semantic cognition. Patients with deficits of controlled semantic retrieval in the context of semantic aphasia (SA) after stroke may benefit from this approach since 'semantic control' is considered an executive process. Deficits in this domain are partially distinct from domain-general deficits of cognitive control. We assessed the effect of both extrinsic and intrinsic motivation in healthy controls and semantic aphasia patients. Experiment 5.1 manipulated extrinsic reward using high or low levels of points for correct responses during a semantic association task. Experiment 5.2 manipulated the intrinsic value of items using self-reference; allocating pictures of items to the participant ('self') or researcher ('other') in a shopping game before people retrieved their semantic associations. These experiments revealed that patients, but not controls, showed better performance when offered high extrinsic reward, consistent with the view that increased external motivation may help to ameliorate patients' semantic control deficits. However, while self-reference was associated with better episodic memory, there was no effect on semantic retrieval. We conclude that semantic control deficits can be reduced when extrinsic rewards are anticipated; this enhanced motivational state is expected to support proactive control, for example, through the maintenance of task representations. It may be possible to harness this modulatory impact of reward to combat the control demands of semantic tasks in SA patients.

5.2. Introduction

Our ability to understand the world relies on flexible access to conceptual information within a semantic store (Jefferies, 2013). Evidence supports the existence of dissociable systems underlying the storage and retrieval of semantic representations (Lambon Ralph et al., 2017). Semantic dementia patients with relatively focal atrophy focussed on the ventrolateral anterior temporal lobes show degraded semantic knowledge, while patients with semantic aphasia (SA) experience deregulated semantic retrieval, or semantic control, following left prefrontal and/or temporoparietal stroke (Jefferies & Lambon Ralph, 2006). Semantic control is an executive process which supports the retrieval of non-dominant aspects of knowledge while overcoming competition from distractors (Hoffman et al., 2018; Jefferies, 2013). Impaired semantic control in SA gives rise to deficits in both verbal communication and organisation of nonverbal actions (Jefferies et al., 2019), consistent with the definition of SA as impaired manipulation of verbal and non-verbal symbolic information (Head, 1926). In line with the damage to left ventrolateral prefrontal cortex and/or left temporoparietal regions in SA, studies of healthy participants employing neuroimaging (Jackson, 2021) and transcranial magnetic stimulation (Hallam et al., 2016) have implicated both left inferior frontal gyrus (IFG) and posterior middle temporal gyrus (pMTG) in semantic control.

In SA, access to semantic knowledge is not universally compromised, but depends on task demands. Semantic retrieval is impaired for subordinate meanings, and when inhibition of task-irrelevant distractors is required (Jefferies, 2013). This results in reduced flexibility when retrieving semantic information in ambiguous contexts (Noonan et al., 2010). Impaired semantic control in SA is also evident when retrieving thematic associations between concepts: identifying weak as opposed to strong associations requires semantic control processes that focus retrieval on non-dominant conceptual information (Thompson et al., 2017). Research has explored manipulations which ameliorate semantic control deficits in SA, such as cueing. Successive phonemic cues (e.g. c.. ca.. cam.. for CAMEL) can facilitate picture naming (Jefferies et al., 2008), while contextually-relevant sentences (Noonan et al., 2010) or emotional and location cues (Lanzoni et al., 2019) can facilitate the retrieval of non-dominant interpretations of ambiguous homonyms. Cues reduce control demands by narrowing down the number of retrievable options and biasing retrieval towards task-relevant information.

An alternative approach to facilitating semantic retrieval involves recruiting processes beyond semantic cognition. Investigations with healthy adults have demonstrated that extrinsic rewards, such as monetary incentives or awarded points, can improve performance in domains including control of visual attention (Padmala & Pessoa, 2011), task-switching (Capa et al., 2013), contextual control (Kouneiher et al., 2009), creative problem solving (Cristofori et al., 2018), interference control (Zhao et al., 2018), and conflict adaptation (Dreisbach & Fischer, 2012). Behavioural benefits of extrinsic reward include increased accuracy, reduced reaction times, and reduced switch-costs (Yee & Braver, 2018). Extrinsic incentives are considered a key element of 'gamification' (Mekler et al., 2017), which uses typical elements of digital games to increase engagement with training activities including post-stroke rehabilitation (Romani et al., 2019). To our knowledge, extrinsic rewards have not been used previously in conjunction with semantic tasks or in SA patients.

Tasks with high control demands are effortful as they draw on limited resources including selective attention and working memory (Yee & Braver, 2018). The cost of mental exertion is typically weighed against the potential benefits of the action (Botvinick & Braver, 2015). As such, tasks perceived as high effort and low in reward may be less appealing than more trivial low effort and high reward actions. Introducing task-based incentives can offset perceived costs (Goschke & Bolte, 2014) and increase preparatory control, and therefore one's ability to sustainably engage with a task (Notebaert & Braem, 2015). This can benefit either cognitive stability or flexibility, depending on recent reward history (Fröber et al., 2019). The neural processing of extrinsic reward has been consistently linked to a network of regions including the ventromedial prefrontal cortex, caudate, and putamen (Lin et al., 2012). Cumulative reward value appears to be tracked and represented in these regions (Juechems et al., 2017). Effects of reward on cognition have been attributed to dopaminergic transmission between these regions and the multiple demand network (MDN), which supports challenging tasks across domains (Camilleri et al., 2018; Parro et al., 2018).

While extrinsic reward refers to incentives provided externally, intrinsic reward refers to inherent enjoyment of or interest in a task (Mori et al., 2018). Intrinsic motivation is relatively difficult to manipulate experimentally, but can be modulated indirectly, through factors such as self-reference. Tamir and Mitchell (2012) demonstrated that self-referential information is intrinsically motivating; participants reliably choose to forgo monetary incentives in order to disclose information about the self, in conjunction with increased activation in brain regions associated with reward processing. The neural substrates

underlying both intrinsic motivation and self-reference show considerable overlap with reward circuitry (Di Domenico & Ryan, 2017; Enzi et al., 2009). Cognition shows biases in favour of self-referenced items, within perception (Sui et al., 2012), attention (Sui & Humphreys, 2015b), working memory (Röer et al., 2013), and recognition memory (Hou et al., 2019). Moreover, Sui and Humphreys (2015a) demonstrated that extrinsic reward and self-reference confer separable but equivalent benefits in associative learning. Self-reference benefits to episodic memory persist in patients with SA (Stampacchia et al., 2019).

If regions associated with reward processing are intact it may be possible to harness modulatory effects of motivation in rehabilitation for post-stroke aphasia. The benefits of increased motivation may be more pronounced in more impaired patients, with greater difficulties constraining internal representations increasing reliance on external prompts. Given evidence of effects of reward and self-reference on cognitive functions across domains, similar benefits may occur for semantic control. However, semantic control is dissociable from domain-general control: the peak activations in fMRI studies that manipulate semantic control demands in healthy participants fall outside MDN (Gao et al., 2021; Noonan et al., 2013), and inhibitory stimulation of semantic control sites temporarily disrupts control-demanding semantic tasks but not demanding visual judgements (Whitney et al., 2011). Moreover, while impaired semantic control is ubiquitous in semantic aphasia, some but not all of these patients have general deficits of cognitive control: lesion-symptom mapping shows that these semantic and non-semantic control deficits are associated with different patterns of structural damage (Souter, Wang, et al., 2022 [Chapter 2 of this thesis]). Given this distinction, there is a need to investigate the effects of motivation in tasks with high semantic control demands, to establish if this domain can benefit from 'gamification' strategies to the same degree as other cognitive tasks. Furthermore, evidence suggests affective abnormalities in SA, including in the ability to categorise facial portrayals according to discrete emotion categories (Souter et al., 2021 [Chapter 3 of this thesis]). This is thought to reflect deficits in constraining internal states beyond the conceptual domain, which may extend to, and therefore limit modulatory effects of, motivation. While people with aphasia generally benefit from the use of motivating 'gamification' strategies, we cannot assume that these benefits will transfer to people with SA for this reason. This is a key motivation for the current study. SA patients have been shown to benefit from the provision of external cues that provide additional information pertaining to semantic decisions (Noonan et al., 2010), but the

influence of reward manipulations, which provide external prompts in the absence of contextually-relevant information, have not been investigated to our knowledge.

The current study aimed to investigate the influence of both extrinsic reward and intrinsic motivation induced through self-reference on the retrieval of strong and weak thematic associations in SA. Experiment 5.1 assessed the effect of cued extrinsic reward, in the form of high or low levels of performance-contingent token points. Experiment 5.2 assessed the effect of self-reference by allocating pictured 'shopping items' either to the participant ('self' condition) or the researcher ('other' condition), prior to semantic judgements about these items. If modulatory effects of motivation can benefit semantic control, high extrinsic reward and/or self-reference might ameliorate patients' semantic deficits. Motivation may support the maintenance of task goals when semantic control is deficient; consequently, any performance gains would likely be greater for weak associations, which place higher demands on semantic control. A better understanding of the effects of motivation on semantic retrieval of strong and weak associations may have implications for the use of gamified approaches for aphasia rehabilitation.

5.3. Method

Ethics approval for this study was granted by the York Neuroimaging Centre at the University of York (date: 24/10/2019, project ID: P1363).

5.3.1. Participants

The sample consisted of 16 SA patients (nine females), and 15 controls (12 females). All participated in Experiment 5.1, while a subset participated in Experiment 5.2 (demographic information is presented separately in Sections 5.4.1.1. and 5.5.1.1., respectively). Patients were recruited from communication support groups across Yorkshire. All had aphasia following left hemisphere stroke and were at least 18 months post-stroke. Patients were selected to show impairments in both verbal and non-verbal semantic cognition, consistent with previous definitions of SA (Jefferies & Lambon Ralph, 2006). The criteria used are explained in the Background Neuropsychology Supplementary Materials sections '*Chapter 5 Sample Summary*'. Controls were healthy adults matched to the patients on age and years in education and reported no history of psychiatric or neurological disorders. Informed consent was obtained for all participants.

5.3.2. Lesion analyses

Ten (of sixteen) patients (P1 – P10) had MRI scans at the York Neuroimaging Centre, using a 3T GE HDx Excite MRI scanner on a T1-weighted 3D fast spoiled gradient echo sequence (TR = 7.8ms, TE = minimum full, flip-angle = 20o, matrix size = 256 x 256, 176 slices, voxel size = 1.13 x 1.13 x 1mm). All were scanned in the chronic stage of stroke (mean (SD) = 8.3 years since stroke (5.4), minimum = 2.5 years). All ten participated in Experiment 5.1, while four (P3 – P6) participated in Experiment 5.2. Structural scans underwent brain extraction in ANTs (version 2.1.0; Avants et al., 2011) using a template from the OASIS Brain Project (https://www.oasis-brains.org/; Marcus et al., 2010). Registration to MNI space was also performed using ANTs. Each patient's lesion was manually traced in MRIcron. Figure 5.1a provides a lesion overlap map for these patients. Eight cases showed damage to left IFG. Several patients showed damage to other regions including pMTG, superior temporal gyrus, and supramarginal gyrus. Clinical acute-stage scans were available for two further patients and revealed damage to left IFG (MRI for P16) and a left frontoparietal lesion (CT for P12). Lesion information was not available for the remaining four patients due to contraindications for scanning and/or closure of scanning facilities during the COVID-19 pandemic.

To assess the impact of patients' lesions on functional networks of interest, we extracted maps from Neurosynth using term-based meta-analyses (Yarkoni et al., 2011) for 'Semantic', 'Demands', and 'Reward' (Figure 5.1b-d). This allowed us to observe the extent to which patients present with damage to regions associated with semantic processing, domain-general task demands, and reward processing. We calculated the average percentage of each map that was damaged across the patients with available lesion maps. Analysis was restricted to left hemisphere aspects of each network, such that it reflects a percentage of all voxels that could possibly be lesioned in an exclusively left-hemisphere stroke sample. While right-hemisphere aspects of these networks may be affected by disconnection (Souter, Wang, et al., 2022 [Chapter 2 of this thesis]), this is beyond the scope of the current paper. As seen in Figure 5.1e, patients showed the most damage to 'Demands' regions, followed by 'Semantic' regions. 'Reward' regions were relatively spared, suggesting it might be possible to harness modulatory impacts of reward.

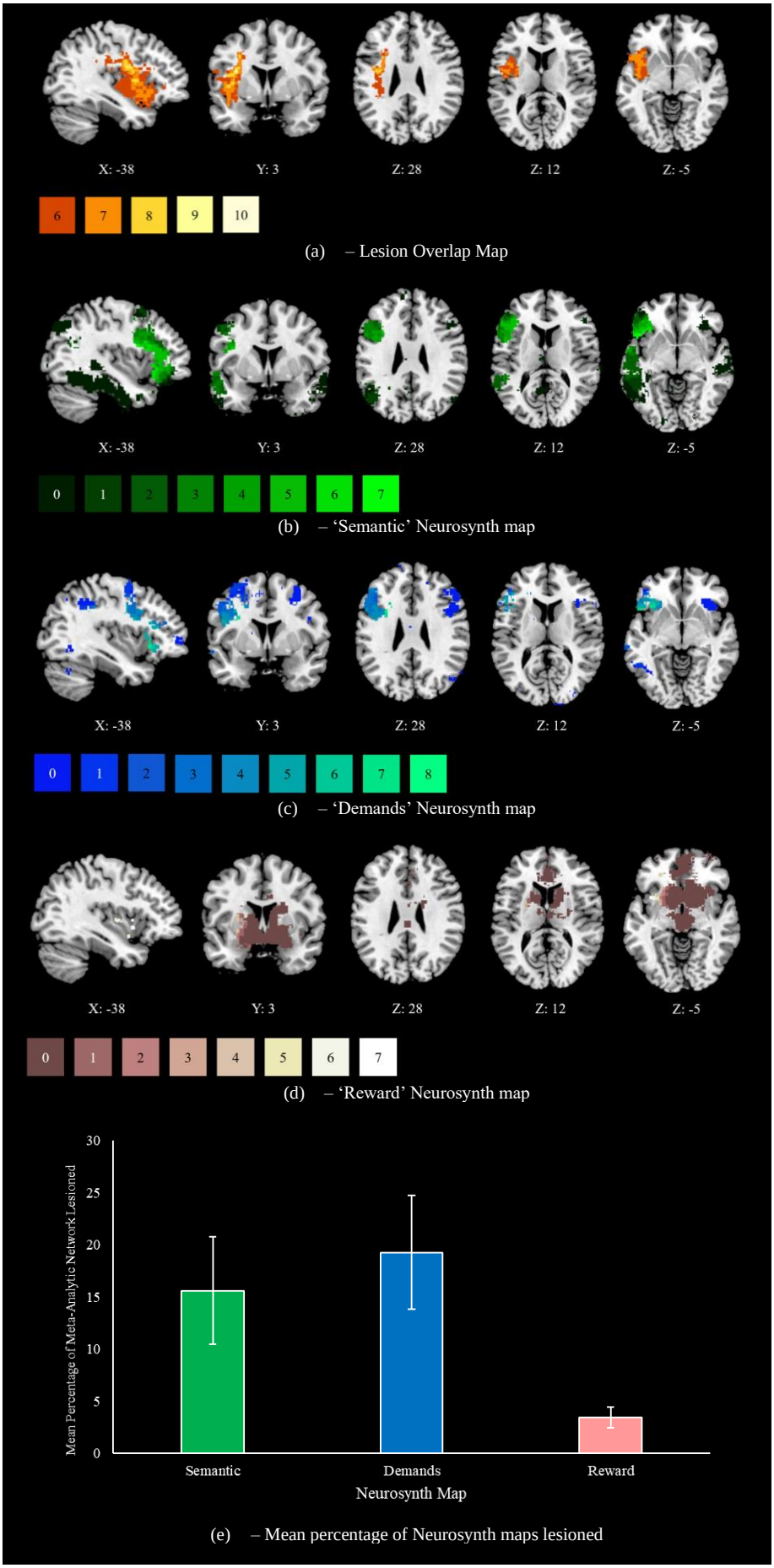


Figure 5.1. Patient lesion analyses, including (a) a lesion overlap map for ten semantic aphasia patients in the current study, created using manual segmentation in MRICron. This map shows lesion overlap in 6 or more patients, with the colour of the lesioned area corresponding to the number of affected cases (bottom left). We assessed the extent of overlap between patient lesions and term-based meta-analytic maps from Neurosynth for the terms (b) 'semantic' (1031 studies), (c) 'demands' (596 studies), and (d) 'reward' (922 studies). Neurosynth maps are coloured according to impact by lesion across the sample, with brighter areas reflecting those more often implicated in lesions. Each map was formatted in MRICron. We present (e) the mean percentage of each map lesioned across patients, with standard error of the mean error bars.

5.3.3. Background neuropsychological testing

Patients completed background tests of language, memory, executive function, and semantic cognition. The control participants tested on the experimental tasks in this study did not complete these background assessments. Each patient's performance on the background neuropsychology measures is shown in Supplementary Table BN.1, while Supplementary Table BN.2 provides data on tests of semantic cognition. Background Neuropsychology Supplementary Materials also provide task descriptions (see Section '*Description of Assessments'*) and an interpretation of the sample's performance on these measures (see Section '*Chapter 5 Sample Summary'*). Patients presented with variable levels of impairment in speech fluency and word repetition. Most patients presented with impaired working memory. Visuospatial processing was largely preserved. Eleven patients showed impairment on at least one test of executive function.

All patients were impaired on at least one verbal and one non-verbal semantic task. All patients performed close to ceiling level on word-picture matching, reflecting low controls demands. On word and picture versions of the Camel and Cactus Test of semantic association, half of the sample showed impairment. Patients presented with considerable variation in picture naming, although performance was improved by successive phonemic cues in all who were able to name at least one picture. Patients presented with the anticipated impairment in tests manipulating semantic control demands, including difficulty retrieving subordinate conceptual information, susceptibility to cues and miscues, and difficulty rejecting strong thematic distractors.

Principal components analysis of the semantic tasks using oblique rotation revealed two components with Eigenvalues greater than 1 (Table 5.1). The first component reflected performance on tasks with high semantic control demands: these factor scores were used as a semantic control composite for each participant. Lower scores reflect greater impairment. This semantic factor was positively correlated with performance on the Brixton Spatial Anticipation Test: $r_s(14) = .837$, $p < .001$. It did not relate to performance on any other manipulation of executive function ($p \geq .200$, see Background Neuropsychology Supplementary Materials Section '*Chapter 5 Sample Summary'*). The second semantic factor loaded on tasks involving object identification.

Table 5.1. Pattern matrix for principal components analysis of semantic aphasia patients' performance on semantic tests with oblique rotation.

Task	Component 1 (Eigenvalue = 4.03)	Component 2 (Eigenvalue = 1.52)
CCT words	**.876**	.083
CCT pictures	**.896**	-.078
Picture naming	.089	**.877**
Word-picture matching	-.062	**.916**
Ambiguity task	**.900**	.057
Synonym judgement task	**.903**	-.154
Object use task	**.801**	.156

Note: Strong loadings for each component are in bold. CCT = Camel and Cactus Test.

5.4. Experiment 5.1: The effect of cued extrinsic reward on semantic retrieval

5.4.1. Method

5.4.1.1. Participants

This sample included 16 patients (nine females) with a mean age of 64.4 years (SD = 12.3), a mean age of leaving education of 17.5 years (SD = 2.9), and a mean of 11.3 years (SD = 6.6) since stroke. These patients were compared with 15 controls (12 females) with a mean age of 70.7 (SD = 9.7), and a mean age of leaving education of 18.8 years (SD = 3.9). Patients and controls were matched for age [$U = 74.0$, $p = .069$], and age of leaving education [$U = 102.0$, $p = .469$].

5.4.1.2. Design

This experiment used a mixed design, with patients and controls making strong and weak thematic associations under the conditions of high and low reward. A three alternative forced choice format was used: participants were asked to select a target word, presented alongside two foils, based on the strongest thematic association to a probe word. The experiment was conducted over two sessions, each consisting of four high and four low reward blocks. Each block contained eight trials split equally across strong and weak associations. High and low reward blocks were alternated. There were 64 trials per session, and 128 trials in total. There was no difference across sessions for accuracy or response time: $p \geq .190$.

5.4.1.3. Stimulus properties

Descriptive statistics for Experiment 5.1 stimulus properties are reported in Supplementary Table 5.1. Target and probe words were taken from the Edinburgh Associative Thesaurus, a publicly available dataset of associative strength between words (Kiss et al., 1973). Probes and targets were more related in strong than weak association trials: $t(67.6) = 42.1$, $p < .001$. There were no differences in association strength across blocks [$t < 1$], or sessions [$t < 1$].

We examined frequency, imageability and length of the target and probe words. Subtlex-UK (Van Heuven et al., 2014) was used to obtain word frequency. Sources for imageability ratings included the MRC Psycholinguistic Database (Coltheart, 1981), N-Watch (Davis, 2005), The Glasgow Norms (Scott et al., 2019), Bird et al. (2001a; 2001b), Cortese and Fugett (2004a; 2004b), and Davey et al. (2015). Frequency and imageability scores were on 7-point Likert scales, and were averaged when multiple sources were available. Overall, 17% of frequency scores could not be retrieved. Missing scores were largely for compound words such as 'snooker ball' or 'space suit'. Imageability ratings were obtained for all but one word. For both target and probe words, three separate 2x2 ANOVAs were run with frequency, imageability and length as dependent variables, examining effects of reward (high/low) and association strength (strong/weak). These ANOVAs are reported in Supplementary Table 5.3. All psycholinguistic properties were matched across reward condition and association strength [$p \geq .071$].

5.4.1.4. Procedure

Each session was preceded by an instructions phase, which included two practice trials to familiarise participants with the procedure. Stimuli for the main experiment were presented on a laptop using PsychoPy3 (Peirce et al., 2019). Each block was preceded by a graphic, informing the participant that correct answers were each worth 1 point (low reward) or 1,000 points (high reward). Due to impaired reading ability, the researcher read all words aloud to the patients. Patients indicated their response by pointing to the screen, with the researcher pressing the corresponding key. Control participants read the words themselves, and keyed in their own responses. Responses were followed by feedback, informing the participant that they had won either 1 or 1,000 points, or that they were incorrect and had not won any points. If a response was not given within ten seconds, participants were informed that they had not won any points. The prospect of gaining points was abstract and not linked to monetary gain. Each block was followed by self-report ratings of task enjoyment, response

confidence, and task focus, each on a 7-point Likert scale. Figure 5.2 provides a summary of the procedure for Experiment 5.1.

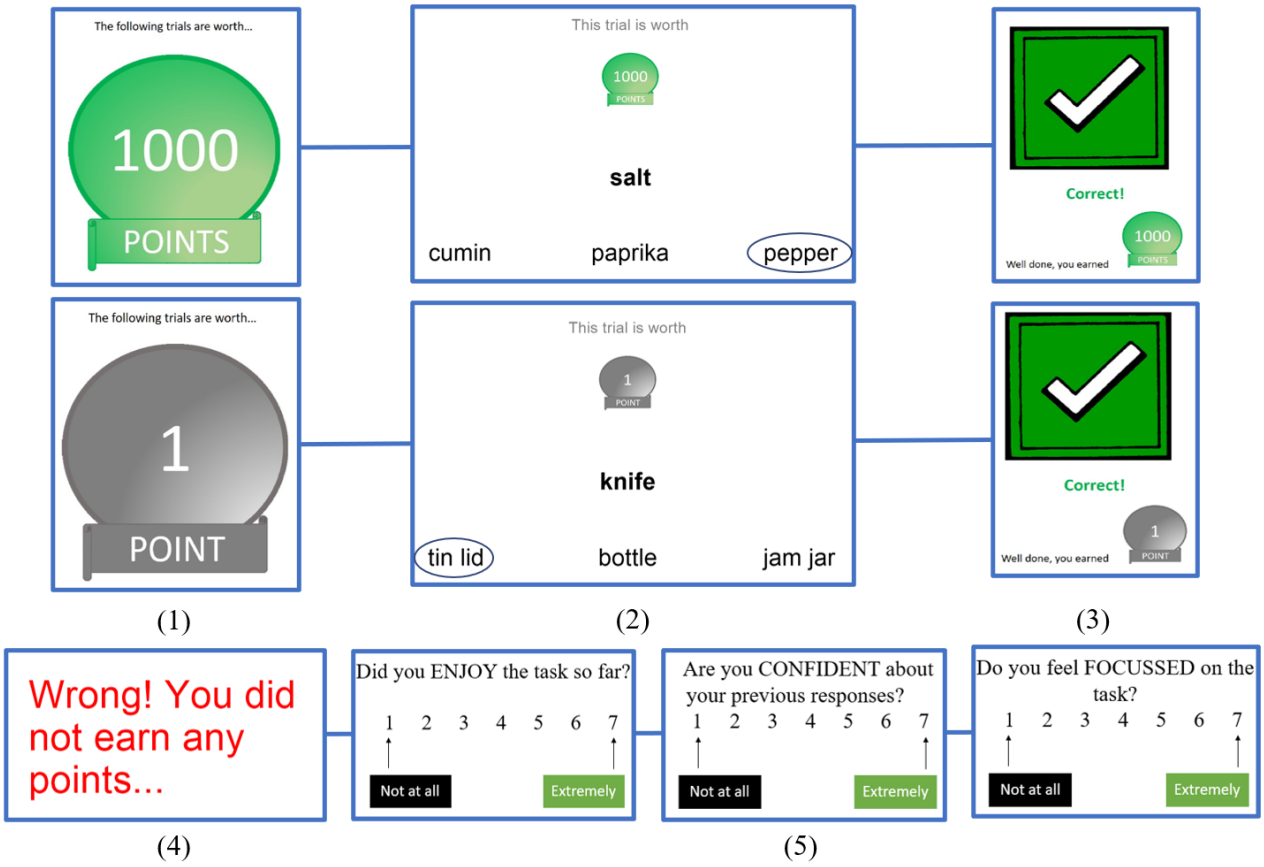


Figure 5.2: Experiment 5.1 procedure. (1) Each block was preceded by a high reward or low reward graphic. (2) Participants made thematic associations, either with strong or weak associations. Participants were provided with feedback as to whether their response was (3) correct or (4) incorrect. (5) Following each block, participants completed ratings of enjoyment, confidence, and focus.

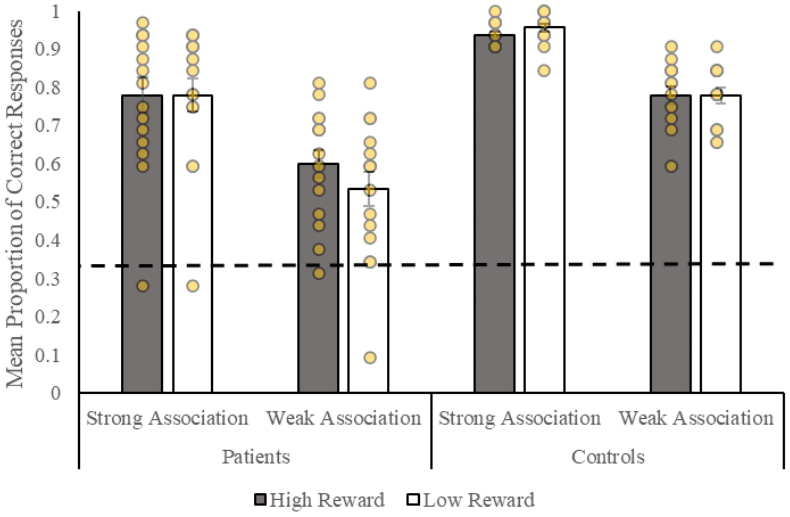
5.4.1.5. Data analysis

Accuracy (proportion of correct responses) was our key dependent measure. As we were specifically interested in effects of reward on patients' accuracy for weak associations, we first ran a repeated measures ANOVA for the patients alone, observing the effects of reward (high/low) and association strength (strong/weak) as within-subject independent variables. Accuracy was then entered into an omnibus mixed ANOVA, adding group (patients/controls) as a between-subjects variable. Post-hoc contrasts for significant interactions are reported with Bonferroni-correction applied. Mixed ANOVAs were

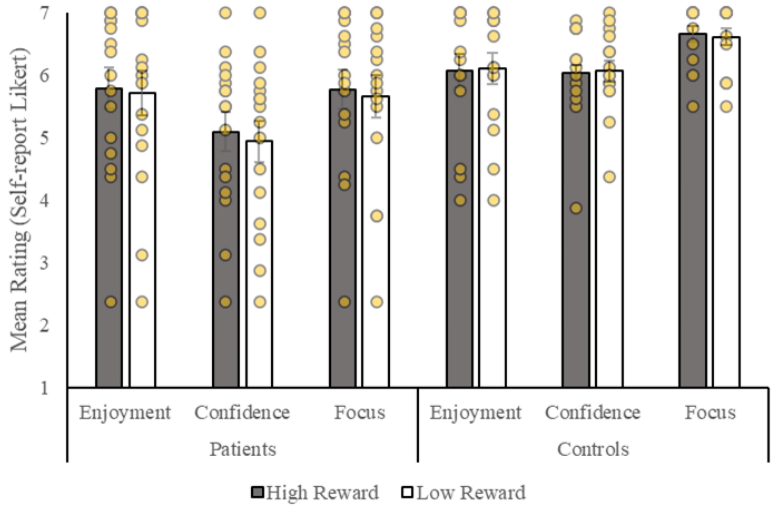
conducted for ratings of enjoyment, confidence, and focus, examining effects of reward and group. Analysis and interpretation of participants' response time can be seen in Supplementary Table 5.4.

5.4.2. Results

Figure 5.3 shows participants' mean accuracy and self-report ratings across reward condition, group, and association strength. Supplementary Table 5.5 provides descriptive statistics for Experiment 5.1.



(a) – Experiment 5.1 accuracy



(b) – Experiment 5.1 self-report ratings

Figure 5.3: Experiment 5.1 bar graphs for (a) mean proportion of correct response (dotted line reflects chance performance, .33), and (b) self-report ratings across reward conditions, participant groups, and association strength, with standard error of the mean error bars. Individual data points are represented by yellow circles.

5.4.2.1. Effects of reward on semantic retrieval in patients

The patient group ANOVA revealed significant main effects of strength [$F(1, 15) = 147.7$, $p < .001$, $\eta_p^2 = .91$] and reward [$F(1, 15) = 5.4$, $p = .034$, $\eta_p^2 = .27$], and a significant reward by strength interaction [$F(1, 15) = 7.0$, $p = .019$, $\eta_p^2 = .32$]. Patients had higher accuracy on high than low reward trials, and on strong than weak association trials. Post-hoc contrasts for the interaction demonstrated that patients were more accurate for weak associations in the high than low reward condition [$t(15) = 3.3$, corrected $p = .010$]. There was no effect of reward on strong associations [$t < 1$][15]. Patients' semantic control composite scores positively correlated with their overall accuracy [$r_s(14) = .70$, $p = .003$], reflecting higher accuracy in less impaired patients. There was no association between the semantic composite and the effect of reward [strong: $r_s(14) = .16$, $p = .563$, weak: $r_s(14) = -.08$, $p = .780$].

5.4.2.2. Omnibus ANOVA comparing effects across patients and controls

ANOVA results are shown in Table 5.2. Controls were more accurate than patients overall. Accuracy was higher for strong than weak association trials. There was a reward by group interaction, with a larger difference in accuracy between high and low reward trials for patients [$t(15) = 2.3$, corrected $p = .068$] than controls [$t < 1$][16], although neither contrast survived correction. There was a reward by strength interaction, with a greater difference in accuracy between the high and low reward conditions for weak [$t(30) = 2.1$, corrected $p = .096$] than for strong association trials [$t < 1$][17], although again neither contrast survived correction. The three-way reward by strength by group interaction was not significant.

Ratings of enjoyment and confidence were not influenced by reward. Controls reported significantly higher confidence and focus than patients. A main effect of reward was found for focus, with higher ratings in the high than low reward condition. As all ratings were taken at the block level, it was not possible to investigate effects of association strength. There were too few participants in the current sample to assess the relationship between these ratings and accuracy.

[15] The assumption of normality was not always met but non-parametric tests elicited the same outcomes. Weak associations: $Z = -2.9$, corrected $p = .008$; strong associations: $Z = -.2$, corrected $p > 1$.
[16] Patients: $Z = -2.1$, corrected $p = .070$, controls: $Z = -.4$, corrected $p > 1$.
[17] Weak association: $Z = -2.4$, corrected $p = .034$, strong association: $Z = -.7$, corrected $p = .976$.

Table 5.2. Omnibus ANOVA results for all Experiment 5.1 (extrinsic reward) dependent variables.

Dependent variable	Main effect/interaction	Result
Accuracy	**Group**	**$F(1, 29) = 18.9$, $p < .001$, $\eta_p^2 = .40$***
	Reward	$F(1, 29) = 1.3$, $p = .263$, $\eta_p^2 = .04$
	Reward by group	**$F(1, 29) = 4.8$, $p = .037$, $\eta_p^2 = .14$***
	Strength	**$F(1, 29) = 215.3$, $p < .001$, $\eta_p^2 = .88$***
	Strength by group	$F(1, 29) = 2.9$, $p = .100$, $\eta_p^2 = .09$
	Reward by strength	**$F(1, 29) = 5.6$, $p = .025$, $\eta_p^2 = .06$***
	Reward by strength by group	$F(1, 29) = 2.0$, $p = .169$, $\eta_p^2 = .06$
Enjoyment	Group	$F(1, 29) = .6$, $p = .438$, $\eta_p^2 = .02$
	Reward	$F(1, 29) = .2$, $p = .690$, $\eta_p^2 < .01$
	Reward by group	$F(1, 29) = .6$, $p = .441$, $\eta_p^2 = .02$
Confidence	**Group**	**$F(1, 29) = 7.7$, $p = .010$, $\eta_p^2 = .21$***
	Reward	$F(1, 29) = 1.4$, $p = .244$, $\eta_p^2 = .05$
	Reward by group	$F(1, 29) = 2.7$, $p = .112$, $\eta_p^2 = .09$
Focus	**Group**	**$F(1, 29) = 6.6$, $p = .016$, $\eta_p^2 = .19$***
	Reward	**$F(1, 29) = 5.8$, $p = .023$, $\eta_p^2 = .17$***
	Reward by group	$F(1, 29) = .8$, $p = .379$, $\eta_p^2 = .03$

Note: ***** reflects a significant result.

5.4.3. Experiment 5.1 summary

Experiment 5.1 studied effects of cued extrinsic reward on semantic aphasia patients' and controls' ability to retrieve thematic associations. An ANOVA for the patient group demonstrated that high reward improved accuracy for weak but not strong associations, suggesting that high extrinsic reward can aid the retrieval of semantic associations when semantic control is deficient. Results from the omnibus ANOVA suggest that benefits of extrinsic reward were greater for the patients than for controls, and for weak than strong associations. Self-reported focus was also higher in the high than low reward condition.

5.5. Experiment 5.2: The effect of self-reference on semantic retrieval

5.5.1. Method

5.5.1.1. Participants

Experiment 5.2 included a subset of Experiment 5.1 participants. This included ten SA patients (six females) with a mean age of 62.4 years (SD = 10.1), a mean age of leaving education of 18.3 years (SD = 3.4), and a mean of 10.1 years (SD = 5.4) since stroke. Eleven control participants (eight females) were included in this sample with a mean age of 69.9 (SD = 10.3), and a mean age of leaving education of 18.9 (SD = 3.6). There was no significant difference between groups for age [$U = 29.0$, $p = .067$], or age leaving education [$U = 52.0$, $p = .831$].

5.5.1.2. Design

This experiment used a mixed design, with patients and controls making strong and weak thematic associations across 'self' and 'other' conditions. A three alternative forced choice format was used. Probe pictures were used, as these were viewed as fitting in the context of the shopping game used to reinforce self-referential encoding (explained in Section 5.5.1.4.). Pictures were selected for 28 pairs of semantically related items (e.g., HARP-LUTE, ANT-WASP). For each pair, one picture was allocated to the participant ('self') and one to the researcher ('other'), counterbalanced across participants. Self and other trials were presented in a random order. The experiment was conducted over two sessions, each containing 56 trials. During the first session, participants completed strong and weak associations for one item in each pair. During the second session, participants completed the same associations for the remaining probes. Foils were thematically related to the target and were also kept consistent across both objects in each pair. Session order was counterbalanced. There was no difference across sessions for accuracy or response time: $p \geq .259$.

5.5.1.3. Stimulus properties

Descriptive statistics for Experiment 5.2 stimulus properties are reported in Supplementary Table 5.2. Association strength between the probe pictures and target words was validated using ratings from an independent sample of healthy adults, on a 7-point Likert scale. Ratings were collected over three surveys, with sample size ranging between 30 and

42. For both probes within each pair, equivalent strong and weak associations were generated. For example, pictures of a HARP and a LUTE were equally strongly and weakly associated with the target words STRINGS and VINYL, respectively. Associations between probes and targets were rated as stronger on strong than on weak association trials: $p < .001$. Association strength within strong and weak association categories was matched across self-reference conditions and sessions: $p \geq .793$.

Frequency, imageability, and length were examined for the target words (using the same sources detailed in Section 5.4.1.3.). Ratings of frequency and imageability could not be retrieved for 14% and 7% of target words, respectively. This was largely the case for compound words. One-way ANOVAs were run for each factor, looking for effects of association strength (see Supplementary Table 5.3). No effects of association strength were found [$p \geq .195$]. Due to counterbalancing, it was not necessary to compare psycholinguistic ratings across conditions or sessions.

5.5.1.4. Procedure

At the start of both sessions, participants completed the allocation phase 'shopping game', intended to reinforce self-referential encoding. Both the participant and researcher had a 'shopping list' in front of them, respectively labelled "My shopping list" and "*researcher's name*'s shopping list", including pictures and names of each object allocated to them. The researcher and participant took turns finding the items on their lists and placing them into their respective baskets. Participants searched through a pile of laminated pictures, found the next item on their list, and placed it into their basket. the researcher provided verbal prompts to reinforce the allocations (e.g., *"The next item on my list is a bagel, so I'll put that in my basket. Your next item is a ciabatta, find that one and put it into your basket."*).

As in Experiment 5.1, the testing phase was preceded by two practice trials. The testing phase was performed on a laptop using PsychoPy3 (Peirce et al., 2019). The probe picture was presented above the three response options. Participants were asked to identify which of the three words was most thematically related to the probe. Participants indicated their responses in the same way as in Experiment 5.1 (see Section 5.4.1.4.). Self-reported ratings of response confidence were taken for each trial. Ratings of task enjoyment and focus were not gathered due to the fully randomised design. It was thought that asking participants to self-report enjoyment and focus after each trial may cause frustration and negatively affect enjoyment or focus.

Finally, participants completed an episodic memory test to test for a self-reference recognition memory effect, shown previously in SA (Stampacchia et al., 2019). Participants were presented with 30 images, 10 of which had been allocated to them ("Mine"), 10 which had been allocated to the researcher ("*researcher's name*"), and 10 which were not present in the allocation or testing phase ("New"). Participants indicated which of these three categories they believed each picture belonged to. The same test was administered after both sessions. A summary of the Experiment 5.2 procedure can be seen in Figure 5.4.

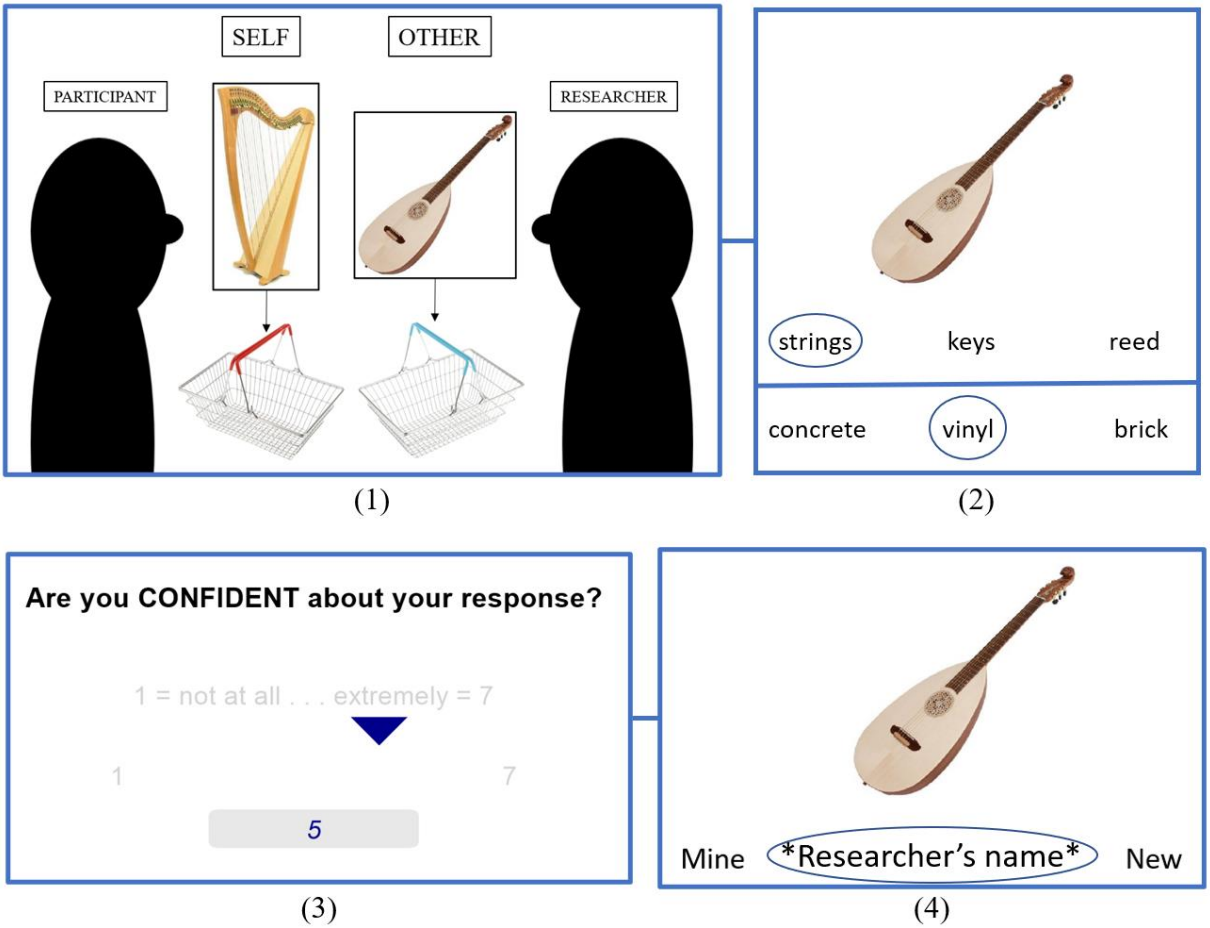


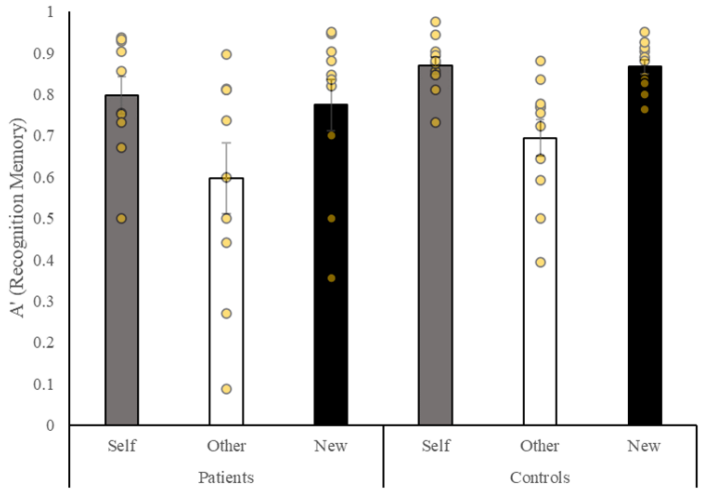
Figure 5.4: Experiment 5.2 procedure. (1) One item from each pair of probe pictures was allocated to the participant, and the other to the researcher. (2) Participants completed strong and weak associations for both the self- and other- allocated items in each pair. (3) After each trial participants gave a rating of response confidence. (4) Participants were tested on source memory for 30 pictures.

5.5.1.5. Data analysis

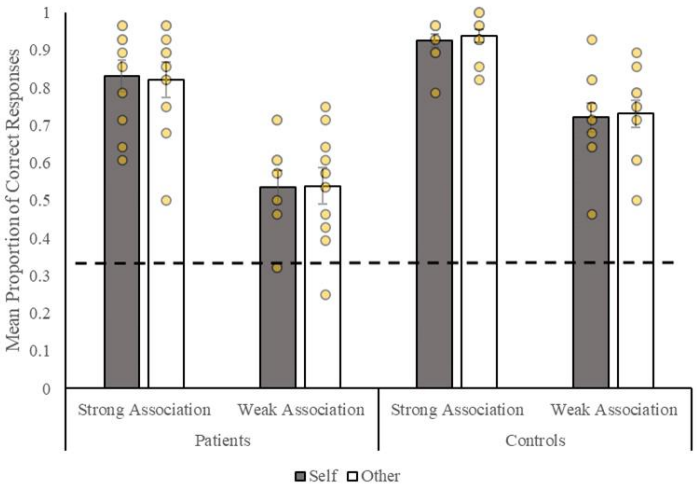
Accuracy (proportion of correct responses) was our key dependent measure. As benefits of self-reference were only expected for patients on weak association trials, a repeated measures ANOVA was first run for patients only with self-reference condition (self/other) and association strength (strong/weak) as within-subjects variables. Accuracy was then entered into an omnibus mixed ANOVA, adding group (patients/controls) as a between-subjects variable. A mixed ANOVA was conducted for confidence ratings, using the same design as above. Analysis of participants' response time can be seen in Supplementary Table 5.4. Results of the episodic memory test were analysed using A', a non-parametric measure of recognition memory based on the ratio of correct 'hits' to false positive responses (Snodgrass & Corwin, 1988). This was calculated for the 'self', 'other', and 'new' conditions. The proportion of correct responses did not vary across sessions for any condition [$p \geq .103$]. Performance was therefore averaged across both sessions. In cases where memory data was only available for one session (N = 5), data for this session were entered into the analysis. The effects of group and self-reference on A' were assessed using a mixed ANOVA.

5.5.2. Results

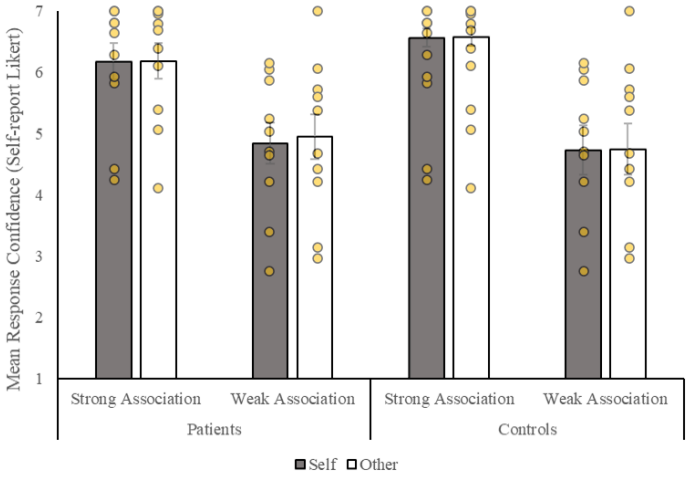
Participants' A' scores, mean accuracy, and response confidence across self-reference condition, group, and association strength can be seen in Figure 5.5. Supplementary Table 5.6 provides descriptive statistics for Experiment 5.2. Results for the recognition memory and omnibus ANOVAs are in Table 5.3.



(a) – Experiment 5.2 recognition memory



(b) – Experiment 5.2 accuracy



(c) – Experiment 5.2 self-reported confidence

Figure 5.5: Experiment 5.2 bar graphs for (a) A', a non-parametric signal detection measure of recognition memory based on the proportion of correct hits and false positives, (b) mean proportion of correct responses (dotted line = chance), and (c) mean self-report ratings of response confidence, with standard error of the mean error bars. Individual data points are represented by yellow circles.

5.5.2.1. Effects of self-reference on recognition memory

We report analysis of recognition memory first in order to show the presence of a self-reference memory effect. Planned comparisons of A' revealed better recognition memory for self-allocated than other-allocated pictures [patients: $t(9) = 3.0$, $p = .014$, controls: $t(10) = 5.6$, $p < .001$], and for new than other-allocated pictures [patients: $t(9) = 3.3$, $p = .010$, controls: $t(10) = 4.9$, $p = .001$], with no difference between self-allocated and new pictures

[patients: t < 1, controls: t < 1] . Both groups therefore showed the expected self-reference memory effect, and effects of novelty.

5.5.2.2. Effects of self-reference on semantic retrieval in SA patients

For patients' semantic judgements, ANOVA revealed a significant main effect of association strength [$F(1, 9) = 251.1$, $p < .001$, $\eta_p^2 = .97$], with higher accuracy on strong than weak association trials. There was no significant main effect of self-reference [$F < 1$] or self-reference by strength interaction [$F < 1$]. Patients' semantic control composite score positively correlated with overall accuracy [$r_s(8) = .90$, $p < .001$], reflecting higher accuracy in less impaired patients.

5.5.2.3. Omnibus self-reference ANOVAs

In the omnibus ANOVA including both groups (see Table 5.3), controls were more accurate than patients. There was a main effect of association strength, reflecting higher accuracy for strong than weak association trials. There were no significant effects or interactions involving self-reference. Ratings of confidence were higher for strong than weak association trials.

Table 5.3. Omnibus ANOVA results for all Experiment 5.2 (self-reference) dependent variables.

Dependent variable	Main effect/interaction	Results
A' (recognition memory)	Group	$F(1, 19) = 2.1$, $p = .168$, $\eta_p^2 = .10$
	Self-reference	**$F(1.6, 29.5) = 24.3$, $p < .001$, $\eta_p^2 = .56$***
	Self-reference by group	$F(1.6, 29.5) = .1$, $p = .861$, $\eta_p^2 < .01$
Accuracy	**Group**	**$F(1, 20) = 12.7$, $p = .002$, $\eta_p^2 = .38$***
	Self-reference	$F(1, 20) = .1$, $p = .767$, $\eta_p^2 < .01$
	Self-reference by group	$F(1, 20) = .3$, $p = .595$, $\eta_p^2 = .01$
	Strength	**$F(1, 20) = 113.3$, $p < .001$, $\eta_p^2 = .87$***
	Strength by group	$F(1, 20) = 3.7$, $p = .068$, $\eta_p^2 = .16$
	Self-reference by strength	$F(1, 20) = .1$, $p = .803$, $\eta_p^2 < .01$
	Self-reference by strength by group	$F(1, 20) = .2$, $p = .677$, $\eta_p^2 < .01$
Confidence	Group	$F(1, 20) = .1$, $p = .776$, $\eta_p^2 < .01$
	Self-reference	$F(1, 20) = .3$, $p = .589$, $\eta_p^2 = .02$
	Self-reference by group	$F(1, 20) = .1$, $p = .746$, $\eta_p^2 < .01$
	Strength	**$F(1, 20) = 94.9$, $p < .001$, $\eta_p^2 = .83$***
	Strength by group	$F(1, 20) = 2.9$, $p = .102$, $\eta_p^2 = .01$
	Self-reference by strength	$F(1, 20) = .2$, $p = .688$, $\eta_p^2 < .01$
	Self-reference by strength by group	$F(1, 20) = .2$, $p = .675$, $\eta_p^2 = .01$

Note: * reflects a significant result.

5.5.3. Experiment 5.2 summary

Experiment 5.2 examined the effect of self-reference on SA patients' and controls' ability to make thematic associations. As in Experiment 5.1, controls were more accurate than the patients, and performance was poorer on weak than strong association trials. Greater response confidence was observed for strong versus weak associations. Despite showing a benefit of self-reference for recognition memory, self/other-allocation did not affect the retrieval of thematic associations.

5.6. Discussion

The current study explored the impact of motivation on controlled semantic retrieval in SA patients with multimodal semantic impairment following left frontoparietal stroke. We assessed the impact of performance-contingent extrinsic reward (Experiment 5.1) and self-referentially encoded pictures (Experiment 5.2) on patients' and controls' ability to retrieve strong and weak thematic associations. As expected, SA patients showed lower accuracy overall. Both groups showed lower accuracy for weak associations, thought to reflect higher semantic control demands. Importantly, extrinsic reward improved SA patients' but not controls' accuracy. Self-reference did not impact participants' semantic performance, despite boosting recognition memory.

SA patients typically show greater semantic impairment for weak associations, when the retrieval of non-dominant information is required (Thompson et al., 2017). In this study, we did not observe the anticipated interactions between group and association strength in accuracy (or response time, see Supplementary Table 5.4), perhaps because the weak association trials were relatively difficult, eliciting frequent errors even in controls, or because our patient sample included mildly impaired individuals. Future research could address these possibilities by observing effects of parametric manipulations of association strength in SA and/or by including more patients with a wider degree of impairment. Experiment 5.1 demonstrated improvements in participants' accuracy for weak but not strong associations following high extrinsic reward. SA patients showed an effect of reward while controls did not, suggesting that when sufficient control over semantic retrieval is harder to

achieve, benefits of extrinsic reward are maximised. Anticipation of extrinsic reward may increase preparatory cognitive control, supporting the ability to maintain task-relevant representations and shield against irrelevant information (Goschke & Bolte, 2014). This is consistent with the current finding that high extrinsic reward increased self-reported task focus. Furthermore, explicit knowledge of task goals has been shown to facilitate semantic judgements (Zhang et al., 2021). Reward may benefit semantic control by augmenting goal-maintenance.

Our findings are also consistent with evidence that extrinsic incentives improve performance on domain-general cognitive control tasks (Capa et al., 2013). Neuroimaging research has shown that introducing extrinsic rewards to cognitive control tasks increases activity across MDN regions (Shashidhara et al., 2019), increases functional connectivity between the ventral striatum and MDN (Cubillo et al., 2019), and improves decoding accuracy of MVPA classifiers for task-set information (Etzel et al., 2016). This reflects enhanced coding of task-relevant information, in line with suggestions that extrinsic reward improves goal maintenance (Goschke & Bolte, 2014). The interaction between reward and semantic control seen in the current study may also be attributable to modulation of MDN regions, as well as regions specifically recruited during semantic control. Indeed, MDN regions are recruited during semantic tasks with high control demands (Wang et al., 2020). Future neuroimaging investigations could elucidate the extent to which motivated semantic control is attributable to modulation or recruitment of domain-general versus semantic control regions. Despite their distinct neurobiological underpinnings (Gao et al., 2021), the current findings suggest that modulatory behavioural effects of reward on semantic control mirror those seen for domain-general control.

While there is evidence that semantic and domain-general control are dissociable (Gonzalez Alam et al., 2018), samples of SA patients can show associations between performance on tests of these functions (Thompson et al., 2018). Semantic and executive control substrates are adjacent, such that damage to one system is frequently accompanied by damage to the other (Souter, Wang, et al., 2022 [Chapter 2 of this thesis]; Wang et al., 2018). Accordingly, the current study revealed a positive correlation between semantic ability and performance on the Brixton Spatial Anticipation Test, a complex nonverbal executive test. Patients' semantic control composite did not correlate with executive measures with verbal requirements including the difference between parts A and B of the Trail Making Test, or with the nonverbal Raven's coloured progressive matrices. While these null results may

reflect a lack of statistical power, our results are sufficient to show that associations between semantic and executive performance are not confined to tests with verbal requirements, consistent with evidence that executive performance is independent of verbal demands in aphasia patients with left IFG lesions (Kendrick et al., 2019; see Chapman et al., 2020 for an alternative view).

The current findings have implications for aphasia rehabilitation. Positive effects of reward are seen in 'gamification' strategies to neurorehabilitation (and education more widely), whereby tasks are made more motivating using typical game features, such as rewards and social competition (Landers, 2014). A preliminary investigation demonstrated that gamification may facilitate the rehabilitation of word production following stroke (Romani et al., 2019). The current findings extend this work to show that SA patients can benefit from this strategy, despite deficits of semantic control being accompanied by difficulties in constraining internal representational states in domains beyond semantic cognition, including emotion perception (Souter et al., 2021 [Chapter 3 of this thesis]) and episodic memory (Stampacchia et al., 2018). These findings merit further investigation of the use of gamified extrinsic incentives in addressing post-stroke impairments in semantic control. SA patients benefit from external prompts which allude to target concepts, including phonemic cues (Jefferies et al., 2008), context-relevant sentences (Noonan et al., 2010), and emotional cues (Lanzoni et al., 2019). The current findings demonstrate that prompts which do not provide additional information concerning target concepts, such as abstract extrinsic incentives, can confer similar benefits.

The current manipulation of self-reference was intended as a proxy for intrinsic motivation, based on evidence of overlapping behavioural effects of self-reference and reward processing (Sui & Humphreys, 2015a), and overlapping neural substrates underlying self-reference and intrinsic motivation (Tamir & Mitchell, 2012). We found expected effects of self-reference on recognition memory, suggesting that we successfully evoked self-referential encoding, consistent with prior evidence from SA (Stampacchia et al., 2019). Self-reference was not found to modulate semantic retrieval. This null result does not preclude the role of intrinsic motivation in semantic performance; the manipulation in the current study may have been insufficient. In future studies, further tailoring may be required to elicit stronger intrinsic motivators. As intrinsic motivation reflects inherent interest or enjoyment (Mori et al., 2018), it may be beneficial to include stimuli which are specifically of interest to, or belong to, the participant.

5.6.1. Limitations

The current study is limited in so far as we did not measure several constructs related to reward processing. Affective abnormalities including apathy (Fishman et al., 2018) and hypo/hyperarousal (Heilman et al., 1978; Laures et al., 2003) are common following stroke, and could interfere with reward sensitivity. This has been demonstrated in relation to apathy, following damage to subcortical reward processing regions (Rochat et al., 2013). The current study cannot account for these effects. It is worth noting, however, that in the current sample, subcortical and medial regions were relatively intact (see Section 5.3.2.). Future investigations into reward processing in post-stroke aphasia may benefit from measuring apathy, reward sensitivity, and physiological arousal to better account for effects of these constructs.

5.6.2. Conclusion

The current study demonstrates that extrinsic reward can improve SA patients' ability to make thematic associations. As with domain-general cognitive control, extrinsic reward may bolster semantic retrieval through increased proactive control. These findings have practical implications for the rehabilitation of post-stroke semantic impairment; language therapy activities for SA patients could be facilitated using a gamification-based approach incorporating external rewards. Effects of self-reference on semantic performance were not observed.

5.7. Link to Chapter 6

Chapter 5 provided evidence that cued extrinsic rewards can ameliorate impairments in semantic control in patients with semantic aphasia (SA). This was the case despite evidence from Chapters 3 and 4 of affective abnormalities in SA. Together, empirical chapters up to this point have provide novel insight into SA as a condition, including its wide reaching impairments and the steps that can be taken to ameliorate them. Chapter 5 also provided further evidence of similarities between semantic and domain-general cognitive control, in so far as both can be bolstered by extrinsic incentives (Swirsky & Spaniol, 2019). This is also consistent with evidence from Chapter 2, which suggested that these two control processes are supported by adjacent fronto-parietal substrates. The final empirical chapter of this thesis aimed to further investigate neural systems that support semantic retrieval, with a specific focus on the role of the default mode network (DMN), as well as considering contributions of the semantic control network (SCN) and multiple demand network (MDN).

DMN has been implicated in a number of higher-order cognitive processes, particularly those with reliance on internally-focused and memory-guided processing (Smallwood et al., 2021). DMN has been linked to semantic representation and processing (Lanzoni et al., 2020), perhaps by virtue of its inclusion of the ventral anterior temporal lobe, a proposed heteromodal semantic hub (Patterson et al., 2007). Beyond this, DMN function has been linked to a number of diverse domains, including reward processing and emotion induction (Mancuso et al., 2022), and the representation of discrete emotion states (Satpute & Lindquist, 2019) and of valence (Lee et al., 2021). Chapter 6 observed the contribution of DMN, and its functionally dissociable subnetworks (Andrews-Hanna et al., 2014), to the generation of semantic contextual and emotional associations. Of particular interest was differential responses of this network according to changing retrieval demands. It may be that activation in DMN subnetworks varies according to such demands. Alternatively, retrieval demands may selectively modulate frontoparietal control regions, orthogonally to the recruitment of task-specific DMN responses. Addressing these questions will provide further insight into the neural bases of semantic retrieval, as well as the similarity in the processing of emotional and more contextual semantic information. If the processing of affective information does rely on semantic control, as suggested by Chapters 3 and 4 of this thesis, it may be that emotional associations recruit SCN to the same extent as contextual associations.

Chapter 6: Default mode network shows distinct emotional and contextual responses yet common effects of retrieval demands across tasks

We do not have sufficient consent to publicly share individual pseudonymized data. Researchers wishing to gain access to the raw data should contact the corresponding authors or the Research Ethics Committee of the York Neuroimaging Centre. Data will be made available when this is possible under the terms of the General Data Protection Regulations (GDPR). Group-level data used in the creation of figures as well as the materials (code) used to run the study are publicly available on the Open Science Framework (OSF; https://osf.io/498ur/). Group-level NIFTI files are available on Neurovault (https://neurovault.org/collections/CFYXAGAU/).

Acknowledgements and author's contribution

The project was conceptualised by Nick Souter, and Elizabeth Jefferies, following conversations with co-authors Jonathan Smallwood and Haakon Engen. Nick Souter oversaw the creation of stimuli, experimental design, coding of experimental scripts in Python, data analysis, and data curation. Co-authors Meichao Zhang, Katya Krieger-Redwood, Tirso Gonzalez Alam, and Elizabeth Jefferies provided input on the creation of the MRI paradigm (e.g., time allocated per phase/scanning parameters). Data was collected by Nick Souter along with co-authors Antonia de Freitas (for whom this project contributed to her MSc project), and Katya Krieger-Redwood and Tirso Gonzalez Alam, who assisted in the scanning of participants. Staff at the York Neuroimaging Centre, including Rebecca Lowndes, Richard Aveyard, Holly Brown, and Andre Gouws, also assisted in scanning participants, and trained Nick Souter as an MRI operator. Antonia de Freitas assisted in the creation of stimuli. Co-authors Meichao Zhang, Ximing Shao, Katya Krieger-Redwood, and Xiuyi Wang assisted Nick Souter in the running of MRI analysis, providing technical advice. Nick Souter wrote the full original draft of this paper, conducted formal analysis, and created all figures. Elizabeth Jefferies edited manuscript drafts, and Antonia de Freitas provided feedback on the current version.

6.1. Abstract

The default mode network (DMN) lies towards the heteromodal end of the principal gradient of intrinsic connectivity, maximally separated from sensory-motor cortex. It supports memory-based cognition, including the capacity to retrieve conceptual and evaluative information from sensory inputs, and to generate meaningful states internally; however, the functional organisation of DMN that can support these distinct modes of retrieval remains unclear. We used fMRI to examine whether activation within subsystems of DMN differed as a function of retrieval demands, or the type of information to be retrieved, or both. In a picture association task, participants retrieved two types of semantic features: contexts and emotions. In the generate phase, these associations were retrieved from a novel picture, while in a switch phase, participants retrieved a new association for the same image. Semantic context and emotion trials were associated with dissociable DMN subnetworks, indicating that a key dimension of DMN organisation relates to the type of information being accessed. Relative to the generate phase, the switch phase recruited clusters closer to the heteromodal apex of the principal gradient. There were no differences in this effect between association types. Instead, memory switching was associated with a distinct subnetwork implicated in controlled internal cognition. These findings delineate *distinct* patterns of DMN recruitment for different kinds of associations yet *common* responses across tasks that reflect retrieval demands.

6.2. Introduction

The default mode network (DMN) is a large-scale distributed network which frequently shows task-related deactivation (Raichle, 2015) yet is also associated with aspects of cognition that are dependent on memory (Murphy et al., 2018; Zhang, Bernhardt, et al., 2022). It is thought to support diverse tasks relating to social cognition, episodic recall, semantic retrieval, and emotion induction (Mancuso et al., 2022). In such domains, DMN is thought to support our interpretation of external events and the distillation of diverse features (Lanzoni et al., 2020), as well as the ability to generate cognitive states that are decoupled from the external world (Smallwood et al., 2021). However, the functional organisation of this network remains unclear, since its activation may be modulated according to the type of information being retrieved, and/or the retrieval demands associated with a particular task.

DMN regions are thought to be maximally distant from sensory-motor cortex on a cortical hierarchy. This topographical organisation is captured by the principal gradient, the dimension of whole-brain intrinsic connectivity that explains the most variance (Margulies et al., 2016). The principal gradient reveals maximal separation of connectivity patterns between unimodal and heteromodal regions and can also explain the order of large-scale networks along the cortical surface, from sensory-motor regions, through attention networks and the frontoparietal control network, to DMN. This separation is thought to allow DMN to support both perceptually-decoupled and abstract thought, since both involve informational states that are at odds with the changing environment (Gordon et al., 2020; Murphy et al., 2018; Smallwood et al., 2021). From picture cues, we can access information about abstract categories that allow us to evaluate and make sense of our experiences, and we can retrieve past events that are no longer taking place (using sensory to DMN pathways). We can also generate sensory-motor features relating to these concepts or past events, even when they do not overlap with features present in the external world (using DMN to sensory pathways).

Nevertheless, DMN contains dissociable subnetworks which might support distinct types of memory-guided cognition. Andrews-Hanna et al. (2014) reported that in addition to a 'core' DMN network focussed on anterior and posterior cingulate cortex and angular gyrus, patterns of intrinsic connectivity reveal a medial temporal (MT) subnetwork (including retrosplenial cortex) and a lateral fronto-temporal (FT) subnetwork[18] (including dorsomedial

[18] Sometimes referred to as the '*dorsal medial subsystem*'.

prefrontal cortex). The MT subnetwork includes aspects of the hippocampus and parahippocampal gyrus, implicated in mental scene construction (Sheldon & Levine, 2016). The FT subnetwork shows greater connectivity with the anterior temporal lobes (ATL; Andrews-Hanna et al., 2014), a brain region thought to provide a heteromodal semantic 'hub' (Chiou & Lambon Ralph, 2019; Lambon Ralph et al., 2017) which is also associated with processing valence (Juran et al., 2016; Spiers et al., 2017; Wang et al., 2019). These subnetworks are consequently associated with different aspects of memory: the MT network is associated with episodic recollections of specific experiences that are typically visuo-spatial in nature, while the FT network is implicated in semantic and social cognition, based on knowledge extracted across many experiences which is typically more abstract in nature (Andrews-Hanna and Grilli, 2021; Andrews-Hanna et al., 2014; Chiou et al., 2020; Gurguryan & Sheldon, 2019; Sheldon et al., 2019). Core DMN regions sit at points where the MT and FT subsystems are spatially interdigitated (Braga & Buckner, 2017; Yeo et al., 2011) and might help to draw together spatial, semantic, and valence information to form coherent patterns of cognition (Lanzoni et al., 2020).

Despite progress in characterising the functional organisation of DMN, several issues remain unresolved. The first concerns the specific task dimensions that separate MT and FT subsystems. While semantic cognition is often considered to involve abstract categories (e.g., types of emotions), we also have general visuo-spatial knowledge about typical scenes and events, acquired over our lifetime. Contrasts of semantic tasks probing contextual information about generic spatial-temporal associations versus valenced associations can establish whether MT and FT subnetworks support distinct types of information processing (scene construction versus evaluative categories). A second unresolved issue concerns how retrieval demands intersect with DMN subnetworks. Research to date has shown similar DMN recruitment for tasks based on meaning as opposed to perceptual features, and for memory-guided 1-back decisions over 0-back trials (Murphy et al., 2018). Nevertheless, very little research has investigated whether retrieval demands equivalently modulate the response of DMN subsystems. One possibility is that FT is more coupled to visual cortex (to allow semantic access from vision) while MT might be more perceptually-decoupled, since episodic tasks rely largely on internal recollection (Chiou et al., 2020). However, internally-focused processes such as mind-wandering also rely on conceptual and evaluative information (Faber & D'Mello, 2018), and so both perceptually-coupled and decoupled retrieval might be supported by both MT and FT subnetworks. Consequently, retrieval

demands might change responses within DMN in a way that is orthogonal to the MT/FT distinction.

Further debate concerns the relationship between DMN and cognitive control networks. DMN regions can support memory-based cognition when executive demands are high (Brown et al., 2019; Murphy et al., 2018; 2019) and DMN is implicated in goal maintenance during controlled semantic retrieval (Wang et al., 2021). This functional similarity between DMN and heteromodal control networks is captured by the principal gradient (Margulies et al., 2016), which identifies these networks as adjacent (Wang et al., 2020). Frontotemporal control regions may also form different alliances depending on task demands (Gonzalez Alam et al., 2022; Niendam et al., 2012; Spreng et al., 2013); they are recruited with attention networks to form the multiple demand network (MDN; Duncan, 2001; 2010; Fedorenko et al., 2013; Hugdahl et al., 2015), and with DMN during semantic tasks. The semantic control network (SCN; Noonan et al., 2013; Jackson, 2021) is situated at the intersection of frontoparietal control regions and DMN (Chiou et al., 2022; Davey et al., 2016; Wang et al., 2020), and is functionally and spatially distinct from MDN (Gao et al., 2021; Humphreys et al., 2015). This network supports semantic control - an executive process crucial for conceptual retrieval of non-dominant aspects of knowledge relevant to the current task. SCN might allow non-dominant memory representations to be prioritised according to goals (Zhang et al., 2021), while MDN prioritises task-relevant sensory-motor input features (Gao et al., 2021). This is reflected in the patterns of intrinsic connectivity of control networks: the 'control A' subnetwork[19] couples with dorsal attention network (DAN), while 'control B' couples with DMN (Dixon et al., 2018; Yin et al., 2022). However, little is known about how control networks for DMN (control B; SCN) relate to the distinction between MT and FT DMN. Weak episodic and semantic associations have been shown to recruit common control regions in SCN (Vatansever et al., 2021), suggesting that distinct memory systems might draw on shared control processes, although DMN subsystems were not examined in this study.

Here, we used functional magnetic resonance imaging (fMRI) to characterise the contribution of DMN subsystems and control networks (SCN and MDN) to the retrieval of emotional associations and meaning-based contexts from picture cues. While both tasks were

[19] The 'control A' and 'control B' terminology is consistent with the labels frequently given to these respective sets of regions from the Yeo et al. (2011) and Schaefer et al. (2018) 17-network parcellations. They have also often been referred to as 'FPCNb' and 'FPCNa', respectively.

reliant on semantic information, they may preferentially activate FT and MT subnetworks, respectively, if these subsystems are sensitive to the type of information being retrieved. Associations were made twice for each picture, allowing us to investigate the effect of varying retrieval demands on these responses. The '*generate'* phase required participants to identify an association from a picture (tapping pathways from visual to heteromodal memory systems). In the '*switch'* phase, participants were asked to retrieve a *new* association from the same picture, tapping processes that drive alternative associations even when the image does not change. We investigated whether responses in FT and MT DMN were modulated by differing retrieval demands across phases, or whether this manipulation was largely independent of association type and instead reflected in control-relevant DMN regions (e.g., control B). This latter possibility is consistent with the observation that brain regions underpinning conceptual abstraction in long-term memory (e.g., ATL) are distinct from SCN regions supporting the control of conceptual retrieval (Jefferies, 2013; Lambon Ralph et al., 2017).

6.3. Materials & Methods

6.3.1. Participants

Participants were right-handed, between the ages of 18 and 35, with normal or corrected to normal vision, no history of neurological disorder, and no current psychiatric disorder. Participants were students at the University of York, recruited through word of mouth and participant pools, and paid for their time or awarded course credit. Thirty-three participants were scanned, with one excluded as they reported having not made associations for the majority (52.1%) of trials during the recall phase (see Section 6.3.4.). The final sample consisted of 32 participants (24 female) with a mean age of 20.1 (SD = 2.4). Ethical approval for this study was granted by the York Neuroimaging Centre at the University of York (date: 23/06/2021, project ID: P1446). Informed consent was obtained from all participants prior to participation.

6.3.2. Design

A within-subjects design was used, with each participant completing both *emotion* and *semantic context* associations. They retrieved these associations over two phases of the task: in the *generate* phase, they retrieved semantic information from a novel picture; in the *switch* phase they were shown the same picture and asked to retrieve a different association.

6.3.3. Materials

Stimuli were taken from the International Affective Picture System (IAPS; Lang et al., 2008), a database of pictures normed for valence and arousal. Thirty-six pictures were selected for *emotion* associations and were classified as either positive (valence mean > 6) or negative (valence mean < 4), with an equal number of positive and negative images in each run. Thirty-six pictures were selected for *semantic context* associations, all of neutral valence (valence mean between 4 and 6). Content was broadly matched, such that *semantic context*, positive *emotion*, and negative *emotion* sets each contained equivalent proportions of people (61.1%) and animals (5.6%). Pictures for *semantic context* associations had significantly lower mean valence than positive *emotion* pictures ($U < 1$, $p < .001$), and higher mean valence than negative *emotion* pictures ($U < 1$, $p < .001$). Ratings of mean arousal were significantly higher for *emotion* than *semantic context* pictures ($U = 221.0$, $p < .001$), but were matched between positive and negative *emotion* images ($U = 153.5$, $p = .791$). Identifiers for each image and normed ratings of valence and arousal can be seen in Supplementary Table 6.1. Python scripts used to present them are available on the Open Science Framework (OSF; https://osf.io/498ur/).

6.3.4. Procedure

A summary of the procedure can be seen in Figure 6.1. Trials were presented across six 4.5 minute long functional runs, each containing one *emotion* mini-block (six trials) and one *semantic context* mini-block (six trials). The order of trials within each run was consistent across participants. Run order was counterbalanced across participants such that a given block could appear in any position (first to sixth).

The day before the scan, participants completed two practice runs (using stimuli not presented in the main experiment) remotely via Zoom (Zoom Video Communications Inc., 2016). During the first run participants reported their associations verbally, in order for the researcher to confirm that they had correctly comprehended the study instructions. During the

second run participants completed the task without verbal responses, to simulate the in-scanner procedure.

At the start of each mini-block, participants were presented with a 2s prompt informing them of the current association type ('SEMANTIC' or 'EMOTION'). Each trial was preceded by a fixation cross, for an average of 1.5s, jittered between 1 and 3s. During the 'GENERATE' phase of *semantic context* associations, participants were shown a picture and asked to reflect on the first event-based association this picture brought to mind. Participants were told not to simply reflect on the content of the picture, nor to recall an episodic memory, but to identify a meaningful context from their general knowledge (e.g., for a picture of a street with washing lines, "walking through a city while on holiday"). During the 'SWITCH' phase, participants were asked to stop reflecting on their initial association, and to reflect on another, perhaps less obvious, context associated with this picture (e.g., "using the sun to dry washing"). During the 'GENERATE' phase of *emotion* associations, participants were shown a picture and asked to reflect on how it made them feel. Participants were asked to avoid simple descriptive labels, but instead to embody emotions caused by the picture (e.g., for a picture of an empty hospital room, thinking about feeling sad). During the 'SWITCH' phase, participants were asked to stop thinking about this emotion, and to switch to another emotional response (e.g., fear). Each *generate* and *switch* phase involved seeing a given picture for the first and second time, respectively. *Generate* and *switch* phases were presented for an average of 5s, jittered between 3.5 and 6.5s. After each *generate* and *switch* phase, participants indicated how strongly related they believed their self-generated association to be to the picture on a scale from 1 (no real relationship) to 7 (very strong relationship). At the end of each trial, participants indicated how difficult they found it to switch from the first to the second association on a scale from 1 (very easy) to 7 (very difficult). Each strength of association and difficulty rating was presented for a set period of 3s.

Immediately following the scan, participants completed a 'recall' assessment. Pictures were presented in the same order as in the scanner, and participants were asked to type which contexts or emotions they had generated, as well as their confidence in the recall accuracy (from 1-7), for both the *generate* and *switch* phases. This data was used to qualitatively validate that each participant had completed the task as intended.

Figure 6.1. Examples of trials for both semantic context (top) and emotion (bottom) associations. Each miniblock was preceded by (a) a probe reflecting the current association type. Each trial was preceded by (b) a fixation cross. This was followed by (c) the 'generate' phase in which dominant response is generated and (d) the 'switch' phase in which a subordinate response is generated. Each trial contained (e) self-report ratings of strength of association between the picture and generated association after each phase, and overall switch difficulty at the end of the trial. The duration of each phase (in seconds) is indicated. Photos used for this figure are taken from stock photo website Pexels, from users Pixabay (emotion) and Elina Sazonova (semantic context).

6.3.5. fMRI acquisition

Participants were scanned at the York Neuroimaging Centre, University of York, using a 3T Siemens MRI scanner with a 64-channel head coil, tuned to 123MHz. A localiser scan and six whole brain functional runs were acquired using a multi-band multi-echo (MBME) EPI sequence (TR = 1.5 s; TEs = 12, 24.83, 37.66 ms; 48 interleaved slices per volume with slice thickness of 3 mm (no slice gap); FoV = 24 cm (resolution matrix = 3x3x3; 80x80); 75° flip angle; 180 volumes per run; 7/8 partial Fourier encoding and GRAPPA (acceleration factor = 3, 36 ref. lines; multi-band acceleration factor = 2). Structural T1-weighted images were acquired using an MPRAGE sequence (TR = 2.3 s, TE = 2.26 s; voxel size = 1x1x1 isotropic; 176 slices; flip angle = 8°; FoV= 256 mm; interleaved slice ordering).

6.3.6. MRI data pre-processing

An MBME sequence was used to optimise signal from the medial temporal lobes while maintaining signal across the whole brain (Halai et al., 2014). Echoes within each functional run were combined using the TE Dependent ANAlysis (tedana; version 0.0.12; Kundu et al., 2011; 2013; The tedana Community et al., 2021) library in Python. Pre-processing was performed before echoes were combined, using the Anatomical Processing Script pipeline in FSL (fsl_anat; https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/fsl_anat). This included re-orientation to standard MNI space (fslreorient2std), automatic cropping (robustfov), bias-field correction (RF/B1 – inhomogeneity-correction, using FAST), linear and non-linear registration to standard-space (using FLIRT and FNIRT), brain extraction (using FNIRT, BET), tissue-type segmentation (using FAST) and subcortical structure segmentation (FAST). The multi-echo data were pre-processed using AFNI (https://afni.nimh.nih.gov/), including de-spiking (3dDespike), slice timing correction (3dTshift; heptic interpolation), and motion correction (3dvolreg applied to echo 1 to realign all images to the first volume; these transformation parameters were then applied to echoes 2 and 3) of all echoes aligned to the first echo (with a cubic interpolation).

6.3.7. Movement

To quantify movement during scanning, first-level analyses were run on data corresponding to the second echo only, without motion correction and combination in tedana. Across the six runs, no participant presented with absolute mean displacement greater than .76mm (sample mean = .18mm), and no relative mean displacement greater than .17mm (sample mean = 0.06mm). No runs were excluded on the basis of movement.

6.3.8. fMRI data analysis

First-, individual-, and group-level analyses were conducted using FSL-FEAT version 6 (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl; Jenkinson et al., 2012; Smith et al., 2004; Woolrich et al., 2009). Denoised optimally-combined time series output from tedana were submitted as input. Pre-processing included high-pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 50s), linear co-registration to native space using the respective participant's structural T1-weighted image, and to MNI152 standard space (Jenkinson & Smith, 2001), spatial smoothing using a Gaussian kernel with full-width-half-maximum of 6 mm, and grand-mean intensity normalisation of the entire 4D dataset by a single multiplicative factor.

EVs in the model included time periods covering (1) *generate* and (2) *switch* phases of *emotion* associations, (3) *generate* and (4) *switch* phases of *semantic context* associations, (5) all self-report rating periods and (6) the association type prompt at the start of each mini-block. Fixation periods between trials were taken as the implicit baseline. Two parametric EVs reflected self-reported switch difficulty for (7) *semantic context* and (8) *emotion* associations, modelled for the *switch* phase of the respective trial. These parametric EV's included demeaned switch difficulty scores for each trial within a run, calculated separately for semantic and emotion associations. One run for one participant was excluded from the model as all *emotion* trials were rated the same for switch difficulty – resulting in each trial weighted as 0. Self-reported ratings of association strength for the *generate* and *switch* phase were not modelled as they both correlated with ratings of switch difficulty across the sample [*generate*: $r_s(2230) = -.14$, $p < .001$, *switch*: $r_s(2234) = -.53$, $p < .001$].

For whole-brain analysis at the group-level, we looked for activation associated with (1) either *semantic context* or *emotion* associations (across generate/switch phases) over baseline, as well as their conjunction (using FSL's 'eaythresh_conj' tool), (2) contrasts of *generate* versus *switch* phases, (3) contrasts of *semantic context* versus *emotion* associations, (4) the interaction of phase and association type, and (5) parametrically higher or lower self-reported switch difficulty[20]. A threshold of $Z > 3.1$ was used for all group-level contrasts.

To search for differences between association types and parse the function of DMN, we examined five resting-state networks taken from the 17-network parcellation from Yeo et

[20] Clusters corresponding to parametric analysis of difficulty can be seen in Supplementary Figure 6.1 and Supplementary Figure 6.2.

al. (2011); these five networks together constitute 96% of voxels of the DMN resulting from the 7-network parcellation. In descending order, the percentage of these networks that make up (Yeo-7) DMN: 'FT DMN' (40.1%), 'core DMN' (37.8%), 'control B' (7.7%), 'auditory' (6.6%), and 'MT DMN' (3.8%). These network maps were mutually exclusive. The auditory and control B networks are often not considered to be subnetworks of DMN but were included here as they constituted more of the Yeo7-DMN than the MT subnetwork, which is relatively small. We also assessed how much of the (Yeo 7) DMN fell within each of these networks: FT DMN = 95.3%, core DMN = 99.7%, auditory = 46.5%, MT DMN = 42.7%, control B = 23.4%. The 7-network DMN covers more of the MT DMN than control B map , despite constituting a smaller portion of the overall network.

We also examined functional maps of control networks. SCN was defined using a meta-analysis of tasks with high > low semantic control demands (Jackson, 2021). A map of MDN was taken from Fedorenko et al. (2013), and reflects activation associated with more demanding versions of cognitive tasks, thresholded at $t > 1.5$. A map of DMN was taken from the 7-network parcellation from Yeo et al. (2011; as above). All maps were mutually exclusive such that (1) voxels contained within both SCN and DMN were removed from each and placed in the 'DMN & SCN' map, and (2) any voxels contained within both SCN and MDN were removed from each and placed in the 'SCN & MDN' map[21]. This reduced the size of DMN by 6.4%, MDN by 8.0%, and SCN by 62.5%. These portions are captured in the joint overlap maps. See Supplementary Table 6.2 for the percentage of each network that falls in each Yeo et al. (2011) 17-network parcellation.

As noted in section 1.3.4., each of these functional control networks defined here show a degree of overlap with regions implicated in language processing. Within DMN resting-state networks, this overlap is particularly striking in the auditory DMN, 62.3% of which falls within the language network (as defined by Neurosynth term-based meta-analysis [Yarkoni et al., 2011], based on 1101 studies and a threshold of $Z > 3.1$). Findings relating to this network can therefore be interpreted as reflecting activation in language regions within the context of DMN. Areas of overlap for this network include the bilateral temporal pole and superior temporal gyrus, and left supramarginal gyrus, precentral gyrus, and dorsomedial prefrontal cortex.

[21] 265 voxels overlapping in DMN and MDN were left in 'DMN'. 149 voxels overlapping in SCN, DMN, and MDN were left in 'SCN & MDN'. These areas of overlap account for small amounts of the overall networks (total voxel numbers; SCN = 6,364, MDN = 28,761, DMN = 30,127).

We ran region of interest (ROI) analysis using the Featquery function of FSL with binarised versions of (1) the resting-state networks overlapping with the DMN and (2) functional control networks. Mean percent signal change was calculated for each ROI in each combination of association type and phase over baseline. Repeated measures ANOVAs were run separately for DMN overlap networks and functionally-defined control networks examining effects and interactions of association type, phase, and network. Both analyses had two levels for association type (*semantic context, emotion*), two levels for phase (*generate, switch*), and five levels for network (DMN overlap networks = FT DMN, core DMN, control B, auditory, FT DMN; control networks = DMN, DMN & SCN, SCN, SCN & MDN, MDN).

To assess the global fit of task activation with network patterns, we ran further supplementary analyses. These used the same structure as our mean percent signal change analyses, observing individual-level Spearman spatial correlations between each network and each combination of association type and phase over baseline (see Chapter 6 Supplementary Materials section '*Individual-level spatial correlations*').

Finally, we characterised the placement of clusters associated with task activation on the principal gradient, reflecting the separation between unimodal and heteromodal regions. We performed Spearman spatial correlations between a map of the principal gradient (from Margulies et al., 2016) and unthresholded contrasts of each combination of association type and phase over baseline. This was performed at the individual-level, such that a coefficient was obtained for each contrast for each participant. We then ran a repeated measures ANOVA examining effects and interactions of association type and phase. Positive mean coefficients reflect that a given condition falls towards the heteromodal end of the gradient, while negative coefficients show that conditions are towards the unimodal end.

6.4. Results

6.4.1. Behavioural results

Descriptive statistics for self-reported association strength, switch difficulty, and recall confidence can be seen in Table 6.1. A repeated-measures ANOVA for association strength revealed significant main effects of association type [$F(1, 31) = 17.1$, $p < .001$, $\eta_p^2 = .36$] and phase [$F(1, 31) = 149.0$, $p < .001$, $\eta_p^2 = .83$], but no association type by phase interaction [$F(1, 31) = 1.6$, $p = .209$, $\eta_p^2 = .05$]. These main effects reflect greater association

strength in the *generate* than the *switch* phase, and for *emotion* than *semantic context* associations. No difference was found between association types for switch difficulty [t(31) = -1.8, p = .089]. For recall confidence, we observed a main effect of phase [F(1, 31) = 80.5, p < .001, η_p^2 = .72], but no effect of association type [F(1, 31) = 0.8, p = .392, η_p^2 = .02] or association type by phase interaction [F(1, 31) < 0.1, p = .827, η_p^2 < .01]. Recall confidence was greater for the *generate* than the *switch* phase.

Table 6.1. Descriptive statistics for self-reported ratings of strength of association, switch difficulty, and recall confidence, split by association type.

	Mean (SD)	
	Semantic context	Emotion
Generate association strength	5.22 (0.69)	5.60 (0.59)
Switch association strength	4.00 (0.67)	4.20 (0.62)
Switch difficulty	4.05 (0.63)	3.86 (0.64)
Generate recall confidence	6.02 (0.58)	5.94 (0.54)
Switch recall confidence	5.26 (0.82)	5.21 (0.78)

Note: All ratings taken on a Likert scale from 1-7.

To validate that participants were using an appropriate strategy for *semantic context* associations, we coded the content of all recalled responses within and across phases (see Supplementary Table 6.3). The majority of associations were 'general semantic' as intended (70%). Some were classified as 'personal semantic' – associations reported in the first person and/or referring to a specific person or place in the participant's life (7%). A small number were classified as 'episodic', as they alluded to discrete events in the participant's life (3%). Although there was considerable variation across participants, *emotion* associations were largely recalled as single words [mean (SD) = 67.3% (27.4)].

6.4.2. Whole-brain analysis

Results of group-level whole-brain analysis are presented in Figure 6.2. Supplementary Figure 6.3 provides the percentage of voxels for each contrast that fall in each of the Yeo et al. (2011) 17-network parcellations. Brain maps throughout this paper were visualised with the BrainNet Viewer (Xia et al., 2013; https://www.nitrc.org/projects/bnv/). Unthresholded versions of group-level nifti files for this project are available on Neurovault (https://neurovault.org/collections/CFYXAGAU/).

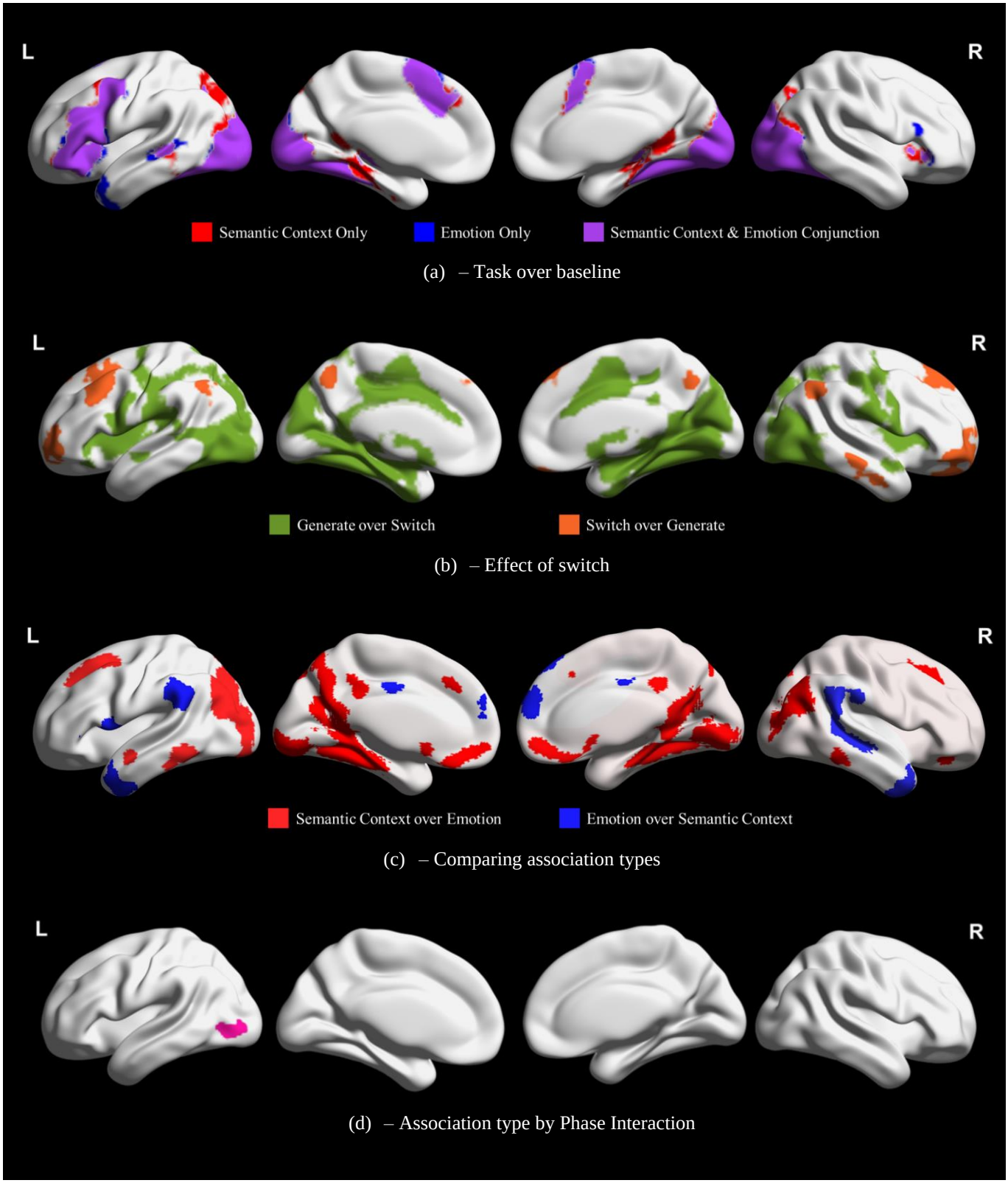


Figure 6.2. Clusters associated (a) with task activation relative to baseline, (b) more with one phase (generate or switch) than the other, (c) more with one association type (emotion or semantic context) than the other, and (d) in the interaction of association type and phase. Clusters taken from group-level analysis in FSL-FEAT with a threshold of Z > 3.1.

Figure 6.2a presents activation associated exclusively with either *semantic context* or *emotion* associations, as well as the conjunction of the two over baseline. Activation across association types is highly converging. All five SCN clusters (Jackson, 2021) are represented, including (1) left IFG, middle frontal gyrus (MFG) and precentral gyrus, (2) left pMTG, (3) bilateral dorsomedial prefrontal cortex (dmPFC), (4) right IFG orbitalis (all for both association types), and (5) right IFG triangularis (for *emotion* only). Visual processing regions are also represented, including the occipital pole, lateral occipital cortex (LOC), and fusiform gyrus, as well as the bilateral thalamus and left caudate and pallidum.

Figure 6.2b presents clusters recruited more for the *switch* or *generate* phase, across association types. Clusters associated with the *generate* phase were extensive and highly overlapping with visual processing regions. The effect of *switch* fell within bilateral angular gyrus (AG), dmPFC, superior frontal gyrus (SFG), precuneus, and frontal pole, right pMTG and left MFG, with many of these clusters within DMN. As seen in Supplementary Figure 6.3e, this contrast shows the greatest overlap with the control B network (46.4%) followed by the core DMN (18.0%) and FT DMN (16.1%). We also found similarity in the effect of *switch* across association types, with overlapping effects across *emotion* and *semantic context* trials in bilateral frontal pole and dorsolateral PFC (see Supplementary Figure 6.4).

Figure 6.2c presents clusters recruited more for *semantic context* or *emotion* associations, across phases. Clusters associated with *semantic context* associations include bilateral LOC, occipital pole, pMTG, ventromedial PFC, posterior cingulate cortex (PCC), precuneus, MFG, SFG, and paracingulate gyrus, left anterior superior temporal gyrus, and right frontal pole. Much of the MT DMN (76%) is represented in these clusters, but this effect of association type extends to visual networks and DAN (given this broader recruitment, only 12.8% of the *semantic context* over *emotion* contrast falls within MT DMN; see Supplementary Figure 6.3b). Clusters showing greater activation for *emotion* associations include the bilateral temporal pole, supramarginal gyrus, dmPFC, and PCC, right AG and pMTG/posterior inferior temporal gyrus, and left IFG pars opercularis. This effect overlaps with the FT DMN; 11.5% of this DMN subnetwork falls within these clusters, with particular overlap in ATL, dmPFC, left IFG, and right pMTG. 34.4% of the *emotion* over *semantic context* contrast falls within FT DMN, with additional overlap in core DMN and language networks, as well as in ventral attention and limbic regions (see Supplementary Figure 6.3c).

Figure 6.2d presents the interaction of association type and phase, comprising one cluster in the left inferior LOC. We extracted mean percent signal change from the peak of this cluster in each phase and association type over baseline. Mean percent signal change was .32 (SD = .04) for *semantic context generate*, .21 (SD = .03) for *semantic context switch*, .34 (SD = .03) for *emotion generate*, and .18 (SD = .03) for *emotion switch*. There was a larger effect of phase for *emotion* associations, relative to *semantic context* associations, in this cluster, primarily because the *switch* phase of *emotion* associations engaged this site less.

6.4.3. DMN overlap networks analysis

We next considered activation differences across phase and association type within DMN subnetworks (as defined in Section 6.3.8). Figure 6.3a presents visualisations of these networks in their full form, including voxels outside the Yeo-7 DMN. Figure 6.3b presents these same networks confined to the Yeo-7 DMN. For the ROI analysis using ANOVA, outlying responses (three standard deviations above or below the group mean for each association type) were excluded. All reported post-hoc tests following significant interaction effects were Bonferroni-corrected for five comparisons (reflecting five networks).

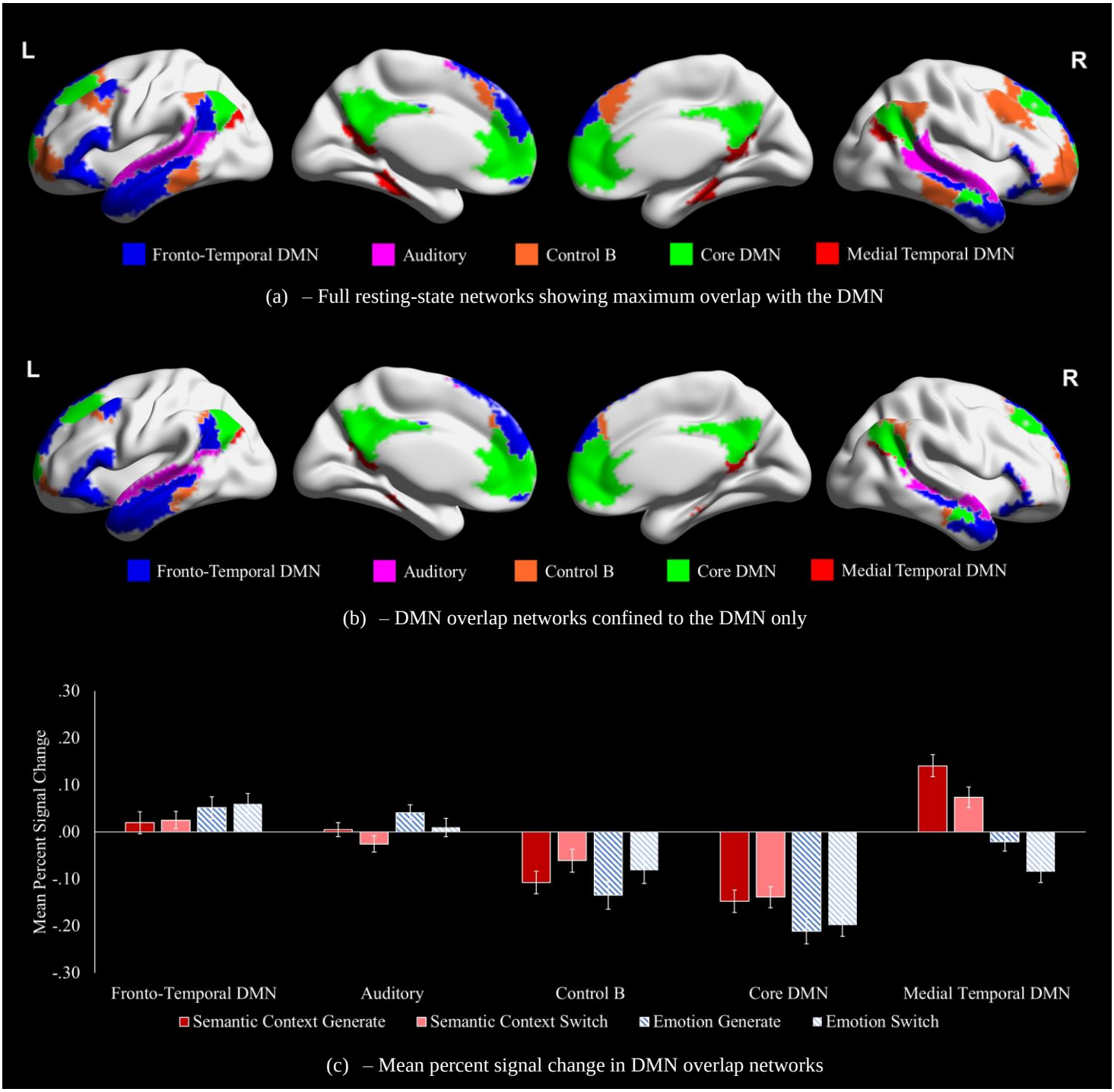


Figure 6.3. (a) Visualisation of complete resting-state networks showing maximum overlap with DMN, taken from the 17-network parcellation from Yeo et al., (2011). (b) Elements of these networks restricted to voxels within the overall DMN map from the 7-network parcellation. (c) Mean percent signal change in DMN resting-state networks in each combination of association type and phase, calculated using the Featquery function of FSL with binarised networks used as regions of interest. Error bars reflect one standard error. DMN = default mode network.

Figure 6.3c presents mean percent signal change in each Yeo-17 network overlapping with DMN, for each condition over the implicit baseline. A repeated-measures ANOVA, reported in Table 6.2, revealed significant main effects of network, association type, and phase, as well as an interaction of association type and network and of phase and network. The main effect of association type reflected more activation for *semantic context* than *emotion,* while the phase main effect reflected more activation for *generate* than *switch*. For the sake of brevity, post-hoc comparisons parsing the network main effect are reported in Supplementary Table 6.4. For the network by association type interaction, more activation was seen for *semantic context* than *emotion* associations for both the MT DMN [t(30) = 11.4, $p < .001$][22] and core DMN [t(30) = 5.1, $p < .001$]. For the core DMN, this reflected more task-related *deactivation* for *emotion* associations. More activation was seen for *emotion* than *semantic context* associations for the auditory network [t(30) = -4.3, $p = .001$] and FT DMN [t(30) = -2.9, $p = .036$]. The control B network showed no difference between association types [t(30) = 1.6, $p = .603$]. For the network by phase interaction, more activation was seen in the *generate* than the *switch* phase for the MT DMN [t(30) = 5.8, $p < .001$]. The control B network showed less task-related deactivation for *switch* than *generate* [t(30) = -2.9, $p = .035$]. No difference was observed between phases for the core DMN [t(30) = -0.1, $p > 1$], FT DMN [t(30) = -1.5, $p = .735$], or auditory network [t(30) = 2.7, $p = .060$]. As seen in analysis of spatial correlations in Supplementary Figure 6.5 and Supplementary Table 6.6, the patterns observed here are broadly supported at the level of a global fit with network patterns.

[22] The assumption of normality was not for tests of these interactions for both the control B and MT DMN networks. Non-parametric tests elicited the same outcomes. Association type comparison: control B [Z = -1.4, $p = .763$], MT DMN [Z = -4.9, $p < .001$]. Phase comparison: control B [Z = -2.7, $p = .038$], MT DMN [Z = -4.1, $p < .001$].

Table 6.2. Repeated measures ANOVA observing main effects and interactions of association type, phase, and network for mean percent signal change in resting-state networks overlapping with the default mode network.

Analysis	Effect	Result
Mean percent signal change	**Association type**	**$F(1, 28) = 52.1$, $p < .001$, $\eta_p^2 = .65$***
	Phase	**$F(1, 28) = 6.3$, $p = .018$, $\eta_p^2 = .18$***
	Network	**$F(1.4, 40.4) = 74.2$, $p < .001$, $\eta_p^2 = .73$***
	Association type x Phase	$F(1, 28) < 0.1$, $p = .778$, $\eta_p^2 < .01$
	Association type x Network	**$F(1.4, 40.0) = 69.4$, $p < .001$, $\eta_p^2 = .71$***
	Phase x Network	**$F(1.6, 45.4) = 29.8$, $p < .001$, $\eta_p^2 = .52$***
	Association type x Phase x Network	$F(2, 56) = 0.5$, $p = .956$, $\eta_p^2 < .01$

Note: * reflects a significant result. Assumption of sphericity violated for 'network'. Greenhouse-Geisser adjustment applied accordingly.

This analysis provides support for functional dissociations within DMN. To summarise, MT and core DMN showed more activation for *semantic context* associations. FT and auditory network showed stronger activation for *emotion* associations. This is consistent with a role of MT DMN in contextual retrieval and scene construction, and of FT DMN in abstract and evaluative processing (Andrews-Hanna and Grilli, 2021). The MT subnetwork also showed a preference for the *generate* phase, which likely required greater focus on visual features of the pictures, while control B (a control network allied to DMN) showed a preference for the *switch* phase.

6.4.4. Control networks analysis

Control networks – both those that are domain-general and those specifically allied to DMN – are expected to be engaged during the retrieval of semantic associations. We next considered whether their recruitment was equivalent across *emotion* and *semantic context* associations, during the *generate* and *switch* phases. Both phases are likely to draw on controlled retrieval but in different ways. The *generate* phase required participants to identify a specific association from an unfamiliar picture and selectively focus on this link (recruiting a pathway from visual cortex to DMN). In contrast, in the *switch* phase, the content of the picture has already activated memory systems that can drive a response, but it is necessary to inhibit the previous response and select a new one.

Control networks are organised systematically along the principal gradient, from DMN regions, through SCN, to MDN regions implicated in domain-general control (Chiou et al., 2022). These were made mutually exclusive, as defined in section 6.3.8. Figure 6.4a presents visualisations of these networks. For analysis below, for each network for each

association type and phase, outliers (three standard deviations above or below the group mean) were excluded from analysis. All interaction post-hoc contrasts are Bonferroni-corrected for five comparisons (reflecting five sets of network regions).

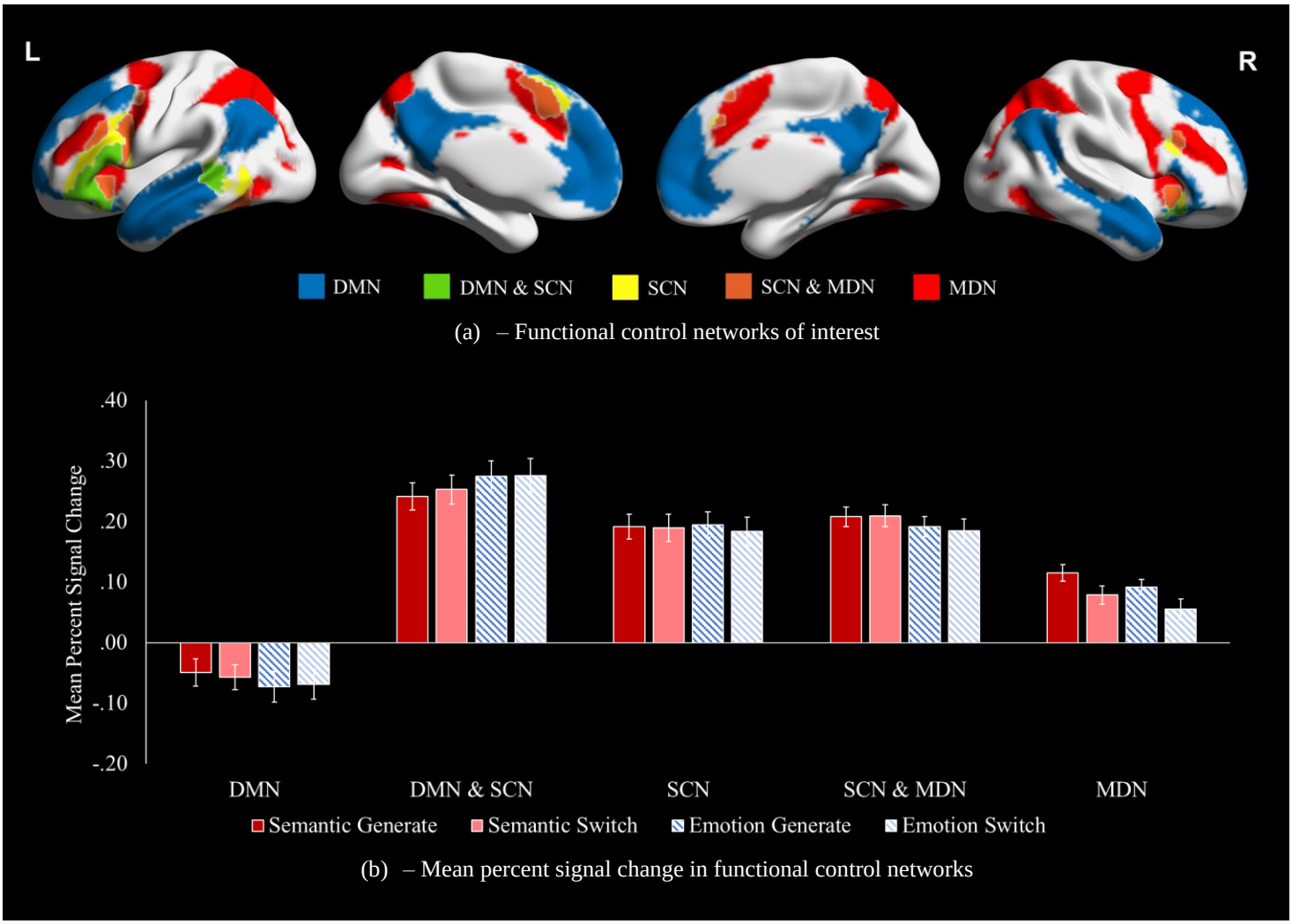


Figure 6.4. (a) Visualisation of functional control networks of interest. (b) Mean percent signal change in functional networks for each combination of association type and phase, calculated using the Featquery function of FSL, with binarised networks used as regions of interest. Error bars reflect one standard error. DMN = default mode network, SCN = semantic control network, MDN = multiple demand network.

Figure 6.4b presents mean percent signal change in each functional network, for each combination of association type and phase over implicit baseline. A repeated-measures ANOVA, shown in Table 6.3, revealed a significant main effect of network, as well as interactions of association type and network, and of phase and network. For the sake of

brevity, post-hoc contrasts for the main effect of network are reported in Supplementary Table 6.5. Overall, DMN & SCN showed more activation than all other networks. No difference was observed between the SCN and SCN & MDN, but both showed greater activation than both DMN and MDN. Finally, MDN showed more activation than DMN. Post-hoc contrasts for the association type by network interaction revealed that MDN was recruited more for *semantic context* than *emotion* associations [$t(31) = 2.9$, $p = .038$][23]. No difference between association types was observed for DMN [$t(30) = 1.8$, $p = .382$], DMN & SCN [$t(31) = -2.1$, $p = .220$], SCN [$t(31) = 0.1$, $p > 1$], or SCN & MDN [$t(31) = 2.0$, $p = .265$]. Post-hoc tests for the phase by network interaction revealed more activation in MDN during the *generate* than the *switch* phase [$t(31) = 3.2$, $p = .016$]. No difference in phases was observed for DMN [$t(30) = 0.2$, $p > 1$], DMN & SCN [$t(31) = -0.5$, $p > 1$], SCN [$t(31) = 0.5$, $p > 1$], or MDN & SCN [$t(31) = 0.3$, $p > 1$][24]. As seen in analysis of spatial correlations in Supplementary Figure 6.5 and Supplementary Table 6.6, these patterns are broadly supported at the level of a global fit with network patterns, although this analysis also provides evidence of considerable overlap with MDN across conditions.

To further parse the contribution of SCN, we conducted ROI analysis with the peaks of five distinct SCN clusters examining each condition over baseline (see Supplementary Figure 6.6 and Supplementary Table 6.9). Left IFG showed a stronger response than other peaks overall (see Supplementary Table 6.10), while an interaction of brain site and phase suggested greater importance of left pMTG in the *generate* phase, and of dmPFC in the *switch* phase, but again no differences between association types.

In summary, these analyses suggest control networks show common responses across association types and phases. The exception was MDN, closer to sensory-motor cortex than SCN along the principal gradient, which showed a preference for *semantic context* associations and the *generate* phase. Strong engagement of SCN was seen under all conditions, and maximally in areas overlapping with DMN. Voxels exclusively in DMN showed consistent task-related deactivation.

[23] The assumption of normality was violated for MDN in this post-hoc test – non-parametric testing of this effect did not survive correction [$Z = -2.8$, $p = .072$]. In any case, this significant interaction appears to be driven by this modest difference.

[24] The assumption of normality was violated for the DMN, SCN, and SCN & MDN for this interaction. Non-parametric tests elicited the same outcomes: DMN [$Z = -0.5$, $p > 1$], SCN [$Z = -1.2$, $p > 1$], SCN & MDN [$Z = -0.8$, $p > 1$].

Table 6.3. Repeated measures ANOVA observing main effects and interactions of association type, phase, and network for mean percent signal change in functional control networks.

Analysis	Effect	Result
Mean percent signal change	Association type	$F(1, 30) = 0.9$, $p = .338$, $\eta_p^2 = .03$
	Phase	$F(1, 30) = 0.7$, $p = .398$, $\eta_p^2 = .02$
	Network	**$F(2.9, 88.3) = 101.4$, $p < .001$, $\eta_p^2 = .77$***
	Association type x Phase	$F(1, 30) < 0.1$, $p = .773$, $\eta_p^2 < .01$
	Association type x Network	**$F(2.3, 68.0) = 6.5$, $p = .002$, $\eta_p^2 = .18$***
	Phase x Network	**$F(2.0, 58.9) = 4.8$, $p = .012$, $\eta_p^2 = .14$***
	Association type x Phase x Network	$F(2.4, 72.1) = 1.8$, $p = .160$, $\eta_p^2 = .06$

Note: * reflects a significant result. Assumption of sphericity violated for 'network'. Greenhouse-Geisser adjustment applied accordingly.

6.4.5. Gradient analysis

We next considered the distribution of task activation on the principal gradient of cortical organisation, which captures the distinction between heteromodal and unimodal cortex. We asked whether *emotion* and *semantic context* associations (and the DMN subsystems that support them) are located at different points in gradient space, and how the contrast of *generate* and *switch* phases for each of these association types changes this topographical pattern.

Figure 6.5a provides visualisations of the three task contrasts of interest ('*semantic context* over *emotion*', '*emotion* over *semantic context*', and '*switch* over *generate*'). There is little overlap between the effect of *switch* and the contrasts relating to association type. However, the *switch* clusters are typically located in brain regions that are equidistant from, and proximal to, both opposing contrasts linked to association type. The *switch* effect falls in between *emotion* and *semantic context* clusters in left and right inferior parietal lobule and right lateral temporal cortex. Bilateral frontal pole switch clusters are also adjacent to both association type effects in medial PFC.

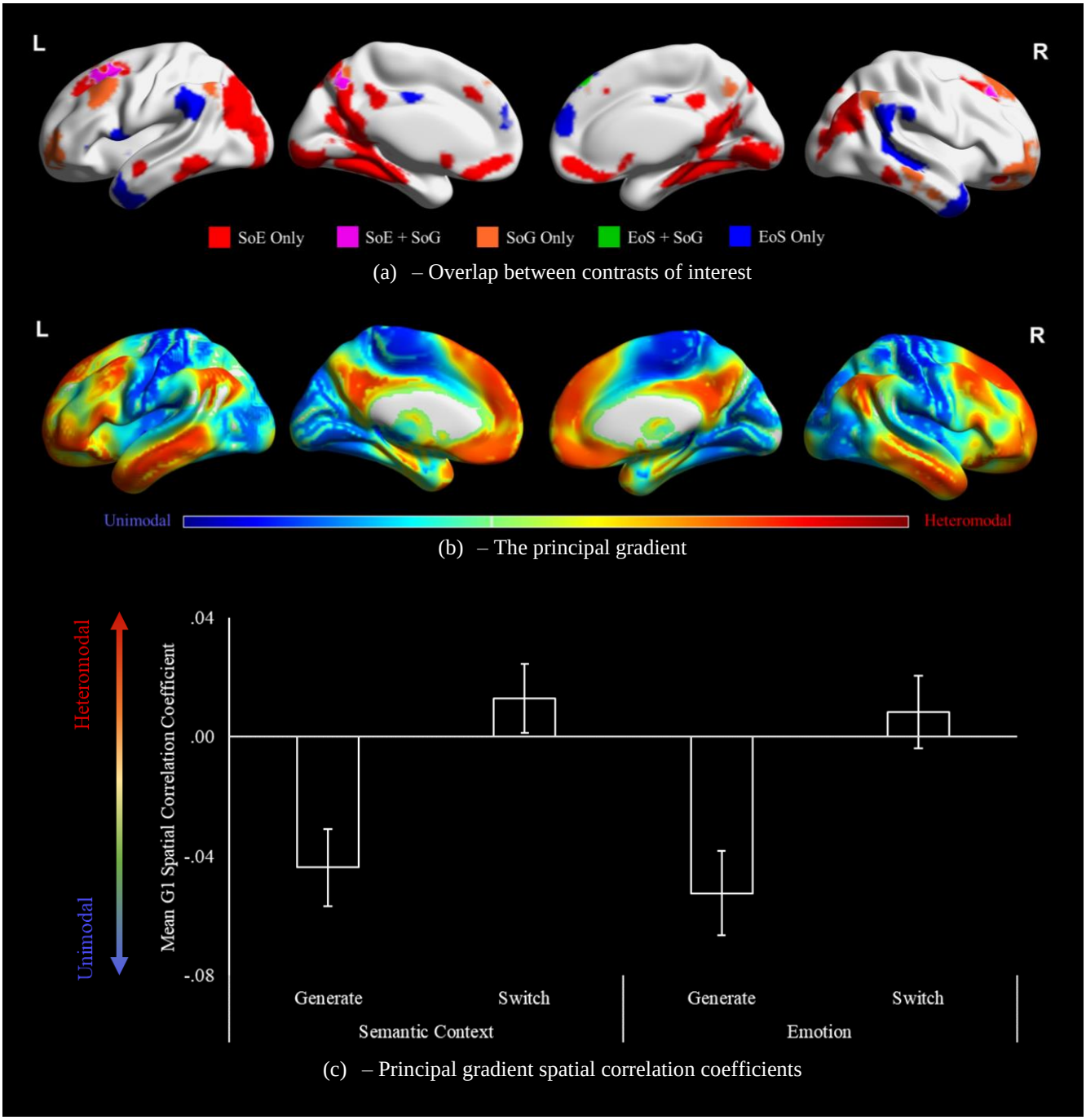


Figure 6.5. (a) Visualisations of overlap between the effect of switch and both contrasts of association type, and of (b) the principal gradient of cortical organisation. (c) Mean spatial correlation coefficients between the principal gradient and unthresholded contrasts of each association type and phase combination over implicit baseline. Error bars reflect one standard error. SoE = semantic context over emotion, EoS = emotion over semantic context, SoG = switch over generate, G1 = gradient 1.

A visualisation of the principal gradient can be seen in Figure 6.5b. Figure 6.5c presents the mean individual-level spatial correlation coefficients between the principal gradient and the unthresholded contrasts of each condition over baseline. A repeated-measures ANOVA of the spatial correlations between task conditions and the principal gradient map revealed a significant main effect of phase [$F(1, 31) = 58.9$, $p < .001$, $\eta_p^2 = .66$], but no effect of association type [$F(1, 31) = 0.8$, $p = .365$, $\eta_p^2 = .03$] or interaction between these factors [$F(1, 31) = 0.3$, $p = .599$, $\eta_p^2 = .01$]. The main effect of phase reflected a stronger response at the DMN-end of the gradient for the *switch* phase, and more sensory activation in the *generate* phase, consistent with our expectation that the *switch* phase would be less reliant on visual-to-semantic pathways and more reliant on heteromodal networks. Both association types showed this difference to the same degree: on the cortical surface this might correspond to a shift in the locus of activation away from DMN subnetworks linked to *semantic contexts* and *emotion* features, and towards common subnetworks across tasks.

This analysis was also conducted for Gradient 2 (reflecting a separation between motor and visual regions) and Gradient 3 (reflecting a separation between DMN and frontoparietal regions; see Supplementary Figure 6.7). These gradients explain the second- and third-largest amounts of variance in the whole-brain decomposition of intrinsic connectivity by Margulies et al. (2016). For Gradient 2, *semantic context* associations were further towards the visual than the motor end, relative to *emotion* associations. The same was observed for the *switch* phase relative to the *generate* phase. This likely reflects the relative importance of visual features in the *semantic context* task, and might reflect a greater importance of motor processes relating to lexical or semantic retrieval or selection in the *generate* phase. For gradient 3, the *switch* phase, relative to the *generate* phase, showed greater reliance on frontoparietal control regions, possibly due to the need to constrain retrieval. Control B, implicated in the *switch* phase, was found to fall further towards the frontoparietal control end of this gradient, while other DMN-allied networks were located towards the opposite end (see Supplementary Figure 6.8c).

6.4.6. Probing for task differences in the switch effect

A key research question is whether the contrasting retrieval demands of *generate* and *switch* phases differentially modulate the response of DMN subsystems linked to *semantic context* and *emotion* associations. In the analyses above, we observed no such differences in the recruitment of specific networks or gradients. Nevertheless, in whole-brain analysis, we observed an interaction of association type and phase in left LOC. This implies that the

mechanisms involved in generating associations from pictures as opposed to switching to new associations are largely orthogonal to the networks that process different association types, but with some overlap of these processes in higher-order visual regions. To stress-test this finding, we performed two supplementary analyses.

First, we split the activation highlighted in the thresholded *switch* over *generate* map into nine distinct, contiguous clusters (see Supplementary Table 6.11). We tested for differences within each cluster. Mean percent signal change in each cluster split by association type and phase can be seen in Supplementary Figure 6.9. This analysis (see Supplementary Table 6.12) revealed that two clusters in this mask activated significantly more for *semantic context* than *emotion* associations. Despite this, again, no significant interaction was observed between association type and phase.

While an interaction of association type and phase was not observed within SCN, networks allied to SCN might show this pattern. We therefore split the full SCN into components based on its overlap with 17-parcellation Yeo et al. (2011) networks. The two dominant networks were FT DMN and Control A, accounting for 30% and 23% of SCN, respectively. We examined voxels identified by the overlap of SCN and these two networks, as well as non-overlapping voxels exclusively within SCN, FT DMN, and Control A. In each network, we examined potential differences in the effect of *switch* over *generate* between association types. Mean percent signal change is shown in Supplementary Figure 6.10, with analysis in Supplementary Table 6.14. While these networks were found to dissociate in their preference for phase, this was not modulated by association type.

Considering these analyses together, we can conclude that the effect of *switch* versus *generate* was largely not modulated by association type in heteromodal cortex. These effects were only recovered in LOC.

6.5. Discussion

This study advances our understanding of the functional organisation of DMN and control networks by comparing activation during the retrieval of semantic context and emotional associations to pictures using fMRI. Each trial was split into a *generate* phase, thought to tap visual to DMN pathways, and a *switch* phase requiring a different association to be retrieved to the same picture, thereby increasing demands on internally-mediated

retrieval processes. Task activation was highly overlapping with the functionally-defined SCN, regardless of association type or phase. This was particularly true of SCN regions within DMN. A functional dissociation within DMN reflected the type of information needed in each task. *Semantic context* associations showed greater reliance on the MT subsystem, associated with scene construction. *Emotion* associations showed greater reliance on the FT subsystem, associated with abstract and evaluative processing. FT and MT subnetworks therefore showed a dissociation within semantic cognition when different meaning-based features were required. This was true regardless of retrieval demands, across the *generate* and *switch* phase. Clusters identified in the *switch* phase were nearer the heteromodal end of the principal gradient than those in the *generate* phase, suggesting internally-oriented retrieval demands. Across multiple analyses, we largely found similarities in this *switch* effect across association types, suggesting that this dimension of DMN organisation related to internal retrieval demands is largely orthogonal to the distinction between MT and FT subnetworks.

These findings contribute to our understanding of the functional specialisation of DMN subsystems. We found a dissociation between these networks when comparing tasks that tapped the retrieval of different meaning-based features (semantic context and emotions). This indicates that this subdivision relates to types of information processing; the MT subsystem supports the retrieval of general knowledge of meaningful contexts acquired over a lifetime. This is supported by studies implicating the MT subnetwork in contextually-specific and perceptually-guided scene construction and the FT subnetwork in abstract and evaluative processing (Andrews-Hanna et al., 2014; Andrews-Hanna and Grilli, 2021; Sheldon et al., 2019). Regions in FT DMN, including dmPFC, are involved in self-reflection about emotions and desires (Ochsner et al., 2004; van der Meer et al., 2010), suggesting the contribution of this network extends beyond simple semantic judgements.

The functional dissociation uncovered between semantic contexts and emotions in MT and FT also extended to additional DMN networks. The auditory network showed greater activation for *emotion* associations, while the core DMN showed less deactivation for *semantic context* associations. The Yeo et al. (2011) 17-network parcellation appears to be finer-grained than the functional dissociation recovered here, such that task differences extended over multiple linked networks. These network pairings may partly reflect spatial proximity – auditory and FT networks are adjacent in lateral temporal regions, while core and MT networks occupy adjacent positions in medial parietal cortex. In addition, language responses in the auditory network may be more relevant for emotion associations due to

importance of language for abstract cognition. In any case, these observations support the claim that DMN is functionally organised according to the type of feature being processed.

We also observed a whole-brain interaction between association type and phase in left inferior LOC – implicated in visual processing of concepts (Coutanche & Thompson-Schill, 2015). The construction of rich scenes during *semantic context* associations may rely on this region across phases, while the *switch* phase of *emotion* associations may be abstract enough for decreased reliance. This mirrors the processing of abstract words, which show greater reliance on emotional content due to a relative lack of sensorimotor features (Kousta et al., 2011; Ponari et al., 2020; Rotaru & Vigliocco, 2019; Vigliocco et al., 2014). Previous studies have found similar regions of inferior LOC show interactions between task demands and modality in the semantic domain. For example, larger effects of inhibitory demands for picture- than word-based stimuli (Gonzalez-Alam et al., 2018). The recruitment of visual object regions in controlled semantic retrieval appears to depend on both the nature of the input (modality; stimulus repetition) and the task demands.

Despite this functional dissociation in the engagement of DMN subsystems, the *emotion* and *semantic context* tasks showed overlapping activation in SCN nodes including left IFG, left pMTG, bilateral dmPFC, and right IFG. This suggests that the contribution of SCN cuts across distinct aspects of memory-based cognition that rely on the FT and MT subnetworks. Previous studies have reported an important role for SCN in contextual associations (Krieger-Redwood et al., 2022). The contribution of this network to emotion associations is predicted by the view that valence is a semantic feature (Lambon Ralph et al., 2017; Martin, 2016) and that the capacity to access emotion categories (e.g., fear) relies on effective semantic cognition (Lindquist et al., 2015). Indeed, post-stroke impairments in semantic control are also associated with impaired categorisation of facial portrayals of emotion (Souter et al., 2021 [Chapter 3 of this thesis]) and classification of words by valence (Souter, Reddy, et al., 2022 [Chapter 4 of this thesis]). Key SCN sites, including left IFG and pMTG, have been implicated in emotion reappraisal (Messina et al., 2015), an emotion regulation strategy that relies on controlled processing (Braunstein et al., 2017). IFG has also been associated with the suppression and substitution of emotional memories (Benoit & Anderson, 2012; Engen & Anderson, 2018; Guo et al., 2018). Our findings further suggest that SCN plays a role in the control of tasks that tap internal representations, including the retrieval of emotion features and meaning-based scenes. Indeed, the contribution of SCN may extend beyond semantic processing given that this network has been implicated in other

domains including episodic retrieval (Vatansever et al., 2021) and social cognition (Diveica et al., 2021). The evidence discussed here suggests that, within the affective domain, SCN may play a role in processing both hedonic valence (positive/negative) as a dimensional and fundamental feature of heteromodal concepts, and discrete emotion states that fall within a superordinate 'emotion' category.

Overall, SCN supported semantic retrieval processes in *generate* and *switch* phases equally; however, supplementary analysis revealed greater importance of left pMTG in the *generate* phase, and of dmPFC in the *switch* phase. Left pMTG has been shown to support semantic control across verbal and picture modalities (Krieger-Redwood et al., 2015; Jackson 2021). Nevertheless, given its proximity to visual and auditory input regions and the focus of the *generate* phase on the initial retrieval of semantic information from an external cue, this finding suggests a stronger role of pMTG in externally-mediated semantic cognition (Davey et al., 2016). In contrast, dmPFC might make a greater contribution to controlling internally-mediated patterns of retrieval or in supporting the cognitive switching process. We also found that MDN showed a modest preference for the *generate* phase. This might reflect the fact that MDN encompasses frontoparietal and dorsal attention networks and is therefore well-suited to supporting external control. In contrast, SCN straddles the frontoparietal and DMN networks (Chiou et al., 2022).

This study revealed functional differences between the functionally-defined SCN meta-analytic map and the control B subnetwork defined by intrinsic connectivity, even though both networks are allied to DMN (e.g., Davey et al., 2016; Dixon et al., 2018; Wang et al., 2020) and contribute to semantic cognition (e.g., Jefferies 2013; Faber et al., 2019). Control B showed less task-related deactivation in the *switch* phase than the *generate* phase, suggesting it may play a role in the control of internally-oriented cognition. The *switch* effect was strongly overlapping with the control B network and located towards the DMN apex of the principal gradient, at a maximal distance from sensory-motor systems. In contrast, SCN strongly overlaps with control A, and minimally with control B (see Supplementary Figure 6.11). Control A is thought to support the control of externally-oriented cognition, as this network couples with dorsal attention regions to respond to external task demands (Yin et al., 2022). One reason for this distinction between the SCN and control B networks might be that SCN is defined according to activation in externally-presented tasks, while the *switch* phase of our experimental task did not involve the presentation of new stimuli. SCN might therefore

support the controlled retrieval of semantic information from perceptual inputs, while control B might be more critical for perceptually-decoupled semantic cognition.

Our findings suggest that a key functional distinction within DMN relates to the type of (semantic) feature being retrieved, reflected by activation differences between FT and MT subsystems. Importantly, this functional dissociation was consistent across the *generate* and *switch* phases, with varying retrieval demands. Though the MT DMN did show a preference for the *generate* over the *switch* phase, this subnetwork still reliably activated for *semantic context* associations, while reliably deactivating for *emotion* associations. These subnetworks may therefore serve separate functions in a context-invariant manner, rather than themselves being sensitive to retrieval demands. Overall, the more internally-oriented retrieval demands of the *switch* phase preferentially activated control B, a network that also falls within and functionally couples with DMN (Dixon et al., 2018). This suggests that retrieval demands and task features are largely orthogonal dimensions of DMN organisation. Control B showed no differences between the *semantic context* and *emotion* tasks. Moreover, analysis positioning these task responses on whole-brain gradients capturing key dimensions of cortical organisation showed that clusters implicated in the *switch* phase tended towards the heteromodal apex of the principal gradient, while no effect of association type was observed. This suggests that *semantic context* associations, associated with the MT subnetwork, were not more perceptually-decoupled than *emotion* associations, associated with the FT subnetwork. This was true despite the MT subnetwork being associated with episodic memory (Andrews-Hanna & Grilli, 2021), even though many episodic memory tasks involve internally-oriented retrieval. Both MT and FT may be able to support access to heteromodal memory representations from visual inputs, as well as sustain more internal pathways to access spatial scenes and abstract, evaluative representations, thought to be supported by these subsystems, respectively.

6.5.1. Limitations

There are limitations to the current study. First, the data do not indicate that the FT subsystem is not involved in the retrieval of semantic information about meaningful contexts; the analysis relies on task contrasts, so we can only conclude that the FT subsystem is less activated by *semantic context* than *emotion* associations. In this way, our data do not contradict the view that anterior and lateral temporal lobe regions act as a ‘semantic hub’, allowing us to integrate the full range of features that we learn about concepts (Lambon Ralph et al., 2017; Patterson et al., 2007). Second, the structure of our task does not

disentangle the experience of seeing a picture for the first time from the generation of a dominant association. There are likely different levels of controlled processing required for the *generate* and *switch* phases, since participants indicated that their associations after the switch tended to be weaker. Future studies are needed to establish whether manipulations of the strength of the association being retrieved have comparable effects on MT and FT subnetworks, in the absence of any differences in the extent to which retrieval is externally- or internally-mediated. Third, while prior studies have implicated the MT DMN in episodic memory (Andrews-Hanna & Grilli, 2021), here we demonstrate its relevance in contextual semantic associations. We cannot say with certainty whether participants drew on episodic strategies in the retrieval of these associations. Participants were asked to avoid retrieving episodic memories. However, participants in prior work have reported using episodic strategies to generate strong semantic links between words (Krieger-Redwood et al., 2022). Future research on this topic may benefit from asking participants to provide detail on the strategy used to generate associations (e.g., Humphreys et al., 2022; Krieger-Redwood et al., 2022). Fourth, it is possible that for a given trial participants may have instantly generated both a dominant and subordinate association in the generate phase, rather than focusing exclusively on a dominant association at this time, despite this contradicting our study instructions. While this cannot be disproven, we did observe behavioural differences in self-reported association strength across these phases, as well as meaningful differences in brain activation, suggesting that dissociable mechanisms were employed in the *generate* and *switch* phases and that on balance the switch phase included a relative focus on subordinate-level associations. Finally, it is unclear the extent to which participants were generating immersive visuospatial scenes and embodied emotional responses to stimuli. Findings from tasks requiring semantic judgements of valence, as conducted here, cannot be directly applied to experiential affect (Itkes & Kron, 2019). Future research may benefit from explicitly considering the role of semantic control in experiential aspects of semantic retrieval. For example, it is unclear if the same MT/FT dissociation would have occurred if the *emotion* associations had been more experiential in this study, given that the FT is associated with abstract aspects of cognition (Andrews-Hanna and Grilli, 2021).

6.5.2. Conclusion

We compared the neural mechanisms underlying the generation of both semantic contextual and emotional associations with pictures. Highly overlapping substrates in SCN support the importance of semantic control across domains. Clusters implicated in the

retrieval of subordinate-level associations were located towards the heteromodal end of the principal gradient, and showed reduced deactivation in a control network allied to DMN. The generation of contextual and emotional associations showed a dissociation across DMN subnetworks corresponding to scene construction and abstract processing, respectively. This dissociation was consistent across the *generate* and *switch* phases, suggesting that the functions of these networks are consistent despite varying retrieval demands.

Chapter 7: General discussion

7.1. Thesis scope and aims

The study of semantic cognition concerns the conceptual knowledge we use to understand the external world. This relies on two dissociable elements; the storage of heteromodal concepts, and our ability to retrieve them in a flexible and context-appropriate manner (Lambon Ralph et al., 2017). The latter process, known as semantic control, is taxed under conditions of increased ambiguity, in the presence of associated distractors, and when access to weakly-encoded information is required (Noonan et al., 2010). This thesis investigated the neural systems supporting semantic control, and aimed to better characterise impairments in semantic aphasia (SA). Patients with SA present with multimodal impairments in semantic control, following left-hemisphere stroke (Jefferies, 2013). Semantic control is supported by a distributed but largely left-lateralised 'semantic control network' (SCN; Jackson, 2021). Key nodes of this network include the left inferior frontal gyrus (IFG) and posterior middle temporal gyrus (pMTG). Evidence suggests that SCN may be involved in diverse domains where flexible and internally-focused processing is required, including episodic retrieval (Vatansever et al., 2021) and social cognition (Diveica et al., 2021). Empirical chapters included a particular focus on the intersection of semantic control and affective processing – including the representation of hedonic valence, processing of discrete emotions, and susceptibility to motivational manipulations. This thesis had three aims:

- To better understand the functional networks implicated in semantic processing. SCN functions in concert with the multiple demand network (MDN), responsible for domain-general cognitive control (Fedorenko et al., 2013), and default mode network (DMN), which supports internal higher-order processing and the integration of diverse features (Lanzoni et al., 2020; Smallwood et al., 2021). DMN sits at the heteromodal end of a principal gradient of cortical organisation, organised according to similarity in the functional connectivity of its nodes (Margulies et al., 2016). Control networks like MDN sit towards the middle of this gradient, with SCN in between MDN and DMN (Chiou et al., 2022). These systems were first examined in SA patients. Using symptom mapping, Chapter 2 investigated patterns of lesion, structural white matter disconnection, and functional network-level disconnection, that predicted greater impairments in both semantic control and domain-general

executive function. This was further investigated using functional magnetic resonance imaging (fMRI) with neurologically healthy adults. In doing so, Chapter 6 investigated how two distinct semantic tasks are supported by dissociable aspects of DMN under varying retrieval demands, as well as contributions of SCN and MDN.

- To investigate the relationship between the processing of conceptual knowledge, and hedonic valence and discrete emotion categories. Chapter 3 first addressed this question from a constructionist viewpoint (Lindquist et al., 2015), testing the prediction that impairments in semantic control may result in greater difficulty accessing constructs of discrete emotion facial expressions. Constructionist models have considered the role of semantic knowledge, but have not accounted for semantic control. Chapter 4 then studied the role of valence as a semantic feature. In doing so this chapter aimed to investigate effects of valence congruency on global semantic matching, as well as effects of semantic relatedness on valence matching. By including SA patients, it was possible to test whether such effects are exaggerated by semantic control impairments, and whether these patients present with baseline impairments in valence matching. The Chapter 6 fMRI study also allowed for investigation of the similarities in the neural bases supporting the generation of semantic contextual and emotional associations.

- To test whether manipulations of extrinsic and intrinsic motivation can ameliorate impairments in semantic control. Semantic control can be considered analogous to domain-general cognitive control, in so far as both are executive processes which require flexibility according to task demands (Thompson et al., 2018). Prior research has demonstrated beneficial effects of reward on cognitive control (e.g., Small et al., 2005), and that such incentives can ameliorate age-related impairments in this domain (Yee et al., 2019). If such an effect held true for semantic control, this could have implications for gamified approaches to rehabilitation (strategies that incorporate typical elements of games) in SA.

These aims were addressed over the course of five empirical chapters, the key findings of which are detailed below.

7.2. Summary of empirical findings

7.2.1. Chapter 2: Mapping lesion, structural disconnection, and functional disconnection to symptoms in semantic aphasia

The first empirical chapter made use of existing structural MRI scans from 23 patients with SA. Lesion site was manually traced on these scans. Two techniques were used which allow insight into diffuse damage beyond lesion site alone. Measures of structural disconnection reflect spreading disconnection throughout white matter tracts that have been physically damaged. Conversely, functional disconnection reveals network-level disruption by highlighting aspects of the brain that would typically be functionally connected to the lesion site. First, typical patterns of lesion, structural disconnection, and functional disconnection were characterised in SA. These measures were then used to map symptoms of impaired semantic cognition and domain-general control. The key findings were:

- Despite all presenting with multimodal semantic control impairments, SA patients presented with variable degrees of impaired executive function. Fourteen of 23 were impaired on the Brixton Spatial Anticipation Test. Executive performance positively correlated with semantic control performance.
- Lesion impacted sites throughout the left hemisphere, centred on frontoparietal sites including IFG. Structural disconnection was extensive, but most convergent within left hemisphere tracts. Functional disconnection was extensive bilaterally.
- Aspects of SCN were most frequently lesioned, followed by core semantic regions and voxels exclusively within MDN. DMN was relatively spared. Extensive structural and functional disconnection beyond lesion site was observed within SCN such that patients who had damage restricted to only one node of this network showed disconnection affecting multiple nodes.
- Semantic impairments were associated with lesions to aspects of SCN including left IFG and pMTG, as well as precentral gyrus, postcentral gyrus, and occipital pole. Clusters implicated in impaired semantic cognition from structural disconnection were small. These aligned with those implicated by lesion symptom mapping, restricted to the left hemisphere. Poorer performance on the executive Brixton test was associated with lesions to frontoparietal sites adjacent to those implicated in semantic control, as well as bilateral structural disconnection across the corpus callosum. For both semantic and Brixton

performance, clusters implicated in functional disconnection were small and largely subcortical.

This study provides evidence of diffuse damage in SA and demonstrates that damage spreads through aspects of SCN even when the broader network is not impacted by the lesion. Different patterns of disconnection may account for the heterogeneous neuropsychological profiles of SA patients despite their common heteromodal semantic impairments. The adjacent brain regions supporting semantic and domain-general control may explain why these functions are frequently impaired together – lesion to one network is likely to impact the other. SA patients who have impairment of semantic cognition in the absence of domain-general executive deficits may have largely left-lateralised disconnection, while those cases with bilateral disconnection show difficulties on the Brixton spatial anticipation test, supporting the largely left-lateralised basis of SCN and bilateral substrates for domain-general control. This chapter provides novel characterisation of SA patients, and insight into the dissociable functional systems that support semantic retrieval and executive control.

7.2.2. Chapter 3: Impaired emotion perception and categorization in semantic aphasia

The second empirical chapter again focused on patients with SA, investigating effects of semantic control impairments on the ability to process discrete emotional facial portrayals. This was assessed over two studies, with samples of seven and six SA patients, respectively, and healthy controls. Study 3.1 adapted a paradigm used previously by Lindquist et al. (2014) with semantic dementia (SD) patients, wherein participants are required to sort facial portrayals into piles according to six emotion categories, with varying levels of task constraint. This study allowed us to directly compare performance in these two patient groups. Study 3.2 similarly required categorization of facial portrayals, this time in an alternative forced choice format with three response options. The demands of this task were manipulated by the presence of audio prosodic cues or miscues. It was predicted that SA patients would be impaired in both Study 3.1 and 3.2, and that impairments would be ameliorated by the addition of task constraints and relevant cues. The key findings were:

- In an unconstrained face sort task, SA patients presented with impaired accuracy relative to controls. Patients benefited from the provision of word anchors which alluded to the discrete emotion categories, but not from the presence of a facial exemplar for each

category. As previously shown in SD, errors were frequently within-valence, such as confusing angry and sad faces. Deficits seen in SA were as severe, and in some cases more severe, than those previously seen in SD.

- In Study 3.2, SA patients again presented with impairments in categorising facial expressions. Patients presented with highest accuracy in the presence of related prosody cues, and poorest performance following within-valence miscues. Control participants showed deleterious effects of within-valence miscues relative to baseline, but did not benefit from cues. Across-valence miscues did not affect performance for either group.

These findings provide evidence of impaired emotion categorization in patients with impaired semantic control. This adds to the constructionist model of emotion, suggesting that the ability to flexibly retrieve emotion concepts is relevant to the perception of facial emotions, as has been previously established for intact long-term knowledge of emotion concepts. It appears that both semantic control and representation may be needed to differentiate between emotion states. In contrast to the retrieval of discrete emotions, semantic impairments do not appear to affect discrimination of faces of positive and negative valence, consistent with predictions of the constructionist model (Lindquist et al., 2014). Consistent with prior evidence in verbal tasks (Noonan et al., 2010), these findings also support the beneficial effects of contextual cueing in SA, as well as the deleterious effects of related miscues which must be inhibited.

7.2.3. Chapter 4: How do valence and meaning interact? The contribution of semantic control

Chapter 4 investigated the importance of valence as a semantic feature. A ‘valence matching’ task required participants to match one of two response option words to a probe word based on valence congruency. Three conditions within this task manipulated semantic relatedness, such that the probe word had either a strong relation or no relation with either the target or foil word. In a ‘semantic matching’ task, participants were required to match one of two response options to a probe word based on strength of association. Across two conditions valence congruency was manipulated, such that the target or foil was congruent with the probe. In a third condition, strength of association was modulated by introducing targets with a weak semantic association to the probe, that could then be compared to performance on

strong associations in the other two conditions. In Experiment 4.1 this was done in a sample of healthy young adults for a sensitive measure of response time, while Experiment 4.2 included five SA patients and age-matched controls. The main findings were:

- For young adults in Experiment 4.1, semantically related targets facilitated valence matching, while related distractors impaired performance. Young adults' semantic matching response time similarly benefited from the presence of valence-congruent targets, relative to valence-congruent distractors.
- SA patients in Experiment 4.2 presented with baseline impairments in valence matching, relative to controls. Participants experienced impaired valence matching in the presence of distractors, an effect that was particularly pronounced in patients. Related targets ameliorated valence matching impairments in patients. Patients and controls benefitted equally from effects of valence congruency on semantic matching. Patients were disproportionately impaired for weak associations.
- Effects of semantic relatedness on valence matching were larger than effects of valence congruency on semantic matching, across experiments.

This study supports prior evidence of the facilitatory effect of valence congruency on semantic matching (Marino Dávolos et al., 2020). Such evidence is consistent with the idea that valence serves as a feature of heteromodal concepts, and as such can cue retrieval. This is further supported by baseline impairments in accessing valence information in SA, consistent with emotion processing impairments observed in Chapter 3. Evidence that semantically related distractors can interfere with valence matching further suggests that ability to use valence effectively can be challenged by the presence of competing features. These findings add to the existing literature on the nature of both semantic retrieval, and processing of hedonic valence.

7.2.4. Chapter 5: Motivated semantic control: Exploring the effects of extrinsic reward and self-reference on semantic retrieval in semantic aphasia

Chapter 5 again studied SA patients and controls, moving from emotion and valence to another affective property – motivation and reward. Based on evidence from literature relating to domain-general control (e.g., Yee et al., 2019), this chapter investigated whether manipulations of both extrinsic and intrinsic motivation could ameliorate impairments in

semantic control. Over two experiment this chapter studied effects of extrinsic reward in the form of token points (Experiment 5.1; 16 patients, 15 controls) and self-reference as a proxy for intrinsic motivation (Experiment 5.2; ten patients, 11 controls) on alternative forced choice semantic matching. Evidence of affective impairments in SA from Chapters 3 and 4 may suggest that value is not processed typically in SA, which may preclude motivational benefits. Alternatively, manipulations of reward may nullify these abnormalities by reducing control demands. The key findings were:

- Across both experiments, controls outperformed patients on semantic matching. Participants performed more accurately on strong than weak associations overall, although an expected interaction of group and association strength was not observed.
- SA patients benefited from the presence of high extrinsic reward during the retrieval of weak, but not strong, semantic associations. Benefits of high extrinsic rewards were greater in SA patients than in controls.
- Patients and controls showed typical self-reference recognition memory effects, suggesting that self-referential processing had been effectively evoked by the manipulation in Experiment 5.2.
- Neither patients nor controls experienced improvements in semantic matching when self-allocated pictures were used as probes for either strong or weak associations.

These findings suggest that impairments in semantic control are susceptible to manipulations of cued extrinsic reward. The manipulation of self-reference used here was intended as a proxy for intrinsic motivation, supported by prior evidence (Madan, 2017). Benefits of self-reference on performance were not observed, implying either that intrinsic motivation was not effective in modulating semantic performance, or that the current manipulation of self-reference was not sufficiently intrinsically motivating.

7.2.5. Chapter 6: Default mode network shows distinct emotional and contextual responses yet common effects of retrieval demands across tasks

The final empirical chapter of this thesis moved from neuropsychology to task-based fMRI. This allowed the thesis to seek convergent evidence for the view that SCN supports not only the controlled retrieval of neutral concepts but also the retrieval of emotion states. A

sample of 32 neurologically healthy young adults were asked to retrieve semantic contextual and emotional associations to pictures. The study investigated whether responses were modulated by retrieval demands across a generate phase, requiring generation of a first association to a picture, and a switch phase, requiring a second subordinate association to the same stimulus. In addition to the response within control networks (SCN and MDN), the chapter considered the role of DMN subnetworks (e.g., Andrews-Hanna et al., 2014), since the medial temporal (MT) and fronto-temporal (FT) subnetworks have been associated with visuospatial scene construction and abstract evaluative processing, respectively (Andrews-Hanna and Grilli, 2021). The key findings were:

- Across both association types and generate and switch phases, strong task activation over the implicit baseline was seen within SCN regions, particularly elements of this network overlapping with DMN.
- Across phases, activation for the two association types showed a dissociation across DMN subnetworks. As predicted, MT DMN showed a relative preference for semantic contextual associations, and FT DMN for emotional associations.
- Clusters implicated in the switch phase showed particular overlap with the control B network, a frontoparietal control network previously shown to be functionally coupled with DMN (Dixon et al., 2018). Clusters showing greater activation in this phase lay towards the heteromodal end of the principal gradient, consistent with the need for internally-focused processing in this phase, and less reliance on the stimulus itself. Switch effects were largely consistent across association types. An interaction was observed in the left lateral occipital cortex, with this region being less engaged for the switch phase of emotion associations.

These findings support a functional dissociation within DMN across semantic context and emotion associations. Importantly, the dissociable role of these DMN subnetworks was found to be consistent across phases with differing retrieval demands – the contrast of switch over generate was instead reflected in a frontoparietal control network allied to DMN. This suggests that effects of retrieval demands in DMN were largely orthogonal to effects of feature type. The equivalent role of SCN in the retrieval of emotional associations along with contextual associations further shows that internally-focussed control processes are recruited across feature types, and shows an importance of SCN in affective processing, in line with Chapters 3 and 4.

7.3. Broader themes

Cutting across these empirical chapters, several broader debates are addressed by the thesis work.

7.3.1. Multiple domains of impairment in semantic aphasia

The study of patients with SA has been foundational in developing our understanding of semantic control. Comparisons of these patients to those with SD provided novel evidence that semantic retrieval dissociates from the storage of semantic concepts (Jefferies & Lambon Ralph, 2006). Patients with SA struggle disproportionately with the retrieval of ambiguous and subordinate conceptual associations (Noonan et al., 2010) and low-relevance conceptual features (Montefinese et al., 2020). Prior research has also consistently demonstrated that semantic control impairments in SA can be ameliorated through the use of external prompts. Despite baseline impairments in SA, phonemic cues alluding to target words can improve picturing naming to near ceiling-level, to a far greater extent than in SD (Jefferies et al., 2008). Noonan et al. (2010) further demonstrated contextual cueing effects, as SA patients benefit from the provision of sentences which allude to the correct interpretation of an ambiguous probe word. Lanzoni et al. (2019) similarly demonstrated that retrieval of ambiguous concepts can be aided by visuospatial and valenced cues.

SA patients are frequently reported to have lesions in SCN sites including left IFG (e.g., Hallam et al., 2018). However, despite common semantic control impairments, lesion profiles within this group are heterogeneous (e.g., Thompson et al.., 2018), with some SA patients showing lesions restricted to left temporoparietal cortex, rather than affecting prefrontal regions (Thompson et al., 2022). Semantic control impairments in SA also frequently co-occur with executive dysfunction (Thompson et al., 2018), although not all cases show this pattern. This thesis provides insight into how semantic and domain-general control processes can dissociate in individuals, despite showing an association in many studies at the group level, as well as the mechanisms by which semantic control impairments may spread into other domains.

Chapter 2 explicitly investigated how impairments in semantic control map onto lesion site and diffuse disconnection. Despite heterogenous lesions, consistent patterns of spreading structural and functional disconnection were observed. This was pronounced within SCN. Patients uniformly presented with both structural and functional disconnection of left-hemisphere SCN sites, even when they were not directly impacted by the lesion. This may explain why SA patients present with common impairments of semantic cognition, despite differences in lesion location. Recent evidence demonstrates that damage to temporo-parietal sites is sufficient to produce impairments in semantic control that are comparable to those in patients with frontal lesions (Thompson et al., 2022).

Next, evidence of adjacent substrates for semantic control and executive function in the left hemisphere in Chapter 2 is consistent with the fact that SA patients often, but not invariably, present with executive dysfunction (Thompson et al., 2018). It is likely that these substrates are frequently lesioned together given their proximity. Beyond this, some patients presented with functional disconnection to right hemisphere control sites and this pattern of disconnection was particularly associated with poor cognitive control. This finding can explain the observation that semantic control and executive function are not necessarily impaired together in SA (Chapman et al., 2020). Damage to either or both SCN and MDN may contribute to the overall picture of deregulated retrieval in this group, spanning multiple domains.

Indeed, this thesis provides further evidence for impairments in SA beyond ostensibly semantic tasks – i.e., in the processing of facial portrayals of discrete emotions and of the hedonic valence of words. Chapter 3 revealed that SA patients present with impaired within-valence discrimination of facial portrayals of discrete emotion categories. Chapter 4 similarly observed that SA patients present with baseline impairments in matching words according to valence. These observations add to a line of research which implicates SCN in tasks requiring the control of internally-focussed representations across different cognitive domains. Stampacchia et al. (2018) provided evidence that SA patients present with multi-modal episodic retrieval impairments that are comparable to their semantic retrieval impairments – suggesting these memory systems may share a single control mechanism. Cogdell-Brooke et al. (2020) further demonstrated that episodic retrieval deficits in SA are inconsistent for single items probed across multiple tasks, as previously demonstrated for semantic retrieval (Jefferies & Lambon Ralph, 2006). Research employing fMRI in healthy volunteers has provided further evidence for a shared control mechanism supporting semantic and episodic

retrieval (Vatansever et al., 2021). A recent meta-analysis similarly implicated key SCN nodes, including left IFG, in a broad range of social cognitive tasks (Diveica et al., 2021). This is likely because semantic control processes inform our ability to select socially-relevant conceptual information and respond appropriately in social situations (Binney & Ramsey, 2020), though this has not yet been investigated in SA. Overall, findings from this thesis are consistent with the notion of widespread and diverse impairments in SA.

On a more applied level, this thesis is relevant to the question of how conceptual retrieval can be facilitated in SA. Chapter 3 demonstrated that the categorisation of discrete emotional portrayals can be aided by the provision of written word anchors and audio prosody cues, consistent with prior evidence of cueing and miscuing of semantic retrieval (Jefferies et al., 2008; Lanzoni et al., 2019; Noonan et al., 2010). Sorting was further impaired by the presence of within-valence prosody miscues. Chapter 4 revealed that impairments in the retrieval of valence could be ameliorated by semantically-related targets, and exacerbated by semantically-related distractors. Conversely, the retrieval of global semantic associations was aided by valence congruency between words. These findings are all consistent with the notion that semantic representations themselves are not inaccessible in SA, but that their retrieval is modulated by contextual factors. In these cases, retrieval can be aided with external prompts designed to disambiguate representations in memory. Lanzoni et al. (2019) similarly demonstrated beneficial effects of the provision of valenced facial expressions in retrieving the meaning of ambiguous homonyms in SA. Chapter 3 of this thesis further demonstrates that cues across modalities can increase the accessibility of emotion concepts themselves. Similarly, Marino Dávolos et al. (2020) demonstrated that valence congruency can cue semantic retrieval in neurologically healthy adults. Chapter 4 was the first to demonstrate that these effects persist despite semantic control impairments, and to demonstrate benefits of semantic relatedness on valence matching.

Chapter 5 goes beyond evidence relating to cueing, in demonstrating beneficial effects of extrinsic reward cues which in themselves do not allude to concept meaning. Prior evidence has consistently demonstrated beneficial effects of extrinsic reward value in bolstering cognitive control (e.g., Capa et al., 2013; Otto & Vassena, 2021; Small et al., 2005). Compensatory effects of reward have also been observed in the context of age-related cognitive decline (Yee et al., 2019). Here, high levels of extrinsic reward were found to similarly ameliorate impairments in semantic matching for SA patients, particularly in the context of weak associations which place greater demands on semantic control resources. As

in the case of reward boosting domain-general cognitive control, this modulation may be a product of increasing engagement with an effortful task (Goschke & Bolte, 2014) via reward-induced modulation of dopamine transmission (Westbrook et al., 2020), although neuroimaging studies of motivated semantic control would be needed to test this. Harnessing a method of ameliorating impairment which does not rely on item-specific information may increase the flexibility of rehabilitation strategies for post-stroke aphasia. Specifically, these findings highlight the potential effectiveness of gamified approaches to rehabilitation, which rely on the use of typical game features including token point systems (Landers, 2014). Recent research provides promising evidence that improvements in semantic matching can be seen in SA through the use of explicit feedback, which may generalise beyond trained items (Stampacchia et al., 2021). The use of gamification strategies including extrinsic reward may play an important role here in improving engagement and strengthening task representations. Conversely, Chapter 5 found no evidence for beneficial effects of self-reference on semantic matching, intended as a proxy for intrinsic motivation (Madan, 2017).

Overall, neuropsychological studies in this thesis contribute to an increasingly coherent picture of SA and its effects. This thesis provides evidence of effects of brain injury that extend beyond locally-damaged regions to affect large scale functional networks, with some patterns associated with impairments to semantic cognition and domain-general control. This thesis also provides evidence of impairments in affective processing, suggesting wide reaching implications of deficient semantic control. Evidence of beneficial cueing effects and reward-induced improvements in performance, however, should be a cause for optimism concerning the potential to lessen the impact of such impairments.

7.3.2. The relationships between emotion, control, and meaning

Traditional models of emotion took a ‘universal’ or ‘basic’ view, with humans possessing an innate capacity to perceive and experience discrete emotion states (Izard, 1994). Such views are rooted in part in early observations by Darwin (1872), who argued that the evolution of innate expressions serves an adaptive communicative function. This is supported by evidence of cross-cultural similarities in the interpretation of facial expressions (Ekman, 1994). Such accounts acknowledge that language may play a role in the identification of existing emotions, but that emotion processing ultimately operates

independently from language (Ekman & Cordaro, 2011; Lindquist et al., 2015). The constructionist model conversely argues that language and conceptual knowledge play a *foundational role* in the ability to possess knowledge of, and perhaps even experience, discrete emotion states (Barrett et al., 2007; Lindquist et al., 2015). In this domain, knowledge can be thought of as a conscious understanding of what anger, for instance, is, while experience reflects one's ability to subjectively feel anger. If conceptual knowledge does facilitate these processes, emotion processing could not be innate without exposure to emotion language and concepts. Several lines of evidence support this position. In neurologically healthy adults, perception of facial portrayals of emotion can be disrupted through semantic satiation (whereby a concept is rendered inaccessible through verbal repetition; Gendron et al., 2012; Lindquist et al., 2006). Furthermore, patients with SD with degraded stores of semantic concepts experience impairments in the within-valence discrimination of facial portrayals (Lindquist et al., 2014). However, the constructionist model has so far not considered the potential role of controlled semantic retrieval.

Chapter 3 provided novel evidence that patients with SA present with emotion categorisation deficits, as observed in SD. Although viewing conditions were different to those in Lindquist et al. (2014) (given remote testing), categorisation impairments in SA were as severe, and in some cases more severe, than those previously observed in SD. Both samples showed greatest difficulty with within-valence discrimination, where boundaries between discrete emotions may be more ambiguous (e.g., anger versus disgust). These findings support the involvement of semantic control in the effective use of emotion concept knowledge. SA patient performance was seen to improve when provided with written labels that alluded to possible response options, suggesting that successful emotion perception may rely on the resolution of ambiguity, as has been observed for verbal associations (Noonan et al., 2010). Conversely, SD patients were found to benefit from perceptual example facial anchors but not from emotion labels (Lindquist et al., 2014). Facilitatory effects of concept knowledge were therefore only seen in patients with impaired semantic control, not in those with degraded conceptual stores. A similar dissociation has previously been observed in effects of phonemic cueing on picture naming, from which SA patients benefit while SD patients do not (Jefferies et al., 2008). The involvement of semantic control in emotion processing is further supported by Chapter 6, using fMRI in healthy adults. Across the retrieval of emotional and contextual associations to pictures, highly overlapping task activation was observed in SCN nodes including left IFG, left pMTG, dorsomedial prefrontal

cortex (dmPFC), and right IFG (Jackson, 2021). This suggests that this network, and semantic control by extension, may be important for the retrieval of discrete emotion states. Chapter 4 similarly demonstrated baseline impairments in SA in matching words by hedonic valence, a core dimension of affect (Lang et al., 1993). Again, these results suggest a role of semantic control in affective processing.

Chapter 4 also investigated the inverse of this relationship – the role that valence plays in facilitating access to global semantic similarity. While the discrete emotion states studied in Chapter 3 reflect members of a superordinate category of emotion, this chapter instead investigated the role of hedonic valence as a facet of heteromodal concepts, beyond emotion states alone. Evidence here of facilitatory effects of valence congruency on semantic matching is consistent with prior findings (Marino Dávolos et al., 2020), although this has not been previously demonstrated in SA patients. The hub and spoke model of semantic cognition argues that representations in a heteromodal hub interact with modality-specific spokes, in domains including vision, sound, praxis, and hedonic valence (Lambon Ralph et al., 2017). Aligning similarity in valence, as in Chapter 4, may add a shared feature that facilitates more efficient access to concept meaning. This is consistent with the notion that heteromodal concepts rely on valence features, as they do with action and perception (Martin, 2016). As such, valence has been argued to play an important role in the lexicon, particularly for the representation of abstract words (Kousta et al., 2011; Vigliocco et al., 2014), where valence information benefits word learning (Ponari et al., 2018; Rotaru & Vigliocco, 2019). Stimuli in Chapter 4 were not uniformly abstract in nature, but facilitatory effects of valence were observed, nonetheless. Valenced words can be emotion-labels, such that they reflect discrete emotion states wherein valence is inherent to their meaning (e.g., ‘fear’), or emotion-laden, such that they do not refer to a single emotion but are imbued with affective connotations (e.g., ‘war’; Zhang et al., 2017). The stimuli used here were predominantly emotion-laden. In such cases, valence is likely attributed as a semantic feature over time due to its reinforcement in the learning context of a given word (Ponari et al., 2020). As predicted, effects of valence congruency on semantic matching in Chapter 4 were not as large as effects of global semantic similarity on valence matching. This is likely the case because valence is only a single feature, while many features contribute to global similarity. While insight from Chapter 3 suggests that discrete emotion states may be a superordinate conceptual category with states of varying similarity within it, Chapter 4 supports the contribution of valence as one of many features of heteromodal concepts. This thesis

therefore provides insight into the relationship between semantics and affect from multiple perspectives.

As mentioned in Section 7.3.1, the current findings add to an established body of literature suggesting that semantic control may be applicable to a diverse range of functions and modalities (Diveica et al., 2021; Vatansever et al., 2021), including semantic and episodic memory, social cognition, and emotion processing. Broadly, there may be two ways of interpreting such a pattern. First, it may be the case that these functions are inherently semantic in nature, and as such necessarily rely on semantic control and storage mechanisms. In the case of Chapters 3 and 6, discrete emotion categories may be semantic constructs, with a representation of ANGER being comparable to the representations of HAMMER, or DOG. These concepts are likely to rely to different degrees on distinct semantic features (i.e., for ANGER, input from bodily sensations and valence will likely be more important than for DOG); nevertheless, emotion concepts may draw on the same semantic store(s) supporting feature integration as other concepts. In this way, ventral anterior temporal lobe (ATL), a heteromodal semantic hub (Patterson et al., 2007), might support representations of both emotions and non-emotive concepts. Alternatively, representations of concepts and emotions may draw on different long-term stores, in a similar fashion to the proposal that semantic and episodic memory draw differentially on the ATL and hippocampus, respectively (Moscovitch et al., 2005)[25]; this could be the case even if both domains activate SCN. By this view, semantic, episodic, and emotion processing might rely on shared retrieval mechanisms despite fundamental differences in long-term representation.

To test the hypothesis that emotions and non-emotive conceptual information are both processed within the same ATL semantic store, ROI analysis using the Featquery function of FSL was performed on the fMRI data in Chapter 6. ROIs were 5mm spheres centred on coordinates from Binney et al. (2010): this paper was chosen because it used distortion-corrected fMRI to image the ATL during semantic processing and showed convergence in the location of activation in healthy participants with the peak atrophy site in SD. This paper has been used to provide ROIs in subsequent studies examining the contribution of ATL to semantic cognition (e.g., Gao et al., 2022). One site was in the middle left fusiform gyrus (FG; see Figure 7.1a); this is the site that was most associated with semantic task performance in Binney et al.'s study. As this peak site is relatively posterior, another site was

[25] Researchers have begun to question the strength of this episodic/semantic distinction (e.g., Renoult et al., 2019).

selected in anterolateral left inferior temporal gyrus (ITG; see Figure 7.1b) to allow for an understanding of how functional contributions may differ across ATL. Mean percent signal change was calculated in both sites for each association type (semantic context, emotion) and phase (generate, switch) over baseline (see Figure 7.1c).

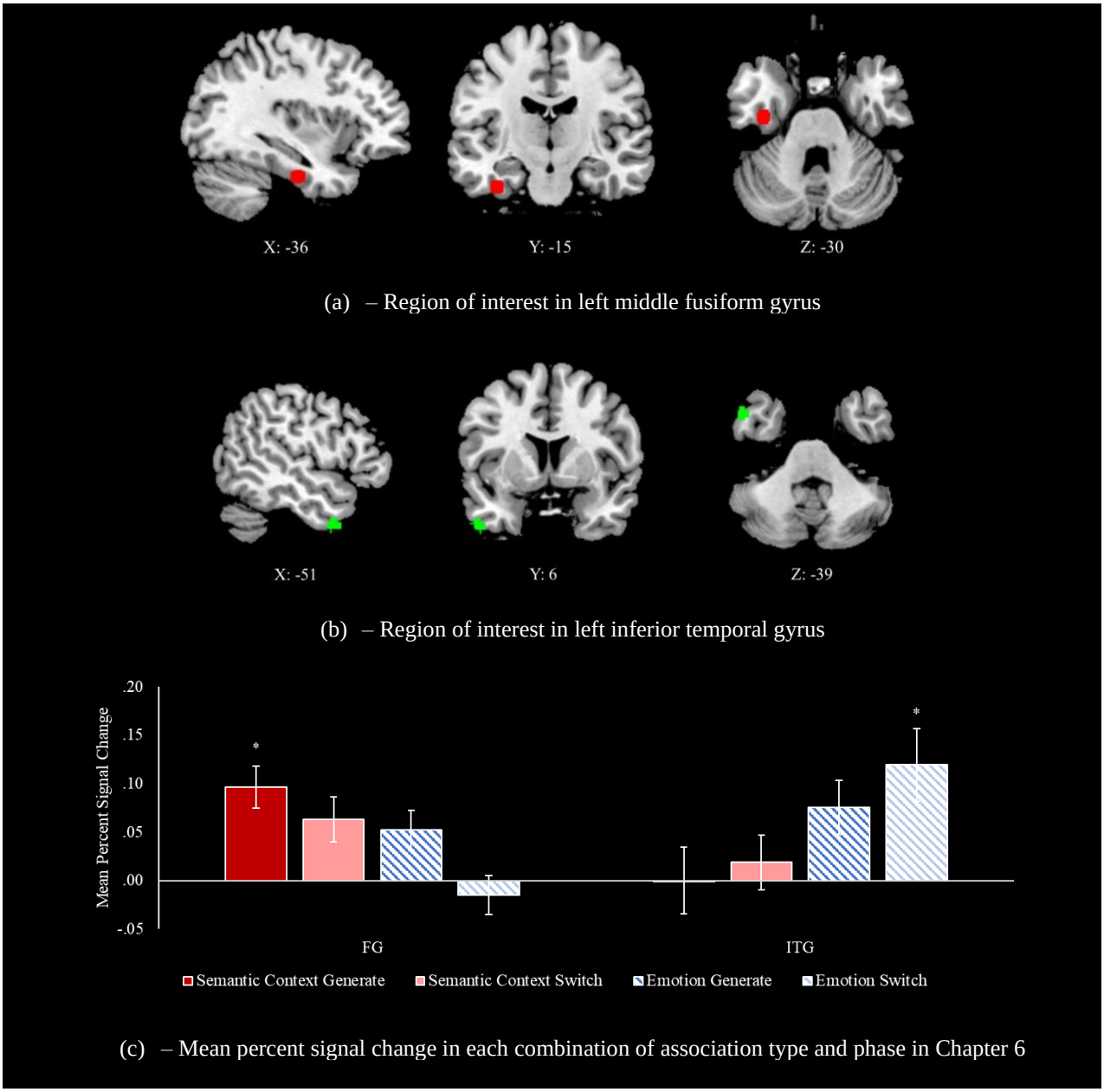


*Figure 7.1. 5mm spheres in the left ventral anterior temporal lobe, used as regions of interest, focusing on (a) left middle FG and (b) left ITG. MNI coordinates are displayed under each view. (c) Mean percent signal change in both sites in each combination of association type and phase from Chapter 6 fMRI task data. Error bars reflect one standard error. * reflects significance difference from 0 according to one-sample t-tests corrected for eight comparisons. FG = fusiform gyrus, ITG = inferior temporal gyrus.*

A repeated measures ANOVA on signal change data can be seen in Table 7.1. Significant effects included an interaction of site and association type, of site and phase, and a three-way interaction between site, association type, and phase. Post-hoc comparisons were run to parse both two-way interactions. For each interaction, contrasts were Bonferroni-corrected for two comparisons. This revealed stronger activation for semantic associations in FG [$t(31) = 4.3$, $p < .001$] and for emotion associations in ITG [$t(29) = -5.8$, $p < .001$], and a preference for the generate phase for the FG [$t(31) = 5.0$, $p < .001$] but no difference between phases for the ITG [$t(29) = -1.0$, $p = .665$]. These results suggest that the semantic site in the relatively posterior FG may support the representation of contextual information and is particularly important for the representation of visual information. In contrast, the anterior ITG may play a more important role in the representation of evaluative concepts.

Table 7.1. Effects of site, association, and phase on mean percent signal change in the left ventral anterior temporal lobe during Chapter 6 task activation.

Effect	Result
Site	$F(1, 29) = 0.1$, $p = .812$, $\eta_p^2 < .01$
Association type	$F(1, 29) = 2.3$, $p = .139$, $\eta_p^2 = .07$
Phase	$F(1, 29) = 2.9$, $p = .100$, $\eta_p^2 = .09$
Site by association type	**$F(1, 29) = 55.8$, $p < .001$, $\eta_p^2 = .66$***
Site by phase	**$F(1, 29) = 15.8$, $p < .001$, $\eta_p^2 = .35$***
Association type by phase	$F(1, 29) = 0.3$, $p = .608$, $\eta_p^2 = .01$
Site by association type by phase	**$F(1, 29) = 9.1$, $p = .005$, $\eta_p^2 = .24$***

Note: * reflects a significant result.

One-sample t-tests were used to establish whether activation in either ROI was significantly different from 0 (and therefore significantly active) in each condition, Bonferroni-corrected for eight comparisons. After correction, FG only significantly activated for *semantic context generate* [$t(31) = 4.4$, $p = .001$]. Differences from 0 for *semantic context switch* [$t(31) = 2.8$, $p = .078$] and *emotion generate* [$t(31) = 2.6$, $p = .125$] were marginally non-significant, and *emotion switch* highly nonsignificant [$t(31) = -0.8$, $p > 1$]. ITG significantly activated for *emotion switch* [$t(31) = 3.2$, $p = .027$] with a marginally nonsignificant effect for *emotion generate* [$t(30) = 2.7$, $p = .091$], and highly nonsignificant differences for *semantic context generate* [$t(31) = 0$, $p > 1$] and *switch* [$t(30) = 0.7$, $p > 1$]. This suggests that FG only responds to contextual retrieval, maximally during the presentation of new pictures. ITG conversely only supports emotion associations, particularly

when retrieving a subordinate association from a picture that has already been seen. Neither site appears to act as a hub that subserves both tasks.

These results are potentially compatible with a graded account of semantic representation (Lambon Ralph et al., 2017), with different aspects of ATL supporting different domains to different degrees (Binney et al., 2016). Indeed, it has been argued that dorsal-polar regions of ATL may support the processing of emotional and valenced information via connections to limbic regions (Binney et al., 2016). However, the graded hub account also predicts that full integration occurs in ventrolateral ATL in regions that are equidistant between different types of feature inputs (Lambon Ralph et al., 2017). In this case, we do not see evidence of integration of emotional and contextual associations in either site, but rather differential specialisation and tuning dependent on the association type required. This is somewhat consistent with the notion of 'mosaic'-like organisation of information in inferior temporal regions, with evidence of category-specific responses (Sato et al., 2013). Overall, this suggests that while control mechanisms may be consistent across such domains, neighbouring yet dissociable ATL regions may serve core representation[26].

Results from this thesis also provide insight into the automaticity of affective processing. Some behavioural studies with neurologically healthy adults suggest that recognition of discrete facial emotions is relatively automatic – with minimal impacts of cognitive load or conscious deliberation on accuracy (Tracy & Robins, 2008). The perception-action model of empathy argues that attending to emotion states automatically activates relevant representations, allowing their effective perception (Preston, 2007). Indeed, evidence suggests that presenting incongruent facial expressions behind emotion labels during a semantic categorisation task interferes with performance, implying rapid activation of emotion concept knowledge upon perceiving facial portrayals (Preston & Stansfield, 2008). This position is somewhat at odds with the Chapter 3 finding that impairments in semantic control disrupt this process. Semantic control reflects one's ability to retrieve concepts under ambiguous conditions: this process is expected to be of little relevance to entirely automatic retrieval. Furthermore, across experiments, emotion state categorisation was improved by increased task constraints and cueing, and impaired by within-valence prosody miscues. Again, such manipulations would likely not cause interference to a purely

[26] From this analysis, it is not possible to discount the possibility that other ATL locations might show significant responses across both tasks – for example, a region between the two ROIs we selected may show this pattern.

automatic process, stressing the importance of control resources in effective discrimination of facial portrayals of emotion. Similarly, Chapter 4 provided evidence that the matching of words by hedonic valence may be disrupted by semantic control impairment, and by semantic distractors. The latter was true in healthy controls, and to a greater extent in SA patients. Prior evidence has suggested that when word meaning is task-relevant, attention to semantic content precedes the extraction of affective qualities (Itkes & Mashal, 2016). The current findings demonstrate that this may also be true when word meaning is implicit and task-irrelevant. It should also be noted, however, that valence congruency influenced semantic matching when it was itself task-irrelevant, suggesting a degree of automaticity to the processing of valence as a stimulus property. It may therefore be the case that word valence is available to drive semantic judgements unless it is superseded by competition from other features. In this case, competition from other features which together constitute higher global similarity may require inhibition and control resources. Overall, it may be the case that the hedonic valence of concepts (positive/negative) is automatically accessed, yet discrete emotion states (e.g., anger, sadness) are not. This is consistent with evidence from semantically impaired patients in Chapter 3 and from Lindquist et al. (2014) showing that emotion classification errors are largely within-valence when semantic cognition is disrupted, with relative sparing of across-valence discrimination.

Using evidence from both neuropsychology and neuroimaging, this thesis therefore provides novel insights into the relationships between emotion, meaning, and control. This evidence suggests that (a) semantic control supports emotion processing by facilitating access to emotion concept knowledge, (b) hedonic valence facilitates the retrieval of concepts by implicitly providing cues as to word meaning, and (c) semantic control aids selection of task-relevant information when valence and other semantic features are in conflict.

7.3.3. Neural systems supporting aspects of cognitive control

Analysis of structural MRI scans from SA patients in Chapter 2 and fMRI data from healthy participants in Chapter 6 allowed further investigation into the functional networks that support semantic retrieval and cognitive control. Prior work has consistently provided evidence of widespread lesions in patients with SA (e.g., Hallam et al., 2018). Symptom mapping in Chapter 2 revealed that lesions to regions within SCN were associated with

poorer semantic performance (see Figure 7.2a). These substrates included left IFG, middle frontal gyrus, frontal pole, pMTG, postcentral gyrus, and lateral occipital cortex. This is consistent with transcranial magnetic stimulation studies which have suggested a causal role of left IFG and pMTG in semantic control (Krieger-Redwood & Jefferies, 2014), as well as compensatory activation from pMTG following IFG disruption (Hallam et al., 2016). Lesioned substrates implicated in domain-general executive function were found to be adjacent to those implicated in semantic cognition, in frontoparietal regions (see Figure 7.2b). This included overlap with typical MDN regions such as the intraparietal sulcus, supramarginal gyrus, and postcentral gyrus. Overall, these findings are consistent with the notion of dissociable substrates supporting semantic control and domain-general control. Regions identified here logically aligned with expected patterns, such as the implication of the anterior IFG in semantic control and posterior IFG in domain-general control, and with pMTG specialised for semantic control (Davey et al., 2016).

SCN nodes were similarly implicated in the generation of contextual and emotional associations in Chapter 6 (see Figure 7.2c). This was particularly true in aspects overlapping with DMN, followed by voxels exclusively within SCN, and those overlapping with MDN. Functional dissociations within SCN were also observed. Left IFG was found to activate more than all other clusters overall, supporting the primary importance of this site in semantic control. Across association types, left pMTG showed higher activation for the generate phase, while bilateral dmPFC showed a preference for the switch phase. This contribution of pMTG to the generate phase may reflect a specialised role of this region in externally-mediated semantic control (Davey et al., 2016), given its proximity to visual and auditory regions. Conversely, dmPFC may play a role in internally-mediated cognitive tasks. Outside SCN, MDN showed a relative preference for the generate phase and for semantic context associations. This preference for the generate phase is consistent with the role of MDN in visual attention (especially the aspects of this network that fall outside SCN), and with its overlap with the dorsal attention network that is specialised for external task demands (Spreng et al., 2013). The generate phase was visually-guided, since it required participants to identify an association to a picture on first exposure. Similarly, semantic context associations likely relied on visuospatial scene construction to a greater extent than relatively abstract emotional associations. These effects support the view that MDN regions are more important for visuo-spatial than semantic cognition (Chiou et al., 2022).

Figure 7.2 presents an overlay of clusters identified in Chapters 2 and 6 with both SCN and MDN (with SCN subtracted). This is done for lesion symptom mapping for (a) poorer semantic performance and (b) poorer Brixton Spatial Anticipation Test performance in Chapter 2, and (c) the statistical conjunction of task activation for semantic contextual and emotional association (across phases) in Chapter 6. All implicate elements of left IFG within SCN. Both impaired semantic cognition lesion-symptom mapping and Chapter 6 task activation show overlap with SCN in left pMTG. To test for functional similarity across chapters, ROI analysis was performed using thresholded ($t > 2.6$) and binarized versions of Chapter 2 semantic and Brixton lesion-symptom mapping clusters, examining each combination of association type and phase from Chapter 6, using the Featquery function of FSL. The resulting mean percent signal change can be seen in Figure 7.2d. For each condition, outliers (three standard deviations above or below the group mean) were removed.

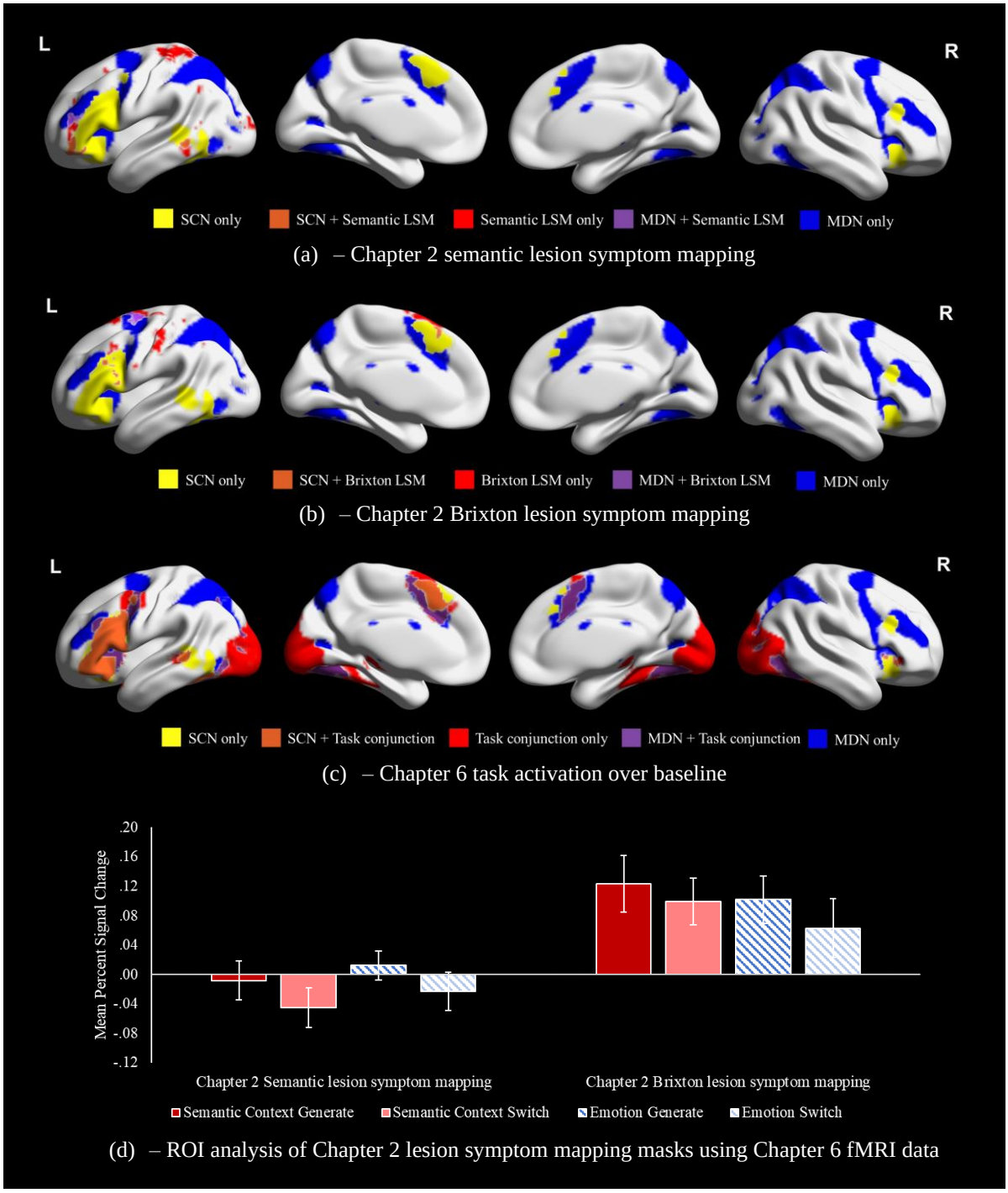


Figure 7.2. Overlap with the Jackson (2021) SCN and Fedorenko et al. (2013) MDN (with SCN removed) for (a) Chapter 2 semantic lesion symptom mapping, (b) Chapter 2 Brixton Spatial Anticipation Test lesion symptom mapping, and (c) the statistical conjunction of task activation for semantic contextual and emotional associations over baseline from Chapter 6. (d) Mean percent signal change in Chapter 2 semantic and Brixton lesion symptom mapping clusters in each Chapter 6 condition over baseline. Error bars reflect one standard error. LSM = lesion-symptom mapping, SCN = semantic control network, MDN = multiple demand network.

Results of a repeated measures ANOVA on this data can be seen in Table 7.2, examining effects of ROI site (defined using semantic versus Brixton symptom mapping), association type (semantic context versus emotion) and phase (generate versus switch). A significant effect of ROI site shows that clusters implicated in Brixton lesion symptom mapping were more active than those implicated in semantic symptom mapping across all the Chapter 6 task conditions. The effect of phase approached but did not reach significance, with numerically more activation in the generate phase. No other effects or interactions approached significance. The stronger task response seen in the Brixton clusters may be attributable to a role of these regions in general task-positive activation, consistent with the nature of MDN (Fedorenko et al., 2013) and the executive demands of the paradigm used in Chapter 6. Clusters implicated by semantic lesion-symptom mapping may be more allied to DMN regions, a network that does not present with reliable task activation (Raichle, 2015). The lack of effects of association type further support the notion that control mechanisms equally contribute to the retrieval of contextual and emotional associations, in line with the interpretation of the data in Chapter 6. Given that subordinate-level and weakly encoded associations impose particularly strong semantic control demands – with stronger activation for weak than strong associations in fMRI studies (e.g., Gao et al., 2021; Krieger-Redwood et al., 2022; Vatansever et al., 2021), plus greater impairment of the retrieval of weak associations in SA (Jefferies et al., 2019; Noonan et al., 2010), one might have expected this network to show a stronger response in the switch than generate phase. However, SA patients also present with impairments in fluency tasks, in which participants are required to self-generate words that fit a semantic category or that start with a given letter under timed conditions (Rogers et al., 2015). This requirement to self-generate task-relevant semantic information is strong in the generate phase of the task from Chapter 6. These results are therefore consistent with the notion that control processes may be taxed both by weak associations and by novel generation of an association under time constraints. While the generate phase may have had high selection demands (given that an association among many competitors must be retrieved), the switch phase may have required inhibition of the initially generated response to identify an alternative and less dominant association.

Table 7.2. Effects of Chapter 2 ROI site and of association type and phase in Chapter 6 on mean percent signal change in clusters implicated in semantic lesion and structural disconnection symptom mapping.

Effect	Result
ROI Site	**$F(1, 28) = 13.6$, $p < .001$, $\eta_p^2 = .33$***
Association type	$F(1, 28) = 1.7$, $p = .203$, $\eta_p^2 = .06$
Phase	$F(1, 28) = 3.1$, $p = .091$, $\eta_p^2 = .10$
ROI Site by association type	$F(1, 28) = 1.0$, $p = .332$, $\eta_p^2 = .03$
ROI Site by phase	$F(1, 28) < 0.1$, $p = .844$, $\eta_p^2 < .01$
Association type by phase	$F(1, 28) = 0.7$, $p = .423$, $\eta_p^2 = .02$
ROI Site by association type by phase	$F(1, 28) = 0.8$, $p = .372$, $\eta_p^2 = .03$

Note: * reflects a significant effect.

Findings across chapters provide insight into the relative lateralisation of SCN and MDN. Prior work has consistently shown left-lateralised activation linked to semantic control demands (Jackson, 2021) and intrinsic connectivity between IFG and pMTG is stronger in the left than right hemisphere (Gonzalez Alam et al., 2019). In contrast, MDN is described as a bilateral network (Duncan, 2001; 2010; Fedorenko et al., 2013) and many studies of non-semantic control show stronger task activation in the right hemisphere (Aron et al., 2014; Gonzalez Alam et al., 2018). Evidence from structural disconnection symptom mapping in Chapter 2 is consistent with these different patterns of lateralisation. Clusters for semantic control were largely confined to left hemisphere regions in and around lesioned areas. Although not implicated in this study, prior work has identified white matter tracts supporting semantic cognition that are largely left-lateralised (Marino Dávolos et al., 2020; Nugiel et al., 2016). In contrast, poorer executive function was associated with cross-hemispheric structural disconnection through the corpus callosum. This is consistent with evidence that executive function is supported by interhemispheric connectivity and the integrity of the corpus callosum (Bodini et al., 2013; Johnson et al., 2017; Jokinen et al., 2007; Voineskos et al., 2012). Chapter 2 therefore supports left-lateralised and bilateral substrates for semantic and domain-general control, respectively. Similarly, in Chapter 6 substrates associated with the generation of associations with pictures were found to align remarkably well with SCN, as seen in Figure 7.2c. This included a large left frontal cluster and only a small right frontal cluster, with substrates in posterior temporal regions restricted to the left hemisphere.

To further test for lateralisation, the analysis in Chapter 6 of functionally defined control networks was rerun in each hemisphere separately. SCN clusters are far larger in the left than right hemisphere. Networks were therefore not simply split by hemisphere; rather,

left hemisphere aspects of each network were projected into the right hemisphere allowing the comparison of two symmetrical maps. ROI analysis using the Featquery function of FSL was run on mean percent signal change in each network (DMN, DMN & SCN, SCN, SCN & MDN, MDN) split by hemisphere (left, right) for each association type (semantic context, emotion) and phase (generate, switch). This data can be seen in Figure 7.3. Outliers (three standard deviations above or below the group mean) were removed.

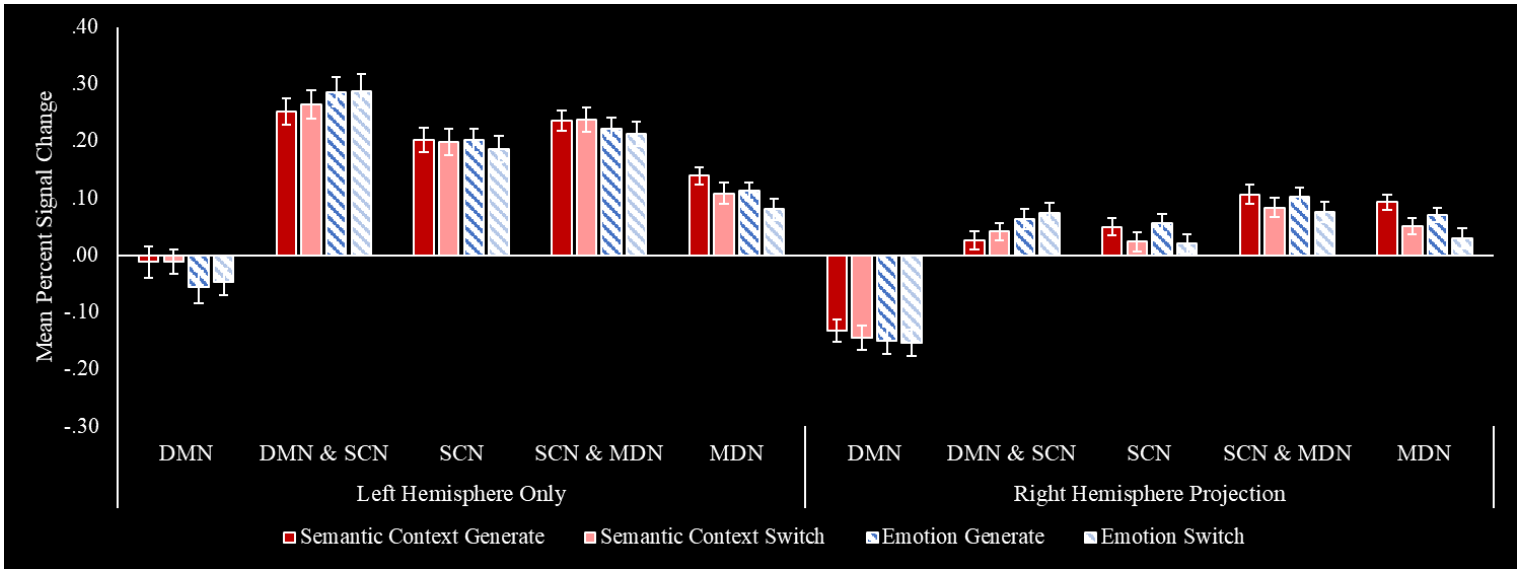


Figure 7.3. Mean percent signal change in functional control networks of interest for Chapter 6 fMRI data, in elements restricted to the left hemisphere and projected from to the left to the right hemisphere. Error bars reflect one standard error.

Repeated measures ANOVA was used to examine the effect of network (five levels) and hemisphere (two levels), averaging across association types and phases. This revealed a significant main effect of hemisphere [$F(1, 27) = 72.2$, $p < .001$, $\eta_p^2 = .73$] and network [$F(2.9, 77.2) = 92.9$, $p < .001$, $\eta_p^2 = .78$] and a hemisphere by network interaction [$F(4, 108) = 28.1$, $p < .001$, $\eta_p^2 = .51$]. The effect of hemisphere reflects more activation for clusters in the left than right hemisphere. For the sake of brevity, contrasts for the main effect of network are not reported. When parsing the observed interaction (contrasts corrected for five comparisons), significant differences between hemispheres were observed for each network [DMN, $t(28) = 5.3$, $p < .001$; DMN & SCN, $t(30) = 10.8$, $p < .001$[27]; SCN, $t(31) = 8.3$, $p <$

[27] The assumption of normality was violated for DMN & SCN. Non-parametric analysis revealed the same result: $Z = -4.9$, $p < .001$

.001; SCN & MDN, t(31) = 8.0, $p < .001$; MDN, t(31) = 4.5, $p < .001$]. This interaction reflects differences in the magnitude of effect of hemisphere, with the largest differences in mean percent signal change for DMN & SCN (.23), followed by SCN (.16), then SCN & MDN (.13), DMN (.12), and finally MDN (.05). This analysis shows that SCN is far less symmetrical across hemispheres in its full form than either DMN or MDN.

It has been argued that a left-lateralised SCN may have emerged in prior work due to the predominant use of verbal stimuli (Jackson, 2021; Rice et al., 2015). Here, left-lateralised activation was observed despite the use of pictorial stimuli without a verbal component. Gonzalez Alam et al. (2021) demonstrated that semantic cognition is more efficient when the 'control B' network, a frontoparietal resting-state network defined by Yeo et al. (2011), is closer to DMN on the principal gradient in the left hemisphere than in the right hemisphere. This lateralisation may allow for stronger coupling between control systems and DMN, facilitating internally-oriented semantic control, while relatively right-lateralised control networks are specialised for externally-oriented tasks. As such, left lateralised semantic control may be adaptive in optimising for efficient control across domains.

Meta-analyses of emotion reappraisal, which involve generating novel interpretations of affective stimuli as in Chapter 6, have also implicated SCN nodes (Buhle et al., 2014; Kohn et al., 2014; Messina et al., 2015; see Figure 1.2). While these analyses tend to implicate bilateral IFG, activation in pMTG is consistently restricted to the left hemisphere, suggesting that the same left-lateralised SCN mechanisms may be implicated. In line with this, task activation in Chapter 6 in SCN was left-lateralised for both the emotion and semantic context task (Figure 7.3).

7.3.4. The role of the default mode network in semantic retrieval

As well as control networks such as MDN and SCN, semantic retrieval may be supported by DMN. Although often associated with task-related deactivation (Raichle, 2015), recent evidence has implicated DMN in higher-order cognitive tasks which require internally-focused and memory-guided processing of heteromodal information (Smallwood et al., 2021). Aspects of DMN have been implicated in semantic representation (Mancuso et al., 2022), including in lateral ATL regions and angular gyrus. Of relevance to empirical data presented here, aspects of DMN have also been associated with emotion induction (Mancuso

et al., 2022), the representation of discrete emotion categories (Satpute & Lindquist, 2019), and emotional valence (Lee et al., 2021).

Using fMRI, Chapter 6 focused on dissociations within DMN during the performance of semantic tasks. Overall task activation was found to be highest in elements of SCN overlapping with DMN. Both SCN and DMN have been implicated in internally-focused processing of heteromodal information (Jefferies et al., 2019; Smallwood et al., 2021), which may account for their shared contribution to this task. The study also found differential contributions of DMN subnetworks to the generation of contextual and emotional associations to pictures. In prior research, MT DMN has been associated with recollections of experiences which rely on mental scene construction that is typically visuospatial in nature, while FT DMN has been implicated in abstract and conceptual processing (Andrews-Hanna and Grilli, 2021; Andrews-Hanna et al., 2014; Chiou et al., 2020; Gurguryan & Sheldon, 2019; Sheldon et al., 2019). This aligns with the observation in Chapter 6 that these networks supported contextual and emotional associations, respectively. Little focus has been given to differential responses within tasks across phases with changing retrieval demands, and here Chapter 6 findings provide novel insight. The generate phase involved retrieving a dominant association to a novel picture. The switch phase involved switching to a new association even when the picture did not change. Modulation of subnetworks differentially responding to task (MT and FT DMN) was found to be independent of changing retrieval demands. While MT DMN activated more for the generate phase overall, this was true across tasks, and no effect of phase was observed for FT DMN.

The switch effect was instead largely supported by the control B network. Control B is associated with internally-focused control of tasks and has been shown to functionally couple with DMN (Dixon et al., 2018; Yin et al., 2022). Clusters implicated in the switch phase also fell towards the heteromodal end of the principal gradient; a hierarchy based on similarity in functional connectivity that captures the distinction between primary sensory-motor and heteromodal cortex and explains the most variance in resting-state fMRI data (Huntenburg et al., 2018; Margulies et al., 2016). This greater activation in the switch phase in heteromodal regions, relative to the generate phase, is likely linked to the requirement to generate a new association even when the visual input did not change, reducing reliance on visual processes. This was equally true across association types, further suggesting independence of retrieval demands and task structure on DMN activation. This is also

consistent with the domain-general nature of the principal gradient, supporting diverse functions (Irish & Vatansever, 2020).

Although other chapters did not explicitly focus on DMN, they provide further insights into its role in semantic cognition. Chapter 2 revealed relative sparing of DMN in patients with SA, with an average of only 5.7% of this network lesioned (although SCN regions falling inside DMN were affected). The sparing of DMN regions not implicated in semantic control might be linked to the way in which SA patients are better at retrieving semantic and emotional information when control demands are reduced through cues or a supportive task structure (see Chapters 3, 4 and 5). Nevertheless, aspects of DMN were implicated by lesion-symptom mapping for both semantic performance and the Brixton Spatial Anticipation Test, including in the frontal pole and posterior temporal regions. Figure 7.4 shows visualisations of resting-state networks that together constitute DMN (Yeo et al., 2011), as described in Chapter 6, alongside thresholded lesion-symptom maps linked to semantic and executive performance.

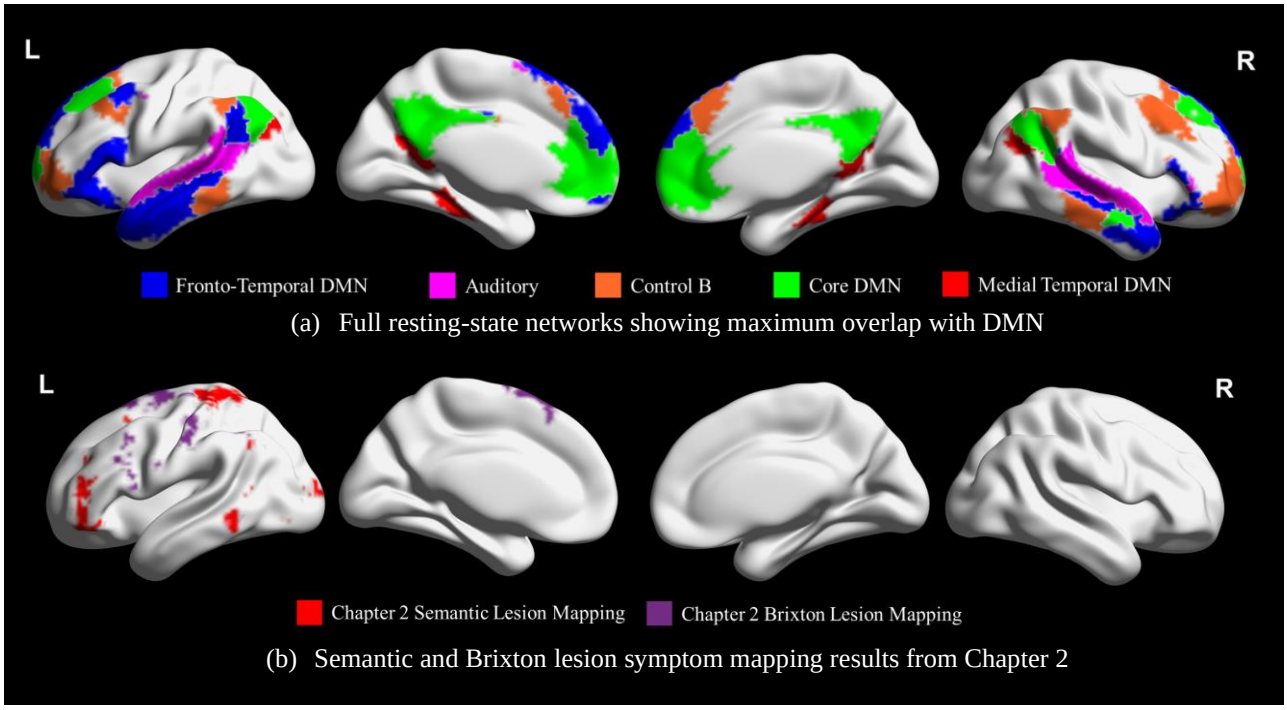


Figure 7.4. (a) Resting-state networks showing maximum overlap with DMN as defined in Chapter 6, from Yeo et al. (2011). (b) Thresholded (t > 2.6) lesion symptom mapping results for poorer semantic and Brixton performance in SA patients in Chapter 2. DMN = default mode network.

The percentage of each lesion-symptom map that falls within each DMN overlap network is shown in Table 7.3. For both maps, noticeable overlap only occurred in control B and FT DMN. For the semantic map, overlap with both networks was observed in left frontal pole, pMTG, and temporo-occipital MTG, while overlap with FT DMN was also seen in left angular gyrus (AG). For the Brixton map, overlap with control B was observed in left AG, dmPFC, and middle frontal gyrus, and overlap with FT DMN in dmPFC, middle frontal gyrus, IFG, and precentral gyrus.

Table 7.3. The percentage of Chapter 2 thresholded semantic and Brixton lesion symptom mapping results to fall in each DMN overlap network as defined in Chapter 6, from Yeo et al. (2011).

Measure	Fronto-temporal DMN	Control B	Auditory	Core DMN	Medial temporal DMN
Semantic	8.79%	9.98%	1.05%	0.22%	0%
Brixton	21.01%	11.35%	1.11%	0.48%	0%

In summary, lesion-symptom mapping implicates DMN subnetworks in both semantic cognition and executive control, consistent with evidence that this network can contribute to highly demanding tasks that include a change in context or task-set (Crittenden et al., 2015). Impairments in domains including valence processing, as seen in SA, may be logically linked to a degree of dysfunction in FT DMN, given its implication in abstract and evaluative processing (Andrews-Hanna et al., 2014). Indeed, SCN overlaps more with FT DMN than any other DMN subsystem, as demonstrated in Chapter 6. SA patients also show impairment in episodic retrieval (Cogdell-Brooke et al., 2020; Stampacchia et al., 2018), a task which one may expect to load onto the MT DMN (Andrews-Hanna et al., 2014). The MT DMN covers medial regions including the hippocampus and parahippocampal gyrus. Such areas are considered ‘watershed’ regions, rarely impacted by stroke due to their position relative to the main trifurcation of the middle cerebral artery and because this watershed region has a dual blood supply from the middle and posterior cerebral arteries (Borden, 2006; Conn, 2003). Indeed, this subnetwork was largely protected from lesion in Chapter 2, likely accounting for its lack of implication in symptom mapping. However, the episodic memory impairment in SA is linked to poor control of retrieval, like the deficit in semantic cognition (Stampacchia et al., 2018; 2019). Left IFG – a region frequently lesioned in SA – has been implicated in the control of both semantic and episodic information (Barredo et al., 2015; Jackson, 2021).

The control B network, also important for controlled processing, was similarly implicated here in symptom mapping, for both semantic and executive performance. This is consistent with evidence from Chapter 6 that this network responds to retrieval demands in DMN orthogonally to processing of task features, and from Dixon et al. (2018) implicating this network in the internally-oriented control of DMN. The exact functional relationship between control B and SCN is not clear. In Chapter 6, control B aided the switch to subordinate level associations. This is a function one may expect to be supported by SCN, given this network's role in processing subordinate information (Jackson, 2021). However, SCN activation as a whole was not found to vary by phase. While both networks are allied to DMN and both support internal aspects of control (Davey et al., 2016; Dixon et al., 2018), little is known about their functional similarities and dissociations. It may be that control B is less perceptually-coupled to task content than SCN, and therefore less important for visually-guided semantic retrieval as in the generate phase. Indeed, as established in Chapter 6, SCN shows far greater overlap with a dissociable frontoparietal control network 'control A' (see Supplementary Figure 6.11), a network that has been implicated in externally-focused control (Dixon et al., 2018). Future research may benefit from exploring the functional relationship between SCN and both frontoparietal control A and control B networks.

Overall, this thesis provides insight into possible roles of DMN in semantic cognition across diverse tasks. Further probing into the contribution of DMN and its subnetworks may be useful in better understanding both functioning semantic control in the healthy brain and impaired semantic control in SA.

7.4. Open questions, limitations, and future research

Several open questions remain, and future investigations may prove effective in addressing limitations of this thesis. First, access to SA patients was disrupted following COVID-19 social distancing restrictions. This resulted in data collection moving to a remote format (for Chapters 3 and 4). This limited the sample size by excluding patients who were unable to engage with remote testing. Even for data not obtained remotely (Chapters 2 and 5), patient sample size was smaller than would have been ideal. This is attributable to challenges in recruiting and testing patients who meet the criteria for SA (which for a single patient may require weekly visits over a three-month period). Conclusions from our data are also limited

by the fact that SA patients rarely present with pure semantic control impairments. Across chapters, patients presented with variable degrees of impairment in working memory, fluency, repetition, and executive function. These broader impairments were not used to exclude patients and are well established in SA (e.g., Thompson et al., 2018). Indeed, this pattern is expected given that SCN and MDN regions occupy adjacent left hemisphere regions. However, contributions of non-semantic impairments to emotion and valence processing cannot be ruled out. Future work with larger samples may allow replication of these findings while statistically controlling for the contributions of non-target impairments.

Second, this thesis suggests an importance of semantic control in the recognition and generation of discrete emotions. However, the current findings may not provide direct insight into the relationship between conceptual information and the *experience* of emotions. Here, experience refers to one's ability to appropriately have subjective feelings of anger, for instance, rather than simply one's ability to know what anger is and perceive it in the world. Barret (2006) argues that experience of discrete emotions is facilitated by conceptualisation of the respective state, in a way that is guided by existing knowledge. Critics have argued that direct links between the role of conceptual knowledge in emotion perception (as in Chapter 3) and emotion experience should not be assumed (Sauter, 2018). Similarly, a distinction can be drawn between semantic valence (*knowing* whether a concept is positive or negative) and affective valence (*experiencing* a stimulus as positive or negative; Itkes et al., 2019; Itkes & Kron, 2019). We have seen from Chapter 3 that SA patients are impaired in classifying facial portrayals of emotion into discrete categories, and from Chapter 4 that they are impaired in matching words by the feature of hedonic valence (positive versus negative). Both can be considered semantic tasks (i.e., *knowing* whether a given face represents anger, or *knowing* that the word 'cake' is positive). It is unclear whether these same patients would experience abnormalities in *experiencing* something as positive or negative – this is worth exploring further. Evidence from Chapter 6 suggests recruitment of SCN regions for the retrieval of emotion features which align with substrates implicated in emotion reappraisal (Buhle et al., 2014; Kohn et al., 2014; Messina et al., 2015), a cognitive strategy that allows for modulation of one's emotional experience of an event. Left IFG in particular has been implicated in the substitution and suppression of emotional memories (Benoit & Anderson, 2012; Engen & Anderson, 2018; Guo et al., 2018). Reappraisal may serve as an ideal lens through which to investigate the relationships between control, semantic retrieval, and emotional experience.

Even within the semantic domain, Chapter 3 was limited in so far as only facial portrayals were studied. Effective interpretation of affective states likely requires integration of cues including facial expressions, bodily states, and vocal prosody. Vigliocco et al. (2020) demonstrated that lesions to IFG and posterior temporal regions predict difficulty in integrating multimodal cues. SA patients, who frequently experience lesion to these sites, are likely to show such impairments and this will impact their processing of valence and semantic information. In patients with frontotemporal dementia, Jastorff et al. (2016) demonstrated that grey matter density in left IFG predicted ability to categorise emotion states based on expressive bodily gait, consistent with the findings of this thesis in the facial domain. Investigations into the role of semantic control in integrating emotion concepts across modalities may provide a more holistic picture.

Furthermore, when considering the structure of affect, a distinction should be made between the representation of discrete emotion states and stimulus valence. Emotions can be considered a superordinate category, containing discrete concepts including anger, happiness, and disgust. Conversely, valence reflects inherent qualities of a stimulus, on a dimension from negative to positive. While this distinction was analysed in Chapter 3, more could have been done in Chapter 6 by comparing differences in activation associated with emotional switches within and across valence. Similarly, while Chapter 4 assessed valence congruency between words, it may also have been possible to manipulate 'emotional congruency'. Indeed, efforts have been made to characterise affective word norms, such as those used in Chapter 4, according to the emotion category they correspond to (Stevenson et al., 2007).

Findings from Chapter 5 suggest facilitatory effects of extrinsic reward on semantic control, ameliorating impairments in SA patients. For domain-general control, such effects have been attributed to dopaminergic modulation of brain regions implicated in cognitive control (Soutschek & Tobler, 2018). The current findings may be attributable to this same modulation. In the absence of patient neuroimaging data, however, this conclusion cannot be made. Original plans to run an fMRI study observing effects of reward on semantic control in patients were disrupted following COVID-19 restrictions. Future use of fMRI to address this question may provide additional insight into the mechanisms underlying motivated semantic control. Also in this chapter, no effects of self-reference on semantic retrieval were observed, despite self-reference recognition memory effects suggesting successful self-referential encoding. Given prior theory and evidence, self-reference was used as a proxy for intrinsic motivation (Madan, 2017) – one's inherent enjoyment or interest in a task (Mori et al., 2018).

It is unclear whether this null effect is attributable to the fact that (a) self-reference does not modulate intrinsic motivation or (b) intrinsic motivation does not benefit semantic retrieval. Future work may benefit from directly measuring the relationship between self-reference and intrinsic motivation, and perhaps exploring more reliable and direct methods of modulating intrinsic motivation in the context of a demanding task.

Chapter 6 provided novel insights into functional dissociations in DMN and found a role of MT DMN in the retrieval of semantic contexts. Prior work has alluded to a role of this subnetwork in episodic recall (Andrews-Hanna et al., 2014), and Chapter 6 appears to add that this network also contributes to the retrieval of generic event contexts from semantic memory. In this study, participants were explicitly asked to avoid using episodic strategies, but it was not possible to completely rule out a contribution from personal episodic memories. The extent to which this subnetwork truly differentiates between episodic and semantic contextual associations is therefore unclear. By one view, this subnetwork supports mental scene construction (Sheldon & Levine, 2016), which is relevant to episodic recollection and the generation of semantic contexts. Alternatively, this subnetwork may dissociate across semantic and episodic tasks. Scanning of a paradigm that decouples these two dimensions (episodic/semantic; scene construction/no scenes) may allow for a clearer delineation of this subnetwork. As discussed above, future research may also benefit from exploring the functional similarities between SCN and control B. In Chapter 6, control B was implicated more in the switch phase while SCN activation was consistent across phases, despite both networks being allied to DMN and both supporting internally-focused control (Davey et al., 2016; Dixon et al., 2018).

Finally, as noted in section 1.3.4, SCN, MDN, and DMN all show degrees of overlap with core language regions. This is likely reflective of the importance of semantic retrieval, control mechanisms, and conceptual knowledge, respectively, in language (Fedorenko, 2014; Jefferies, 2013). Throughout this thesis I have not conducted explicit analysis of the language network. Rather, aspects of language processing regions were represented across these functional networks and across DMN subnetworks. Language regions were not specifically interrogated because here semantic control was conceptualised as a multimodal process encompassing both verbal and nonverbal tasks. However, with this approach it is not possible to definitely conclude whether language processing regions play a meaningful role in driving network effects observed in Chapter 2 and Chapter 6. Future work could address this by

explicitly focusing on effects of lesion on the language network in patients with SA, or on this network's role in the retrieval of contextual and emotional associations.

7.5. Conclusion

Using a combination of cognitive neuropsychology and task-based neuroimaging, this thesis has provided novel insight into the structure of semantic cognition. Through the study of semantic aphasia patients with impaired semantic control, empirical chapters have provided evidence of (a) adjacent neural substrates for semantic control and executive function with left-lateralised and bilateral bases, respectively, (b) impairments in the discrimination of discrete emotion categories that are sensitive to task constraints, (c) baseline impairments in word valence matching that are heightened in the context of related distractors, and (d) sensitivity to cued extrinsic reward value, which can ameliorate semantic impairments. These facets of semantic aphasia have not been previously observed and add to our understanding of the wide-reaching impairments in this group. More generally, this thesis has contributed to our understanding of the role of semantic cognition in affective processing. Adding to constructionist models of emotion processing, this thesis has suggested the importance of semantic control mechanisms in accessing discrete emotion categories. Evidence also suggests that access to word valence is modulated by semantic control demands, even in neurologically healthy adults. Finally, using fMRI this thesis implicates DMN in semantic retrieval, as well as providing evidence of a functional dissociation within DMN. While this dissociation been previously reported, this thesis demonstrates for the first time that processing of retrieval demands is largely independent of the processing of task features, supported by a frontoparietal control network than is allied to DMN. Together, these findings add to our understanding of controlled semantic retrieval and of the structure of emotion and valence processing, as well as providing practical implications for the conceptualisation and amelioration of deficits in SA.

Supplementary materials

Background Neuropsychology supplementary materials

Individual Patient Performance Data

Supplementary Table BN.1. Patient performance on background neuropsychological testing for Chapters 3, 4, and 5.

Test	Max	Cut-off	Patients Mean	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	# Impaired
Chapter 3							✓		✓				✓	✓	✓			✓	✓	
Chapter 4							✓		✓					✓	✓				✓	
Chapter 5				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Non-semantic language tests																				
PALPA 9 real word repetition	80	73 †	60.93	NA	**71**	**42**	**7**	78	79	**1**	NA	74	77	79	75	**67**	**50**	74	79	6
Cookie theft (words/minute)	-	50 ‡	36.79	**0**	**18**	**9**	**38**	60	**37**	**0**	NA	54	**37**	77	80	**34**	NA	**16**	55	9
Category Fluency (8 categories) (words/minute)	-	7.75	5.19	NA	**3.3**	**1.9**	8.6	**1.8**	**3.3**	NA	NA	10	**7.1**	9.4	11.3	**3.8** §	**0**§	**3.8**	**3.5**	9
Letter Fluency (F, A, S) (words/minute)	-	7.27	2.54	NA	**0.7**	**0.7**	**4**	**1**	**2**	NA	NA	**5.3**	**3**	**4.3**	**4.3**	**1**	**1.3**	**2.7**	**2.7**	13
Verbal working memory																				
Digit Span Forward	8	5.54	3.00	**0**	**4**	**1**	6	6	**4**	NT	**0**	**4**	**4**	**4**	**4**	**3**	**0**	**2**	**3**	13
Digit Span Backward	7	3.66	1.27	**0**	**2**	**0**	4	**2**	**0**	NT	**0**	**2**	**3**	**2**	**2**	**0**	**0**	**0**	**2**	14
Visuospatial processing																				
VOSP dot counting	10	8	9.25	**7**	10	10	10	10	10	8	8	10	10	10	9	9	9	8	10	1
VOSP position discrimination	20	18	18.87	19	20	**15**	20	**17**	20	19	20	20	20	20	20	**17**	20	**15**	20	4
VOSP number location	10	7	8.44	8	10	**5**	8	10	10	10	8	**5**	10	10	10	**4**	9	8	10	3
VOSP cube analysis	10	6	8.25	8	9	**4**	8	7	9	10	9	10	10	9	10	**5**	9	**5**	10	3
Executive and spatial processing																				
TEA: counting without distraction	7	4.2	5.53	**2**	5	6	5	**4**	NT	7	5	5	7	5	6	6	7	6	7	2

TEA: counting with distraction	10	2.6	3.73	**1**	3	**1**	3	**2**	NT	7	**1**	**2**	6	**2**	9	4	**2**	3	10	7
Raven's coloured matrices	36	28 †	29.00	31	**27**	31	33	**19**	30	34	**24**	**21**	33	34	32	**20**	32	**27**	36	6
Brixton spatial anticipation	54	28	26.94	**21**	**7**	**18**	39	**24**	**23**	31	34	31	30	41	32	30	**21**	**18**	31	7
Trail Making Test A	24	24 †	22.88	**19**	**22**	**23**	24	24	**23**	24	24	24	24	24	24	24	**16**	**23**	24	6
Trail Making Test B	23	17.4 †	17.37	**2**	23	**16**	21	**1**	**5**	23	23	19	22	22	20	19	20	20	22	4

Note: Scores are number of correct responses unless otherwise specified. NT = unavailable for testing; NA = testing was not attempted because patients were non-fluent; TEA = Test of Everyday Attention, elevator counting subtest; VOSP = Visual Object and Space Processing battery; PALPA = Psycholinguistic Assessments of Language Processing in Aphasia. Cut-offs for impairment correspond to two standard deviations below control mean performance (separate from the control sample used within empirical chapters here), with impaired scores underlined and in bold. These are taken from control norms from respective tests manuals, unless otherwise specified (see below). The top three throws indicate, through ticks, the chapters that a given patient participated in. Data for Chapter 2 are presented separately, given that this chapter used a larger number of patients from separate samples.

† Cut-offs taken from control testing at the University of York. Number of controls: Raven's = 20; Trail Making Test = 14.

‡ Cut-off reflects the 'very slow' classification taken from Kerschensteiner, Poeck and Brunner (1972).

§ Patients P13 and P14 completed only 4 categories (animals, fruit, birds, breeds of dog) for the test of category fluency, while the other patients completed 8 (animals, fruit, birds, breeds of dog, household objects, tools, vehicles, types of boat).

Supplementary Table BN.2. Patient performance on the Cambridge Semantic Battery and tests of semantic control for Chapters 3, 4, and 5.

Test	Max	Cut-off	Patient Mean	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	# Impaired
Chapter 3							✓		✓				✓	✓	✓			✓	✓	
Chapter 4							✓		✓					✓	✓				✓	
Chapter 5				✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Semantic composite score				-1.36	-1.21	-1.07	1.32	.37	.34	.63	.40	.63	.96	1.26	.92	-.75	-1.69	-.89	.13	-
Cambridge Semantic Battery																				
Picture Naming (no cues)	64	59	41.00	**1**	61	**19**	**46**	60	**50**	**3**	**0**	**56**	62	59	63	**54**	**33**	**51**	**38**	11
Picture Naming (with cues)	64	-	51.19	3	63	58	64	64	64	10	0	62	64	64	64	63	52	63	61	-
Word-Picture Matching	64	62.7	60.88	63	**62**	**60**	63	**62**	**62**	**52**	**56**	64	**62**	64	**62**	**62**	**58**	**59**	63	11
Word CCT	64	56.6	49.88	**39**	**43**	**29**	**56**	59	**52**	57	**56**	61	60	59	59	**48**	**28**	**45**	**47**	9
Picture CCT	64	52.7	50.94	**31**	**44**	**45**	61	**45**	57	54	61	53	61	62	59	**44**	**35**	**51**	**52**	8
Ambiguity task																				
Miscued dominant	30	30	18.93	**12**	**13**	**13**	**26**	**20**	**19**	**21**	NT	**24**	**26**	**22**	**25**	**16**	**12**	**21**	**14**	15
Miscued subordinate	30	26.6	15.20	**7**	**10**	**14**	28	**10**	**15**	**18**	NT	**18**	**19**	**22**	**18**	**13**	**12**	**13**	**11**	14
No cue dominant	30	28.4	24.38	**22**	**18**	**24**	**27**	**24**	**26**	**27**	**25**	**28**	**28**	**27**	30	**25**	**11**	**22**	**26**	15
No cue subordinate	30	27.6	16.81	**11**	**9**	**14**	**21**	**19**	**17**	**19**	**16**	**21**	**19**	28	**26**	**12**	**14**	**12**	**11**	15
Cued dominant	30	30	24.13	**23**	**21**	**19**	**29**	**24**	**23**	**23**	NT	**27**	**29**	**28**	30	**23**	**19**	**24**	**20**	14
Cued subordinate	30	28.8	21.87	**25**	**14**	**20**	28	**19**	28	**24**	NT	**23**	**25**	**26**	29	**19**	**16**	**15**	**17**	12
Synonym with distractors																				
Strong distractors	42	35.4	19.94	**15**	**12**	**13**	38	**21**	**23**	**30**	**16**	**22**	**17**	**27**	**13**	**17**	**17**	**13**	**25**	15
Weak distractors	42	40.4	29.31	**25**	**23**	**29**	**36**	**27**	**30**	**31**	**33**	**28**	**39**	**35**	**35**	**25**	**16**	**24**	**33**	16
Object use																				
Alternative	37	33.67	22.06	**14**	**13**	**14**	**32**	34	**22**	**22**	**22**	**26**	**29**	**31**	**29**	**12**	**17**	**9**	**27**	15
Canonical	37	35.9	33.56	**32**	**31**	**29**	37	37	**35**	**33**	**35**	37	37	**34**	**35**	**29**	**34**	**28**	**34**	12

Note: Scores are number of correct responses. NT = unavailable for testing, CCT = Camel and Cactus Test. Cut-offs for impairment are taken from testing at the University of York and correspond to two standard deviations below mean control performance (separate from the control sample used in empirical chapters here), with impaired scores underlined and in bold. Number of controls: Cambridge Semantic Battery = 10, Ambiguity task, Synonym with distractors, Object use = 8. Semantic composite score reflects regression scores derived from principal components analysis (see Table 5.1), including tests with high control demands [CTT words, CCT pictures, Ambiguity task (no cue: dominant + subordinate), Object use task (alternative + canonical), Synonym with distractors (strong + weak)]. Lower composite scores reflect greater impairment. The top three throws indicate, through ticks, the chapters that a given patient participated in. Data for Chapter 2 are presented separately, given that this chapter used a larger number of patients from separate samples.

Description of Assessments

Patients across empirical chapters completed a series of background tests of language, memory, and executive function. For Chapters 3, 4, and 5, individual patients' performance on tests of background neuropsychology are reported in Supplementary Table BN.1, and performance on semantic tests in Supplementary Table BN.2. A description of the tasks used is presented here, followed by a summary of performance within each of these three samples on the following pages. **Chapter 2 used a larger pool of patients from three separate sample. As such, background neuropsychology for this sample is presented and interpreted separately, in the Chapter 2 Supplementary Materials. Pseudonymised patient identifiers are consistent across Chapters 3, 4, and 5, but not for Chapter 2.**

Repetition of single words was assessed using a test from the Psycholinguistic Assessments of Language Processing in Aphasia battery (Kay et al., 1992). Working memory was assessed using forward and backward digit span (Wechsler Memory Scale III; Wechsler, 1997). Spontaneous speech was evaluated using patients' description of 'The Cookie Theft Picture' (Goodglass et al., 2001). Performance was judged non-fluent for a given patient as consistent with the 'very slow' classification from Kerschensteiner et al. (1972) [fewer than 50 words per minute]. Letter fluency was assessed by asking patients to generate words beginning with F, A, and S, with a minute provided for each letter. Category fluency was similarly assessed using the eight categories: animals, fruit, birds, breeds of dog, household objects, tools, vehicles, types of boat. Visuospatial processing was examined using four subtests of the Visual Object and Space Perception battery (Warrington & James, 1991), including judgements of dot counting, position discrimination, number location identification, and cube analysis. Executive function was tested using multiple assessments, including the elevator counting subtest of the Test of Everyday Attention (Robertson et al., 1994), Raven's Coloured Progressive Matrices (Raven, 1962), The Brixton Spatial Anticipation Test (Burgess & Shallice, 1997), and the Trail Making Test A & B (Reitan, 1958).

Simple semantic tasks were taken from the Cambridge Semantic Battery (Bozeat, Lambon Ralph, et al., 2000). This includes Picture Naming, whereby participants must provide a verbal label for 64 line drawings. Though not part of the Cambridge Semantic Battery, successive phonemic cues were provided for words that patients were initially unable to retrieve, to test whether this facilitated naming. Word-Picture Matching required patients to match a spoken word to one of ten semantically-related pictures. Word and picture versions of the Camel and Cactus Test (CCT) were used to examine the retrieval of thematic

associations between concepts. Participants linked a probe word or concept (e.g., ORANGE) to one of four semantically-related options (e.g., target: JUICE, foils: WATER, MILK, WINE). In the word version, the items were presented in print and read aloud by the researcher.

The ambiguity task (Noonan et al., 2010) required patients to make thematic associations between a probe and target word, presented alongside three foils. Each probe was a homonym, with a dominant (e.g., PEN – PENCIL) and subordinate association (e.g., PEN – PIG). These probes were presented alone or following a sentence either cueing the correct interpretation of the probe in relation to the upcoming target (e.g., PEN – PIG: "the labourers cleaned out the pen"), or miscuing the incorrect interpretation (e.g., PEN – PIG: "he signed his name with a fountain pen"). Cues should facilitate semantic retrieval while miscues should impair it. Subordinate associations should confer greater semantic control demands than dominant associations.

The synonym judgement task (Samson et al., 2007) required patients to select which of three possible targets was a synonym of a probe word. Each trial included either a weak distractor, not expected to interfere with retrieval (e.g., probe: HAZARD, target: DANGER, distractor: LIGHT), or a strong distractor, which had a strong thematic association with the probe (e.g., probe: DESERT, target: WILDERNESS, distractor: SAND). Strong distractors should confer greater semantic control demands by requiring inhibition of irrelevant conceptual information (Noonan et al., 2010).

The object use task (Corbett et al., 2011) provides a non-verbal measure of semantic control. Patients are required to identify the appropriate object, of six options, to perform an action (e.g., "Crack a nut"). The target objects could be either be 'canonical' such that they are typically used to complete this action (e.g., NUT CRACKER), or an 'alternative' object which could be used to complete the action if necessary (e.g., HAMMER). Alternative trials should require greater semantic control as they require access to non-dominant information about the target object, and inhibition of dominant information (e.g., that hammers are typically used in construction). Conversely, targets and probes in canonical trials have strong associations, allowing for relatively automatic retrieval of dominant information.

Chapter 3 Sample Summary

Of the seven patients in Chapter 3, only one showed evidence of impaired word repetition. Four patients showed evidence of non-fluent speech when describing The Cookie Theft Picture. Four patients were impaired for category fluency (eight categories), while all seven were impaired for letter fluency (F, A, S). Six patients showed impairment for both forward and backward digit span. One patient presented with impairments in visuospatial processing. Three patients showed evidence of impairment on at least one assessment of executive function.

Core semantic ability was measured using the Cambridge Semantic Battery. Four patients were impaired on the Picture Naming task [Mean (SD) = 82.4% (14.3)]. Providing phonemic cues as to the correct target label improved all patients' performance to ceiling or near-ceiling level [Mean (SD) = 99.1% (1.8)]. Four patients showed impaired performance on Word-Picture Matching [Mean (SD) = 97.1% (2.5)]. Four patients were impaired on the word version of the Camel and Cactus Test [Mean (SD) = 84.4% (9.5)], while only two were impaired on the picture version [Mean (SD) = 90.0% (7.0)].

The ambiguity task required patients to make thematic associations between words. In the no cue condition, patients performed better for dominant [Mean (SD) = 88.6% (8.1)] than subordinate trials [Mean (SD) = 63.8% (21.6)]. Relative to no cue, cued trials improved performance on subordinate [Mean (SD) = 80.0% (18.9)] but not dominant trials [Mean (SD) = 87.1% (12.7)]. Miscued trials considerably impaired accuracy on dominant [Mean (SD) = 72.9% (14.6)], but not subordinate trials [Mean (SD) = 60.0% (19.2)]. Contextual cues therefore improved accuracy on the most difficult trials, while contextual miscues impaired performance on the easiest trials.

On the synonym judgement task, the sample performed better on weak distractor trials [Mean (SD) = 78.9% (11.6)] than strong distractor trials [Mean (SD) = 53.1% (21.2)]. Each patient showed this expected pattern, with the exception of P4 (the least impaired patient).

On the non-verbal object use task, patients performed better on canonical [Mean (SD) = 92.7% (8.2)] than on alternative trials [Mean (SD) = 69.1% (21.6)]. This was true for all seven patients.

Chapter 4 Sample Summary

Of the five patients in Chapter 4, only one showed evidence of impaired word repetition. Two patients showed evidence of non-fluent speech when describing The Cookie Theft Picture. Two patients were impaired for category fluency (eight categories), while all five were impaired for letter fluency (F, A, S). Four patients showed impairment for both forward and backward digit span. Two patients showed evidence of impairment on at least one test of executive function. The relatively low degree of executive impairment in the current sample may reflect the fact that the remote testing requirements imposed by COVID-19 social distancing restrictions selected for less impaired patients than in typical samples.

Core semantic ability was measured using the Cambridge Semantic Battery. Three patients were impaired on the Picture Naming task [Mean (SD) = 80.0% (15.7)]. Providing phonemic cues as to the correct target label improved all patients' performance to ceiling or near-ceiling level [Mean (SD) = 99.1% (2.1)]. Two patients showed impaired performance on Word-Picture Matching [Mean (SD) = 98.1% (1.3)]. Three patients were impaired on the word version of the Camel and Cactus Test [Mean (SD) = 85.3% (8.0)], while only one was impaired on the picture version [Mean (SD) = 90.9% (6.2)].

The ambiguity task required patients to make thematic associations between words. In the no cue condition, patients performed better for dominant [Mean (SD) = 90.1% (5.5)] than subordinate trials [Mean (SD) = 68.7% (22.9)]. Relative to no cue, cued trials improved performance on subordinate [Mean (SD) = 85.3% (16.4)] but not dominant trials [Mean (SD) = 86.7% (14.3)]. Miscued trials considerably impaired accuracy on dominant [Mean (SD) = 70.7% (16.2)], and to a lesser extent on subordinate trials [Mean (SD) = 62.7% (21.8)]. Contextual cues therefore improved accuracy on the most difficult trials, while contextual miscues impaired performance on the easiest trials.

On the synonym judgement task, patients performed better on weak distractor trials [Mean (SD) = 80.5% (5.7)] than strong distractor trials [Mean (SD) = 60.0% (21.3)]. Each patient showed this expected pattern, with the exception of P4 (the least impaired patient).

On the non-verbal object use task, patients performed better on canonical [Mean (SD) = 94.6% (3.3)] than on alternative trials [Mean (SD) = 76.2% (10.7)]. This was true for all five patients.

Chapter 5 Sample Summary

Sixteen patients were in this sample in total, with variable proportions completing each individual assessments. Six patients showed impaired repetition of single words. Thirteen and fourteen cases (of fifteen tested) showed impaired forward and backward digit span, respectively. Evaluation of spontaneous speech when describing 'The Cookie Theft Picture' non-fluent speech in nine patients. All patients showed impaired letter fluency (words beginning with F, A, and S) and nine (of 13 tested) had impaired category fluency (8 categories) – three more cases in the group had little speech output and did not attempt these tasks. Visuospatial processing was largely preserved. Eleven patients showed impairment on at least one test of executive function.

Simple semantic tasks were taken from the Cambridge Semantic Battery. There was considerable variation in performance on Picture Naming, likely due to variable impairment in speech production [Mean (SD) = 64.1% (35.8)]. Apart from for patients showing near-floor or -ceiling performance, naming improved when phonemic cues were presented [Mean (SD) = 80.0% (36.8), Z = -3.4, p = .001], consistent with the view that SA cases retain knowledge of the names of items that they often fail to retrieve. All patients performed close to ceiling level on word-picture matching [Mean (SD) = 95.1% (5.0)]. On the Camel and Cactus Test, there was considerable variation in performance, with half of the sample falling below the normal cut-off for impairment. There was no difference in performance between the word [mean (SD) = 77.9% (16.7)] and picture versions [mean (SD) = 79.6% (14.9)]: Z = -.7, p = .477.

The ambiguity task required patients to make thematic associations between words. A repeated measures ANOVA assessed the effect of cue condition (no cue, cue, miscue) and dominance (dominant, subordinate). This revealed a significant main effect of cue condition: $F(2, 28) = 35.1$, $p < .001$, $\eta_p^2 = .72$, and dominance: $F(1, 14) = 42.6$, $p < .001$, $\eta_p^2 = .75$, and a cue by dominance interaction: $F(2, 28) = 8.0$, $p = .002$, $\eta_p^2 = .37$. Planned contrasts confirmed that cues improved performance on subordinate ($t(15) = -4.8$, $p < .001$) but not dominant trials ($t < 1$). Conversely, while miscues did not affect performance on subordinate

trials (t(15) = 1.6, p = .130), they did impair performance on dominant trials [t(15) = 5.4, p < .001][28].

On the synonym judgement task, patients showed a significant difference in accuracy according to distractor strength: t(15) = -5.2, p < .001. In all but one case, accuracy was lower on trials with strong distractors [Mean (SD): 47.5% (17.3)] than with weak distractors [Mean (SD): 69.8% (14.1)].

On the non-verbal object use task, patients showed a significant difference in accuracy between canonical and alternative trials: t(15) = 8.2, p < .001. All patients performed better on canonical trials [Mean (SD): 90.7% (8.1)] than on alternative trials [Mean (SD): 59.6% (21.7)].

Overall, every patient showed impairment on at least one verbal and one non-verbal test of semantic cognition, indicating multi-modal impairment in semantic retrieval. Additionally, all patients showed effects of cues, miscues, and strong thematic distractors, as expected for patients with semantic control deficits. This profile is consistent with the classification of SA, and replicate the results of previous studies (e.g., Stampacchia et al., 2018). These impairments occurred in conjunction with variable impairments in language affecting both verbal fluency and repetition. Most cases also showed some evidence of executive dysfunction.

As detailed in section 5.3.3. of Chapter 5, a 'semantic control composite score' was derived using principal components analysis. In order to examine associations between semantic control and executive function, we calculated Spearman correlations between the semantic control composite and each test tapping executive function. This correlation was only found to be significant for the Brixton Spatial Anticipation Test:

- Brixton: **$r_s(14) = .837, p < .001$***
- Ravens: $r_s(14) = .338, p = .200$
- Test of Everyday Attention (with distraction) - Test of Everyday Attention (without distraction): $r_s(13) = -.275, p = .320$
- Trail Making Test B - Trail Making Test A: $r_s(14) = -.024, p = .931$
- Digit span backwards - digit span forwards: $r_s(13) = .300, p = .278$

[28] The assumption of normality was not always met but non-parametric tests elicited the same outcomes. Cue effect for subordinate trials: Z = -3.2, p = .001, cue effect for dominant trials: Z = -.3, p = .752, miscue effect for subordinate trials: Z = -1.7, p = .090, miscue effect for dominant trials: Z = -3.3, p = .001.

The finding that only the Brixton Spatial Anticipation Test was associated with semantic control performance may be partially due to low power in the current sample. Alternatively, this association may reflect the demanding nature of the Brixton test, which requires the identification of rules, updating/switching in accordance with new information, and the inhibition of learned rules. This measure has been shown to be sensitive to executive impairment (van den Berg et al., 2009). Other manipulations used here may be comparatively less demanding. Raven's Progressive Coloured Matrices requires the discovery of rules, but not the ability to switch between them. The Trail Making Test requires switching, but between well-learned sequences (letters and numbers). Finally, contrasts for the Test of Everyday Attention and digit span tax attentional resources, but present little demand beyond this. Overall, the demands of the Brixton test may be comparable to those of tests implicated in the semantic control composite score, while the other manipulations of executive function used here may be less demanding.

Chapter 2 supplementary materials

Background Neuropsychology Sample Summary

Patients completed a series of background tests probing language, memory, and executive function. See the Background Neuropsychology Supplementary Materials section '*Description of Assessments*' for descriptions of the tasks employed here. Each individual patient's performance on these tests can be seen in Supplementary Table 2.1. Of the 15 patients tested, seven showed evidence of impaired word repetition. Of the 17 patients tested, 15 were impaired for category fluency (eight categories), while 16 were impaired for letter fluency (F, A, S). Sixteen of 22 patients presented with impaired forward digit span, while 14 of 19 presented with impaired backward digit span. Eight patients presented with impairments in visuospatial processing. All patients completed at least one test of executive function, with fourteen showing some evidence of impairment.

The Cambridge Semantic Battery was used as a measure of core semantic ability. Each individual patient's performance on these tests can be seen in Supplementary Table 2.2. Of the 20 tested, 16 patients were impaired on the Picture Naming task. Providing phonemic cues as to the correct target label improved all patients' performance to ceiling or near-ceiling level [Mean (SD) = 75.3% (41.5)]. Of the 21 tested, 12 patients showed impaired performance on Word-Picture Matching [Mean (SD) = 91.5% (9.4)] For the associative Camel and Cactus Test (CCT), twenty-one patients completed full versions, while the remaining two (P22 and P23) completed shortened versions. Of those who completed the full task, 18 patients were impaired on the word version of the CCT [Mean (SD) = 74.1% (18.3)], while 12 were impaired on the picture version [Mean (SD) = 74.5% (21.8)]. The two patients who completed the short versions of the CCT were impaired on both the word and pictures versions.

The ambiguity task required patients to make thematic associations between words. Twenty-one patients completed the no cue version of the task, with 14 also completing the cue and miscue versions. In the no cue condition, patients performed better for dominant [Mean (SD) = 79.0% (13.8)] than subordinate trials [Mean (SD) = 53.5% (15.1)]. Relative to no cue, cued trials improved performance on subordinate [Mean (SD) = 71.9% (15.6)] but not dominant trials [Mean (SD) = 77.4% (14.6)]. Miscued trials impaired accuracy on dominant [Mean (SD) = 61.2% (21.3)], and somewhat on subordinate trials [Mean (SD) = 45.0%

(19.9)]. Contextual cues therefore improved accuracy on the most difficult trials, while contextual miscues impaired performance on the easiest trials.

On the synonym judgement task, patients performed better on weak distractor trials [Mean (SD) = 69.3% (13.4)] than strong distractor trials [Mean (SD) = 49.6% (16.6)]. All but one patient (P13) showed this expected pattern.

On the non-verbal object use task, patients performed better on canonical [Mean (SD) = 92.7% (7.5)] than on alternative trials [Mean (SD) = 59.5% (19.7)]. This was true for all 20 patients.

Supplementary Table 2.1. Patient performance on background neuropsychological testing.

	Language			Verbal working memory			Executive			Visual Object and Space Processing battery			
	PALA 9 Word repetition	Category Fluency	Letter Fluency	Forwards digit span	Backwards digit span	Brixton	Ravens	TEA without distraction	TEA with distraction	Dot counting	Position discrimination	Number location	Cube analysis
Max	80	-	-	8	7	54	36	7	10	10	20	10	10
Cut-off	73	62	18	5.54	3.66	28	28 [a]	4.2	2.6	8	18	7	6
Mean	62.2	32.3	7.8	3.6	1.8	23.7	26.0	5.0	4.1	8.7	18.4	8.3	6.8
P01	**68.8**	**49**	**14**	6	**2**	28	20	7	9	8	19	9	**4**
P02	**64**	**18**	**0**	**4**	2	**7**	**12**	6	3	10	18	9	**3**
P03	75.2	**24**	19	8	4	28	31	5	9	NT	NT	NT	NT
P04	76.8	**11**	**8**	**4**	**1**	**14**	**6**	**2**	3	**6**	**16**	8	**4**
P05	80	**25**	**14**	6	**3**	**11**	**13**	7	9	**3**	**15**	**2**	**4**
P06	**64.8**	**25**	**5**	**3**	2	34	26	**3**	**2**	10	20	10	**5**
P07	NT	**61**	**13**	**5**	3	37	29	5	6	NT	NT	NT	NT
P08	NT	NT	NT	**0**	**0**	34	**24**	5	**1**	8	20	8	9
P09	75	**26**	**2**	5	**2**	**26**	**24**	5	**1**	9	19	10	**4**
P10	**42**	**15**	**2**	**1**	**0**	**18**	31	6	**1**	10	**15**	**5**	**4**
P11	**1**	NT	NT	**2**	NT	31	34	7	7	8	19	10	10
P12	**71**	**26**	**2**	**4**	**2**	**7**	**27**	5	3	10	20	10	9
P13	**7**	69	**12**	6	4	39	33	5	3	10	20	8	8
P14	74	80	**16**	**4**	**2**	31	**21**	5	**2**	10	20	**5**	10
P15	NT	NT	NT	**0**	**0**	**21**	31	**2**	**1**	**7**	19	8	8
P16	NT	**4**	**3**	**3**	NT	NT	31	7	3	NT	NT	NT	NT
P17	79	**26**	**6**	**4**	**0**	**23**	30	NT	NT	10	20	10	9
P18	77	**57**	**9**	**4**	**3**	30	33	7	6	10	20	10	10
P19	NT	NT	NT	NT	NT	**6**	32	NT	NT	NT	**16**	9	NT
P20	78	**14**	**3**	6	**2**	**24**	**19**	**4**	**2**	10	**17**	10	7
P21	NT	**19**	**5**	**3**	**3**	30	**25**	**2**	6	9	18	9	8
P22	NT	NT	NT	**0**	**0**	16	35	NT	NT	NT	NT	NT	NT
P23	NT	NT	NT	**2**	NT	27	30	NT	NT	NT	NT	NT	NT
# Tested	15	17	17	22	19	22	23	19	19	17	18	18	17
# Impaired	7	15	16	16	14	8	9	5	7	3	5	3	7

Note: Scores are number of correct responses unless otherwise specified. NT = unavailable for testing; TEA = Test of Everyday Attention, elevator counting subtest; VOSP = Visual Object and Space Processing battery. Category fluency corresponds to 8 categories (animals, fruit, birds, breeds of dog, household objects, tools, vehicles, types of boat). Letter fluency corresponds to F, A, S. Cut-offs for impairment correspond to two standard deviations below control mean performance, with impaired scores underlined and in bold. These are taken from control norms from respective tests manuals, unless otherwise specified (see below).

[a] Cut-offs taken from control testing at the University of York. Number of controls = 20.

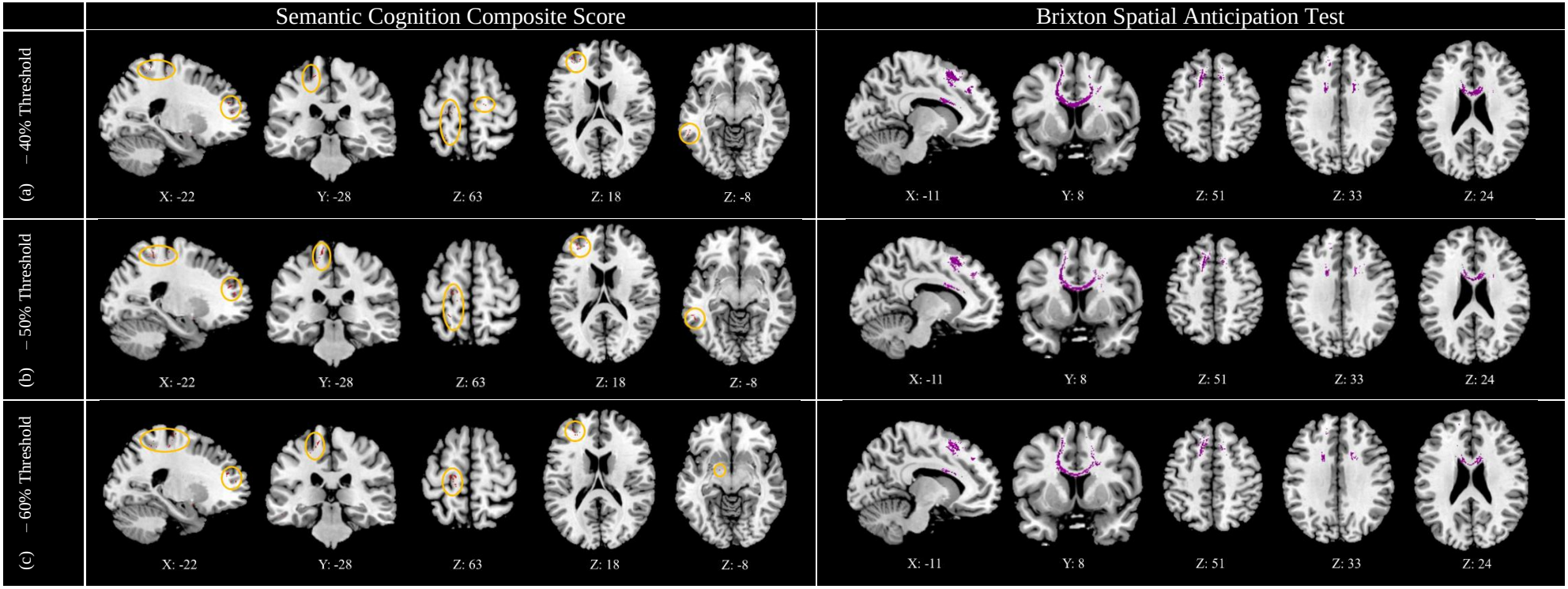
Supplementary Table 2.2. Patient performance on the Cambridge Semantic Battery and tests of semantic control.

	Semantic cognition composite score	Picture Naming		Word-picture matching	CCT		Ambiguity						Synonym with distractors		Object use	
		No cues	With cues		Word	Picture	Miscued dominant	Miscued subordinate	No cue dominant	No cue subordinate	Cued dominant	Cued subordinate	Strong distractor	Weak distractor	Alternative	Canonical
Max	-	64	64	64	64	64	30	30	30	30	30	30	42	42	37	37
Cut-off	-	59	-	62.7	56.6	52.7	30	26.6	28.4	27.6	30	28.8	35.4	40.4	33.7	35.9
Mean	-	35.0	48.2	58.6	47.4	47.7	18.4	13.5	23.7	16.1	23.2	21.6	20.8	29.1	22.0	34.3
P01	.76	**51**	NT	**50**	**54**	54	NT	NT	**26**	**23**	NT	NT	NT	NT	**24**	35
P02	-.71	**30**	NT	**54**	**41**	**46**	NT	NT	**19**	**10**	NT	NT	NT	NT	NT	NT
P03	-.51	**21**	NT	**46**	**42**	**44**	NT	NT	**21**	**13**	NT	NT	NT	NT	**12**	**30**
P04	-2.62	**5**	NT	**48**	**16**	**15**	**5**	**7**	**11**	**10**	**12**	**14**	**15**	**18**	**9**	**31**
P05	-1.62	**5**	NT	**50**	**33**	**13**	**19**	**9**	**23**	**10**	**24**	**17**	**18**	**34**	**13**	**31**
P06	-.72	**55**	NT	**60**	**39**	**36**	**18**	**10**	**23**	**13**	**22**	**22**	**19**	**24**	**24**	37
P07	1.30	62	NT	64	60	61	NT	NT	29	**24**	NT	NT	**29**	**36**	**31**	37
P08	.66	**0**	0	**56**	**56**	61	NT	NT	**25**	**16**	NT	NT	**16**	**33**	**22**	35
P09	.22	**50**	63	64	**53**	56	**14**	**8**	**22**	**14**	**22**	**18**	**20**	**24**	**21**	35
P10	-.72	**19**	58	**60**	**29**	**45**	**13**	**14**	**24**	**14**	**19**	**20**	**13**	**29**	**14**	**29**
P11	.73	**3**	10	**52**	57	54	**21**	**18**	**27**	**19**	**23**	**24**	**30**	**31**	**22**	**33**
P12	-.78	61	63	**62**	**43**	**44**	**13**	**10**	**18**	**9**	**21**	**14**	**12**	**23**	**13**	**31**
P13	.96	**46**	64	63	**56**	61	**26**	28	**27**	**21**	**29**	**28**	38	**36**	**32**	37
P14	.96	**56**	62	64	61	53	**24**	**18**	**28**	**21**	**27**	**23**	**22**	**28**	**26**	37
P15	-.98	**1**	3	63	**39**	**31**	**12**	**7**	**22**	**11**	**23**	**25**	**15**	**25**	**14**	**32**
P16	.24	**50**	63	63	**48**	**51**	**27**	**16**	**25**	**18**	**27**	**25**	NT	NT	**27**	37
P17	.52	**50**	64	**62**	**52**	57	**19**	**15**	**26**	**17**	**23**	**28**	**23**	**30**	**22**	35
P18	1.04	62	64	**62**	60	61	**26**	**19**	**28**	**19**	**29**	**25**	**17**	**39**	**29**	37
P19	.55	NT	NT	61	**50**	59	NT	NT	**27**	**17**	NT	NT	NT	NT	**24**	**33**
P20	.43	60	64	**62**	59	**45**	**20**	**10**	**24**	**19**	**24**	**19**	**21**	**27**	34	37
P21	.28	**12**	NT	64	**48**	54	NT	NT	**23**	**19**	**NT**	**NT**	**25**	**29**	**27**	37
P22	-	NT	NT	NT	**7** [a]	**10** [a]	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
P23	-	NT	NT	NT	**13** [a]	**10** [a]	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
# Tested	-	20	12	21	23	23	14	14	21	21	14	14	16	16	20	20
# Impaired	-	16	-	12	18	12	14	13	20	21	14	14	15	16	19	8

Note: Scores are number of correct. NT = unavailable for testing, CCT = Camel and Cactus Test. Cut-offs for impairment are taken from testing at the University of York and correspond to two standard deviations below mean control performance, with impaired scores underlined and in bold. Number of controls: CCT, Picture naming, and Word-picture matching = 10, Ambiguity task, Synonym with distractors, Object use = 8. Semantic composite score reflects regression scores derived from principal components analysis, including performance on CTT words, CCT pictures, and the Ambiguity task (no cue: dominant + subordinate). Lower composite scores reflect greater impairment.

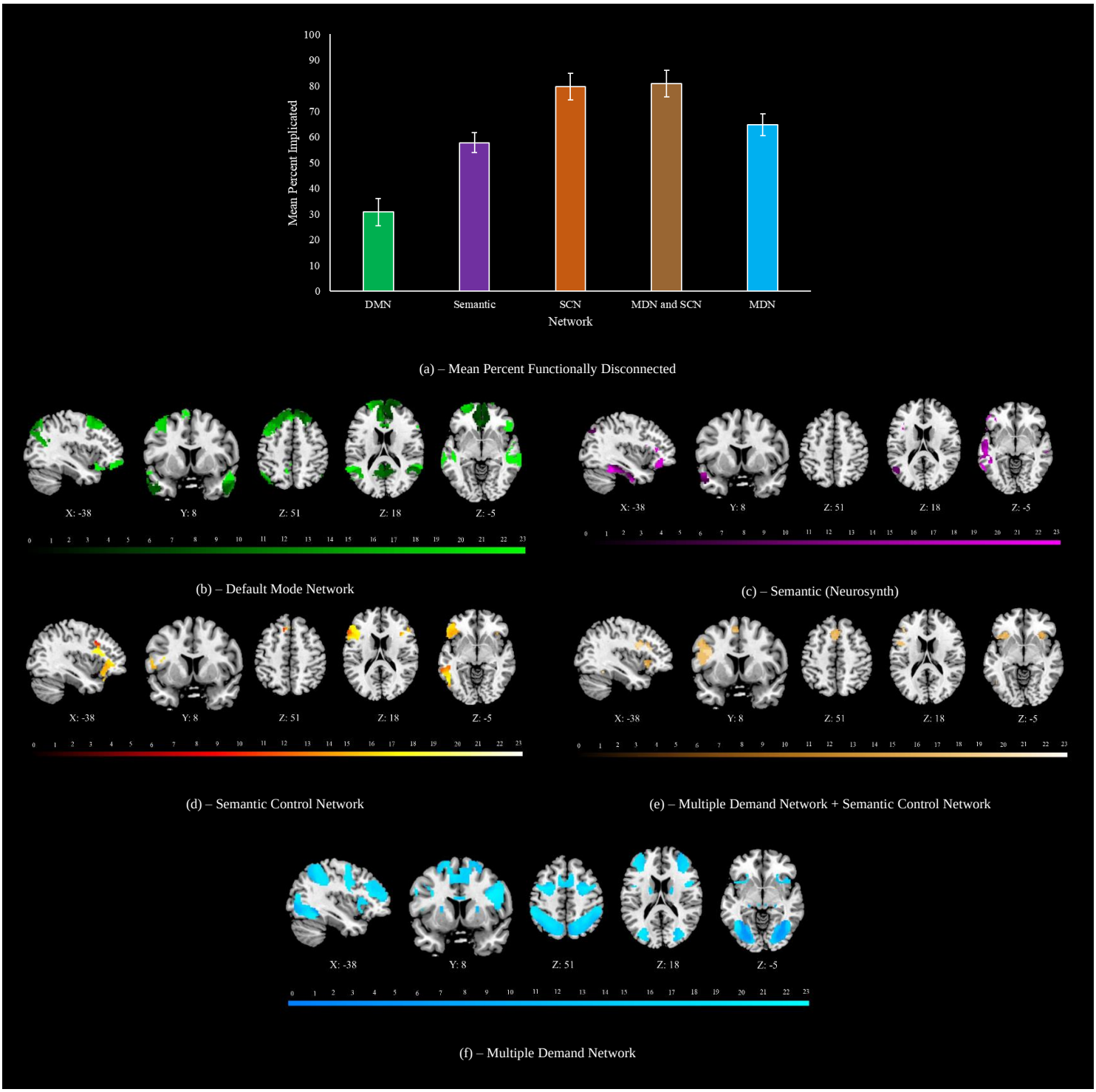
[a] Patients P22 and P23 completed short versions of the CCT tasks, each comprising 25 trials. Cut-off for impairment for the word and picture versions of the task is 20.7 and 19.6, respectively. As these patients do not have scores for the long version of the CCT tasks or the Ambiguity task, they do not have semantic composite scores.

Alternative Structural Disconnection Symptom Mapping



Supplementary Figure 2.1. Replication of the structural disconnection symptom mapping from Chapter 2, but at alternative probability thresholds. This includes 40% in Supplementary Figure 2.1a, 50% in Supplementary Figure 2.1b, which is the default threshold used in the paper, and 60% in Supplementary Figure 2.1c. In each case, symptom mapping is presented for patients' Semantic Cognition Composite Score on the left, and performance on the Brixton Spatial Anticipation Test on the right. Generated using non-parametric permutation tests in Randomise with threshold-free cluster enhancement. Highlighted voxels have a t-value of 2.6 or higher. Small clusters are highlighted in orange circles. 3D rendering generated in SurfIce. Results are consistent at each threshold. For the Semantic Cognition Composite Score, this includes very small voxels located in the left the frontal pole, precentral and postcentral gyri, pMTG, and occipital pole. The only conceptual deviation from the default threshold is a single voxel highlighted in the right precentral gyrus at a threshold of 40%. Clusters are too small to provide clinical significance. For the Brixton Spatial Anticipation Test, at each threshold performance is predicted by structural disconnection across the corpus callosum. N = 20

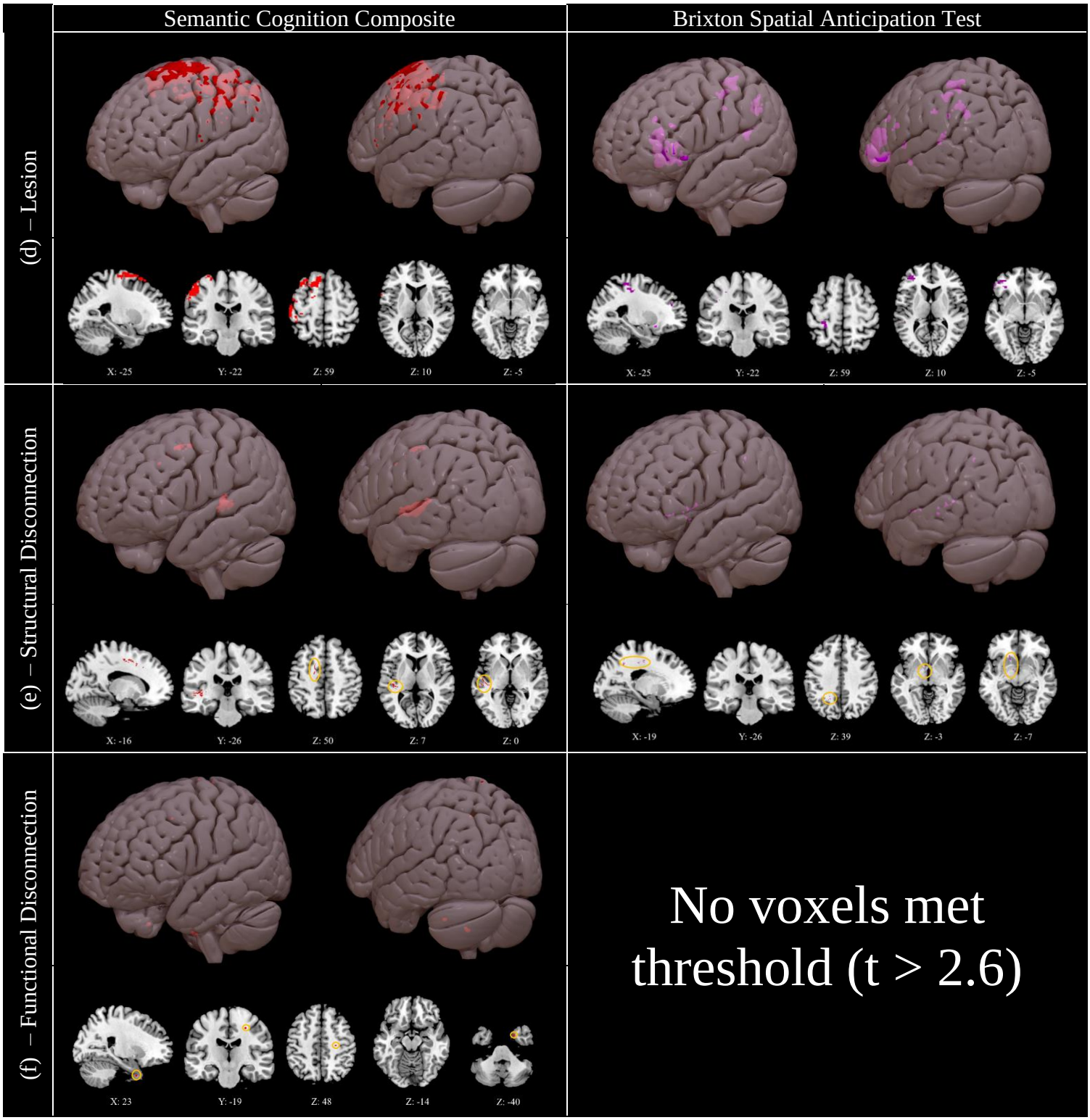
Network Functional Disconnection



Supplementary Figure 2.2. (a) The mean percent of each network of interest overlapping with patient functional disconnection maps, generated in CONN. DMN = default mode network, SCN = semantic control network, MDN = multiple demand network. This peaks in SCN at 85%, followed by areas shared between MDN and SCN at 81%, core semantic regions at 80%, regions exclusive to MDN both at 75%, and DMN at 44%. Locations of most frequent damage are displayed for each network in following sections. (b) DMN, functional

disconnection peaks in the right inferior frontal gyrus (pars triangularis), left frontal orbital cortex, left temporooccipital part of the middle temporal gyrus, and left posterior supramarginal gyrus. (c) Core semantic regions, functional disconnection peaks in the left temporooccipital part of the inferior temporal gyrus, left temporooccipital part of the middle temporal gyrus, and left inferior lateral occipital cortex. (d) SCN, functional disconnection peaks in the bilateral inferior frontal gyrus (pars opercularis), and left temporooccipital part of the inferior temporal gyrus. (e) Regions shared by SCN and MDN, functional disconnection peaks in the left precentral gyrus, left inferior frontal gyrus (pars triangularis), and left temporooccipital part of the inferior temporal gyrus. (f) MDN, functional disconnection peaks in the bilateral precentral gyrus, right inferior frontal gyrus (pars opercularis) and left temporooccipital part of the inferior temporal gyrus. Keys under each map reflects the number of patients whose map overlap in a given voxel. N = 23

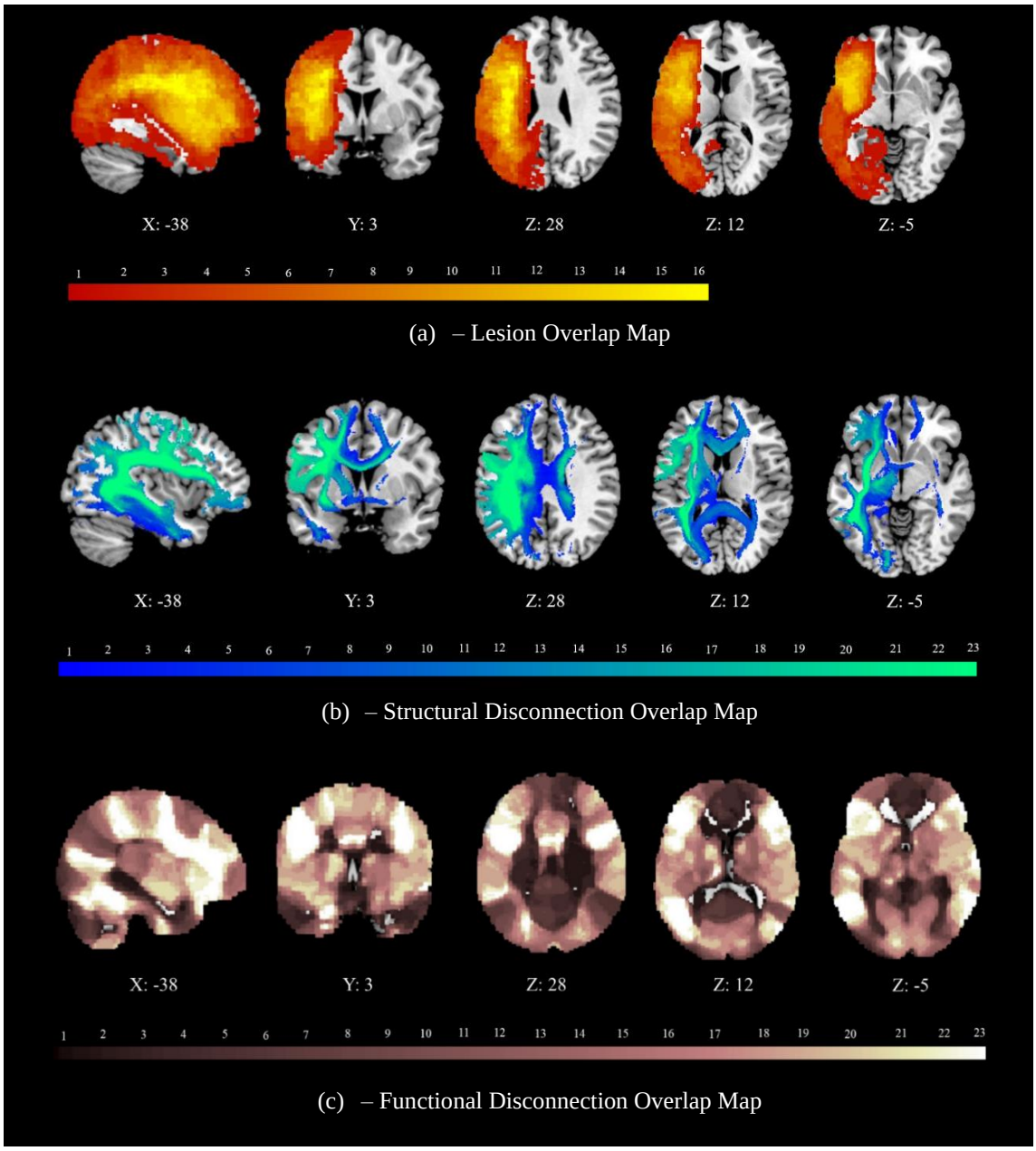
Positive Symptom Mapping



Supplementary Figure 2.3. Voxels associated with higher semantic cognition composite scores (left) and better performance on the Brixton Spatial Anticipation Test (right), for (a) lesion, (b) structural disconnection, and (c) functional disconnection data. Generated using a non-parametric permutation tests in Randomise with threshold-free cluster enhancement.

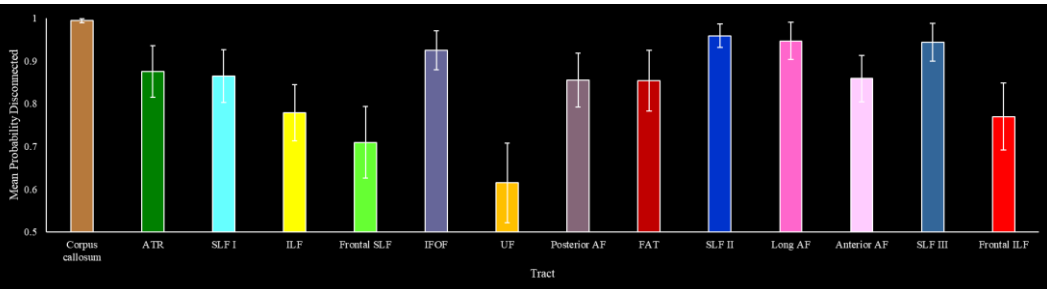
Highlighted voxels reflect those with a t-value of 2.6 or higher. Small clusters are highlighted in orange circles for visibility. 3D rendering generated in SurfIce. Lesioned clusters associated with better semantic cognition are left fronto-parietal, and implicate the precentral, postcentral, and superior frontal gyri. Lesioned clusters associated with better Brixton performance include the frontal pole, planum temporale, angular gyrus, and postcentral gyrus. Structurally disconnected clusters associated with better semantic cognition include a small bilateral group of voxels in the parietal cortex which do not implicate specific regions or tracts, as well as a cluster in the left Heschl's gyrus. Structurally disconnected clusters associated with better Brixton performance are similarly sparse, but implicate the putamen, occipital pole, superior parietal lobule and precentral gyrus. Functionally disconnected clusters associated with better semantic cognition include several sparse voxels, including in the brain stem, right temporal pole, and in white matter proximal to the right precentral gyrus. No clusters met the threshold of t > 2.6 for functionally disconnected clusters associated with better Brixton performance. N = 20

Unthresholded Overlap Maps

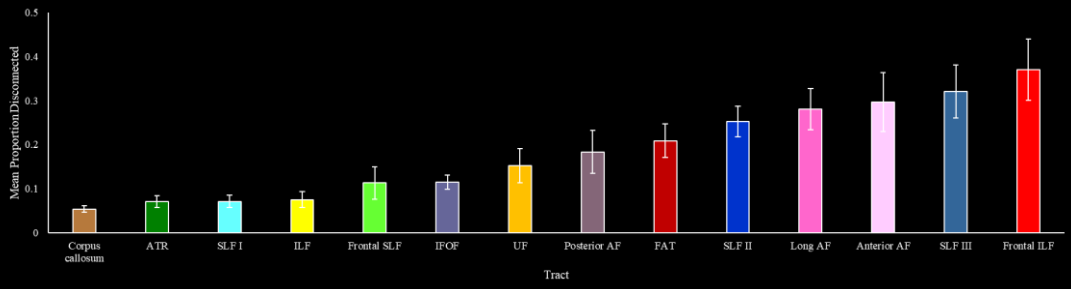


Supplementary Figure 2.4. Unthresholded overlap maps for (a) lesion sites, (b) structural disconnection maps, generated using the BCB Toolkit, and (c) functional disconnection maps, generated using CONN. Lesions are confined to the left hemisphere and subsume much of the cortex, affecting each lobe, peaking in the precentral and middle frontal gyri. Maximum overlap is 16 cases. Structural disconnection is largely left lateralised but with some spreading to the right hemisphere. Most left hemisphere white matter is implicated here, but this peaks in the left superior longitudinal fasciculus and inferior fronto-occipital fasciculus. Maximum overlap is all 23 cases. Functional disconnection is bilateral and extensive, subsuming almost the entirety of the brain. This disconnection peaks in the left temporooccipital part of the inferior temporal gyrus, and right inferior frontal gyrus (pars opercularis). Maximum overlap is all 23 cases. N = 23

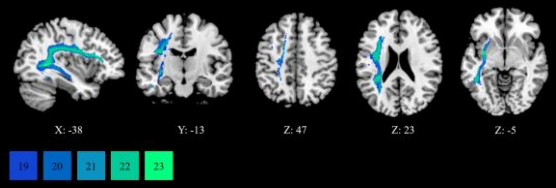
Probability and Proportion of Tract Disconnection



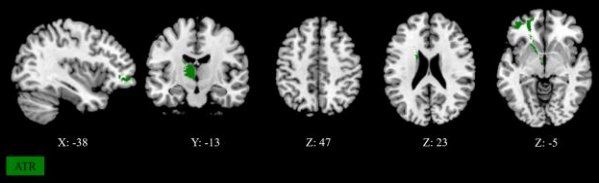
(a) – Mean Probability of Disconnection



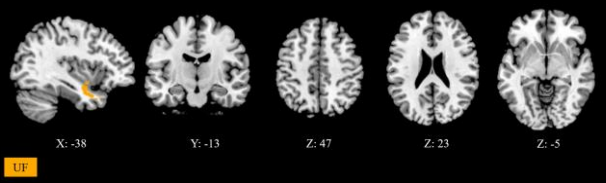
(b) – Mean Proportion Disconnected



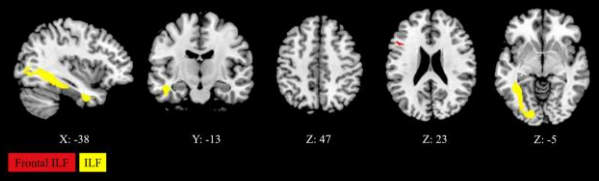
(c) – Sructural Disconnection Overlap Map



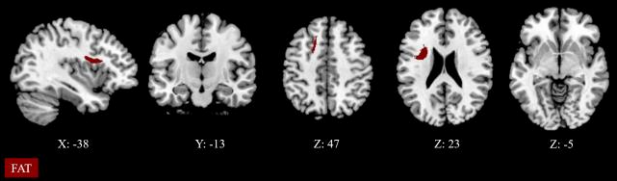
(d) – Anterior Thalamic Radiation



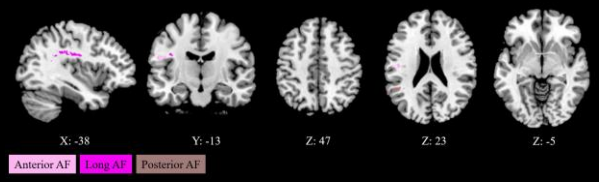
(e) – Uncinate Fasciculus



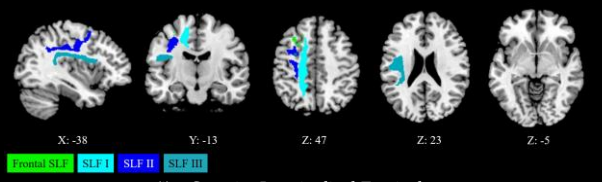
(f) – Inferior Longitudinal Fasciculus



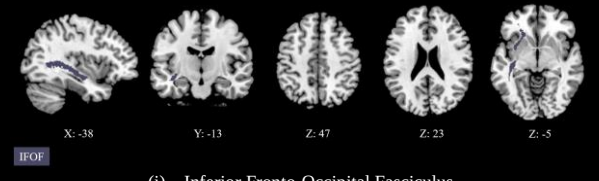
(g) – Frontal Aslant Tract



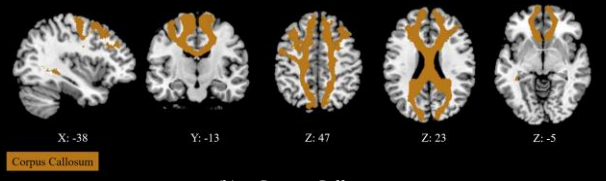
(h) – Arcuate Fasciculus



(i) – Superior Longitudinal Fasciculus



(j) – Inferior Fronto-Occipital Fasciculus



(k) – Corpus Callosum

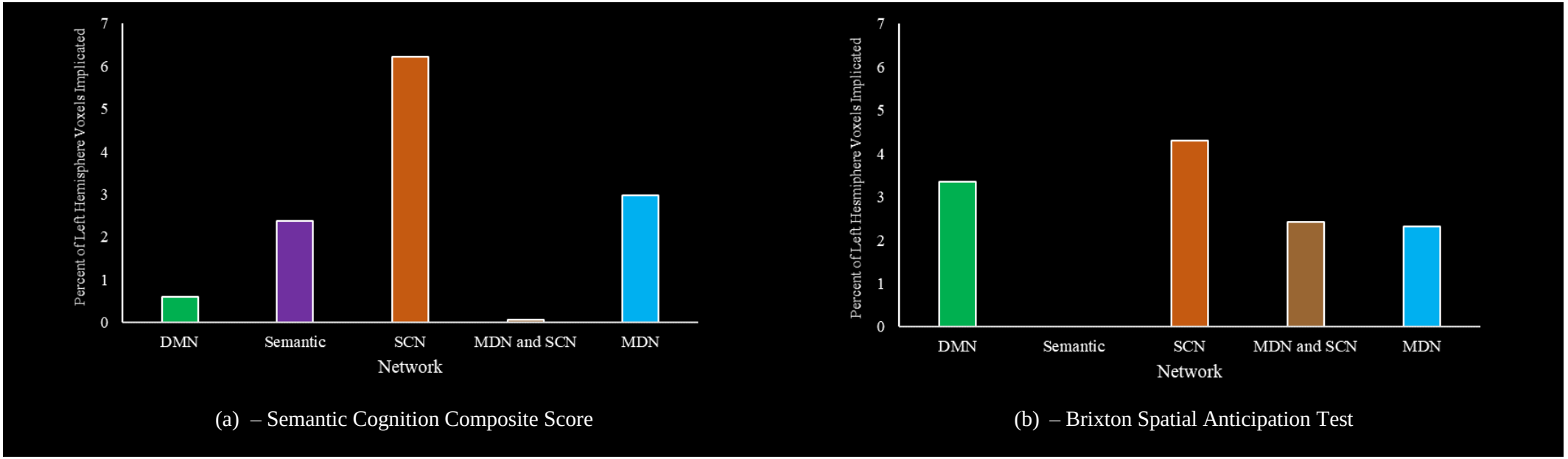
Supplementary Figure 2.5. (a) The mean probability of a given white matter tract being disconnected across the sample, and (b) the mean proportion disconnected. Generated using the Tractotron component of the BCB Toolkit (Foulon et al., 2018). Error bars reflect standard error of the mean. ATR = Anterior thalamic radiation, IFOF = Inferior fronto-occipital fasciculus, UF = Uncinate fasciculus, SLF = Superior longitudinal fasciculus, ILF = Inferior longitudinal fasciculus, AF = Arcuate fasciculus, FAT = Frontal aslant tract. The mean probability of disconnection is highest in the corpus callosum at .99, followed by SLF 2 at .96, the AF long at .95, and SLF 3 at .94. The lowest probability of disconnection is in the UF at .61. Mean estimated proportion disconnected peaks in the frontal ILF at .37, followed by the SLF 3 at .32, and the anterior AF at .30. The lowest estimated mean proportion disconnected is in the corpus callosum, at .05. (c) The structural disconnection overlap map for the sample, thresholded at 19 cases. Structural disconnection is left lateralised at this threshold and shows maximal overlap with the superior longitudinal fasciculus and inferior fronto-occipital fasciculus. Visualisations of the (d) ATR, (e) UF, (f) ILF, (g) FAT, (h) AF, (i) SLF, (j) IFOF, and (k) corpus callosum are presented. All tracts are confined to the left hemisphere. N = 23

Network Main Effects

Supplementary Table 2.3. Main effects of network followed by Wilcoxon contrasts comparing the extent of both lesion and functional disconnection (percent of network impacted) between all functional networks of interest.

Lesion					
Network main effect	**$F(2.2, 47.7) = 10.1$, $p < .001$, $\eta_p^2 = .32$***				
	DMN	Semantic	SCN	SCN & MDN	MDN
DMN					
Semantic	$Z = -2.4$, $p = .186$				
SCN	**$Z = -3.2$, $p = .015$***	$Z = -2.5$, $p = .137$			
SCN & MDN	**$Z = -3.5$, $p = .005$***	$Z = -1.9$, $p = .569$	$Z = -1.3$, $p > 1$		
MDN	**$Z = -4.2$, $p < .001$***	$Z = -0.7$, $p > 1$	$Z = -2.1$, $p = .333$	$Z = -2.1$, $p = 358$	
Functional Disconnection					
Network main effect	**$F(1.7, 38.2) = 27.2$, $p < .001$, $\eta_p^2 = .55$***				
	DMN	Semantic	SCN	SCN & MDN	MDN
DMN					
Semantic	**$Z = -3.9$, $p < .001$***				
SCN	**$Z = -3.9$, $p < .001$***	**$Z = -3.3$, $p = .008$***			
SCN & MDN	**$Z = -3.8$, $p = .002$***	**$Z = -3.1$, $p = .019$***	$Z = -1.0$, $p > 1$		
MDN	**$Z = -3.0$, $p = .030$***	$Z = -1.8$, $p = .727$	$Z = -2.5$, $p = .138$	**$Z = -3.1$, $p = .019$***	

Note: Non-parametric contrasts reported due to violation of the normality assumption. Results in both sections Bonferroni corrected for ten comparisons. * = significant result. N = 23.



Supplementary Figure 2.6. The percentage of voxels in each network of interest, restricted to the left hemisphere, implicated in the group level lesion-symptom mapping output for (a) the semantic cognition composite score and (b) the Brixton Spatial Anticipation Test. DMN = default mode network, SCN = semantic control network, MDN = multiple demand network.[29] *For the Semantic Cognition Composite Score, This peaks at 6.2% for SCN, followed by 3.0% for MDN, 2.4% for core semantic regions, 0.6% for DMN, and 0.1% for areas shared by SCN and MDN. For the Brixton Spatial Anticipation Test, numbers peak in SCN at 4.3%, followed by DMN at 3.6%, areas shared by SCN and MDN at 2.4%, and MDN at 2.3%, with 0% of core semantic regions implicated.*

[29] Note that these percentages will be impacted by differences in the relative size of each network. The number of voxels implicated over the total size of the respective number of voxels in each network for the Semantic Cognition Composite Score is: DMN: 82/13,618, Semantic: 84/3,549, SCN: 220/3,538, MDN & SCN: 1/1,777, MDN: 380/12,731. For the Brixton Spatial Anticipation Test, it's: DMN: 457/13,618, Semantic: 0/3,549, SCN: 152/3,538, MDN & SCN: 43/1,777, MDN: 296/12,731. Due to these differences in size, comparisons for a give network between graphs will be most informative.

Chapter 3 supplementary materials

Experimental Stimuli

Supplementary Table 3.1. Identity codes for Study 1 and Study 2 stimuli, from the IASLab Face Set.

Study 3.1		Study 3.2	
Emotion	Stimulus	Emotion	Stimulus
Anger	F1ang_o_st	Anger	F06ang_c_st
	F02ang_o_st		F07ang_c_st
	F08ang_o_st		F22ang_c_st
	M1ang_o_st		F23ang_c_st
	M3ang_o_st		F29ang_c_st
	M11ang_o_st		F32ang_c_st
Disgust	F1disg_c_st		M07ang_c_st
	F02disg_c_st		M08ang_c_st
	F8disg_c_st		M11ang_c_st
	M1disg_c_st		M13ang_c_st
	M3disg_c_st		M16ang_c_st
	M11disg_c_st1		M17ang_c_st
Fear	F1fear_c_st	Happiness	F06hap_c_st
	F02fear_c_st		F07hap_c_st
	F8fear_c_st		F22hap_c_st
	M1fear_c_st		F23hap_c_st
	M3fear_c_st		F29hap_c_st
	M11fear_c_st		F32hap_c_st
Happiness	F1hap_c_st		M07hap_c_st
	F02hap_c_st3		M08hap_c_st
	F8hap_c_st		M11hap_c_st
	M1hap_c_st		M13hap_c_st
	M3hap_c_st		M16hap_c_st
	M11hap_c_st		M17hap_c_st
Neutral	F1neut_o_st	Sadness	F06sad_c_st
	F02neut_o_st		F07sad_c_st
	F08neut_o_st		F22sad_c_st
	M1neut_o_st		F23sad_c_st
	M3neut_o_st		F29sad_c_st
	M11neut_o_st		F32sad_c_st
Sadness	F1sad_o_st		M07sad_c_st
	F02sad_o_st		M08sad_c_st
	F08sad_o_st		M11sad_c_st
	M1sad_o_st		M13sad_c_st
	M3sad_o_st		M16sad_c_st
	M11sad_o_st		M17sad_c_st

Note: The complete set of pictorial stimuli used in this study cannot be made directly available by the author. The full database of stimuli can be requested for download through https://www.affective-science.org/face-set.shtml.[30]

[30] Development of the Interdisciplinary Affective Science Laboratory (IASLab) Face Set was supported by the National Institutes of Health Director's Pioneer Award (DP1OD003312) to Lisa Feldman Barrett.

Descriptive Statistics

Supplementary Table 3.2. Percent of all participants' responses corresponding to each error type across Study 3.1 tasks.

		P4	P6	P10	P11	P12	P15	P16	Comparison Group Mean (SD)
Emotion free Sort	# piles	6	4	4	4	5	5	7	5.7 (1.35)
	NEG-NEUT	5.56%	0%	0%	0%	0%	0%	2.78%	3.82% (3.76)
	POS-NEUT	0%	0%	0%	0%	0%	0%	0%	0% (0)
	NEG-NEG	36.11%	52.78%	**66.67%**	47.22%	44.44%	**61.11%**	27.78%	26.42% (17.76)
	NEUT-NEG	5.56%	**16.67%**	**16.67%**	13.89%	13.89%	**16.67%**	5.56%	5.14% (5.52)
	POS-NEG	0%	0%	0%	0%	0%	**2.78%**	0%	0.08% (0.48)
	NEG-POS	0%	0%	0%	2.78%	**5.56%**	**5.56%**	0%	0.86% (2.34)
	NEUT-POS	0%	0%	0%	**2.78%**	**2.78%**	0%	0%	0.42% (1.01)
	% total errors	47.22%	69.44%	**83.33%**	66.67%	66.67%	**86.11%**	36.11%	36.74% (21.98)
	% correct	52.78%	30.56%	**16.67%**	33.33%	33.33%	**13.89%**	63.89%	63.26% (21.98)
Number anchored sort	# piles	6	6	5	6	6	6	6	6 (0)
	NEG-NEUT	0%	5.56%	0%	0%	5.56%	0%	0%	4.23% (3.95)
	POS-NEUT	0%	0%	0%	0%	0%	0%	0%	0% (0)
	NEG-NEG	38.89%	41.67%	30.56%	**55.56%**	**44.44%**	**55.56%**	41.67%	20.49% (13.41)
	NEUT-NEG	**16.67%**	5.56%	11.11%	**16.67%**	2.78%	**16.67%**	**16.67%**	4.72% (4.93)
	POS-NEG	0%	0%	0%	0%	2.78%	2.78%	0%	0% (0)
	NEG-POS	0%	0%	**5.56%**	0%	0%	2.78%	0%	0.51% (1.47)
	NEUT-POS	0%	**2.78%**	**5.56%**	0%	**2.78%**	0%	0%	0.43% (1.27)
	% total errors	55.56%	55.56%	52.78%	**72.22%**	58.33%	**77.78%**	58.33%	30.38% (17.02)
	% correct	44.44%	44.44%	47.22%	**27.78%**	41.67%	**22.22%**	41.67%	69.62% (17.02)
Word anchored sort	# piles	6	6	6	6	6	6	6	6 (0)
	NEG-NEUT	8.33%	13.89%	5.71%	11.11%	8.33%	**19.44%**	5.56%	7.00% (6.31)
	POS-NEUT	0%	0%	0%	0%	0%	0%	0%	0.08% (0.48)
	NEG-NEG	13.89%	**30.56%**	**40.00%**	27.78%	25.00%	27.78%	**36.11%**	16.26% (6.96)
	NEUT-NEG	**8.33%**	**8.33%**	2.86%	0%	0%	**8.33%**	0%	2.61% (2.86)
	POS-NEG	0%	0%	0%	0%	0%	0%	0%	0% (0)
	NEG-POS	0%	0%	0%	0%	**5.56%**	0%	2.78%	0.76% (1.88)
	NEUT-POS	0%	0%	0%	**2.78%**	0%	0%	0%	0.08% (0.48)
	% total errors	30.56%	**52.78%**	**48.57%**	41.67%	38.89%	**55.56%**	44.44%	26.80% (10.87)
	% correct	69.44%	**47.22%**	**51.43%**	58.33%	61.11%	**44.44%**	55.56%	73.20% (10.87)

Face anchored sort	# piles	6	6	6	6	6	6	6	6% (0)
	NEG-NEUT	8.33%	11.11%	11.11%	5.56%	8.33%	11.11%	11.11%	5.39% (3.92)
	POS-NEUT	0%	0%	0%	0%	**5.56%**	0%	0%	0.08% (0.48)
	NEG-NEG	13.89%	**33.33%**	**33.33%**	22.22%	**33.33%**	**44.44%**	**38.89%**	15.24% (8.37)
	NEUT-NEG	8.33%	**11.11%**	5.56%	8.33%	**5.56%**	0%	2.78%	3.96% (3.87)
	POS-NEG	0%	0%	0%	0%	0%	0%	0%	0% (0)
	NEG-POS	0%	2.78%	0%	0%	2.78%	0%	**5.56%**	0.42% (1.57)
	NEUT-POS	0%	**2.78%**	0%	0%	**5.56%**	0%	**2.78%**	0.08% (0.48)
	% total errors	30.56%	**61.11%**	**50.00%**	36.11%	**61.11%**	**55.56%**	**61.11%**	25.17% (11.72)
	% correct	69.44%	**38.89%**	**50.00%**	63.89%	**38.89%**	**44.44%**	**38.89%**	74.83% (11.72)

Note: With the exception of '# piles' and '% correct', all metrics reflect the percent of all responses which classified as the corresponding error type. Cases where patients were impaired relative to comparison participants (based on Singlims analysis) are underlined and in bold. NEG-NEUT = errors in which negative faces were put in a pile of predominantly neutral faces; POS-NEUT = refers to errors in which positive faces were put in a pile of predominantly neutral faces; NEG-NEG = errors in which one type of negative face was put in a pile consisting predominantly of another negative face, or negative faces which were sorted together into a pile with no one dominant expression; NEUT-NEG = errors in which neutral faces were put in a pile of predominantly negative faces; POS-NEG = errors in which positive faces were put in a pile of predominantly negative faces; NEG-POS = errors in which negative faces were put in a pile of predominantly positive faces; NEUT-POS = errors in which neutral faces were put in a pile of predominantly positive faces.

Supplementary Table 3.3. Percent of all participants' responses corresponding to each error type across tasks from Lindquist et al. (2014).

		EG	FZ	CP	Comparison Group Mean
Emotion free sort	# piles	3	4	4	7.82 (SD = 2.99)
	NEG-NEUT	1.66%	0%	0%	2.88%
	POS-NEUT	0%	0%	0%	0.13%
	NEG-NEG	**46.67%**	**44.44%**	**36.11%**	21.72%
	NEUT-NEG	5.83%	0%	0%	2.8%
	POS-NEG	0%	0%	0%	0.27%
	NEG-POS	1.66%	0%	2.77%	0.55%
	NEUT-POS	**5.83%**	0%	0%	1.69%
	% total errors	**61.66%**	44.44%	38.89%	30.04%
	% correct	**38.34%**	55.56%	61.11%	69.96%
Number anchored sort	# piles	NT	5	6	NT
	NEG-NEUT	NT	0%	2.86%	NT
	POS-NEUT	NT	0%	0%	NT
	NEG-NEG	NT	33.33%	34.29%	NT
	NEUT-NEG	NT	0%	0%	NT
	POS-NEG	NT	0%	0%	NT
	NEG-POS	NT	2.78%	0%	NT
	NEUT-POS	NT	2.78%	2.86%	NT
	% total errors	NT	38.89%	39.0%	NT
	% correct	NT	61.11%	61.0%	NT
Word anchored sort	# piles	NT	8	6	NT
	NEG-NEUT	NT	0%	5.71%	NT
	POS-NEUT	NT	0%	0%	NT
	NEG-NEG	NT	27.78%	31.48%	NT
	NEUT-NEG	NT	0%	0%	NT
	POS-NEG	NT	0%	0%	NT
	NEG-POS	NT	2.78%	0%	NT
	NEUT-POS	NT	0%	0%	NT
	% total errors	NT	30.56%	36.0%	NT
	% correct	NT	69.44%	64.0%	NT
Face anchored sort	# piles	6	6	6	NT
	NEG-NEUT	0%	0%	5.71%	NT
	POS-NEUT	0%	0%	0%	NT
	NEG-NEG	0%	19.44%	17.14%	NT
	NEUT-NEG	0%	0%	0%	NT
	POS-NEG	0%	0%	0%	NT
	NEG-POS	0%	0%	0%	NT
	NEUT-POS	0%	0%	0%	NT
	% total errors	0%	19.44%	22.0%	NT
	% correct	100%	80.56%	78.0%	NT

Note: Apart from '# piles' and '% correct', metrics reflect the percent of all responses classified as the respective error type. Cases where patients were impaired relative to controls (using a modified t-test; Crawford & Howell, 1998) are underlined and in bold. NT = 'not tested'. NEG-NEUT = errors in which negative faces were put in a pile of predominantly neutral faces; POS-NEUT = refers to errors in which positive faces were put in a pile of predominantly neutral faces; NEG-NEG = errors in which one type of negative face was put in a pile consisting predominantly of another negative face; NEUT-NEG = errors in which neutral faces were put in a pile of predominantly negative faces; POS-NEG = errors in which positive faces were put in a pile of predominantly negative faces; NEG-POS = errors in which negative faces were put in a pile of predominantly positive faces; NEUT-POS = errors in which neutral faces were put in a pile of predominantly positive faces.

Identity Sort Task Performance

Supplementary Table 3.4. Output for Study 3.1 mixed effects linear regression for performance on the identity sort task, looking at the effect of group and emotion.

Variable	Estimate	Lower 95% CI	Upper 95% CI	Likelihood Ratio Test
Intercept	4.36	1.19	7.53	-
Group	3.61	-0.29	7.51	$\chi(1) = 3.14$, $p = .077$
Emotion	-	-	-	$\chi(5) = 0.53$, $p = .991$
Group by Emotion	-	-	-	$\chi(5) = 0.25$, $p = .998$

Note: CI = confidence interval. Model run in R using lme4 package (version 1.1-25; Bates et al., 2015). As this is a logistic model, estimate coefficients reflect log transformation of odds ratios (Larsen et al., 2000). Overall emotion effect and group by emotion interaction do not include an estimate value, as these effects are not provided by the overall model. The respective likelihood ratio test results were obtained by comparing the full model to nested versions in which all condition main effects or interactions were removed.

Response Time Analysis

Supplementary Table 3.5. Output for Study 3.2 mixed effects linear regression for response time, observing effects of group and specific condition comparisons.

Variable	Estimate	Lower 95% CI	Upper 95% CI	Likelihood Ratio Test
Intercept	4.60	4.18	5.03	-
Group	**-1.07**	**-1.58**	**-0.57**	**$\chi(1) = 13.2, p < .001$***
Condition	**-**	**-**	**-**	**$\chi(3) = 11.8, p = .008$***
Group by Condition	-	-	-	$\chi(3) = 6.54, p = .088$

Note: * reflects significance at the .05 threshold. CI = confidence interval. Model was run in R using lmerTest package (version 3.1-3; Kuznetsova et al., 2017). Overall condition effect and group by condition interaction do not include an estimate value, as these effects are not provided by the overall model. The respective likelihood ratio test results were obtained by comparing the full model to nested versions in which all condition main effects or interactions were removed.

Supplementary Table 3.6. Post-hoc pairwise contrasts of the Study 3.2 response time mixed effects logistic regression, comparing the estimated mean response time across conditions within the patient and comparison groups.

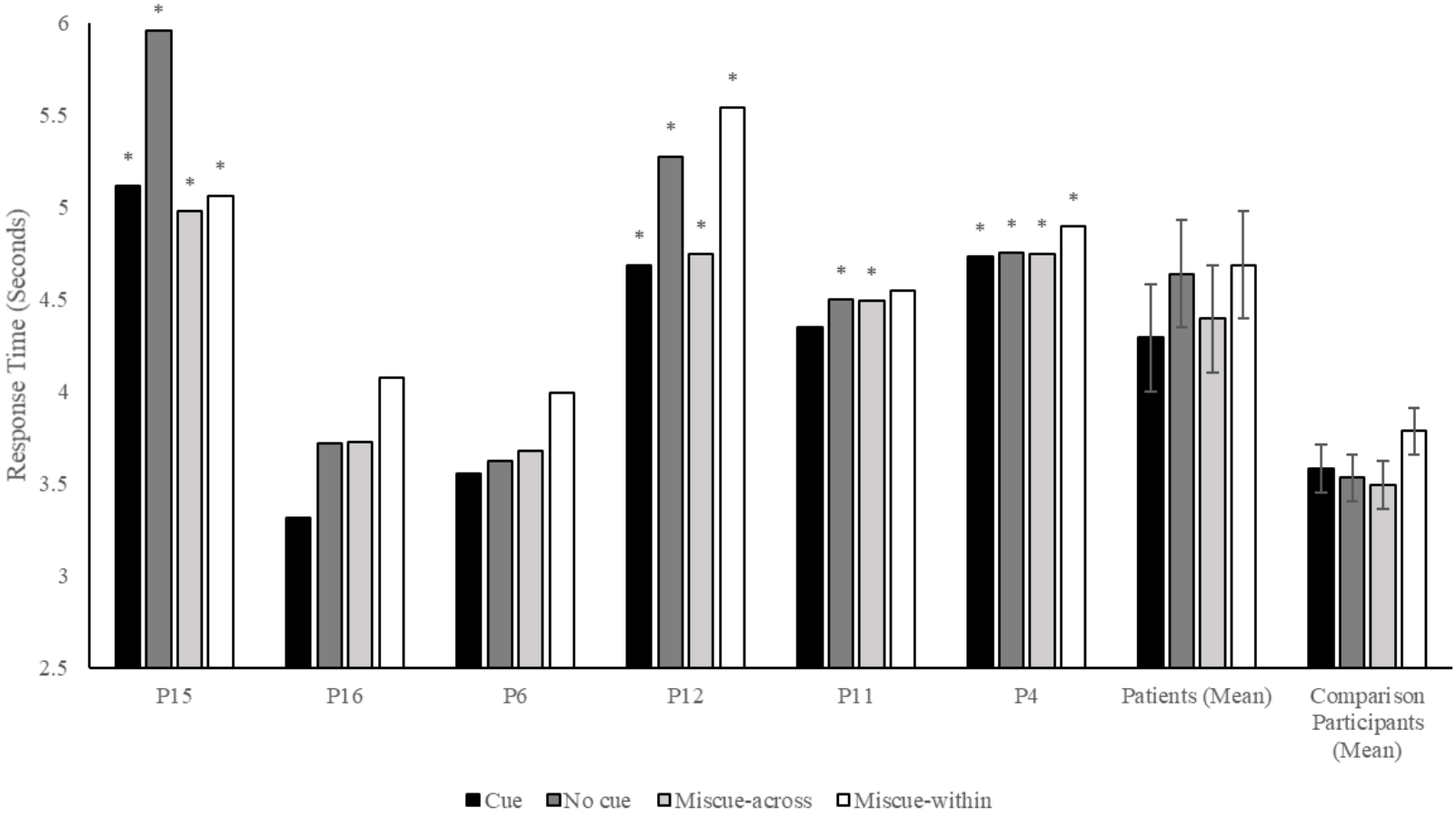
Contrast	Patients	Comparison Participants
No cue – cue	**$t = 2.60, p = .046$***	$t = -0.63, p = .921$
No cue – miscue across-valence	$t = 1.67, p = .347$	$t = 0.55, p = .947$
No cue – miscue within-valence	$t = -0.67, p = .908$	**$t = -2.99, p = .015$***
Cue – miscue across-valence	$t = -0.92, p = .792$	$t = 1.18, p = .640$
Cue – miscue within-valence	**$t = -2.94, p = .018$***	$t = -2.43, p = .072$
Miscue across-valence – miscue within-valence	$t = -2.12, p = .149$	**$t = -3.46, p = .003$***

Note: * reflects significance at the .05 threshold. P-values were corrected using the Tukey HSD method for multiple comparisons. Contrasts were run using the emmeans package in R.

Interpretation

Participants' mean response times across all conditions can be seen below in Supplementary Figure 3.1. As the current data was collected remotely over Zoom, factors such as poor internet speed may have in some cases influenced response time. These results should therefore be interpreted cautiously. The response time mixed effects logistic regression (Supplementary Table 3.5) was run in R (R Core Team, 2020) using the lmerTest package (Kuznetsova et al., 2017). Likelihood ratio tests were used to look for significant main effects or interactions of condition and group. These tests compare two nested models using the chi-square distribution, to determine whether removing a specific predictor (e.g.,

effect of group) significantly changes the overall model. Comparison participants demonstrated faster response times than patients. An overall main effect of condition was observed. Post-hoc pairwise comparisons (Supplementary Table 3.6) were run using the emmeans package in R (Lenth, 2020). Patients showed a significantly faster response time in the cue trials in relation to both the no cue baseline and the miscue within-valence trials. Comparison participants did not show an effect of cue trials but showed slower response time during miscue within-valence trials relative to both the no cue baseline and miscue across-valence trials. These results suggest beneficial effects of relevant cueing on response time in patients but not comparison participants, suggesting facilitation of emotion concept information in SA patients. Both groups showed some evidence of slowed response time on miscue within-valence trials, which present with the highest semantic control demands by requiring inhibition of a conceptually association emotion state.



*Supplementary Figure 3.1. Mean response time in the Cue, No cue, Miscue across-valence, and Miscue within-valence conditions, for each individual patient and for the mean patient and comparison participant response times. Patients are ordered (left to right) from the most to least semantically impaired, based on their semantic control composite score. Errors bars created using standard error of the mean. * = impaired performance based on Singlims analysis.*

Chapter 4 supplementary materials

Stimulus Properties

For stimuli in the current study, metrics of word frequency were taken from Subtlex-UK (Van Heuven et al., 2014). Ratings of imageability and familiarity were taken from the MRC Psycholinguistic Database (Coltheart, 1981). We also measured word length (number of letters). We assessed the strength of association between each probe-target and probe-foil pair using word2vec (Mikolov et al., 2013), a measure of semantic distance between words based on their co-occurrence in text. An association was considered 'strong' if word2vec was above 0.2, 'weak' if between 0.1 and 0.2, and negligible if below 0.1. Using ANOVAs, we established that frequency, familiarity, imageability, length, probe association strength, and valence were matched across all six experimental conditions, word type (probe/target/foil), categorical valence (positive/neutral/negative), session (1/2), and association strength categories (negligible/weak/strong). These tests also show that valence was different across positive, negative and neutral words, while word2vec scores varied across strong, weak and negligible associations, by design. See Supplementary Table 4.1 for all ANOVAs. Effects logically expected to be significant are highlighted in green. Several unanticipated interactions were also found to be significant, these are highlighted in red. While such effects were not designed to be significant, we do not anticipate that they are likely to have meaningfully affected task performance.

A possible exception is that negative words had significantly higher mean arousal ratings than positive words. Though unintended, this is in line with prior findings that these two factors can be conflated (Ito et al., 1998). In the current study, this was a consequence of sourcing representative valenced stimuli while attempting to balance for strength of association and psycholinguistic factors. To verify that this confound had not affected the results of the current study, all main paper and supplementary mixed models were repeated with the addition of arousal congruency between probe and target word as an added continuous variable. Congruency was determined as the absolute difference between mean arousal ratings for each word, such that a lower score would indicate greater similarity in arousal. Results of these models can be seen in Supplementary Table 4.2. The effect of arousal was not significant in any model, nor did the inclusion of this effect change the significance of any other main effect or interaction. It is therefore likely that observed effects of valence congruency can be attributed to valence itself, and not to arousal as a confound.

Supplementary Table 4.1. Effects of experimental factors on word valence, arousal, psycholinguistics, and probe association strength.

	Valence	Arousal	Frequency	Length	Familiarity	Imageability	Word2Vec
Condition	$F(5, 413) = 0.9$, $p = .502$	$F(5, 413) = 0.7$, $p = .591$	$F(5, 413) = 0.9$, $p = .450$	$F(5, 413) = 0.6$, $p = .689$	$F(5, 413) = 0.7$, $p = .614$	$F(5, 413) = 0.4$, $p = .843$	$F(5, 279) = 0.3$, $p = .924$
Word type	$F(2, 413) = 1.2$, $p = .317$	$F(2, 413) = 0.1$, $p = .870$	$F(2, 413) = 2.9$, $p = .058$	$F(2, 413) = 0.1$, $p = .898$	$F(2, 413) = 0.4$, $p = .642$	$F(2, 413) = 1.6$, $p = .197$	-
Word valence	**$F(2, 413) = 2755.4$, $p < .001$***	**$F(2, 413) = 6.2$, $p = .002$***	$F(2, 413) = 1.0$, $p = .370$	$F(2, 413) = 0.6$, $p = .552$	$F(2, 413) = 0.2$, $p = .850$	$F(2, 413) = 0.7$, $p = .495$	$F(2, 279) = 0.1$, $p = .914$
Session	$F(1, 413) = 0.2$, $p = .667$	$F(1, 413) < 0.1$, $p = .835$	$F(1, 413) < 0.1$, $p = .946$	$F(1, 413) < 0.1$, $p = .831$	$F(1, 413) = 0.1$, $p = .727$	$F(1, 413) = 1.7$, $p = .192$	$F(1, 279) < 0.1$, $p = .916$
Condition x Word type	$F(10, 413) = 0.2$, $p = .996$	$F(10, 413) = 0.2$, $p = .998$	$F(10, 413) = 1.2$, $p = .317$	$F(10, 413) = 1.3$, $p = .209$	$F(10, 413) = 1.2$, $p = .295$	$F(10, 413) = 0.7$, $p = .707$	-
Condition x Word valence	$F(5, 413) = 1.4$, $p = .211$	$F(5, 413) = 0.6$, $p = .711$	$F(5, 413) = 0.1$, $p = .993$	$F(5, 413) = 1.0$, $p = .443$	$F(5, 413) = 0.2$, $p = .969$	$F(5, 413) = 0.1$, $p = .987$	$F(5, 279) = 1.8$, $p = .118$
Condition x Session	$F(5, 413) = 0.1$, $p = .983$	$F(5, 413) = 1.0$, $p = .399$	$F(5, 413) = 1.0$, $p = .392$	$F(5, 413) = 1.4$, $p = .206$	**$F(5, 413) = 2.5$, $p = .033$***	$F(5, 413) = 1.1$, $p = .345$	**$F(5, 279) = 2.8$, $p = .016$***
Word Type x Word valence	**$F(2, 413) = 4.8$, $p = .009$***	$F(2, 413) = 0.4$, $p = .689$	$F(2, 413) = 1.1$, $p = .339$	$F(2, 413) = 1.2$, $p = .312$	$F(2, 413) = 0.8$, $p = .462$	**$F(2, 413) = 5.8$, $p = .003$***	-
Word type x Session	$F(2, 413) = 0.3$, $p = .777$	$F(2, 413) = 0.6$, $p = .577$	$F(2, 413) = 0.1$, $p = .927$	$F(2, 413) < 0.1$, $p = .955$	$F(2, 413) = 0.1$, $p = .902$	$F(2, 413) = 0.7$, $p = .501$	-
Word valence x Session	$F(2, 413) = 0.1$, $p = .925$	$F(2, 413) = 0.7$, $p = .485$	$F(2, 413) = 0.1$, $p = .928$	$F(2, 413) < 0.1$, $p = .995$	$F(2, 413) < 0.1$, $p = .981$	$F(2, 413) = 0.1$, $p = .875$	$F(2, 279) = 0.1$, $p = .944$
Condition x Word type x Word valence	$F(10, 413) = 1.3$, $p = .216$	$F(10, 413) = 0.2$, $p = .993$	$F(10, 413) = 0.6$, $p = .815$	$F(10, 413) = 0.2$, $p = .992$	$F(10, 413) = 0.4$, $p = .939$	$F(10, 413) = 0.8$, $p = .647$	-
Condition x Word type x Session	$F(10, 413) = 1.5$, $p = .123$	**$F(10, 413) = 2.1$, $p = .024$***	$F(10, 413) = 1.0$, $p = .473$	$F(10, 413) = 0.3$, $p = .984$	$F(10, 413) = 1.7$, $p = .087$	$F(10, 413) = 1.4$, $p = .162$	-
Condition x Word valence x Session	$F(5, 413) = 1.0$, $p = .388$	$F(5, 413) = 0.3$, $p = .925$	$F(5, 413) = 0.3$, $p = .891$	$F(5, 413) = 0.6$, $p = .707$	$F(5, 413) = 0.5$, $p = .790$	$F(5, 413) = 0.4$, $p = .854$	$F(5, 279) = 0.8$, $p = .560$
Word type x Word valence x Session	$F(2, 413) < 0.1$, $p = .997$	$F(2, 413) = 0.4$, $p = .652$	$F(2, 413) = 0.9$, $p = .415$	$F(2, 413) = 0.5$, $p = .580$	$F(2, 413) < 0.1$, $p = .992$	$F(2, 413) = 0.1$, $p = .937$	-
Condition x Word type x Word valence x Session	$F(9, 413) = 0.7$, $p = .672$	$F(9, 413) = 0.4$, $p = .912$	$F(9, 413) = 0.7$, $p = .713$	$F(9, 413) = 1.4$, $p = .191$	$F(9, 413) = 0.6$, $p = .813$	$F(9, 413) = 0.4$, $p = .910$	-
Strength	-	-	-	-	-	-	**$F(2, 279) = 470.9$, $p < .001$***
Word valence x Strength	-	-	-	-	-	-	$F(2, 279) = 1.0$, $p = .375$
Condition x Strength	-	-	-	-	-	-	$F(3, 279) = 0.6$, $p = .611$
Session x Strength							$F(2, 279) = 0.1$, $p = .907$
Word valence x Condition x Strength	-	-	-	-	-	-	$F(3, 279) = 1.7$, $p = .172$
Word valence x Strength x Session	-	-	-	-	-	-	$F(1, 279) < 0.1$, $p = 1$
Condition x Strength x Session	-	-	-	-	-	-	**$F(3, 279) = 3.2$, $p = .024$***
Word valence x Condition x Strength x Set	-	-	-	-	-	-	$F(3, 279) = 0.2$, $p = .870$

Note: Ratings of Valence and arousal taken from the Warriner et al. (2013) norms. Ratings of frequency taken from Subtlex-UK. Ratings of familiarity and imageability taken from the MRC Psycholinguistic Database. Strength scores reflect word2vec values between the target/foil word and the probe word. Fixed factors split on the following levels: condition (valence – *associated target*, valence – *no association*, valence – *associated distractor*, semantic – *congruent target*, semantic – *congruent distractor*, semantic – *weak association*), word type (probe, target, foil), word valence (positive, negative, neutral), session (1, 2), strength (strong, weak, negligible). Results highlighted in green reflect significant effects intuitively expected to be significant. Results highlighted in red reflect significant effects not expected to be significant. Effects and interactions of strength not investigated for most factors as this metric is not applicable for probe words in each triad. For the same reason effects and interactions of word type on word2vec score are not reported.

Supplementary Table 4.2. All mixed effects models (main paper and supplementary) with main effect of probe-target arousal congruency added.

Experiment	Model	Variable	Estimate	Lower 95% CI	Upper 95% CI	Likelihood Ratio Test
Experiment 4.1	Valence Matching (Binary) – Accuracy	Intercept	4.13	3.61	4.65	-
		Condition	**-**	**-**	**-**	**$\chi(2) = 39.9, p < .001$***
		Arousal	-0.27	-0.62	0.09	$\chi(1) = 2.15, p = .142$
	Valence Matching (Binary) – Response Time	Intercept	0.71	0.64	0.78	-
		Condition	**-**	**-**	**-**	**$\chi(2) = 28.3, p < .001$***
		Arousal	**0.05**	**0.01**	**0.09**	**$\chi(1) = 4.96, p = .026$***
	Semantic Matching (Binary) – Accuracy	Intercept	5.01	4.13	5.89	-
		Association strength	**-1.62**	**-2.56**	**-0.68**	**$\chi(1) = 10.92, p = .001$***
		Arousal	-0.35	-1.02	0.32	$\chi(1) = 1.03, p = .309$
	Semantic Matching (Binary) – Response Time	Intercept	0.57	0.50	0.65	-
		Association strength	**0.29**	**0.23**	**0.36**	**$\chi(1) = 53.7, p < .001$***
		Arousal	0.03	-0.02	0.08	$\chi(1) = 1.69, p = .194$
	Task Comparison – Accuracy	Intercept	4.26	3.64	4.88	-
		Task	**0.18**	**-0.46**	**0.82**	$\chi(1) = 0.30$, p = .584
		Difficulty	-0.40	-1.16	0.35	$\chi(1) = 1.09$, p = .296
		Task by difficulty	**-1.81**	**-2.84**	**-0.78**	**$\chi(1) = 11.3$, p = .001***
		Arousal	**-0.30**	**-0.66**	**0.05**	$\chi(1) = 2.79$, p = .095
	Task Comparison – Response Time	Intercept	0.69	0.61	0.77	-
		Task	**0.14**	**0.07**	**0.20**	**$\chi(1) = 16.9$, p < .001***
		Difficulty	**-0.09**	**-1.17**	**-0.01**	**$\chi(1) = 4.57$, p = .032***
		Task by difficulty	**0.13**	**0.01**	**0.24**	**$\chi(1) = 3.79$, p = .029***
		Arousal	**0.04**	**0.01**	**0.08**	**$\chi(1) = 5.04$, p = .025***
	Semantic Matching (Parametric) – Accuracy	Intercept	2.67	2.05	3.29	-
		Valence congruency	1.22	-0.56	3.01	$\chi(1) = 1.77, p = .184$
		Association strength	**5.92**	**3.97**	**7.86**	**$\chi(1) = 34.6, p < .001$***
		Valence by strength	**-6.35**	**-11.42**	**-1.28**	**$\chi(1) = 5.75, p = .017$***
		Arousal congruency	-0.15	-0.51	0.21	$\chi(1) = 0.68, p = .411$
	Semantic Matching (Parametric) – Response Time	Intercept	0.96	0.88	1.03	-
		Valence congruency	**-0.36**	**-0.53**	**-0.19**	**$\chi(1) = 16.9, p < .001$***
		Association strength	**-0.76**	**-0.92**	**-0.59**	**$\chi(1) = 66.3, p < .001$***
		Valence by strength	**0.86**	**0.38**	**1.34**	**$\chi(1) = 12.0, p = .001$***

		Arousal congruency	0.01	-0.02	0.05	$\chi(1) = 0.56$, $p = .453$
	Valence Matching (Parametric) – Accuracy	Intercept	3.63	2.94	4.32	-
		Condition	**-1.72**	**-2.63**	**-0.81**	**$\chi(1) = 12.5$, $p < .001$***
		Target association	**2.10**	**0.28**	**3.92**	**$\chi(1) = 5.08$, $p = .024$***
		Condition x target association	3.00	-9.55	15.56	$\chi(1) = 0.18$, $p = .671$
		Arousal congruency	-0.20	-0.56	0.15	$\chi(1) = 1.27$, $p = .260$
	Valence Matching (Parametric) – Response Time	Intercept	0.90	0.81	0.98	-
		Condition	0.10	-0.01	0.20	$\chi(1) = 3.34$, $p = .068$
		Target association	**-0.63**	**-0.80**	**-0.46**	**$\chi(1) = 44.5$, $p < .001$***
		Condition x target association	-0.28	-1.86	1.30	$\chi(1) = 0.12$, $p = .726$
		Arousal congruency	0.02	-0.02	0.05	$\chi(1) = 1.06$, $p = .304$
Experiment 4.2	Valence Matching	Intercept	3.35	2.41	4.29	-
		Group	**1.64**	**0.80**	**2.49**	**$\chi(1) = 11.9$, $p = .001$***
		Condition	**-**	**-**	**-**	**$\chi(2) = 54.8$, $p < .001$***
		Group by condition	**-**	**-**	**-**	**$\chi(2) = 9.56$, $p = .008$***
		Arousal congruency	-0.27	-0.72	0.18	$\chi(1) = 1.38$, $p = .240$
	Semantic Matching (Binary)	Intercept	4.01	3.05	4.97	-
		Group	**1.32**	**0.41**	**2.24**	**$\chi(1) = 7.44$, $p = .006$***
		Association strength	**-3.05**	**-3.82**	**-2.28**	**$\chi(1) = 66.4$, $p < .001$***
		Group by association strength	**0.90**	**0.21**	**1.59**	**$\chi(1) = 6.55$, $p = .011$***
		Arousal congruency	-0.11	-0.56	0.33	$\chi(1) = 0.25$, $p = .614$
	Semantic Matching (Parametric)	Intercept	0.91	-0.12	1.94	-
		Group	**2.38**	**1.49**	**3.26**	**$\chi(1) = 19.2$, $p < .001$***
		Valence congruency	**4.11**	**1.03**	**7.19**	**$\chi(1) = 6.93$, $p = .008$***
		Probe-Target association	**10.01**	**6.56**	**13.47**	**$\chi(1) = 40.2$, $p < .001$***
		Group by congruency	-1.27	-4.05	1.50	$\chi(1) = 0.79$, $p = .374$
		Group by association	-2.92	-6.35	0.51	$\chi(1) = 2.77$, $p = .096$
		Valence congruency by association	**-13.08**	**-21.59**	**-4.58**	**$\chi(1) = 8.15$, $p = .004$***
		Group by association by congruency	2.17	-5.50	9.85	$\chi(1) = 0.30$, $p = .585$
		Arousal congruency	-0.09	-0.56	0.38	$\chi(1) = 0.14$, $p = .707$
	Task Comparison	Intercept	3.11	2.09	4.13	-
		Group	**1.80**	**0.87**	**2.73**	**$\chi(1) = 12.4$, $p < .001$***
		Task	0.79	-0.15	1.73	$\chi(1) = 2.74$, $p = .098$
		Difficulty	0.95	-0.25	2.15	$\chi(1) = 2.47$, $p = .116$

	Group by task	-0.21	-1.15	0.74	$\chi(1) = 0.18$, $p = .670$
	Group by difficulty	-0.99	-2.11	0.13	$\chi(1) = 3.04$, $p = .081$
	Task by difficulty	**-4.37**	**-5.96**	**-2.78**	**$\chi(1) = 30.9$, $p < .001$***
	Group by task by difficulty	**1.90**	**0.45**	**3.34**	**$\chi(1) = 6.64$, $p = .010$***
	Arousal congruency	-0.30	-0.75	0.15	$\chi(1) = 1.76$, $p = .185$
Valence Matching (Parametric)	Intercept	2.40	1.26	3.53	-
	Group	**2.16**	**1.12**	**3.20**	**$\chi(1) = 14.6$, $p < .001$***
	Condition	**-2.37**	**-3.65**	**-1.09**	**$\chi(1) = 13.3$, $p < .001$***
	Target association	**4.58**	**1.56**	**7.59**	**$\chi(1) = 9.57$, $p = .002$***
	Group x condition	0.03	-1.03	1.08	$\chi(1) < 0.01$, $p = .961$
	Group x target association	**-2.99**	**-6.03**	**0.04**	**$\chi(1) = 3.87$, $p = .049$***
	Condition x target association	3.14	-14.69	20.96	$\chi(1) = 0.12$, $p = .733$
	Group x condition x target association	11.27	-2.35	24.89	$\chi(1) = 2.51$, $p = .113$
	Arousal congruency	-0.18	-0.62	0.26	$\chi(1) = 0.63$, $p = .427$

Note: * reflects significance at the .05 threshold. Models were run in R packages lme4 (version 1.1-25; Bates et al., 2015) and lmerTest (version 3.1-3; Kuznetsova et al., 2017). All Experiment 4.1 accuracy models and all Experiment 4.2 models are logistic models; estimate coefficients reflect log transformation of odds ratios (Larsen et al., 2000). All models include participant identity and item as crossed random factors. Estimates are not provided for the Experiment 4.2 valence matching condition effect and group by condition interaction. Respective likelihood ratio test results were obtained by comparing the full model to nested versions with all condition main effects or interactions removed. Significant effects of arousal are highlighted in red. CI = confidence interval.

Valence Congruency Mixed Effects Models

Experiment 4.1

To mirror the parametric analysis conducted for the semantic matching task, we observed for parametric effects of probe-target association strength on accuracy and response time (RT) in the valence matching task for Experiment 4.1. We compared the *associated distractor* condition to the *no association* condition, due to the fact that probe-target association strength was matched across these two conditions. The *associated target* condition was not observed here, due to the fact that this condition explicitly manipulated probe-target association strength to be higher than in the other conditions. This analysis was conducted using mixed effects models in R. In both cases, we used condition (*no association* / *congruent distractor*) and target association (continuous, based on Word2Vec score between target and probe word) as fixed effects, and observed their interaction, and used participant identity and item (trial) as crossed random factors. In the case of accuracy, a logistic mixed effects regression was used with the likelihood of a correct response as the outcome variable. In the case of RT, a mixed effects linear regression was used. RT outliers were addressed by removing any values larger than 10 seconds, or any larger than 3 standard deviations above a given participant's mean RT in a given condition. RT data were then log transformed such that residuals were approximately normally distributed. In each case, likelihood ratio tests were used to determine the significance of effects and interactions, by statistically comparing the full model to nested versions with specific effects removed.

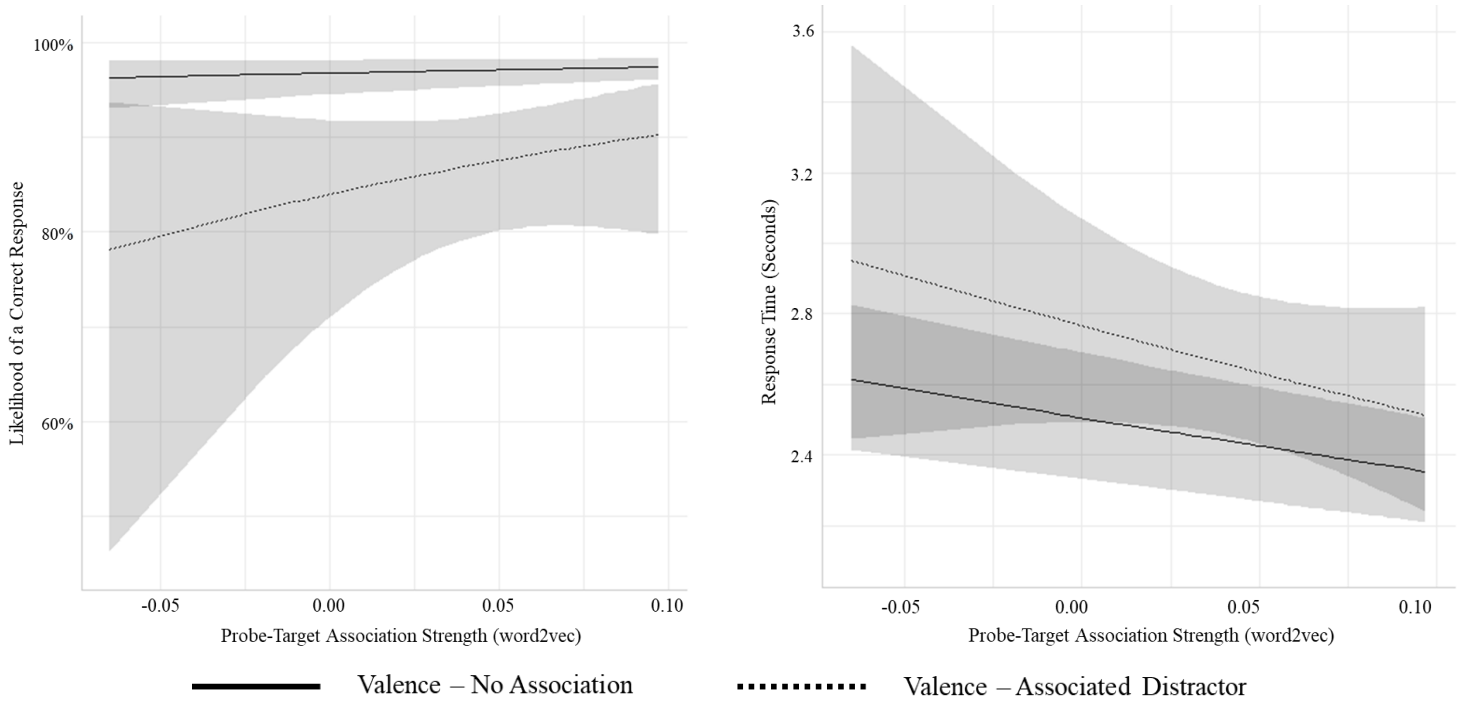
Results of these models can be seen in Supplementary Table 4.3. More accurate and faster responses were predicted by higher strength of association between probe and target. The absence of semantically-related distractors led to more accurate responses, but did not affect RT. No interaction was found for either accuracy or RT. Visualisations of the linear relationship between association strength and both probability of a correct response and RT in each condition created using the ggpredict function of the ggeffects package (Lüdecke, 2018) can be seen in Supplementary Figure 4.1[31].

[31] Although RT was estimated using a linear mixed effects model, the trends visualised are curved as response time values were log-transformed. Similarly, accuracy was estimated using log transformation of odds ratios.

Supplementary Table 4.3. Output of Experiment 4.1 valence matching mixed effects regressions.

Measure	Variable	Estimate	Lower 95% CI	Upper 95% CI	Likelihood Ratio Test
Accuracy	Intercept	3.39	2.85	3.94	-
	Condition	**-1.74**	**-2.64**	**-0.84**	**$\chi(1) = 12.69$, $p < .001$***
	Target association	**2.28**	**0.49**	**4.07**	**$\chi(1) = 6.14$, $p = .013$***
	Condition x target association	3.60	-8.63	15.83	$\chi(1) = 0.26$, $p = .611$
Response Time	Intercept	0.92	0.85	0.99	-
	Condition	0.10	-0.005	0.20	$\chi(1) = 3.48$, $p = .062$
	Target association	**-0.64**	**-0.81**	**-0.47**	**$\chi(1) = 47.84$, $p < .001$***
	Condition x target association	-0.35	-1.9	1.23	$\chi(1) = 0.19$, $p = .665$

Note: * reflects a significant result. The Accuracy model was run in R using lme4 package (version 1.1-25; Bates et al., 2015). As this is a logistic model, estimate coefficients reflect log transformation of odds ratios (Larsen et al., 2000). The Response Time model was run in R using lmerTest package (version 3.1-3; Kuznetsova et al., 2017). CI = confidence interval.



Supplementary Figure 4.1. Associations between probe-target association strength and both the likelihood of a correct response and response time for the Experiment 4.1 valence matching task. Grey shaded areas reflect confidence intervals based on the standard errors.

Experiment 4.2

To mirror the parametric analysis conducted for the semantic matching task, we observed for parametric effects of probe-target association strength on accuracy in the valence matching task for Experiment 4.2. We compared the *associated distractor* condition to the *no association* condition, due to the fact that probe-target association strength was matched across these two conditions. The *associated target* condition was not observed here, due to the fact that this condition explicitly manipulated probe-target association strength to be higher than in the other conditions. This analysis was conducted using a mixed effects logistic regression in R. We used group (patients/controls), condition (*no association*/ *congruent distractor*) and target association (continuous, based on Word2Vec score between target and probe word) as fixed effects, and observed their interactions. Participant identity and item (trial) were used as crossed random factors. In each case, likelihood ratio tests were used to determine the significance of effects and interactions, by statistically comparing the full model to nested versions with specific effects removed.

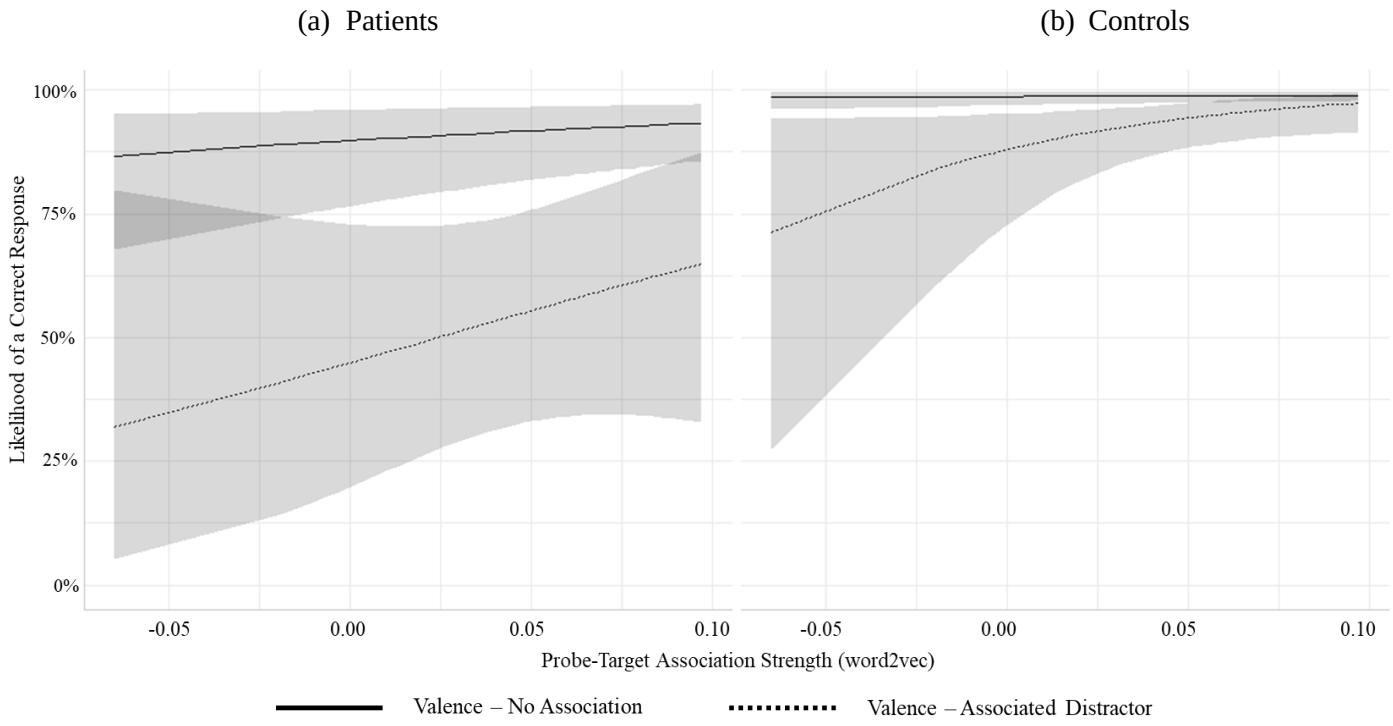
Results of this model can be seen in Supplementary Table 4.4. More accurate responses were predicted both by the absence of semantically related distractors, and by higher strength of association between the probe and target. Controls were also shown to be significantly more accurate than patients. A marginal but significant interaction between group and association strength was observed. We used the emtrends function of the emmeans package (Lenth, 2020) to parse this interaction by observing the relationship between association strength and probability of a correct response in each group. Visualisations of these trends, split by group, were created using the ggpredict function of the ggeffects package (Lüdecke, 2018), and can be seen in Supplementary Figure 4.2. In controls, a positive relationship was found between association strength and the probability of a correct response (association = 9.16, LCL = 0.78, UCL = 17.50). No such relationship was found for patients (association = 6.60, LCL = -2.41, UCL = 15.60).

Overall, these results suggest that greater probe-target association strength facilitated valence matching across conditions. Contrary to Experiment 4.1, no significant interaction was found between association strength and condition. The effect of association strength was only seen to be reliable in the control group.

Supplementary Table 4.4. Output of Experiment 4.2 valence matching mixed effects logistic regression.

Variable	Estimate	Lower 95% CI	Upper 95% CI	Likelihood Ratio Test
Intercept	2.18	1.18	3.17	-
Group	**2.16**	**1.12**	**3.21**	**$\chi(1) = 14.6, p < .001$***
Condition	**-2.38**	**-3.67**	**-1.10**	**$\chi(1) = 13.5, p < .001$***
Target association	**4.75**	**1.76**	**7.74**	**$\chi(1) = 10.6, p = .001$***
Group x condition	0.03	-1.02	1.09	$\chi(1) < 0.01, p = .954$
Group x target association	**-3.01**	**-6.05**	**0.03**	**$\chi(1) = 3.88, p = .049$***
Condition x target association	3.69	-14.28	21.67	$\chi(1) = 0.16, p = .687$
Group x condition x target association	11.14	-2.50	24.79	$\chi(1) = 2.45, p = .118$

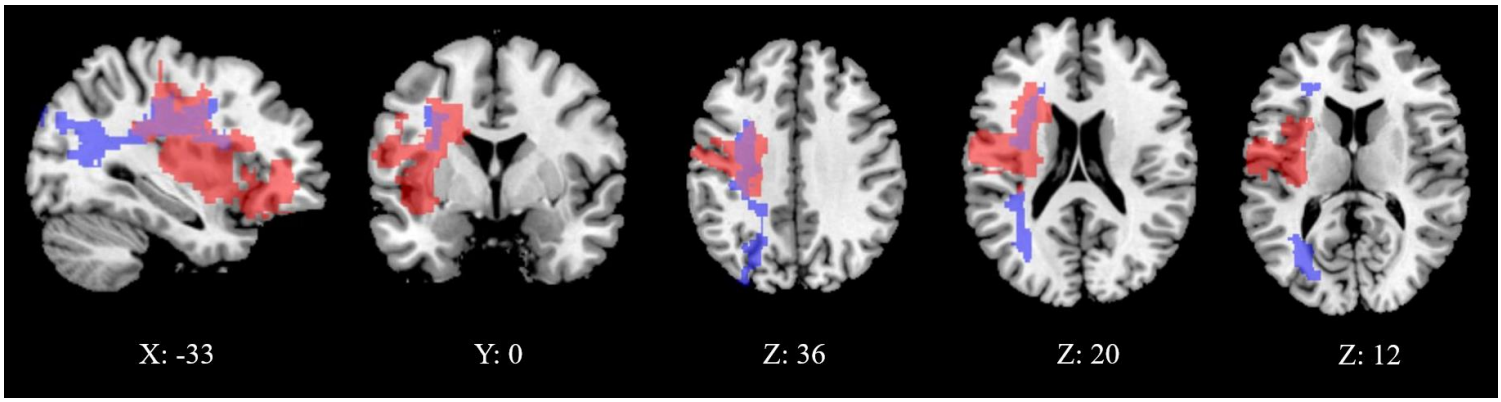
Note: * reflects a significant result. The model was run in R using lme4 package (version 1.1-25; Bates et al., 2015). As this is a logistic model, estimate coefficients reflect log transformation of odds ratios (Larsen et al., 2000).



Supplementary Figure 4.2. Associations between probe-target association strength and the likelihood of a correct response for the Experiment 4.2 valence matching task in (a) semantic aphasia patients and (b) control participants. Grey shaded areas reflect confidence intervals based on the standard errors.

Lesion Analysis

For P4 and P6, structural T1 scans were obtained at the York Neuroimaging Centre using a 3T GE HDx Excite MRI scanner on a T1-weighted 3D fast spoiled gradient echo sequence (TR = 7.8ms, TE = minimum full, flip-angle = 20^{o}, matrix size = 256 x 256, 176 slices, voxel size = 1.13 x 1.13 x 1mm). These scans underwent extraction and registration to MNI space in ANTs (Avants et al., 2011), using a template from the OASIS Brain project (Marcus et al., 2010). Lesions for these patients were manually traced in MRICron. An overlay in Supplementary Figure 4.3 provides evidence of widespread frontoparietal damage. It was not possible to obtain T1 scans for the remaining patients. Clinical acute-stage scans were obtained for P16 (MRI) which showed evidence of a left frontal lesion, and for P12 (CT) which showed evidence of a left frontoparietal lesion.



Supplementary Figure 4.3. Manually segmented lesion location for P4 (red) and P6 (blue). Both lesions impact the left inferior frontal gyrus. Voxel coordinates are displayed under each slice.

Within-Group Contrasts

Supplementary Table 4.5. Within-group post-hoc contrasts for the Experiment 4.2 valence mixed effects model.

Group	Contrast	Result
Patients	Associated target – No association	OR = .25, p = .247
	No association – Associated distractor	**OR = 16.09, p < .001***
Controls	Associated target – No association	OR = .94, p > 1
	No association – Associated distractor	**OR = 10.61, p < .001***

Note: Contrasts Bonferroni corrected for four comparisons. * reflects a significant result. OR = odds ratio. Run using the emmeans package (Lenth, 2020), in R.

Chapter 5 supplementary materials

Psycholinguistics

Supplementary Table 5.1. Stimulus properties for Experiment 5.1.

	Experiment 5.1 (Reward) – Stimulus Properties [Mean (SD)]			
	High Reward		**Low Reward**	
	Strong Association	**Weak Association**	**Strong Association**	**Weak Association**
Probe frequency	3.72 (.65)	3.68 (.76)	3.62 (.64)	3.75 (.63)
Target frequency	4.08 (.92)	4.25 (.69)	4.43 (.59)	4.26 (.64)
Probe imageability	4.92 (.96)	5.22 (.95)	5.05 (.86)	5.08 (.90)
Target imageability	5.22 (.83)	5.21 (1.08)	5.41 (.76)	5.27 (.91)
Probe length	7.31 (2.07)	6.41 (2.23)	7.03 (1.86)	7.53 (2.53)
Target length	7.22 (2.42)	6.48 (2.46)	6.25 (2.26)	6.03 (2.33)
Association strength	5.70 (.10)	2.87 (.55)	5.71 (.10)	2.98 (.49)

Note: ratings of familiarity, frequency, and imageability taken on a 7-point Likert scale, taken from established databases of linguistic norms. Length corresponds with the numbers of letters in a word. Association strength taken on a 7-point Likert scale, based on ratings taken from the Edinburgh Associative Thesaurus (Kiss et al., 1973).

Supplementary Table 5.2. Stimulus properties for Experiment 5.2.

	Experiment 5.2 (Self-Reference) – Stimulus Properties [Mean (SD)]	
	Strong Association	**Weak Association**
Target frequency	4.22 (.73)	4.05 (.84)
Target imageability	5.27 (.99)	4.93 (.87)
Target length	6.46 (2.41)	6.82 (2.83)
Set 1 association strength	5.91 (.64)	2.78 (.61)
Set 2 association strength	5.89 (.66)	2.82 (.58)

Note: ratings of familiarity, frequency, and imageability taken on a 7-point Likert scale, taken from established databases of linguistic norms. Length corresponds with the numbers of letters in a word. Association strength taken on a 7-point Likert scale, based on online validation surveys.

Supplementary Table 5.3. ANOVAs for Experiment 5.1 and Experiment 5.2 psycholinguistic factors.

Experiment	Word type	Factor	Main effect/interaction	Results
Experiment 5.1: Reward	Probe	Frequency	Association strength	$F(1, 98) = .1$, $p = .721$, $\eta_p^2 < .01$
			Reward condition	$F(1, 98) < .1$, $p = .949$, $\eta_p^2 < .01$
			Reward condition by association strength	$F(1, 98) < .1$, $p = .524$, $\eta_p^2 < .01$
		Imageability	Association strength	$F(1, 123) = 1.1$, $p = .304$, $\eta_p^2 < .01$
			Reward condition	$F(1, 123) < .1$, $p = .965$, $\eta_p^2 < .01$
			Reward condition by association strength	$F(1, 123) = .7$, $p = .413$, $\eta_p^2 < .01$
		Length	Association strength	$F(1, 124) = .3$, $p = .600$, $\eta_p^2 < .01$
			Reward condition	$F(1, 124) = 1.2$, $p = .277$, $\eta_p^2 = .01$
			Reward condition by association strength	$F(1, 124) = 3.3$, $p = .071$, $\eta_p^2 = .03$
	Target	Frequency	Association strength	$F(1, 106) < .1$, $p = .973$, $\eta_p^2 < .01$
			Reward condition	$F(1, 106) = 1.7$, $p = .194$, $\eta_p^2 = .02$
			Reward condition by association strength	$F(1, 106) = 1.5$, $p = .224$, $\eta_p^2 = .01$
		Imageability	Association strength	$F(1, 124) = .2$, $p = .624$, $\eta_p^2 < .01$
			Reward condition	$F(1, 124) = .7$, $p = .416$, $\eta_p^2 < .01$
			Reward condition by association strength	$F(1, 124) = .1$, $p = .700$, $\eta_p^2 < .01$
		Length	Association strength	$F(1, 124) = .3$, $p = .607$, $\eta_p^2 < .01$
			Reward condition	$F(1, 124) = 2.2$, $p = .142$, $\eta_p^2 = .02$
			Reward condition by association strength	$F(1, 124) = .4$, $p = .515$, $\eta_p^2 < .01$
Experiment 5.2: Self-reference	Target	Frequency	Association strength	$F(1, 46) = .6$, $p = .441$, $\eta_p^2 = .01$
		Imageability	Association strength	$F(1, 46) = 1.7$, $p = .195$, $\eta_p^2 = .03$
		Length	Association strength	$F(1, 46) = .3$, $p = .609$, $\eta_p^2 < .01$

Response Time

Supplementary Table 5.4. Analysis and interpretation of response time (seconds) in Experiment 5.1 and Experiment 5.2.

Experiment	Main effect/interaction	Results
Experiment 5.1: reward	**Group**	**$F(1, 29) = 80.7$, $p < .001$, $\eta_p^2 = .74$***
	Reward	$F(1, 29) < .1$, $p = .827$, $\eta_p^2 < .01$
	Reward by group	$F(1, 29) = 1.0$, $p = .315$, $\eta_p^2 = .04$
	Strength	**$F(1, 29) = 357.7$, $p < .001$, $\eta_p^2 = .93$***
	Strength by group	$F(1, 29) = 2.7$, $p = .113$, $\eta_p^2 = .08$
	Reward by strength	$F(1, 29) = 3.9$, $p = .057$, $\eta_p^2 = .12$
	Reward by strength by group	$F(1, 29) < .1$, $p = .830$, $\eta_p^2 < .01$
Experiment 5.2: self-reference	**Group**	**$F(1, 20) = 18.2$, $p < .001$, $\eta_p^2 = .48$***
	Self-reference	$F(1, 20) = .2$, $p = .662$, $\eta_p^2 = .01$
	Self-reference by group	$F(1, 20) = 1.2$, $p = .278$, $\eta p^2 = .06$
	Strength	**$F(1, 20) = 345.2$, $p < .001$, $\eta_p^2 = .95$***
	Strength by group	$F(1, 20) = 3.2$, $p = .089$, $\eta p^2 = .14$
	Self-reference by strength	$F(1, 20) = .2$, $p = .669$, $\eta p^2 < .01$
	Self-reference by strength by group	$F(1, 20) = .1$, $p = .811$, $\eta p^2 < .01$

The observed significant main effects of group on response time reflect that controls responded more quickly than patients in both Experiment 5.1, and Experiment 5.2. The observed main effects of strength reflect that all participants responded more slowly for weak than strong association trials in both Experiment 5.1 and Experiment 5.2. No effects or interactions of either reward or self-reference for RT were observed. Patients' semantic control composite did not correlate with overall RT in Experiment 5.1 [$r_s(14) = -.41$, $p = .113$], but did negatively correlate with overall RT in Experiment 5.2 [$r_s(8) = -.64$, $p = .048$], suggesting slower responses in more impaired patients.

Descriptive Statistics

Supplementary Table 5.5. Descriptive statistics for Experiment 5.1.

Experiment 5.1 – Extrinsic Reward								
	Patients (N = 16)				Controls (N = 15)			
	Mean	**SD**	**Minimum**	**Maximum**	**Mean**	**SD**	**Minimum**	**Maximum**
Proportion of correct responses								
High-strong	.779	.183	.28	.97	.938	.031	.91	1
High-weak	.600	.144	.31	.81	.777	.095	.59	.91
Low-strong	.779	.176	.28	.94	.956	.042	.84	1
Low-weak	.533	.179	.09	.81	.779	.083	.66	.91
Response time (seconds)								
High-strong	5.48	.931	4.51	8.03	3.02	.664	2.05	4.59
High-weak	6.22	.913	4.96	8.01	3.94	.743	2.78	5.64
Low-strong	5.33	.708	4.46	6.79	3.02	.584	2.00	4.02
Low-weak	6.27	.779	5.51	7.85	4.10	.631	3.01	5.28
Self-reported enjoyment								
High reward	5.79	1.31	2.38	7	6.08	1.03	4.00	7
Low reward	5.71	1.44	2.38	7	6.10	.963	4.00	7
Self-reported confidence								
High reward	5.09	1.24	2.38	7	6.04	.773	3.88	6.88
Low reward	4.94	1.33	2.38	7	6.07	.671	4.38	7
Self-reported focus								
High reward	5.77	1.26	2.38	7	6.67	.497	5.50	7
Low reward	5.66	1.34	2.38	7	6.62	.550	5.50	7

Note: The naming of levels of task-based dependent variables is based on the reward condition and association strength of these trials (e.g., High-Strong = high reward, strong association). All self-report ratings were taken on a 7-point Likert scale.

Supplementary Table 5.6. Descriptive statistics for Experiment 5.2.

Experiment 5.2 – Self-Reference								
	Patients (N = 10)				Controls (N = 11)			
	Mean	**SD**	**Minimum**	**Maximum**	**Mean**	**SD**	**Minimum**	**Maximum**
Recognition memory – Proportion of hits								
Self	.810	.181	.40	1	.832	.108	.60	.95
Other	.425	.199	.15	.75	.468	.169	.25	.80
New	.760	.263	.10	1	.900	.087	.75	1
Recognition memory – Proportion of false positives								
Self	.365	.196	.10	.75	.241	.120	0	.40
Other	.295	.236	.10	.90	.218	.108	.10	.40
New	.320	.195	.05	.75	.341	.130	.10	.55
Recognition memory - A'								
Self	.797	.142	.50	.94	.870	.065	.73	.98
Other	.597	.269	.09	.90	.695	.148	.40	.88
New	.774	.199	.36	.95	.866	.057	.76	.95
Proportion of correct responses								
Self-strong	.831	.127	.61	.96	.925	.054	.79	.96
Self-weak	.536	.136	.32	.71	.721	.120	.46	.93
Other-strong	.821	.139	.50	.96	.938	.058	.82	1
Other-weak	.539	.147	.25	.75	.731	.117	.50	.89
Response time (seconds)								
Self-strong	5.01	1.04	3.76	7.07	3.30	.656	2.41	4.40
Self-weak	6.32	.864	4.97	7.89	4.87	.812	3.55	6.12
Other-strong	4.95	1.08	3.61	7.32	3.38	.629	2.48	4.49
Other-weak	6.28	1.06	4.55	7.95	5.02	.686	3.91	6.24
Self-reported confidence								
Self-strong	6.17	.993	4.25	7.00	6.56	.507	5.11	7.00
Self-weak	4.84	1.07	2.75	6.15	4.73	1.33	1.50	6.07
Other-strong	6.18	.943	4.11	7.00	6.57	.477	5.32	7.00
Other-weak	4.95	1.22	2.96	7.00	4.74	1.40	1.61	6.14

Note: A’ is a non-parametric signal detection theory statistic, which factors in the proportion of both correct hits and false positive responses. The formula used is from Snodgrass and Corwin (1988). Overall, participants selected ‘self’ significantly more than ‘other’ ($Z = -3.9$, $p < .001$) and ‘new’ significantly more than ‘other’ ($Z = -3.3$, $p = .001$). Given that these responses are believed to reflect genuine recognition memory effects, and given the reported output of A’ analysis, this was not considered to be the result of spurious response bias. The naming of levels of task-based dependent variables is based on the self-reference condition and association strength of these trials (e.g., Self-Strong = self-allocated, strong association). Self-report ratings of confidence were taken on a 7-point Likert scale.

Chapter 6 supplementary materials

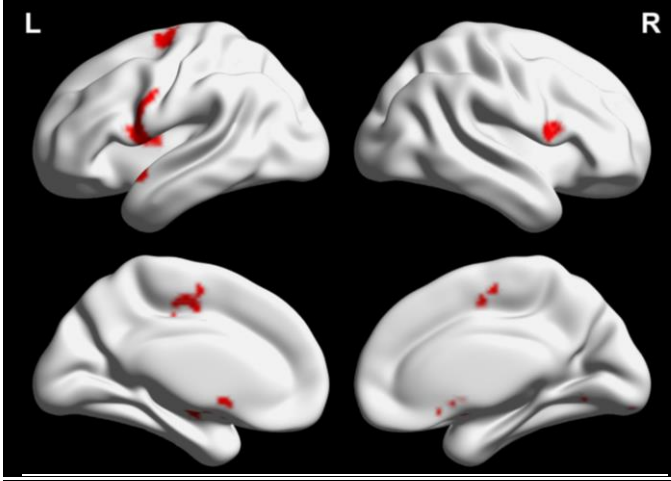
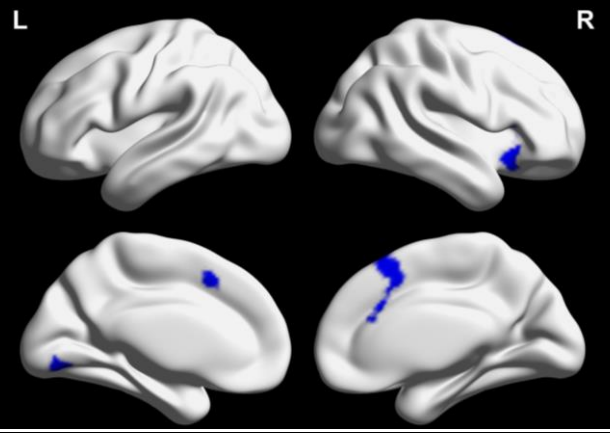
Experimental Stimuli

Supplementary Table 6.1. Identifiers for stimuli taken from the International Affective Picture System with mean and SD of valence and arousal ratings, and allocation of association type and categorical valence in the current study.

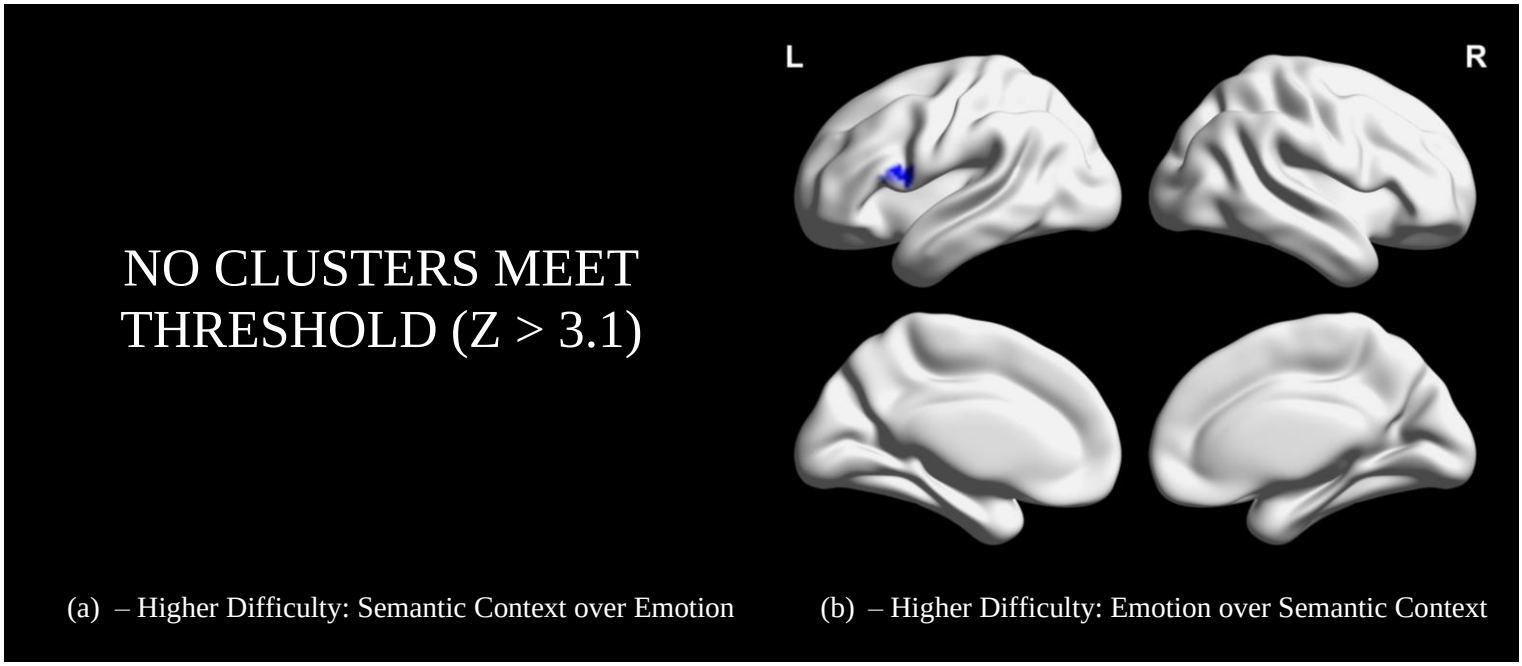
ID	Description	Valence Mean	Valence SD	Arousal Mean	Arousal SD	Association Type	Valence
1120	Snake	3.79	1.93	6.93	1.68	Emotion	Negative
1350	Pig	5.25	1.96	4.37	1.76	Semantic Context	Neutral
1390	Bees	4.5	1.56	5.29	1.97	Semantic Context	Neutral
1659	Gorilla	6.57	1.98	4.89	1.97	Emotion	Positive
1675	Buffalo	5.24	1.48	4.37	2.15	Semantic Context	Neutral
1999	Mickey	7.43	1.47	4.77	2.4	Emotion	Positive
2002	Man	4.95	1.36	3.35	1.87	Semantic Context	Neutral
2036	Woman	5.8	1.28	3.24	1.88	Semantic Context	Neutral
2039	Woman	3.65	1.44	3.46	1.94	Emotion	Negative
2092	Clowns	6.28	1.9	4.32	2.29	Emotion	Positive
2156	Family	7.12	1.46	4.34	2.11	Emotion	Positive
2191	Farmer	5.3	1.62	3.61	2.14	Semantic Context	Neutral
2217	Class	6.24	1.52	4.08	1.85	Emotion	Positive
2360	Family	7.7	1.76	3.66	2.32	Emotion	Positive
2377	Reading	5.19	1.31	3.5	1.95	Semantic Context	Neutral
2382	Artist	5.67	1.19	3.75	1.97	Semantic Context	Neutral
2383	Secretary	4.72	1.36	3.41	1.83	Semantic Context	Neutral
2390	Couple	5.4	1.18	3.57	1.92	Semantic Context	Neutral
2397	Men	4.98	1.11	2.77	1.74	Semantic Context	Neutral
2455	SadGirls	2.96	1.79	4.46	2.12	Emotion	Negative
2456	CryingFamily	2.84	1.27	4.55	2.16	Emotion	Negative
2488	Musician	5.73	1.14	3.91	1.87	Semantic Context	Neutral
2489	Musician	5.66	1.44	3.8	1.93	Semantic Context	Neutral
2490	Man	3.32	1.82	3.95	2	Emotion	Negative
2595	Women	4.88	1.24	3.71	1.88	Semantic Context	Neutral
2635	Cowboy	5.22	1.65	4.42	1.98	Semantic Context	Neutral
2691	Riot	3.04	1.73	5.85	2.03	Emotion	Negative
2718	DrugAddict	3.65	1.58	4.46	2.03	Emotion	Negative
2745.1	Shopping	5.31	1.08	3.26	1.96	Semantic Context	Neutral
2751	DrunkDriving	2.67	1.87	5.18	2.39	Emotion	Negative
2870	Teenager	5.31	1.41	3.01	1.72	Semantic Context	Neutral
2980	FoodBasket	5.61	1.5	3.09	1.91	Semantic Context	Neutral
5300	Galaxy	6.91	1.8	4.36	2.62	Emotion	Positive
5455	Cockpit	5.79	1.37	4.56	2.17	Semantic Context	Neutral
5500	Mushroom	5.42	1.58	3	2.42	Semantic Context	Neutral
5621	SkyDivers	7.57	1.42	6.99	1.95	Emotion	Positive
5623	Windsurfers	7.19	1.44	5.67	2.32	Emotion	Positive

5814	Mountain	7.15	1.54	4.82	2.4	Emotion	Positive
5900	Desert	5.93	1.64	4.38	2.1	Semantic Context	Neutral
5910	Fireworks	7.8	1.23	5.59	2.55	Emotion	Positive
6240	Gun	3.79	1.8	5.27	2.2	Emotion	Negative
7001	Buttons	5.32	1.19	3.2	2.15	Semantic Context	Neutral
7033	Train	5.4	1.57	3.99	2.14	Semantic Context	Neutral
7036	Shipyard	4.88	1.08	3.32	2.04	Semantic Context	Neutral
7081	Luggage	5.36	1.3	3.96	2.24	Semantic Context	Neutral
7130	Truck	4.77	1.03	3.35	1.9	Semantic Context	Neutral
7234	IroningBoard	4.23	1.58	2.96	1.9	Semantic Context	Neutral
7325	Watermelon	7.06	1.65	3.55	2.07	Emotion	Positive
7492	Ferry	7.41	1.68	4.91	2.46	Emotion	Positive
7493	Man	5.35	1.34	3.39	2.08	Semantic Context	Neutral
7495	Store	5.9	1.6	3.82	2.33	Semantic Context	Neutral
7496	Street	5.92	1.66	4.84	1.99	Semantic Context	Neutral
7503	CardDealer	5.77	1.39	4.21	2.39	Semantic Context	Neutral
7506	Casino	5.34	1.46	4.25	1.95	Semantic Context	Neutral
7509	Paintbrush	6.03	1.35	3.43	2.02	Emotion	Positive
7520	Hospital	3.83	1.56	4.57	1.85	Emotion	Negative
7530	House	6.71	1.36	4	2.14	Emotion	Positive
7560	Freeway	4.47	1.65	5.24	2.03	Semantic Context	Neutral
7710	Bed	5.42	1.58	3.44	2.21	Semantic Context	Neutral
8158	Hiker	6.53	1.66	6.49	2.05	Emotion	Positive
8180	CliffDivers	7.12	1.88	6.59	2.12	Emotion	Positive
8312	Golf	5.37	1.41	3.32	2.06	Semantic Context	Neutral
8325	RaceCars	5.63	1.5	4.47	2.19	Semantic Context	Neutral
8499	Rollercoaster	7.63	1.41	6.07	2.31	Emotion	Positive
9090	Exhaust	3.56	1.5	3.97	2.12	Emotion	Negative
9110	Puddle	3.76	1.41	3.98	2.23	Emotion	Negative
9220	Cemetery	2.06	1.54	4	2.09	Emotion	Negative
9342	Pollution	2.85	1.41	4.49	1.88	Emotion	Negative
9445	Skeleton	3.87	1.57	4.49	2.01	Emotion	Negative
9622	Jet	3.1	1.9	6.26	1.98	Emotion	Negative
9630	Bomb	2.96	1.72	6.06	2.22	Emotion	Negative
9832	Cigarettes	2.94	1.58	4.46	2.06	Emotion	Negative

Parametric Difficulty Analysis

	(a) – Higher Difficulty	(b) – Lower Difficulty
Semantic Context	NO CLUSTERS MEET THRESHOLD (Z > 3.1)	
Emotion		SIGNIFICANT CLUSTER IN RIGHT CEREBELLUM ONLY
Statistical Conjunction	NO CLUSTERS MEET THRESHOLD (Z > 3.1)	NO CLUSTERS MEET THRESHOLD (Z > 3.1)

Supplementary Figure 6.1. Clusters corresponding to (a) higher and (b) lower self-report switch difficulty during semantic context associations, emotion associations, and the statistical conjunction of the two. Clusters taken from group-level analysis in FSL-FEAT with a threshold of Z > 3.1. Maps visualised with the BrainNet Viewer (Xia et al., 2013; https://www.nitrc.org/projects/bnv/).



Supplementary Figure 6.2. Clusters associated with (a) higher parametric self-reported difficulty for semantic context associations relative to emotion associations and (b) higher parametric self-reported difficulty for emotion associations relative to semantic context associations. Clusters taken from group-level analysis in FSL-FEAT with a threshold of Z > 3.1. Maps visualised with the BrainNet Viewer (Xia et al., 2013; https://www.nitrc.org/projects/bnv/).

Interpretation

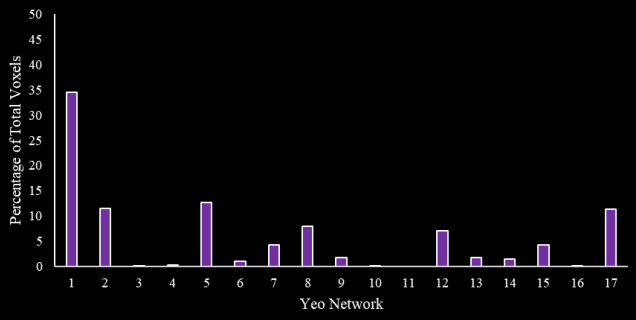
Supplementary Figure 6.1 displays clusters associated with both higher and lower self-reported switch difficulty, separately for both *semantic context* and *emotion* associations. The statistical conjunction across association types (generated using FSL's 'eaythresh_conj' tool) is also presented. For higher difficulty, clusters only survive thresholding for *emotion* associations. There are no significant clusters for *semantic context* associations or for the conjunction of association types. For lower difficulty, clusters for *semantic context* associations are observed in the cortex, with *emotion* associations only yielding one small cluster in the right cerebellum. Again, no clusters are implicated in the statistical conjunction. As seen in Supplementary Figure 6.2, there are no clusters associated more so with higher difficulty for *semantic context* associations compared to *emotion* associations. One cluster implicating aspects of the left inferior frontal gyrus and precentral gyrus is associated with greater difficulty for *emotion* associations, relative to *semantic context* associations.

Yeo Network Overlap

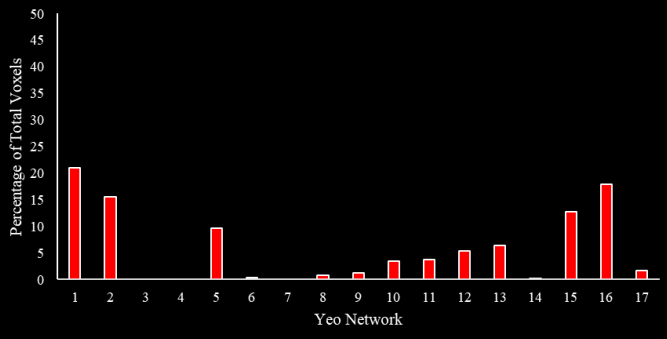
Supplementary Table 6.2. The percentage of each functional network (exclusive and conjunction) which falls within a given Yeo et al. (2011) 17-network parcellation.

Network	Label	DMN	DMN & SCN	SCN	SCN & MDN	MDN
Yeo 1	Visual peripheral	0	0	0.29	0	8.77
Yeo 2	Visual central	0	0	0	0	1.16
Yeo 3	Somatosensor A	0	0	0	0	0.38
Yeo 4	Somatosensor B	0	0	0	0	0.01
Yeo 5	DAN A	0	0	4.94	9.28	13.19
Yeo 6	DAN B	0	0	0.92	1.87	9.01
Yeo 7	VAN	0	0	1.67	1.74	4.32
Yeo 8	Salience	0.81	0.45	5.19	34.60	9.56
Yeo 9	Limbic A	0	0	0	0	0
Yeo 10	Limbic B	1.05	0.22	2.93	0	0
Yeo 11	Control C	2.31	0	0	0	2.40
Yeo 12	Control A	0	0	34.95	29.89	13.78
Yeo 13	Control B	8.00	3.64	11.30	7.91	3.21
Yeo 14	Auditory	6.62	6.66	2.22	0.50	0.07
Yeo 15	Medial temporal DMN	4.06	0	0	0	0
Yeo 16	Core DMN	40.39	0.45	0.08	0	0
Yeo 17	Fronto-temporal DMN	36.77	88.58	5.90	7.82	0.04
Total		100	100	70.41	93.60	65.89

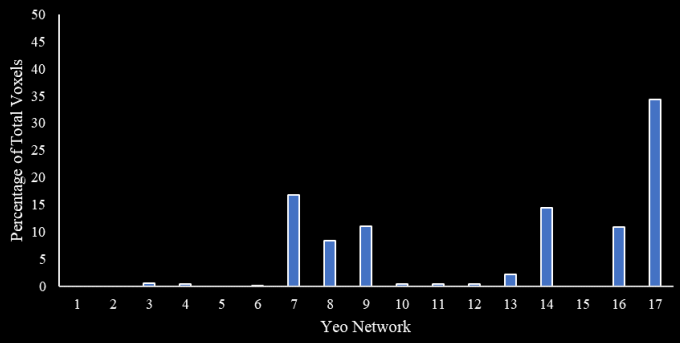
Note: Totals for each network do not add to 100% in each case as aspects of some networks fall outside this 17-network parcellation. Colour grading used gives brighter colours to larger percentages. DAN = dorsal attention network, VAN = ventral attention network, DMN = default mode network, SCN = semantic control network, MDN = multiple demand network.



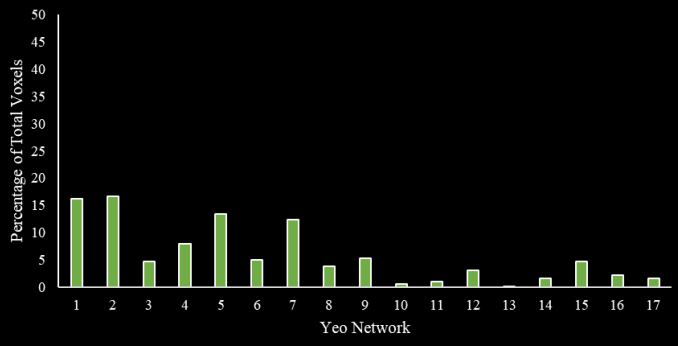
(a) – Task over Baseline



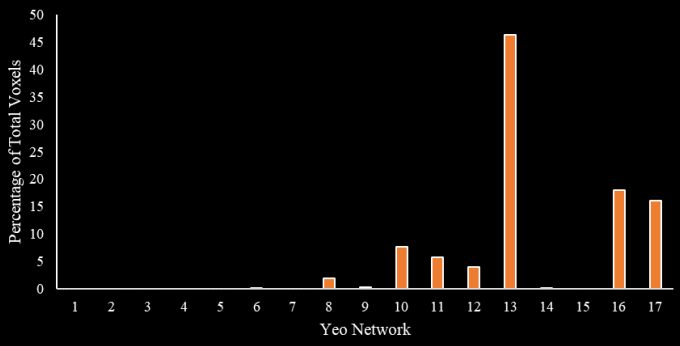
(b) – Semantic Context over Emotion



(c) – Emotion over Semantic Context



(d) – Generate over Switch



(e) – Switch over Generate

Yeo 1	Visual peripheral	Yeo 2	Visual central	Yeo 3	Somatosensor A
Yeo 4	Somatosensor B	Yeo 5	DAN A	Yeo 6	DAN B
Yeo 7	VAN	Yeo 8	Salience	Yeo 9	Limbic A
Yeo 10	Limbic B	Yeo 11	Control C	Yeo 12	Control A
Yeo 13	Control B	Yeo 14	Auditory	Yeo 15	Default C (Medial Temporal)
Yeo 16	Default A (Core)	Yeo 17	Default B (Fronto-Temporal)		

(f) – Yeo et al. (2011) 17-network parcellation labels

Supplementary Figure 6.3. The percentage implicated in each Yeo et al. (2011) 17-network parcellation for clusters associated with (a) the conjunction of semantic context and emotion associations over baseline, (b) greater activation for semantic context than emotion associations, (c) greater activation for emotion than semantic context associations, (d) greater activation in the generate than the switch phase, and (e) greater activation in the switch than the generate phase. Each contrast was masked by the 17 networks for this figure,

such that bars for each contrast add up to 100% together[32]*. (f) Labels are presented for each network.*

[32] Variable portions of each contrast fell within the addition of all 17 Yeo networks before masking: task over baseline [70.0%], *semantic context* over *emotion* [85.5%], *emotion* over *semantic context* [89.5%], *generate* over *switch* [62.3%], *switch* over *generate* [93.5%].

Coding Semantic Context Recall Responses

Supplementary Table 6.3. The mean percentage (standard deviation) of semantic context associations that fall in each coding category, split by phase and overall.

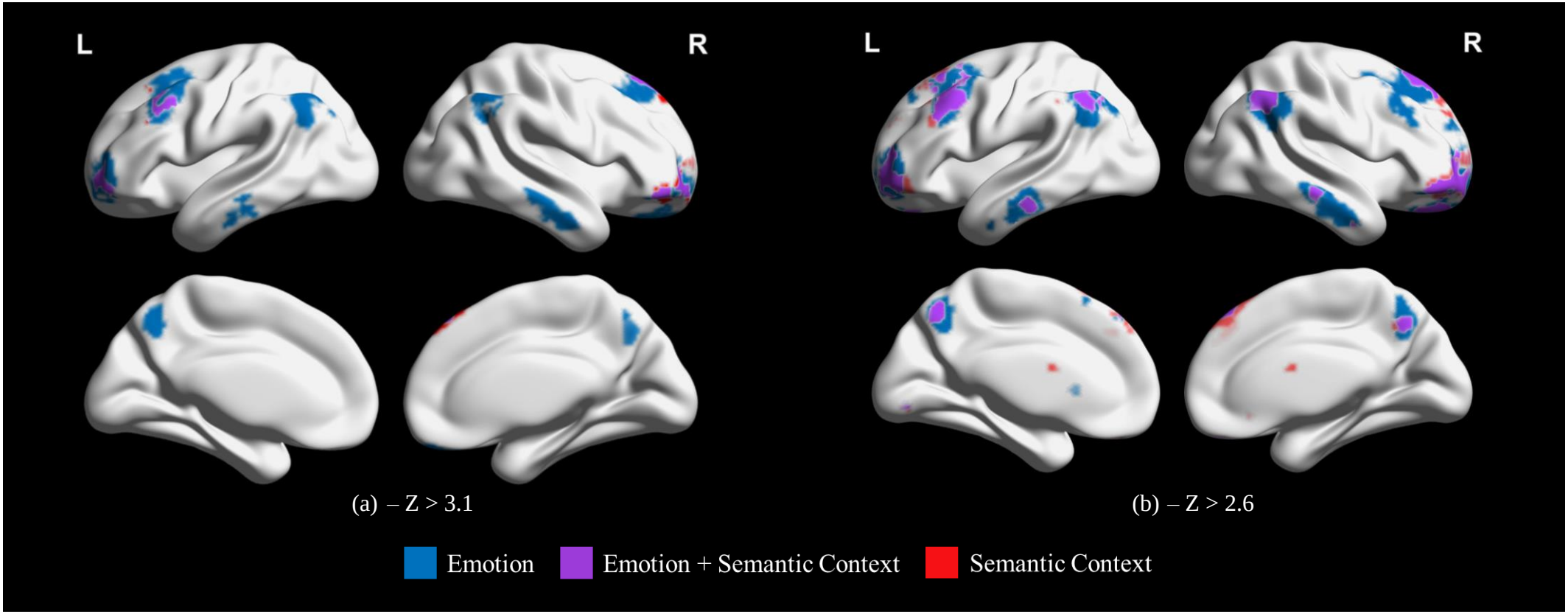
	General semantic	No association made	Personal semantic	Picture label	Episodic	Emotion association retrieved	Can't remember
Generate	75.8 (20.3)	3.8 (5.8)	8.9 (10.7)	4.6 (8.6)	2.9 (5.4)	0.3 (1.1)	3.8 (7.1)
Switch	64.7 (18.1)	10.9 (10.8)	5.6 (8.2)	1.9 (4.2)	3.3 (7.6)	0.4 (1.0)	13.2 (14.5)
Overall	70.2 (17.7)	7.3 (7.1)	7.3 (8.6)	3.3 (6.1)	3.1 (6.3)	0.4 (0.9)	8.5 (10.1)

All categories are mutually exclusive, such that percentages add to 100% in each phase. Scores are taken from coding of recall data. It is not possible to say how accurately these reflect associations made in the scanner, although participants were generally confident in their recall (see Table 6.1). Criteria used for each category are explained below:

- **General semantic** – Appropriate *semantic context* associations that reflect contextual associations free from personal semantics or specific episodes.
- **No association made** – Trials where participant report not having been able to generate an association for a given phase.
- **Personal semantic** – Associations that are semantic in nature but refer to specific people or places in the participant's life, and/or are reported in the first person.
- **Picture label** – Brief descriptions which do not provide anything beyond the content of the picture, e.g., "gambling" for a picture of a casino.
- **Episodic** – Associations that appear to reflect a specific event or memory in the participant's life, suggesting episodic recall rather than generation of a semantic contextual association.
- **Emotion association retrieved** – Associations for which participants appear to have mistakenly thought they were in an *emotion* block, and as such have reported an emotional response to a *semantic context* stimulus.
- **Can't remember** – Associations were participants report not being able to remember the association they generated. It is important to note that associations in this category may have fallen in any of the other categories in reality.

Switch over Generate Split by Condition

In Supplementary Figure 6.4 is the effect of *switch* over *generate* split across *emotion* and *semantic context* conditions, including the overlap of the two. The threshold of Z > 3.1 appears to reflect differences in the effect of *switch* across conditions. This data has therefore also been presented at a lower threshold of Z > 2.6 to demonstrate that clusters are similar across conditions, despite effects being slightly more modest for *semantic context* associations.



Supplementary Figure 6.4. Clusters associated more with the switch than the generate phase split by association type (emotion or semantic context) at thresholds of (a) Z > 3.1 and (b) Z > 2.6. Maps visualised with the BrainNet Viewer (Xia et al., 2013; https://www.nitrc.org/projects/bnv/).

Mean Percent Signal Change Network Main Effect Contrasts

Supplementary Table 6.4. Post-hoc contrasts for the main effect of network on mean percent signal change in resting-state networks overlapping with DMN.

	Control B	Auditory	Medial temporal DMN	Core DMN
Auditory	**t(29) = -5.3, *p* < .001***	-	-	-
Medial temporal DMN	**t(29) = -4.3, *p* = .002***	t(29) = -1.2, *p* > 1	-	-
Core DMN	**t(29) = 4.2, *p* = .002***	**t(29) = 10.5, *p* < .001***	**t(29) = 8.8, *p* < .001***	-
Fronto-temporal DMN	**t(29) = -6.9, *p* < .001***	t(29) = -2.2, *p* = .327	t(29) = -0.6, *p* > 1	**t(29) = -18.5, *p* < .001***

Note: post-hoc contrasts Bonferroni-corrected for ten comparisons. * reflects a significant result. DMN = default mode network.[33]

Supplementary Table 6.5. Post-hoc contrasts for the main effect of network on mean percent signal change in functional control networks.

	DMN	DMN & SCN	SCN	SCN & MDN
DMN & SCN	**t(30) = -18.9, *p* < .001***	-	-	-
SCN	**t(30) = -15.6, p < .001***	**t(31) = 5.8, *p* < .001***	-	-
SCN & MDN	**t(30) = -12.5, p < .001***	**t(31) = 3.7, *p* < .001***	t(31) = -0.6, *p* > 1	-
MDN	**t(30) = -7.8, p < .001***	**t(31) = 8.1, *p* = .009***	**t(31) = 5.6, *p* < .001***	**t(31) = 7.7, *p* < .001***

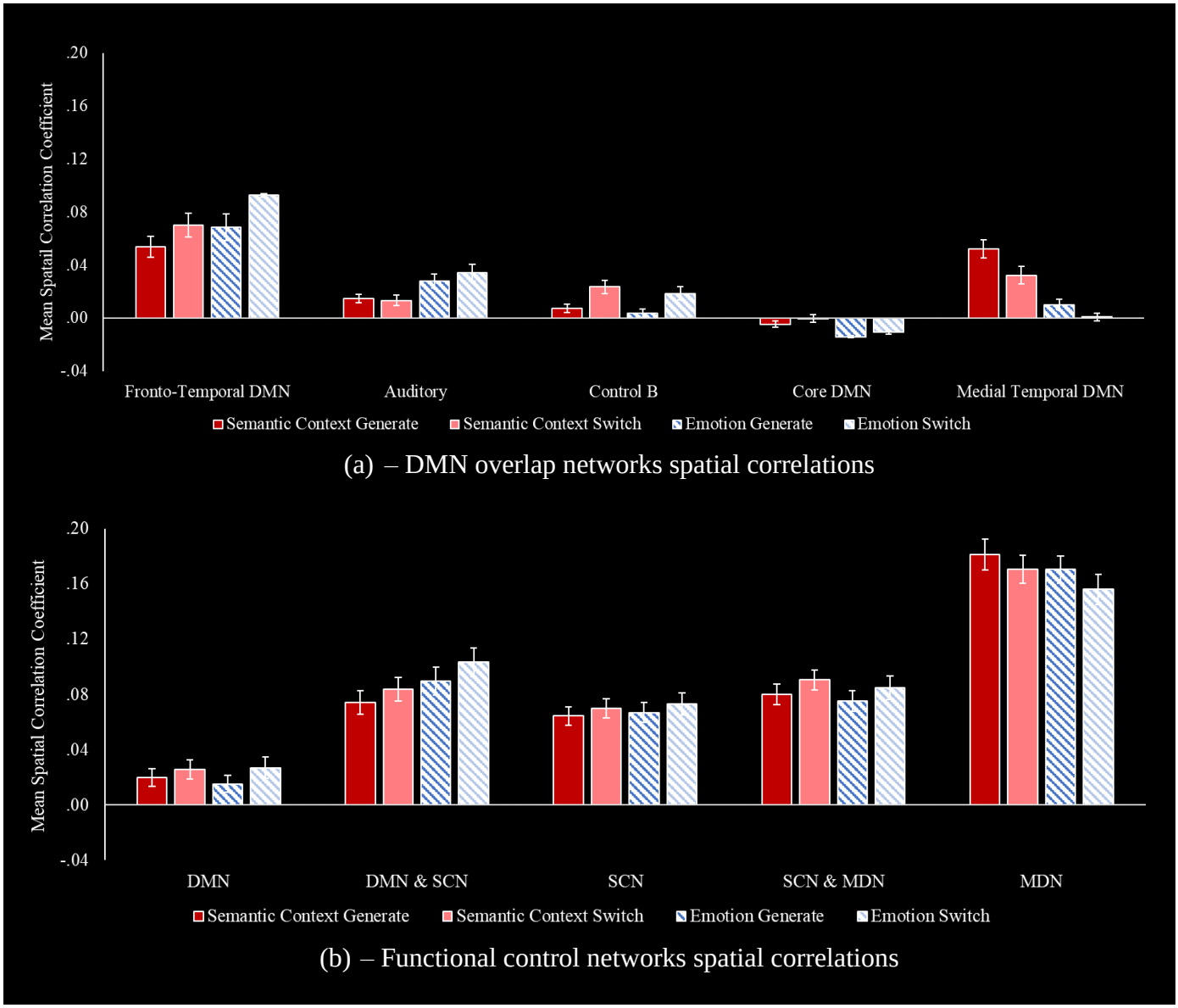
Note: post-hoc contrasts Bonferroni-corrected for ten comparisons. * reflects a significant result. DMN = default mode network, SCN = semantic control network, MDN = multiple demand network.

[33] The assumption of normality was violated for both the control B network and medial temporal DMN. While parametric contrasts are used in this table, non-parametric equivalents elicited the same outcomes: control B – auditory [Z = -3.9, *p* = .001], control B – medial temporal DMN [Z = -3.5, *p* = .004], control B – core DMN [Z = -3.5, *p* = .004], control B – fronto-temporal DMN [Z = -4.6, *p* < .001], medial temporal DMN – auditory network [Z = -0.7, *p* > 1], medial temporal DMN – core DMN [Z = -4.8, *p* < .001], medial temporal DMN – fronto-temporal DMN [Z = -0.5, *p* > 1].

Individual-level spatial correlations

To assess the global fit of task activation with network patterns, Spearman spatial correlations were run between the four contrasts comprising each combination of association type and phase (e.g., *semantic context generate*) over implicit baseline and each network of interest, including functional networks and resting-state networks overlapping with DMN. This was done at the individual-level, providing a coefficient for each participant for each contrast and network. Binarised versions of each network were correlated with thresholded ($Z > 3.1$)[34] and binarised versions of each contrast, such that these correlations are logistic in practice. Using these coefficients, repeated measures ANOVAs were run separately for DMN overlap networks and functional networks, observing for effects and interactions of association type (two levels), phase (two levels), and network (five levels). Significant effects and interactions were parsed using post-hoc contrasts, with Bonferroni correction applied. In addition to the mean percent signal change in each network, this analysis allows us to consider the extent to which the topographical activation pattern we see for each condition corresponds with the spatial distribution of each network. This helps to confirm that association type differences are emerging from network-level organisation, and not from fluctuating BOLD responses in individual brain regions. Mean spatial correlation coefficients for these analyses can be seen in Supplementary Figure 6.5.

[34] This threshold was selected as it is consistent with the threshold used for our group-level analysis output.



Supplementary Figure 6.5. Mean correlation coefficients from individual-level spatial correlations between participants' thresholded (Z > 3.1) and binarised contrasts for each combination of association type and phase over baseline and (a) resting-state DMN networks and (b) functional control networks. Error bars reflect one standard error. DMN = default mode network, SCN = semantic control network, MDN = multiple demand network.

Supplementary Figure 6.5a presents mean individual-level spatial correlation coefficients for resting state networks overlapping with DMN (including voxels outside the Yeo-7 DMN). The results of a repeated-measures ANOVA on these statistics can be seen in Supplementary Table 6.6. This shows significant main effects of phase and network, as well as interactions of association type and network, and of phase and network. The phase main effect reflected higher spatial correlations for the *switch* phase than the *generate* phase. Post-

hoc comparisons parsing the network main effect are reported in Supplementary Table 6.7. For the network by association type interaction, stronger positive spatial correlations with *semantic context* associations were observed for the medial temporal DMN [t(30) = 7.0, p < .001][35] and core DMN [t(28) = 4.5, p = .001]. Stronger positive spatial correlations with *emotion* associations were observed for the auditory network [t(31) = -5.4, p < .001] and fronto-temporal DMN [t(31) = -3.1, p = .019]. There was no difference between association types for the control B network [t(30) = 1.4, p = .894]. For the network by phase interaction, stronger positive spatial correlations with the *generate* phase were observed for the medial temporal DMN [t(30) = 5.0, p < .001]. Stronger positive spatial correlations with the *switch* phase were observed for the control B network [t(30) = -5.0, p < .001], core DMN [t(28) = -4.4, p = .001], and fronto-temporal DMN [t(31) = -4.1, p = .001]. There was no difference between phases for the auditory network [t(31) = -1.0, p > 1]. In summary, this analysis confirms that different DMN networks show topographical similarity with *emotion* and *semantic context* activation (FT and MT, respectively). The control-B network, linked to the *switch* phase, was not spatially correlated with either type of association.

Supplementary Figure 6.5b presents mean individual-level spatial correlation coefficients for functional control networks of interest. A repeated-measures ANOVA, shown in Supplementary Table 6.6, revealed a significant main effect of network, and interactions of association type and network, and of phase and network. Post-hoc tests of interactions are corrected for five comparisons. Post-hoc contrasts for the network main effect are reported in Supplementary Table 6.8. These showed, overall, stronger positive correlations with task activation in MDN compared to all other networks. This was followed by DMN & SCN, which showed stronger correlations than both SCN and MDN separately, but not the SCN & MDN conjunction. There was no difference between SCN and SCN & MDN, but both showed stronger correlations than DMN. While no contrasts survive correction, the association type by network interaction reflected a trend of stronger spatial correlation between MDN and *semantic context* associations [t(31) = 2.4, p = .126], and between DMN & SCN and *emotion* associations [t(31) = -2.5, p = .097]. There were no effects of association type for DMN [t(30) = 0.5, p > 1], SCN [t(31) = -0.5, p > 1], or SCN & MDN [t(31) = 1.0, p

[35] The assumption of normality was violated across the board for these interactions, with the exception of the fronto-temporal DMN when comparing phases. However, non-parametric tests elicit the same outcomes as reported here. Association type comparison: control B [Z = -1.1, p > 1], auditory [Z = -4.5, p < .011], medial temporal DMN [Z = -4.9, p < .001], core [Z = -3.8, p < .001], fronto-temporal DMN [Z = -2.8, p = .028]. Phase comparison: control B [Z = -4.0, p < .001], auditory [Z = -0.9, p > 1], medial temporal DMN [Z = -4.0, p < .001], core [Z = -3.7, p = .001].

> 1]. The phase by network interaction reflected stronger positive spatial correlations between both DMN [t(30) = -2.8, p = .041][36] and DMN & SCN [t(31) = -3.2, p = .015] with the *switch* phase, relative to the *generate* phase. No difference between phases was observed for SCN [t(31) = -1.8, p = .415], SCN & MDN [t(31) = -2.5, p = .088], or MDN [t(31) = 2.1, p = .213]. In summary, task activation correlates most with MDN, likely due to the implication of lateral occipital regions, followed by regions in SCN, then DMN. MDN trends towards preferentially correlating with *semantic context* associations, while regions in the DMN & SCN prefer *emotion* associations. Voxels in DMN and overlapping in DMN & SCN correlate more with the *switch* than the *generate* phase, consistent with the abstract nature of this phase.

Supplementary Table 6.6. Repeated measures ANOVAs observing main effects and interactions of association type, phase, and network for spatial correlations with resting-state networks overlapping with the default mode network and functional control networks of interest.

Analysis	Effect	Result
DMN overlap networks	Association type	$F(1, 26) = 3.2$, $p = .087$, $\eta_p^2 = .11$
	Phase	**$F(1, 26) = 10.5$, $p = .003$, $\eta_p^2 = .29$***
	Network	**$F(1.7, 45.3) = 29.5$, $p < .001$, $\eta_p^2 = .53$***
	Association type x Phase	$F(1, 26) = 1.9$, $p = .179$, $\eta_p^2 = .07$
	Association type x Network	**$F(2.1, 53.4) = 20.0$, $p < .001$, $\eta_p^2 = .44$***
	Phase x Network	**$F(2.7, 70.6) = 29.3$, $p < .001$, $\eta_p^2 = .53$***
	Association type x Phase x Network	$F(2.8, 73.8) = 2.6$, $p = .063$, $\eta_p^2 = .09$
Functional control networks	Association type	$F(1, 30) < 0.1$, $p = .995$, $\eta_p^2 < .01$
	Phase	$F(1, 30) = 2.6$, $p = .120$, $\eta_p^2 = .08$
	Network	**$F(1.9, 55.7) = 71.8$, $p < .001$, $\eta_p^2 = .71$***
	Association type x Phase	$F(1, 30) = 0.2$, $p = .624$, $\eta_p^2 = .01$
	Association type x Network	**$F(2.6, 78.0) = 5.9$, $p = .002$, $\eta_p^2 = .16$***
	Phase x Network	**$F(2.2, 65.6) = 11.4$, $p < .001$, $\eta_p^2 = .28$***
	Association type x Phase x Network	$F(1.7, 51.7) = 0.5$, $p = .582$, $\eta_p^2 = .02$

Note: * reflects a significant result. For both analyses, assumption of sphericity violated for 'network'. Greenhouse-Geisser adjustment has been applied accordingly.

[36] The assumption of normality was violated for DMN for this comparison. A non-parametric test elicited the same outcome: Z = -3.7, p = .002.

Supplementary Table 6.7. Post-hoc contrasts for the main effect of network on individual-level Spearman spatial correlations between each combination of association type and phase over baseline and resting-state networks overlapping with DMN.

	Control B	Auditory	Medial temporal DMN	Core DMN
Auditory	t(30) = -2.4, p = .208	-	-	-
Medial temporal DMN	t(29) = -1.5, p > 1	t(30) = -0.1, p > 1	-	-
Core DMN	**t(27) = 6.8, p < .001***	**t(28) = 7.8, p < .001***	**t(27) = 6.2, p < .001***	-
Fronto-temporal DMN	**t(30) = -7.3, p < .001***	**t(31) = -7.2, p < .001***	**t(30) = -4.4, p = .001***	**t(28) = -9.2, p < .001***

Note: post-hoc contrasts Bonferroni-corrected for ten comparisons. * reflects a significant result. DMN = default mode network.[37]

Supplementary Table 6.8. Post-hoc contrasts for the main effect of network on individual-level Spearman spatial correlations between each combination of association type and phase over baseline and functional control networks.

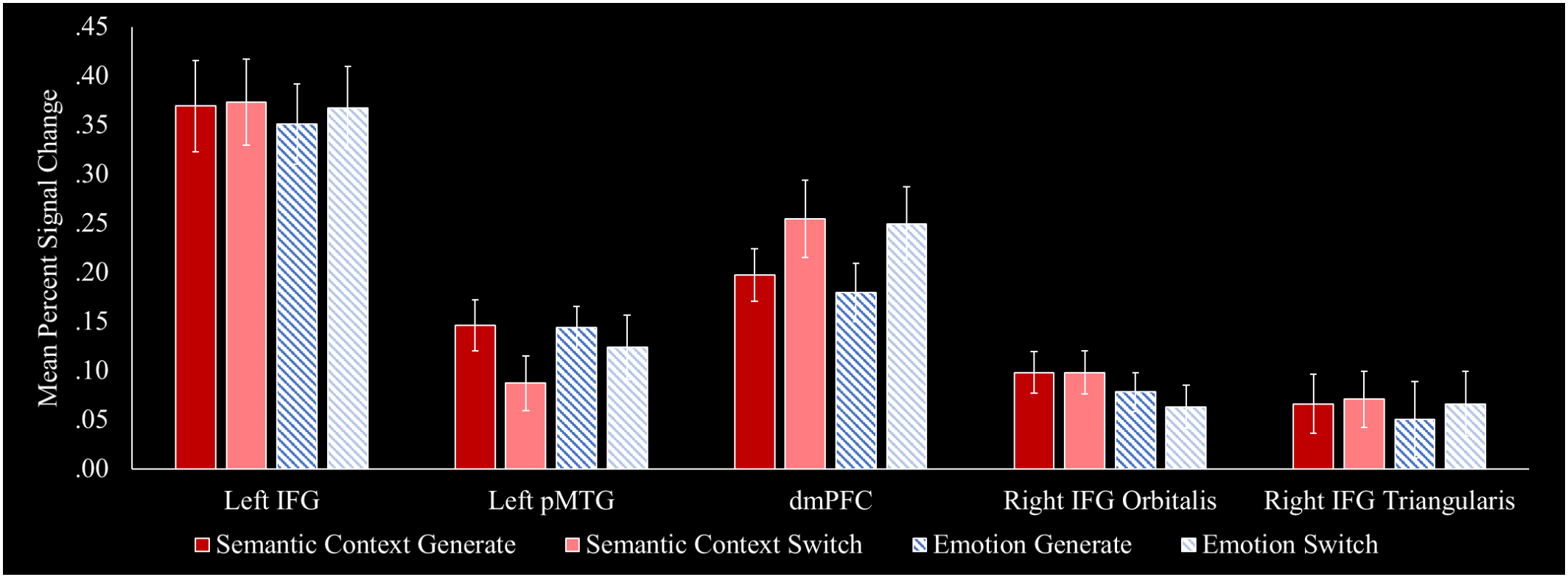
	DMN	DMN & SCN	SCN	SCN & MDN
DMN & SCN	**t(30) = -12.1, p < .001***	-	-	-
SCN	**t(30) = -18.2, p < .001***	**t(31) = 3.3, p = .022***	-	-
SCN & MDN	**t(30) = -9.4, p < .001***	t(31) = 0.6, p > 1	t(31) = -2.4, p = .243	-
MDN	**t(30) = -12.4, p < .001***	**t(31) = -6.0, p < .001***	**t(31) = -9.0, p < .001***	**t(31) = -9.4, p < .001***

Note: post-hoc contrasts Bonferroni-corrected for ten comparisons. * reflects a significant result. DMN = default mode network, SCN = semantic control network, MDN = multiple demand network.[38]

[37] The assumption of normality was violated for both the auditory network, medial temporal DMN, and core DMN. While parametric contrasts are used in this table, non-parametric equivalents elicited the same outcomes: control B = auditory [Z = -2.3, p = .208], control B – medial temporal DMN [Z = -1.3, p > 1], control B – core DMN [Z = -4.5, p < .001], auditory – medial temporal DMN [Z = -0.3, p > 1], auditory = core DMN [Z = -4.6, p < .001], auditory – fronto-temporal DMN [Z = -4.8, p < .001], medial temporal DMN – core DMN [Z = -4.4, p < .001], medial temporal DMN – fronto-temporal DMN [Z = -3.4, p = .008], core DMN – fronto-temporal DMN [Z = -4.7, p < .001].

[38] Assumption of normality was violated for DMN. Non-parametric tests elicit the same outcomes: DMN – DMN & SCN [Z = -4.9, p < .001], DMN – SCN [Z = -4.7, p < .001], DMN – SCN & MDN [Z = -4.8, p < .001], DMN – MDN [Z = -4.9, p < .001].

Semantic Control Network Peak Analysis



Supplementary Figure 6.6. Mean percent signal change in the five peaks of the Jackson (2021) meta-analytic Semantic Control Network map, for each combination of association type (emotion or semantic context) and phase (generate or switch) over baseline. Error bars reflect one standard error. Analysis run using the Featquery function of FSL, with binarised 5mm spheres around each peak, based on voxel coordinates, used as regions of interest. IFG = inferior frontal gyrus, pMTG = posterior middle temporal gyrus, dmPFC = dorsomedial prefrontal cortex. N = 32.

Supplementary Table 6.9. A repeated measures ANOVA observing main effects and interactions of association type, phase, and network for the five peaks of the semantic control network.

Effect	Result
Association type	$F(1, 28) = 0.9$, $p = .354$, $\eta_p^2 = .03$
Phase	$F(1, 28) = 0.2$, $p = .623$, $\eta_p^2 = .01$
Peak	**$F(4, 112) = 19.9$, $p < .001$, $\eta_p^2 = .42$***
Association type x Phase	$F(1, 28) = 0.3$, $p = .617$, $\eta_p^2 = .01$
Association type x Peak	$F(4, 112) = 1.0$, $p = .392$, $\eta_p^2 = .04$
Phase x Peak	**$F(4, 112) = 5.3$, $p < .001$, $\eta_p^2 = .16$***
Association type x Phase x Peak	$F(2.8, 80.4) = 1.4$, $p = .258$, $\eta_p^2 = .05$

Note: * reflects a significant result.

The main effect of network is parsed below in Supplementary Table 6.10. These tests are Bonferroni-corrected for ten comparisons. This reveals significantly higher overall activation in left IFG than in any other peak. In turn, dmPFC shows higher overall activation than either right IFG cluster. No other differences between peaks were observed.

Supplementary Table 6.10. Post-hoc tests for the main effect of semantic control network peak on mean percent signal change.

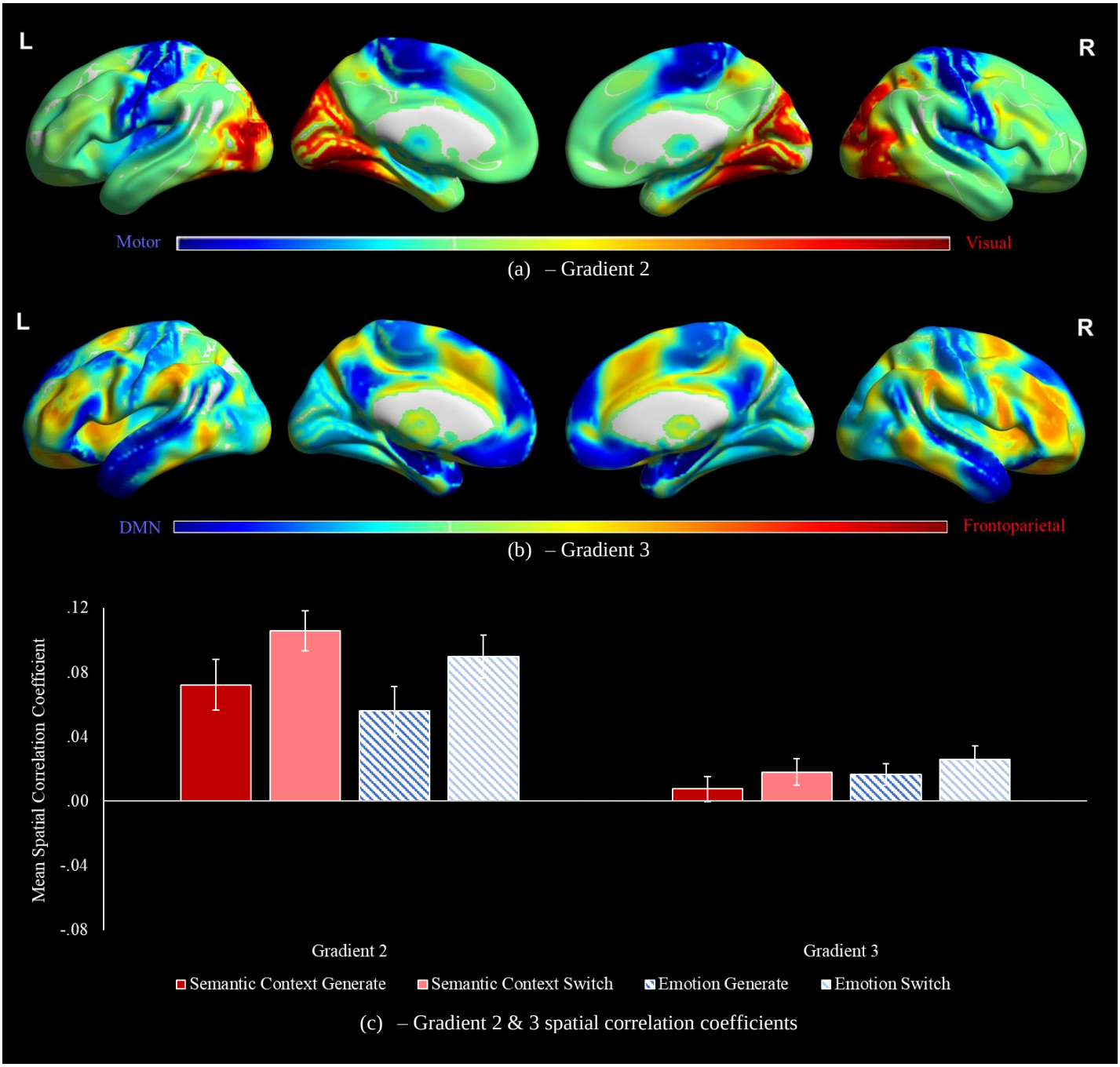
	Left IFG	Left pMTG	dmPFC	Right IFG orbitalis
Left IFG	-	-	-	-
Left pMTG	**$t(29) = 6.5$, $p < .001$***	-	-	-
dmPFC	**$t(29) = 3.4$, $p = .021$***	$t(29) = -3.0$, $p = .050$	-	-
Right IFG orbitalis	**$t(30) = 6.5$, $p < .001$***	$t(30) = 0.9$, $p > 1$	**$t(30) = 3.6$, $p = .010$***	-
Right IFG triangularis	**$t(30) = 6.2$, $p < .001$***	$t(30) = 1.2$, $p > 1$	**$t(30) = 3.6$, $p = .011$***	$t(31) = 0.7$, $p > 1$

Note: * reflects a significant different. IFG = inferior frontal gyrus, pMTG = posterior middle temporal gyrus, dmPFC = dorsomedial prefrontal cortex.[39]

Post-hoc comparisons for the phase by peak interaction are Bonferroni-corrected for five comparisons. While no contrast survives correction, left pMTG trends towards being more implicated in the *generate* phase than the *switch* phase [$t(30) = 2.7$, $p = .061$]. Conversely, dmPFC trends towards being more implicated in the *switch* phase than the *generate* phase [$t(30) = -2.5$, $p = .083$]. Highly non-significant differences between phases was observed for the left IFG [$t(30) = -0.7$, $p > 1$], right IFG orbitalis [$t(31) = 1.0$, $p > 1$], and right IFG triangularis [$t(31) = -0.5$, $p > 1$].

[39] Assumption of normality violated for pMTG and dmPFC. However, non-parametric tests elicit the same results: pMTG – left IFG [$Z = -4.5$, $p < .001$], pMTG – dmPFC [$Z = -2.6$, $p = .104$], pMTG – right IFG orbitalis [$Z = -1.1$, $p > 1$], pMTG – right IFG triangularis [$Z = -1.1$, $p > 1$], dmPFC – left IFG [$Z = -2.9$, $p = .041$], dmPFC – right IFG orbitalis [$Z = -3.3$, $p = .011$], dmPFC – right IFG triangularis [$Z = -3.3$, $p = .009$].

Gradients 2 & 3 Analysis

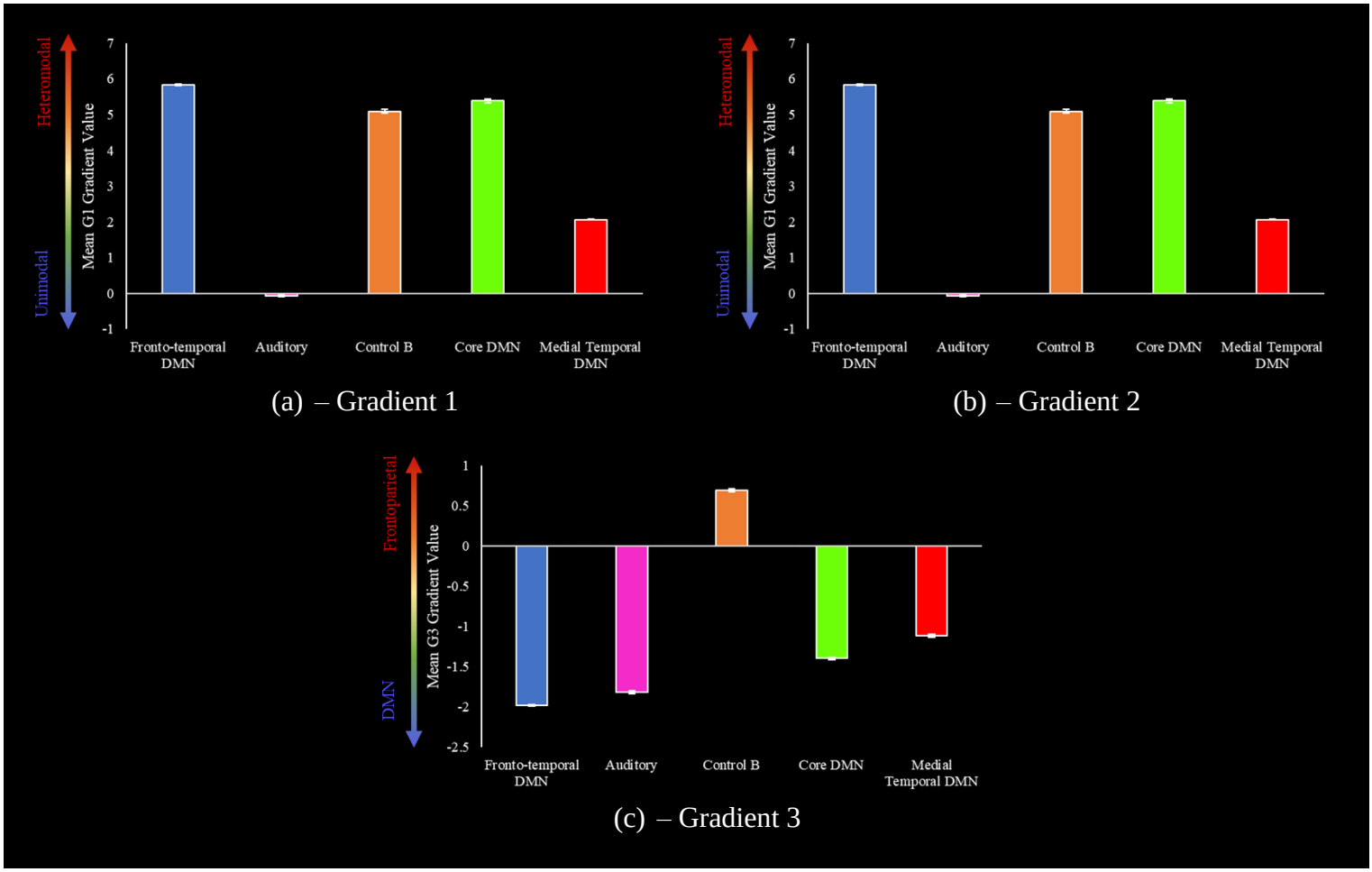


Supplementary Figure 6.7. Visualisations of (a) gradient 2 and (b) gradient 3. (c) Mean spatial correlation coefficients between each gradient and unthresholded contrasts of each association type and phase combination over implicit baseline. Error bars reflect one standard error.

For gradient 2, we observed a main effect of association type [$F(1, 31) = 4.5$, $p = .041$, $\eta_p^2 = .13$] and of phase [$F(1, 31) = 18.4$, $p < .001$, $\eta_p^2 = .37$], but no association type by phase interaction

[F(1, 31) < 0.1, p = .981, η_p^2 < .01]. The observed main effects reflect that *semantic context* associations were higher than *emotion* associations, while the *switch* phase was higher than the *generate* phase. Given their focus on scene construction, greater importance of visual information for *semantic context* associations is intuitive. The phase main effect likely suggests a relative importance of motor information for the *generate* phase, compared to the *switch* phase.

For gradient 3, we observed a significant main effect of phase [F(1, 31) = 7.2, p = .012, η_p^2 = .19], but no main effect of association type [F(1, 31) = 2.9, p = .097, η_p^2 = .09] or association type by phase interaction [F(1, 31) = 0.1, p = .764, η_p^2 < .01]. The main effect of phase reflects that the *switch* phase was higher than the *generate* phase. This suggests greater reliance on frontoparietal control regions for the *switch* phase. Indeed, aspects of the control B network, implicated in clusters associated with the *switch* phase, sit further towards the frontoparietal control end of this gradient while other DMN-allied networks sit towards the lower end (see Supplementary Figure 6.8c).



Supplementary Figure 6.8. Mean gradient values for each resting-state DMN overlap network, for (a) gradient 1, (b) gradient 2, and (c) gradient 3. Error bars reflect one standard error. DMN = default mode network, G1 = gradient 1, G2 = gradient 2, G3 = gradient 3.

Analysis of Contiguous Clusters within the Switch over Generate Contrast

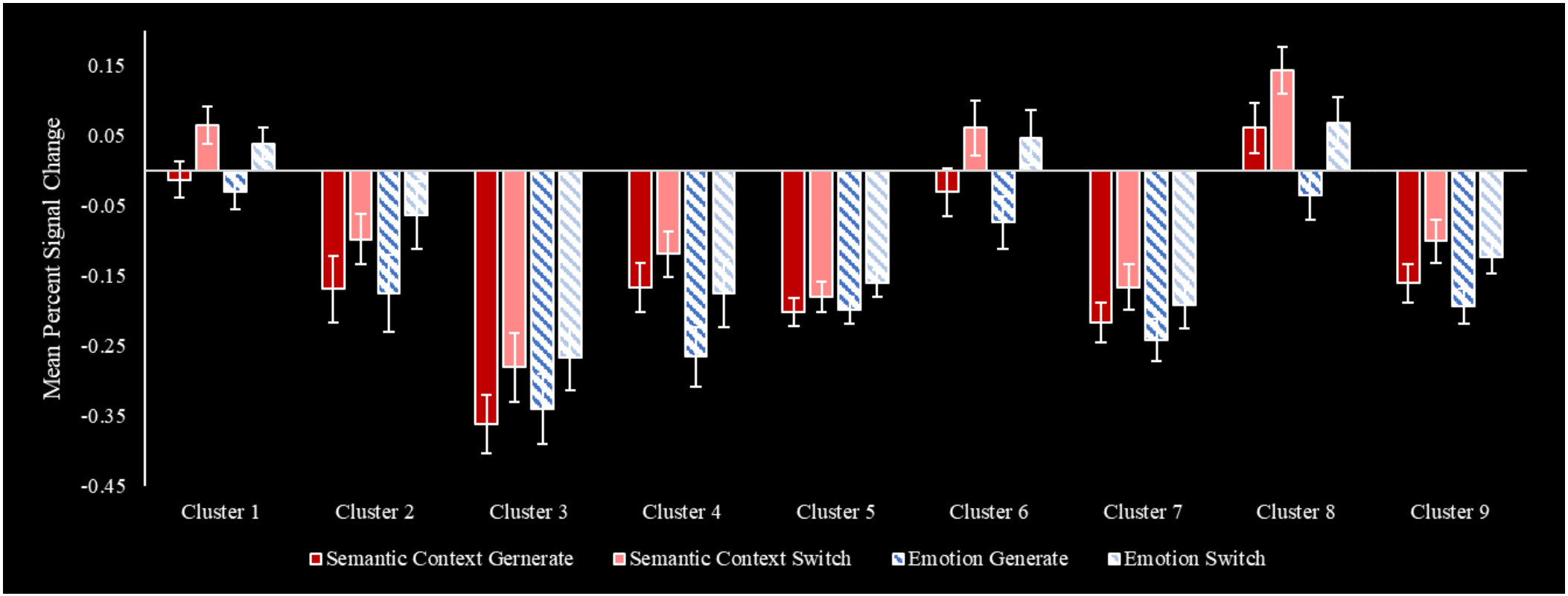
To test whether effects of association type on the effect of *switch* were being masked, we separated the thresholded contrast of *switch* over *generate* into all its separate contiguous clusters. There were nine clusters in total. The location and size of these are characterised in Supplementary Table 6.11.

Supplementary Table 6.11. Contiguous clusters that comprise the thresholded (Z > 3.1) switch over generate contrast, including characterisation of regions implicated, size in voxels, and location in MNI coordinates.

	Cluster Number								
	1	2	3	4	5	6	7	8	9
Regions	R cerebellum	L AG L pSMG L superior LOC	R AG R pSMG R superior LOC	Precuneus	R pMTG R aMTG R pSTG R pITG	L frontal pole	R SFG R MFG R frontal pole L SFG L frontal pole	L SFG L MFG L frontal pole	R frontal pole R OFC
Size (voxels)	222	237	345	360	480	626	772	1099	1104
Peak (MNI)	(42, -68, -45)	(-40, -70, 44)	(48, -54, 48)	(-6, -62, 50)	(58, -12, -27)	(-30, 62, -2)	(12, 32, 54)	(-38, 20, 44)	(15, 41, -23)

Note: R = right, L = left, AG = angular gyrus, pSMG = posterior supramarginal gyrus, LOC = lateral occipital cortex, pMTG = posterior middle temporal gyrus, aMTG = anterior middle temporal gyrus, pSTG = posterior superior temporal gyrus, pITG = posterior inferior temporal gyrus, SFG = superior frontal gyrus, MFG = middle frontal gyrus, OFC = orbitofrontal cortex.

We used binarised versions of each cluster as ROIs in Featquery, interrogating them relative to each combination of association type and phase over implicit baseline. Doing so may reveal whether any of these clusters were particularly important for either association type. Outliers were removed at each level by identifying data points three standard deviations above or below the group mean. The resulting data can be seen in Supplementary Figure 6.9. Results of a repeated measures ANOVA run on this data can be seen in Supplementary Table 6.12.



Supplementary Figure 6.9. Mean percent signal change in contiguous clusters that comprise the overall thresholded (Z > 3.1) switch over generate contrast for each combination of association type and phase over implicit baseline. Error bars reflect one standard error. N = 32.

Supplementary Table 6.12. Repeated measures ANOVA for effects of association type and phase on contiguous switch over generate clusters.

Effect	Result
Association type	**F(1, 29) = 4.6, *p* = .041, np2 = .14***
Phase	**F(1, 29) = 25.6, *p* < .001, np2 = .47***
Cluster	**F(5.3, 153.6) = 30.6, *p* < .001, np2 = .51***
Association type by Phase	F(1, 29) = 2.3, *p* = .137, np2 = .08
Association type by Cluster	**F(2.5, 73.0) = 4.2, *p* = .013, np2 = .13***
Phase by Cluster	**F(4.7, 135.3) = 4.3, *p* = .002, np2 = .13***
Association type by Phase by Cluster	F(4.9, 142.2) = 1.2, *p* = .296, np2 = .04

Note: * reflects a significant effect. Assumption of sphericity violated for 'cluster'. Greenhouse-Geisser adjustment applied accordingly.

The significant effect of association type reflects more overall activation for *semantic context* than *emotion* associations, while the main effect of phase reflects more overall activation for the *switch* phase than the *generate* phase. The main effect of cluster was not of interest here, and as such post-hoc tests of this effect are not reported. Post-hoc contrasts for the observed interactions can be seen in Supplementary Table 6.13. As seen here, two clusters activated significantly more for the *semantic context* than the *emotion* condition. Unsurprisingly, given that these clusters came from the *switch* over *generate* contrast, all clusters except two activate significantly more for the *switch* than *generate* phase (although the two which do not meet significance after correction are marginal). These results do imply a slight preference of *switch* clusters for *semantic context* associations. However, the absence of any interaction between association type and phase here is consistent with overall evidence of parity in *switch* effects across association types.

Supplementary Table 6.13. Post-hoc contrasts for significant switch over generate cluster interactions.

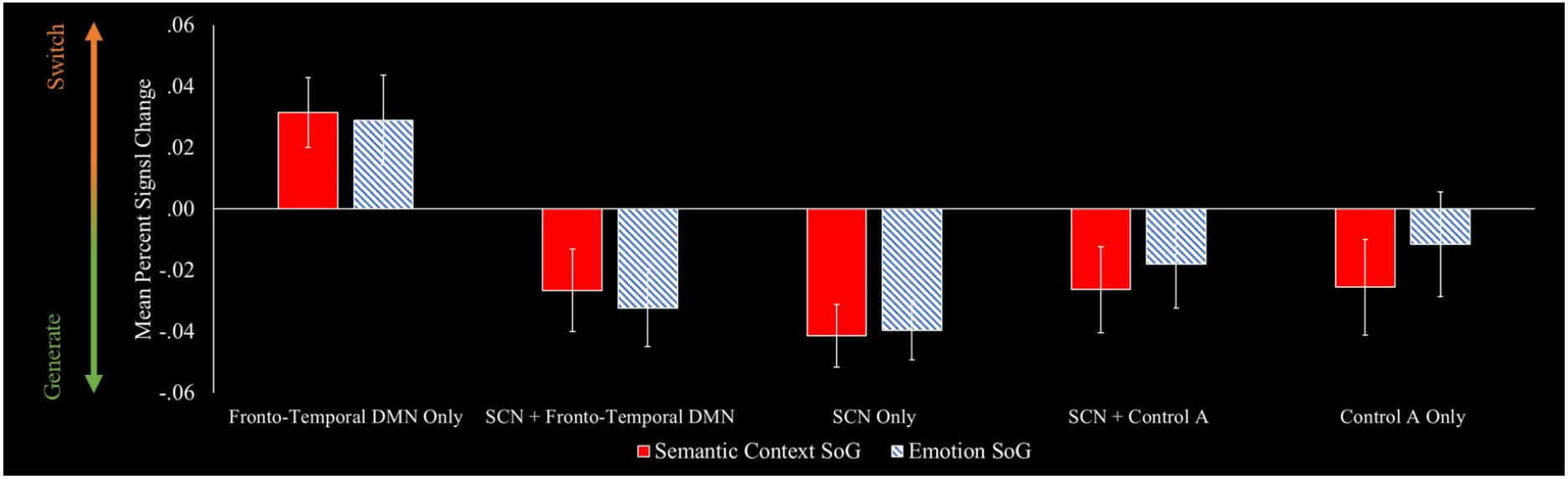
Cluster	Association type by cluster	Phase by cluster
1	t(31) = 1.5, *p* > 1	**t(31) = -4.9, *p* < .001***
2	t(31) = -0.3, *p* > 1[40]	**t(31) = -4.2, *p* = .002***
3	t(30) = -0.9, *p* > 1	t(30) = -2.8, *p* = .086
4	**t(30) = 4.8, *p* < .001***	**t(30) = -3.8, *p* = .006***
5	t(31) = -0.9, *p* > 1	t(31) = -2.9, *p* = .055
6	t(31) = 1.3, *p* > 1	**t(31) = -5.2, *p* < .001***[41]
7	t(31) = 1.5, *p* > 1	**t(31) = -3.2, *p* = .029***
8	**t(31) = 5.8, *p* < .001***	**t(31) = -5.5, *p* < .001***
9	t(31) = 2.1, *p* = .435	**t(31) = -5.4, *p* < .001***

Note: * reflects a significant difference.

[40] Assumption of normality violated, non-parametric test elicits the same result: Z = -3.7, *p* = .002*
[41] Assumption of normality violated, non-parametric test elicits the same result: Z = -4.2, *p* < .001*

SCN and Yeo Overlap Analysis

We first identified networks from the Yeo et al. (2011) 17-network parcellation which accounted for the highest percentage of the full SCN. These were the control A network (30%) and fronto-temporal DMN (23%). We created five mutually exclusive ROIs, capturing voxels lying exclusively within SCN and each of these two networks, as well as voxels falling both within SCN and either network. These ROIs were interrogated in Featquery, observing mean percent signal change in the *switch* over *generate* contrast, separately for *semantic context* and *emotion* associations. Outliers were removed at each level by identifying data points three standard deviations above or below the group mean. The resulting data can be observed in Supplementary Figure 6.10.



Supplementary Figure 6.10. Mean percent signal change in SCN and Yeo 17-parcellation networks showing maximum overlap with SCN for the switch of generate effect across association types. Error bars reflect one standard error. SCN = semantic control network, DMN = default mode network. N = 32.

A repeated measures ANOVA on this data provided evidence of a main effect of network [$F(2.5, 70.3) = 18.1$, $p < .001$, $\eta_p^2 = .39$], but no effect of association type [$F(1, 28) < 0.1$, $p = .977$, $\eta_p^2 < .01$] and no network by association type interaction [$F(2.3, 63.3) = 1.8$, $p = .177$, $\eta_p^2 = .06$]. Post-hoc contrasts parsing this main effect of network can be seen in Supplementary Table 6.14.

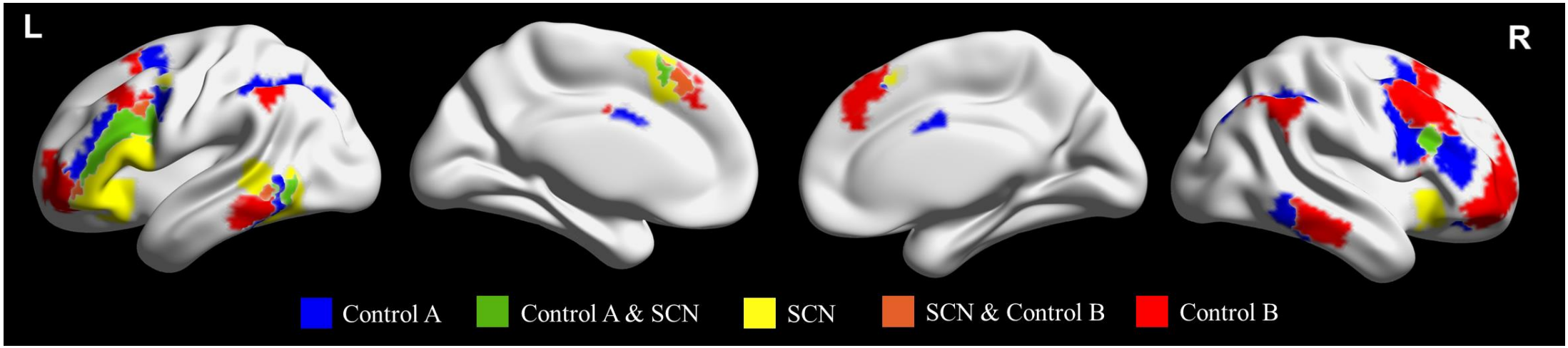
Supplementary Table 6.14. Post-hoc contrasts for the main effect of network on mean percent signal change for networks comprising the SCN for the switch over generate contrast.

	Fronto-temporal DMN only	Fronto-temporal DMN and SCN	SCN only	Control A and SCN
Fronto-temporal DMN and SCN	**$t(29) = 6.7$, $p < .001$***	-	-	-
SCN only	**$t(29) = 7.6$, $p < .001$***	$t(30) = 1.8$, $p = .774$	-	-
Control A and SCN	**$t(29) = 4.4$, $p = .001$***	$t(30) = -0.8$, $p > 1$	$t(30) = -2.7$, $p = .104$	-
Control A only	**$t(29) = 4.2$, $p = .003$***	$t(30) = -0.5$, $p > 1$	$t(29) = -2.1$, $p = .450$	$t(29) = 0.3$, $p > 1$

Note: contrasts corrected for ten comparisons. * reflects a significant result.

These results suggest a relative preference for voxels only within the fronto-temporal DMN compared to all other networks, but no other differences between networks. Importantly, this analysis suggests no impact of association type on this pattern of results, suggesting the involvement of SCN overlap networks in the *switch* over *generate* contrast is consistent across *semantic context* and *emotion* associations.

SCN and Control Network Overlap



Supplementary Figure 6.11. Overlap between SCN, taken from Jackson (2021), and control A and control B, taken from the Yeo et al. (2011) 17-network parcellation. SCN = semantic control network.

The percentage of control A that falls within SCN (16.8%; 1,489/8,848 voxels) is the larger than the percentage of control B that falls within SCN (5.1%; 508/9,951 voxels). Conversely, a larger percentage of SCN falls within control A (23.4%; 1,489/6,364 voxels) than within control B (8.0%; 508/6,364 voxels).

References

Agosta, F., Henry, R. G., Migliaccio, R., Neuhaus, J., Miller, B. L., Dronkers, N. F., Brambati, S. M., Filippi, M., Ogar, J. M., Wilson, S. M., & Gorno-Tempini, M. L. (2010). Language networks in semantic dementia. *Brain, 133*(1), 286-299. https://doi.org/10.1093/brain/awp233.

Almairac, F., Herbert, G., Moritz-Gasser, S., Menjot de Champfleur, N., & Duffau, H. (2015). The left inferior fronto-occipital fasciculus subserves language semantics: A multilevel lesion study. *Brain Structure and Function, 220,* 1983-1995. https://doi.org/10.1007/s00429-014-0773-1.

Andreottia, J., Dierks, T., Wahlund, L-O., & Grieder, M. (2017). Diverging progression of network disruption and atrophy in Alzheimer's disease and semantic dementia. *Journal of Alzheimer's Disease, 55,* 981-993. https://doi.org/10.3233/JAD-160571.

Andrews-Hanna, J. R., & Grilli, M. D. (2021). Mapping the imaginative mind: Charting new paths forward. *Current Directions in Psychological Science, 30*(1), 82-89. https://doi.org/10.1177/0963721420980753.

Andrews-Hanna, J. R., Smallwood, J., & Spreng, R. N. (2014). The default network and self-generated thought: component processes, dynamic control, and clinical relevance. *Annals of the New York Academy of Sciences, 1316*(1), 29-52. https://doi.org/10.1111/nyas.12360.

Anwyl-Irvine, A. L., Massonnié, J., Flitton, A., Kirkham, N., & Evershed, J. K. (2020). Gorilla in our midst: An online behavioral experiment builder. *Behavior Research Methods, 52,* 388-407. https://doi.org/10.3758/s13428-019-01237-x.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2014). Inhibition and the right inferior frontal cortex: One decade on. *Trends in Cognitive Sciences, 18*(4), 177-185. https://doi.org/10.1016/j.tics.2013.12.003.

Arthurs, O. J., & Boniface, S. (2002). How well do we understand the neural origins of the fMRI BOLD signal? *Trends in Neurosciences, 25*(1), 27-31. https://doi.org/10.1016/S0166-2236(00)01995-0.

Avants, B. B., Tustison, N. J., Song, G., Cook, P. A., Klein, A., & Gee, J. C. (2011). A reproducible evaluation of ANTs similarity metric performance in brain image registration. *NeuroImage, 54*(3), 2033-2044. https://doi.org/10.1016/j.neuroimage.2010.09.025.

Avants, B. B., Tustison, N. J., Stauffer, M., Song, G., Wu, B., & Gee, J. C. (2014). The Insight ToolKit image registration framework. *Frontiers in Neuroscience, 8*, 44. https://doi.org/10.3389/fninf.2014.00044.

Aviezer, H., Hassin, R. R., Ryan, J., Grady, C., Susskind, J., Anderson, A., Moscovitch, M., & Bentin, S. (2008). Angry, disgusted, or afraid?: Studies on the malleability of emotion perception. *Psychological Science, 19*(7), 724-731. https://doi.org/10.1111/j.1467-9280.2008.02148.x.

Badre, D., Poldrack, R. A., Paré-Blagoev, E. J., Insler, R. Z., & Wagner, A. D. (2005). Dissociable controlled retrieval and generalized selection mechanisms in ventrolateral prefrontal cortex. *Neuron, 47*(6), 907-918. https://doi.org/10.1016/j.neuron.2005.07.023.

Badre, D., & Wagner, A. D. (2007). Left ventrolateral prefrontal cortex and the cognitive control of memory. *Neuropsychologia, 45*(13), 2883–2901. https://doi.org/10.1016/j.neuropsychologia.2007.06.015.

Barredo, J., Öztekin, I., & Badre, D. (2015). Ventral fronto-temporal pathway supporting cognitive control of episodic memory retrieval. *Cerebral Cortex, 25*(4), 1004-1019. https://doi.org/10.1093/cercor/bht291.

Barrett, L. F. (2006). Solving the emotion paradox: categorization and the experience of emotion. *Personality and Social Psychology Review, 10*(1), 20-46. https://doi.org/10.1207/s15327957pspr1001_2.

Barrett, L. F., Lindquist, K. A., & Gendron, M. (2007). Language as context for the perception of emotion. *Trends in Cognitive Science, 11*(8), 327-332. https://doi.org/10.1016/j.tics.2007.06.003.

Barsalou, L. W. (1999). Perceptual symbol systems. *Brain and Behavioural Sciences, 22*(4), 577-609. https://doi.org/10.1017/s0140525x99002149.

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. *Journal of Statistical Software, 67*(1), 1-48. https://doi.org/10.18637/jss.v067.i01.

Bates, E., Wilson, S. M., Saygin, A. P., Dick, F., Sereno, M. I., Knight, R. T., & Dronkers, N. F. (2003). Voxel-based lesion-symptom mapping. *Nature Neuroscience, 6*, 448-450. https://doi.org/10.1038/nn1050.

Becker, M., Sommer, T., & Kühn, S. (2020). Inferior frontal gyrus involvement during search and solution in verbal creative problem solving: A parametric fMRI study. *NeuroImage, 206*, 116294. https://doi.org/10.1016/j.neuroimage.2019.116294.

Behzadi, Y., Restom, K., Liau, J., & Liu, T. T. (2007). A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. *NeuroImage, 37*(1), 90-101. https://doi.org/10.1016/j.neuroimage.2007.04.042.

Bell, A., Fairbrother, M., & Jones, K. (2019). Fixed and random effects models: Making an informed choice. *Quality & Quantity, 53*, 1051-1074. https://doi.org/10.1007/s11135-018-0802-x.

Benoit, R. G., & Anderson, M. C. (2012). Opposing mechanisms support the voluntary forgetting of unwanted memories. *Neuron, 76*(2), 450-4650. https://doi.org/10.1016/j.neuron.2012.07.025.

Bertoux, M., Duclos, H., Caillaud, M., Segobin, S., Merck, C., de La Sayette, V., Belliard, S., Desranges, B., Eustache, F., & Laisney, M. (2020). When affect overlaps with concept: emotion recognition in semantic variant of primary progressive aphasia. *Brain, 143*, 3850-3864. https://doi.org/10.1093/brain/awaa313.

Binder, J. R., & Desai, R. H. (2011). The neurobiology of semantic memory. Trends in Cognitive Sciences, 15(11), 527-536. https://doi.org/10.1016/j.tics.2011.10.001.

Binney, R. J., Embleton, K. V., Jefferies, E., Parker, G. J., & Lambon Ralph, M. A. (2010). The ventral and inferolateral aspects of the anterior temporal lobe are crucial in semantic memory: Evidence from a novel direct comparison of distortion-corrected fMRI, rTMS, and semantic dementia. *Cerebral Cortex, 20*(11), 2728–2738. https://doi.org/10.1093/cercor/bhq019.

Binney, R. J., Hoffman, P., & Lambon Ralph, M. A. (2016). Mapping the multiple graded contributions of the anterior temporal lobe representational hub to abstract and social concepts: evidence from distortion-corrected fMRI. *Cerebral Cortex, 26*(11), 4227-4241. https://doi.org/10.1093/cercor/bhw260.

Binney, R. J., Parker, G. J. M., & Lambon Ralph, M. A. (2012). Convergent connectivity and graded specialization in the rostral human temporal lobe as revealed by diffusion-weighted imaging probabilistic tractography. *Journal of Cognitive Neuroscience, 24*(10), 1998-2014. https://doi.org/10.1162/jocn_a_00263.

Binney, R. J., & Ramsey, R. (2020). Social semantics: The role of conceptual knowledge and cognitive control in a neurobiological model of the social brain. *Neuroscience and Biobehavioral Reviews, 112,* 28-38. https://doi.org/10.1016/j.neubiorev.2020.01.030.

Bird, H., Franklin, S., & Howard, D. (2001a). Age of acquisition and imageability ratings for a large set of words, including verbs and function words. *Behavior Research Methods, Instruments, & Computers, 33*, 73–79. https://doi.org/10.3758/BF03195349.

Bird, H., Franklin, S., & Howard, D. (2001b). ratings.csv. Retrieved April 4, 2020 from Springer Link: https://link.springer.com/article/10.3758%2FBF03195349#SecESM1.

Bodini, B., Cercignani, M., Khaleeli, Z., Miller, D. H., Ron, M., Penny, S., Thompson, A. J., & Ciccarelli, O. (2013). Corpus callosum damage predicts disability progression and cognitive dysfunction in primary-progressive MS after five years. *Human Brain Mapping, 34,* 1163-1172. https://doi.org/10.1002/hbm.21499.

Boes, A. D. (2021). Lesion network mapping: Where do we go from here? *Brain, 144(1),* e5. https://doi.org/10.1093/brain/awaa350.

Bonner, M. F., Peelle, J. E., Cook, P. A., & Grossman, M. (2013). Heteromodal conceptual processing in the angular gyrus. *NeuroImage, 71,* 175-186. https://doi.org/10.1016/j.neuroimage.2013.01.006.

Borden, N. M. (2006). *3D angiographic atlas of neurovascular anatomy and pathology*. Cambridge: Cambridge University Press.

Botvinick, M., & Braver, T. (2015). Motivation and cognitive control: from behavior to neural mechanism. *Annual Review of Psychology, 66,* 83-113. https://doi.org/10.1146/annurev-psych-010814-015044.

Bowen, H. J., Ford, J. H., Grady, C. L., & Spaniol, J. (2020). Frontostriatal functional connectivity supports reward-enhanced memory in older adults. *Neurobiology of Aging, 90,* 1-12. https://doi.org/10.1016/j.neurobiolaging.2020.02.013.

Bowren, M., Bruss, J., Manzel, K., Edwards, D., Liu, C., Corbetta, M., Tranel, D., & Boes, A. D. (2022). Post-stroke outcomes predicted from multivariate lesion-behaviour and lesion network mapping. *Brain*, awac010. https://doi.org/10.1093/brain/awac010.

Bozeat, S., Gregory, C. A., Lambon Ralph, M. A., & Hodges, J. R. (2000). Which neuropsychiatric and behavioural features distinguish frontal and temporal variants of frontotemporal dementia from Alzheimer's disease? *Journal of Neurology, Neurosurgery, and Psychiatry, 69*(2), 178-186. https://doi.org/10.1136/jnnp.69.2.178.

Bozeat, S., Lambon Ralph, M. A., Patterson, K., Garrard, P., & Hodges, J. R. (2000). Non-verbal semantic impairment in semantic dementia. *Neuropsychologia, 9*, 1207-1215. https://doi.org/10.1016/s0028-3932(00)00034-8.

Braem, S., & Egner, T. (2018). Getting a grip on cognitive flexibility. *Current Directions in Psychological Science, 27*(6), 470-476. https://doi.org/10.1177/0963721418787475.

Braga, R. M., & Buckner, R. L. (2017). Parallel interdigitated distributed networks within the individual estimated by intrinsic functional connectivity. *Neuron, 95*(2), 457-471. https://doi.org/10.1016/j.neuron.2017.06.038.

Braunstein, L. M., Gross, J. J., & Ochsner, K. N. (2017). Explicit and implicit emotion regulation: A multi-level framework. *Social Cognitive and Affective Neuroscience, 12*(10), 1545-1557. https://doi.org/10.1093/scan/nsx096.

Brooks, J. A., & Freeman, J. B. (2018). Conceptual knowledge predicts the representational structure of facial emotion perception. *Nature Human Behaviour, 2,* 581-591. https://doi.org/10.1038/s41562-018-0376-6.

Brown, C. A., Schmitt, F. A., Smith, C. D., & Gold, B. T. (2019). Distinct patterns of default mode and executive control network circuitry contribute to present and future executive function in older adults. *NeuroImage, 195,* 320-332. https://doi.org/10.1016/j.neuroimage.2019.03.073.

Buckner, R. L. (2013). The cerebellum and cognitive function: 25 years of insight from anatomy and neuroimaging. *Neuron, 80*(3), 807-815. https://doi.org/10.1016/j.neuron.2013.10.044.

Buhle, J. T., Silvers, J. A., Wager, T. D., Lopez, R., Onyemekwu, C., Kober, H., Weber, J., & Ochsner, K. N. (2014). Cognitive reappraisal of emotion: a meta-analysis of human neuroimaging studies. *Cerebral Cortex, 24,* 2981-2990. https://doi.org/10.1093/cercor/bht154.

Burgess, P. W., & Shallice, T. (1997). *The Hayling and Brixton Tests*. Bury St Edmunds: Thames Valley Test Company.

Camilleri, J. A., Müller, V. I., Fox, P., Laird, A. R., Hoffstaedter, F., & Kalenscher, T. (2018). Definition and characterization of an extended multiple-demand network. *NeuroImage, 165,* 138-147. https://doi.org/10.1016/j.neuroimage.2017.10.020.

Capa, R. L., Bouquet, C. A., Dreher, J-C., & Dufor, A. (2013). Long-lasting effects of performance-contingent unconscious and conscious reward incentives during cued task-switching. *Cortex, 49,* 1943-1954. https://doi.org/10.1016/j.cortex.2012.05.018.

Caramazza, A., & McCloskey, M. (1988). The case for single-patient studies. *Cognitive Neuropsychology, 5*(5), 517-528. https://doi.org/10.1080/02643298808253271.

Carroll, N., C., & Young, A. W. (2005). Priming of emotion recognition. *Quarterly Journal of Experimental Psychology, 58A*(7), 1173-1197. https://doi.org/10.1080/02724980443000539.

Catani, M., & Mesulam, M. (2008). The arcuate fasciculus and the disconnection theme in language and aphasia: History and current state. *Cortex, 44*(8), 953-961. https://doi.org/10.1016/j.cortex.2008.04.002.

Catricalà, E., Della Rosa, P. A., Plebani, V., Vigliocco, G., & Cappa, S. F. (2014). Abstract and concrete categories? Evidences from neurodegenerative diseases. *Neuropsychologia, 64,* 271-281. https://doi.org/10.1016/j.neuropsychologia.2014.09.041.

Celeghin, A., Diano, M., Bagnis, A., Viola, M., & Tamietto, M. (2017). Basic emotions in human neuroscience: Neuroimaging and beyond. *Frontiers in Psychology, 8,* 1432. https://doi.org/10.3389/fpsyg.2017.01432.

Chapman, C. A., Hasan, O., Schulz, P. E., & Martin, R. C. (2020). Evaluating the distinction between semantic knowledge and semantic access: Evidence from semantic dementia and comprehension-impaired stroke aphasia. *Psychonomic Bulletin & Review, 27,* 607-639. https://doi.org/10.3758/s13423-019-01706-6.

Chen, T., Becker, B., Camilleri, J., Wang, L., Yu, S., Eickhoff, S. B., & Feng, C. (2018). A domain-general brain network underlying emotional and cognitive interference processing: Evidence from coordinate-based and functional connectivity meta-analyses. *Brain Structure and Function, 223,* 23813-3840. https://doi.org/10.1007/s00429-018-1727-9.

Chen, Y., Chen, K., Ding, J., Zhang, Y., Yang, Q., Lv, Y., Guo, Q., & Han, Z. (2017). Brain network for the core deficits of semantic dementia: A neural network connectivity-behavior mapping study. *Frontiers in Human Neuroscience, 11,* 267. https://doi.org/10.3389/fnhum.2017.00267.

Chiou, R., Humphreys, G. F., Jung, J., & Lambon Ralph, M. A. (2018). Controlled semantic cognition relies upon dynamic and flexible interactions between the executive 'semantic control' and hub-and-spoke 'semantic representation' systems. *Cortex, 103,* 100-116. https://doi.org/10.1016/j.cortex.2018.02.018.

Chiou, R., Humphreys, G. F., & Lambon Ralph, M. A. (2020). Bipartite functional fractionation within the default network supports disparate forms of internally oriented cognition. *Cerebral Cortex, 30,* 5484-5501. https://doi.org/10.1093/cercor/bhaa130.

Chiou, R., Jefferies, E., Duncan, J., Humphreys, G. F., & Lambon Ralph, M. A. (2022). A middle ground where executive control meets semantics: The neural substrates of semantic control are topographically

sandwiched between the multiple-demand and default-mode systems. *Cerebral Cortex*, bhac358. https://doi.org/10.1093/cercor/bhac358.

Chiou, R., & Lambon Ralph, M. A. (2019). Unveiling the dynamic interplay between the hub- and spoke-components of the brain's semantic system and its impact on human behaviour. *NeuroImage, 199*, 114-126. https://doi.org/10.1016/j.neuroimage.2019.05.059.

Citron, F. M. M., Gray, M. A., Critchley, H. D., Weekes, B. S., & Ferstl, E. C. (2014). Emotional valence and arousal affect reading in an interactive way: Neuroimaging evidence for an approach-withdrawal framework. *Neuropsychologia, 56*, 79-89. https://doi.org/10.1016/j.neuropsychologia.2014.01.002.

Cogdell-Brooke, L., Stampacchia, S., Jefferies, E., Violante, I. R., & Thompson, H. (2020). Consistently inconsistent: Multimodal episodic deficits in semantic aphasia. *Neuropsychologia*, *140*, 107392. https://doi.org/10.1016/j.neuropsychologia.2020.107392.

Cohen, M. S. (1997). Parametric analysis of fMRI data using linear systems methods. *NeuroImage, 6*(2), 93-103. https://doi.org/10.1006/nimg.1997.0278.

Cohen, A. L., Fair, D. A., Dosenbach, N. U. F., Miezin, F. M., Dierker, D., Van Essen, D. C., Schlaggar, B. L., & Petersen, S. E. (2008). Defining functional areas in individual human brains using resting functional connectivity MRI. *NeuroImage, 41*(1), 45-57. https://doi.org/10.1016/j.neuroimage.2008.01.066.

Cohen, A. L., Ferguson, M. A., & Fox, M. D. (2021). Lesion network mapping predicts post-stroke behavioural deficits and improves localization. *Brain, 144*(4), 1-4. https://doi.org/10.1093/brain/awab002.

Coifman, R. R., Lafon, S., Lee, A. B., Maggioni, M., Nadler, B., Warner, F., & Zucker, S. W. (2005). Geometric diffusions as a tool for harmonic analysis and structure definition of data: Diffusion maps. *PNAS, 102*(21), 7426-7431. https://doi.org/10.1073/pnas.0500334102.

Coltheart, M. (1981). The MRC psycholinguistic database. *Quarterly Journal of Experimental Psychology, 33*, 497–505. https://doi.org/10.1080/14640748108400805.

Conn, M. (2003). *Neuroscience in medicine*. Totowa, NJ: Humana Press.

Corbett, F., Jefferies, E., & Lambon Ralph, M. A. (2009). Exploring multimodal semantic control impairments in semantic aphasia: Evidence from naturalistic object use. *Neuropsychologia, 47*, 2721-2731. https://doi.org/10.1016/j.neuropsychologia.2009.05.020.

Corbett, F., Jefferies, E., & Lambon Ralph, M. A. (2011). Deregulated semantic cognition follows prefrontal and temporo-parietal damage: Evidence from the impact of task constraint on nonverbal object use. *Journal of Cognitive Neuroscience, 23(5)*, 1125-1135. https://doi.org/10.1162/jocn.2010.21539.

Cortese, M. J., & Fugett, A. (2004a). Imageability ratings for 3,000 monosyllabic words. *Behavior Research Methods, Instruments, & Computers, 36*, 384–387. https://doi.org/10.3758/BF03195585.

Cortese, M. J., & Fugett, A. (2004b). cortese2004norms.csv. Retrieved April 4, 2020 from Springer Link: https://link.springer.com/article/10.3758%2FBF03195585#SecESM1.

Coutanche, M. N., & Thompson-Schill, S. L. (2015). Creating concepts from converging features in human cortex. *Cerebral Cortex, 25*(9), 2584-2593. https://doi.org/10.1093/cercor/bhu057.

Crawford, J. R., Garthwaite, P. H., & Porter, S. (2010). Point and interval estimates of effect sizes for the case-controls design in neuropsychology: Rationale, methods, implementations, and proposed reporting standards. *Cognitive Neuropsychology, 27*, 245-260. https://doi.org/10.1080/02643294.2010.513967.

Crawford, J. R., & Howell, D. C. (1998). Comparing an individual's test score against norms derived from small samples. *The Clinical Neuropsychologist, 12*, 482-486. https://doi.org/10.1076/clin.12.4.482.7241.

Cristofori, I., Salvi, C., Beeman, M., & Grafman, J. (2018). The effects of expected reward on creative problem solving. *Cognitive, Affective, & Behavioral Neuroscience, 18*, 925-931. https://doi.org/10.3758/s13415-018-0613-5.

Crittenden, B. M., Mitchell, D. J., & Duncan, J. (2015). Recruitment of the default mode network during a demanding act of executive control. *eLife, 4*, e06481. https://doi.org/10.7554/eLife.06481.

Cubillo, A., Makwana, A. B., & Hare, T. A. (2019). Differential modulation of cognitive control networks by monetary reward and punishment. *Social Cognitive and Affective Neuroscience, 14*(3), 305-317. https://doi.org/10.1093/scan/nsz006.

Darwin, C. R. (1872). *The expression of the emotions in man and animals.* London: John Murray.

Davey, J., Cornelissen, P. L., Thompson, H. E., Sonkusare, S., Hallam, G., Smallwood, J., & Jefferies, E. (2015). Automatic and controlled semantic retrieval: TMS reveals distinct contributions of posterior middle temporal gyrus and angular gyrus. *The Journal of Neuroscience, 35*(46), 15230-15239. https://doi.org/10.1523/JNEUROSCI.4705-14.2015.

Davey, J., Thompson, H. E., Hallam, G., Karapanagiotidis, T., Murphy, C., De Caso, I., Krieger-Redwood, K., Bernhardt, B. C., Smallwood, J., & Jefferies, E. (2016). Exploring the role of the posterior middle temporal gyrus in semantic cognition: Integration of anterior temporal lobe with executive processes. *NeuroImage, 137*, 165-177. https://doi.org/10.1016/j.neuroimage.2016.05.051.

Davis, C. J. (2005). N-Watch: A program for deriving neighborhood size and other psycholinguistic statistics. *Behavior Research Methods, 37*(1), 65-70. https://doi.org/10.3758/BF03206399.

Davis, C. P., & Yee, E. (2019). Features, labels, space, and time: Factors supporting Taxonomic relationships in the anterior temporal lobe and thematic relationships in the angular gyrus. *Language, Cognition and Neuroscience, 34*(10), 1347-1357. https://doi.org/10.1080/23273798.2018.1479530.

Del Gaizo, J., Fridriksson, J., Yourganov, G., Hillis, A. E., Hickok, G., Misic, B., Rorden, C., & Bonilha, L. (2017). Mapping language networks using the structural and dynamic brain connectomes. *ENEURO, 4*(5), e0204-17. https://doi.org/10.1523/ENEURO.0204-17.2017.

Di Domenico, S. I., & Ryan, R. M. (2017). The emerging neuroscience of intrinsic motivation: A new frontier in self-determination research. *Frontiers in Human Neuroscience, 11*, 145. https://doi.org/10.3389/fnhum.2017.00145.

Diachek, E., Blank, I., Siegelman, M., Affourtit, J., & Fedorenko, E. (2020). The domain-general multiple demand (MD) network does not support core aspects of language comprehension: A large-scale fMRI investigation. *The Journal of Neuroscience, 40*(23), 4536-4550. https://doi.org/10.1523/JNEUROSCI.2036-19.2020.

Dick, A. S., Garic, D., Graziano, P., & Tremblay, P. (2019). The frontal aslant tract (FAT) and its role in speech, language and executive function. *Cortex, 111,* 148-163. https://doi.org/10.1016/j.cortex.2018.10.015.

Ding, J., Chen, K., Zhang, N., Luo, M., Du, X., Chen, Y., Yang, Q., Lv, Y., Zhang, Y., Song, L., Han, Z., & Guo, Q. (2020). White matter networks dissociate semantic control from semantic knowledge representations: Evidence from voxel-based lesion-symptom mapping. *Cognitive Neuropsychology, 37*(7-8), 450-465. https://doi.org/10.1080/02643294.2020.1767560.

Diveica, V., Koldewyn, K., & Binney, R. J. (2021). Establishing a role of the semantic control network in social cognitive processing: A meta-analysis of functional neuroimaging studies. *NeuroImage, 245,* 118702. https://doi.org/10.1016/j.neuroimage.2021.118702.

Dixon, M. L., De La Vega, A., Mills, C., Andrews-Hanna, J., Spreng, R. N., Cole, M. W., & Christoff, K. (2018). Heterogeneity within the frontoparietal control network and its relationship to the default and dorsal attention networks. *PNAS, 115*(7), E1598-1607. https://doi.org/10.1073/pnas.1715766115.

Døli, H., Helland, T., & Helland, W. A. (2017). Self-reported symptoms of anxiety and depression in chronic stroke patients with and without aphasia. *Aphasiology, 31*(12), 1392-1409. https://doi.org/10.1080/02687038.2017.1280595.

Doyle, C. M., Gendron, M., & Lindquist, K. A. (2021). Language is a unique context for emotion perception. *Affective Science, 2,* 171-177. https://doi.org/10.1016/j.tics.2007.06.003.

Dreisbach, G., & Fischer, R. (2012). The role of affect and reward in the conflict-triggered adjustment of cognitive control. *Frontiers in Human Neuroscience, 6*(342), 1-5. https://doi.org/10.3389/fnhum.2012.00342.

Duncan, J. (2001). An adaptive coding model of neural function in prefrontal cortex. *Nature Reviews Neuroscience, 2,* 820-829. https://doi.org/10.1038/35097575.

Duncan, J. (2010). The multiple-demand (MD) system of the primate brain: mental programs for intelligent behaviour. *Trends in Cognitive Sciences, 14*(4), 172-179. https://doi.org/10.1016/j.tics.2010.01.004.

Ekman, P. (1994). Strong evidence for universals in facial expressions: A reply to Russell's mistaken critique. *Psychological Bulletin, 115*(2), 268-287. https://doi.org/10.1037/0033-2909.115.2.268.

Ekman, P., & Cordaro, D. (2011). What is mean by calling emotions basic. *Emotion Review, 3*(4), 364-370. https://doi.org/10.1177/1754073911410740.

Engen, H. G., & Anderson M. C. (2018). Memory control: A fundamental mechanism of emotion regulation. *Trends in Cognitive Sciences, 22*(11), 982-992. https://doi.org/10.1016/j.tics.2018.07.015.

Enzi, B., de Greck, M., Prösch, U., Tempelmann, C., & Northoff, G. (2009). Is our self nothing but reward? Neuronal overlap and distinction between reward and personal relevance and its relation to human personality. *PLoS ONE, 4*(12), e8429. https://doi.org/10.1371/journal.pone.0008429.

Etzel, J. A., Cole, M. W., Zacks, J. M., Kay, K. N., & Braver, T. S. (2016). Reward motivation enhances task coding in frontoparietal cortex. *Cerebral Cortex, 26*(4), 1647-1659. https://doi.org/10.1093/cercor/bhu327.

Faber, M., & D'Mello, S. K. (2018). How the stimulus influences mind wandering in semantically rich task contexts. *Cognitive Research: Principles and Implications, 3,* 35. https://doi.org/10.1186/s41235-018-0129-0.

Faber, M., Przeździk, I., Fernández, G., Haak, K. V., & Beckmann, C. F. (2019). Overlapping connectivity gradients in the anterior temporal lobe underlie semantic cognition. *BioRxiv*. https://doi.org/10.1101/2020.05.28.121137.

Fang, Y., Wang, X., Zhong, S., Song, L., Han, Z., Gong, G., & Bi, Y. (2018). Semantic representation in the white matter pathway. *PLOS Biology, 16*(4), e2003993. https://doi.org/10.1371/journal. pbio.2003993.

Fedorenko, E. (2014). The role of domain-general cognitive control in language comprehension. *Frontiers in Psychology, 5*(335), 1-10. https://doi.org/10.3389/fpsyg.2014.00335.

Fedorenko, E., Duncan, J., & Kanwisher, N. (2013). Broad domain generality in focal regions of frontal and parietal cortex. *PNAS, 110*(41), 16616-16621. https://doi.org/10.1073/pnas.1315235110.

Fedorenko, E., & Varley, R. (2016). Language and thought are not the same thing: evidence from neuroimaging and neurological patients. *Annals of the New York Academy of Sciences, 1369*(1), 132-153. https://doi.org/10.1111/nyas.13046.

Ferguson, M. A., Lim, C., Cooke, D., Darby, R. R., Wu, O., Rost, N. S., Corbetta, M., Grafman, J., & Fox, M. D. (2019). A human memory circuit derived from brain lesions causing amnesia. *Nature Communications, 10,* 3497. https://doi.org/10.1038/s41467-019-11353-z.

Fernandino, L., Binder, J. R., Desai, R. H., Pendl, S. L., Humphries, C. J., Gross, W. L., Conant, L. L., & Seidenberg, M. S. (2016). Concept representation reflects multimodal abstraction: A framework for embodied semantics. *Cerebral Cortex, 26,* 2018-2034. https://doi.org/10.1093/cercor/bhv020.

Fishman, K. N., Ashbaugh, A. R., Lanctôt, K. L., Cayley, M. L., Herrmann, N., Murray, B. J., Sicard, M., Lien, K., Sahlas, D. J., & Swartz, R. H. (2018). Apathy, not depressive symptoms, as a predictor of semantic and phonemic fluency task performance in stroke and transient ischemic attack. *Journal of Clinical and Experimental Neuropsychology, 40*(5), 449-461. https://doi.org/10.1080/13803395.2017.1371282.

Fornito, A., Zalesky, A., & Breakspear, M. (2015). The connectomics of brain disorders. *Nature Reviews Neuroscience, 16,* 159-172. https://doi.org/10.1038/nrn3901.

Foulon, C., Cerliani, L., Kinkingnéhun, S., Levy, R., Rosso, C., Urbanski, M., Volle, E., & Thiebaut de Schotten, M. (2018). Advanced lesion symptom mapping analyses and implementation as BCBtoolkit. *GigaScience, 7*(3), 1-17. https://doi.org/10.1093/gigascience/giy004.

Fröber, K., Pfister, R., & Dreisbach, G. (2019). Increasing reward prospect promotes cognitive flexibility: Direct evidence from voluntary task switching with double registration. *Quarterly Journal of Experimental Psychology, 72*(8), 1926-1944. https://doi.org/10.1177/1747021818819449.

Fugate, J. M. B., Gendron, M., Nakashima, S. F., & Barrett, L. F. (2018). Emotion words: adding face value. *Emotion, 18*(5), 693-706. https://doi.org/10.1037/emo0000330.

Gainotti, G. (2014). Old and recent approaches to the problem of non-verbal conceptual disorders in aphasic patients. *Cortex*, 53, 78–89. https://doi.org/10.1016/j.cortex.2014.01.009.

Gao, C., Weber, C. E., Wedell, D. H., & Shinkareva, S. V. (2020). An fMRI study of affective congruence across visual and auditory modalities. *Journal of Cognitive Neuroscience, 32*(7), 1251-1262. https://doi.org/10.1162/jocn_a_01553.

Gao, Z., Zheng, L., Chiou, R., Gouws, A., Krieger-Redwood, K., Wang, X., Varga, D., Lambon Ralph, M. A., Smallwood, J., & Jefferies, E. (2021). Distinct and common neural coding of semantic and non-semantic control demands. *NeuroImage, 236,* 118230. https://doi.org/10.1016/j.neuroimage.2021.118230.

Gao, Z., Zheng, L., Gouws, A., Krieger-Redwood, K., Wang, X., Varga, D., Smallwood, J., & Jefferies, E. (2022). Context free and context-dependent conceptual representation in the brain. *Cerebral Cortex,* bhac058. https://doi.org/10.1093/cercor/bhac058.

Garcea, F. E., Greene, C., Grafton, S. T., & Buxbaum, L. J. (2020). Structural disconnection of the tool use network after left hemisphere stroke predicts limb apraxia severity. *Cerebral Cortex Communications, 1*(1), tgaa035. https://doi.org/10.1093/texcom/tgaa035.

Garrido, L., Duchaine, B., & DeGutis, J. (2018). Association vs dissociation and setting appropriate criteria for object agnosia. *Cognitive Neuropsychology, 35*(1-2), 55-58. https://doi.org/10.1080/02643294.2018.1431875.

Gazzaniga, M. S. (2005). Forty-five years of split-brain research and still going strong. *Nature Reviews Neuroscience, 6,* 653-659. https://doi.org/10.1038/nrn1723.

Gendron, M., Lindquist, K. A., Barsalou, L., & Barrett, L. F. (2012). Emotion words shape emotion percepts. *Emotion, 12*(2), 314-325. https://doi.org/10.1037/a0026007.

Gilboa, A., & Moscovitch, M. (2021). No consolidation without representation: Correspondence between neural and psychological representations in recent and remote memory. *Neuron, 109*(14), 2239-2255. https://doi.org/10.1016/j.neuron.2021.04.025.

Gonzalez Alam, T. R. D. J., Karapanagiotidis, T., Smallwood, J., & Jefferies, E. (2019). Degrees of lateralisation in semantic cognition: Evidence from intrinsic connectivity. *NeuroImage, 202,* 116089. https://doi.org/10.1016/j.neuroimage.2019.116089.

Gonzalez Alam, T. R. J., Krieger-Redwood, K., Evans, M., Rice, G. E., Smallwood, J., & Jefferies, E. (2021). Intrinsic connectivity of anterior temporal lobe relates to individual differences in semantic retrieval for landmarks. *Cortex, 134,* 76-91. https://doi.org/10.1016/j.cortex.2020.10.007.

Gonzalez Alam, T. R. D. J., McKeown, B. L. A., Gao, Z., Bernhardt, B., Vos de Wael, R., Margulies, D. S., Smallwood, J., & Jefferies, E. (2022). A tale of two gradients: Differences between the left and right hemispheres predict semantic cognition. *Brain Structure and Function, 227,* 631-654. https://doi.org/10.1007/s00429-021-02374-w.

Gonzalez Alam, T., Murphy, C., Smallwood, J., & Jefferies, E. (2018). Meaningful inhibition: Exploring the role of meaning and modality in response inhibition. *NeuroImage, 181,* 108-119. https://doi.org/10.1016/j.neuroimage.2018.06.074.

Goodglass, H., Kaplan, E., & Barresi, B. (2001). *The Boston Diagnostic Aphasia Examination*. Baltimore: Lippincott, Williams & Wilkins.

Gordon, E. M., Laumann, T. O., Marek, S., Raut, R. V., Gratton, C., Newbold, D. J., Greene, D. J., Coalson, . S., Snyder, A. Z., Schlaggar, B. L., Petersen, S. E., Dosenbach, N. U. F., & Nelson, S. M. (2020). Default-mode network streams for coupling to language and control systems. *PNAS, 117*(29), 17308-17319. https://doi.org/10.1073/pnas.2005238117.

Goschke, T., & Bolte, A. (2014). Emotional modulation of control dilemmas: The role of positive affect, reward, and dopamine in cognitive stability and flexibility. *Neuropsychologia, 62,* 403-423. https://doi.org/10.1016/j.neuropsychologia.2014.07.015.

Glisky, E. L., & Marquine, M. J. (2009). Semantic and self-referential processing of positive and negative trait adjectives in older adults. *Memory, 17*(2), 144-157. https://doi.org/10.1080/09658210802077405.

Gray, T. (2020). The relationship between language control, semantic control and nonverbal control. *Behavioral Sciences, 10*(11), 169. https://doi.org/10.3390/bs10110169.

Guo, C. C., Gorno-Tempini, M. L., Gesierich, B., Henry, M., Trujillo, A., Shany-Ur, T., & Rankin, K. P. (2013). Anterior temporal lobe degeneration produces widespread network-driven dysfunction. *Brain, 136*(10), 2979–2991. https://doi.org/10.1093/brain/awt222.

Guo, Y., Schmitz, T. W., Mur, M., Ferreira, C. S., & Anderson, M. C. (2018). A supramodal role of the basal ganglia in memory and motor inhibition: Meta-analytic evidence. *Neuropsychologia, 108,* 117-134. https://doi.org/10.1016/j.neuropsychologia.2017.11.033.

Gurguryan, L., & Sheldon, S. (2019). Retrieval orientation alters neural activity during autobiographical memory recollection. *NeuroImage, 199,* 534-544. https://doi.org/10.1016/j.neuroimage.2019.05.077.

Halai, A. D., Welbourne, S. R., Embleton, K., & Parkers, L. M. (2014). A comparison of dual gradient-echo and spin-echo fMRI of the inferior temporal lobe. *Human Brain Mapping, 35*(8), 4118-4128. https://doi.org/10.1002/hbm.22463.

Hallam, G. P., Thompson, H. E., Hymers, M., Millman, R. E., Rodd, J. M., Lambon Ralph, M. A., Smallwood, J., & Jefferies, E. (2018). Task-based and resting-state fMRI reveal compensatory network changes following damage to left inferior frontal gyrus. *Cortex, 99*, 150-165. https://doi.org/10.1016/j.cortex.2017.10.004.

Hallam, G. P., Whitney, C., Hymers, M., Gouws, A. D., & Jefferies, E. (2016). Charting the effects of TMS with fMRI: Modulation of cortical recruitment within the distributed network supporting semantic control. *NeuropsycholCogia, 93*, 40-52. https://doi.org/10.1016/j.neuropsychologia.2016.09.012.

Hamann, S. (2012). Mapping discrete and dimensional emotions onto the brain: controversies and consensus. *Trends in Cognitive Sciences, 16*(9), 458-466. https://doi.org/10.1016/j.tics.2012.07.006.

Hamari, J., Koivisto, J., & Sarsa, H. (2014). Does gamification work? – A literature review of empirical studies on gamification. In B. A. Carreras, D. E. Newman, & I. Dobson (Eds.), *HICSS '14: Proceedings of the 2014 47th Hawaii International Conference on System Sciences* (pp. 3025-3030). Washington, DC: IEEE Computer Society. https://doi.org/10.1109/HICSS.2014.377.

Han, Z., Ma, Y., Gong, G., He, Y., Caramazza, A., & Bi, Y. (2013). White matter structural connectivity underlying semantic processing: evidence from brain damaged patients. *Brain, 136*, 2952-2965. https://doi.org/10.1093/brain/awt205.

Hanson, G. K., & Chrysikou, E. G. (2018). Attention to distinct goal-relevant features differentially guides semantic knowledge retrieval. *Journal of Cognitive Neuroscience, 29*(7), 1178-1193. https://doi.org/10.1162/jocn_a_01121.

Head, H. (1926). *Aphasia and kindred disorders of speech* (Vol. II). New York: Cambridge University Press.

Heilman, K. M., Schwartz, H. D., & Watson, R. T. (1978). Hypoarousal in patients with the neglect syndrome and emotional indifference. *Neurology, 28*(3), 229. https://doi.org/10.1212/WNL.28.3.229.

Hennessee, J. P., Castel, A. D., & Knowlton, B. J. (2017). Recognizing what matters: Value improves recognition by selectively enhancing recollection. *Journal of Memory and Language, 94*, 195-205. https://doi.org/10.1016/j.jml.2016.12.004.

Herbert, G., Zemmoura, I., & Duffau, H. (2018). Functional anatomy of the inferior longitudinal fasciculus: From historical reports to current hypotheses. *Frontiers in Neuroanatomy, 12*, 77. https://doi.org/10.3389/fnana.2018.00077.

Hippmann, B., Kuhlemann, I., Bäumer, T., Bahlmann, J., Münte, T. F., & Jessen, S. (2019). Boosting the effect of reward on cognitive control using TMS over the left IFJ. *Neuropsychologia, 125*, 109-115. https://doi.org/10.1016/j.neuropsychologia.2019.01.016.

Hobson, H., Chiu, E. G., Ravenscroft, C., Partridge, K., Bird, G., & Demeyere, N. (2020). The association between communication impairments and acquired alexithymia in chronic stroke patients. *Experimental Neuropsychology, 42*(5), 495-504. https://doi.org/10.1080/13803395.2020.1770703.

Hodges, J. R., & Patterson, K. (2007). Semantic dementia: A unique clinicopathological syndrome. *The Lancet Neurology, 6*(11), 1004-1014. https://doi.org/10.1016/S1474-4422(07)70266-1.

Hodgson, V. J., Lambon Ralph, M. A., & Jackson, R. L. (2021). Multiple dimensions underlying the functional organization of the language network. *NeuroImage, 241*, 118444. https://doi.org/10.1016/j.neuroimage.2021.118444.

Hoemann, K., Xu, F., & Barrett, L. F. (2019). Emotion words, emotion concepts, and emotional development in children: A constructionist hypothesis. *Developmental Psychology, 55*(9), 1830-1849. https://doi.org/10.1037/dev0000686.

Hoffman, P. (2018). An individual differences approach to semantic cognition: Divergent effects of age on representation, retrieval and selection. *Scientific Reports, 8*(8145), 1-10. https://doi.org/10.1038/s41598-018-26569-0.

Hoffman, P. (2019). Divergent effects of healthy ageing on semantic knowledge and control: Evidence from novel comparisons with semantically impaired patients. *Journal of Neuropsychology, 13*, 462-484. https://doi.org/10.1111/jnp.12159.

Hoffman, P., Cogdell-Brooke, L., & Thompson, H. E. (2020). Going off the rails: Impaired coherence in the speech of patients with semantic control deficits. *Neuropsychologia, 146*, 107516. https://doi.org/10.1016/j.neuropsychologia.2020.107516.

Hoffman, P., McClelland, J. L., & Lambon Ralph, M. A. (2018). Concepts, control, and context: a connectionist account of normal and disordered semantic cognition. *Psychological Review, 125*(3), 293-328. https://doi.org/10.1037/rev0000094.

Hope, T. M. H., Leff, A. P., & Price, C. J. (2018). Predicting language outcomes after stroke: Is structural disconnection a useful predictor? *NeuroImage: Clinical, 19*, 22-29. https://doi.org/10.1016/j.nicl.2018.03.037.

Hou, M., Grilli, M. D., & Glisky, E. L. (2019). Self-reference enhances relational memory in young and older adults. *Aging, Neuropsychology, and Cognition, 26*(1), 105-120. https://doi.org/10.1080/13825585.2017.1409333.

Huang, X., Du, X., Song, H., Zhang, Q., Jia, J., Xiao, T., & Wu, J. (2015). Cognitive impairments associated with corpus callosum infarction: A ten cases study. *International Journal of Clinical and Experimental Medicine, 8*(11), 21991-21998.

Hugdahl, K., Raichle, M. E., Mitra, A., & Specht, K. (2015). On the existence of a generalized non-specific task-dependent network. *Frontiers in Human Neuroscience, 9*, 430. https://doi.org/10.3389/fnhum.2015.00430.

Humphreys, G. F., Halai, A. D., Branzi, F. M., & Lambon Ralph, M. A. (2022). The angular gyrus is engaged by autobiographical recall not object-semantics, or event-semantics: Evidence from contrastive propositional speech production. *bioRxiv*. https://doi.org/10.1101/2022.04.04.487000.

Humphreys, G. F., Hoffman, P., Visser, M., Binney, R. J., & Lambon Ralph, M. A. (2015). Establishing task- and modality-dependent dissociations between the semantic and default mode networks. *PNAS, 112*(25), 7857-7862. https://doi.org/10.1073/pnas.1422760112.

Humphreys, G. F., & Lambon Ralph, M. A. (2017). Mapping domain-selective and counterpointed domain-general higher cognitive functions in the lateral parietal cortex: Evidence from fMRI comparisons of difficulty-varying semantic versus visuo-spatial tasks, and functional connectivity analyses. *Cerebral Cortex, 27,* 4199-4212. https://doi.org/10.1093/cercor/bhx107.

Huntenburg, J. M., Bazin, P-L., & Margulies, D. S. (2018). Large-scale gradients in human cortical organization. *Trends in Cognitive Sciences, 22*(1), 21-31. https://doi.org/10.1016/j.tics.2017.11.002.

Hurley, R. S., Bonakdarpour, B., Wang, X., & Mesulam, M. M. (2015). Asymmetric connectivity between the anterior temporal lobe and the language network. *Journal of Cognitive Neuroscience, 27*(3), 464-473. https://doi.org/10.1162/jocn_a_00722.

Huskey, R., Craighead, B., Miller, M. B., & Weber, R. (2018). Does intrinsic reward motivate cognitive control? A naturalistic-fMRI study based on the synchronization theory of flow. *Cognitive, Affective, & Behavioral Neuroscience, 18,* 902-924. https://doi.org/10.3758/s13415-018-0612-6.

Hymes, K., Hammer, J., Seyalioglu, H., Dow-Richards, C., Brown, D., Hambridge, T., Ventrice, J., Baker, M., Kim, Y. J., Hutchings, T., & Evans, W. S. (2021). Designing game-based rehabilitation experiences for people with aphasia. *Proceedings of the ACM on Human-Computer Interaction, 5*(CHI PLAY), 1-31. https://doi.org/10.1145/3474697.

IBM Corp. (2020). *IBM SPSS Statistics for Windows, Version 27.0*. Armonk, NY: IBM Corp.

Irish, M., & Vatansever, D. (2020). Rethinking the episodic-semantic distinction from a gradient perspective. *Current Opinion in Behavioral Sciences, 32,* 43-49. https://doi.org/10.1016/j.cobeha.2020.01.016.

Itkes, O., Eviatar, Z., & Kron, A. (2019). Semantic and affective manifestations of ambi (valence). *Cognition and Emotion, 33*(7), 1356-1369. https://doi.org/10.1080/02699931.2018.1564249.

Itkes, O., Kimchi, R., Haj-Ali, H., Shapiro, A., & Kron, A. (2017). Dissociating affective and semantic valence. *Journal of Experimental Psychology: General, 146*(7), 924-942. https://doi.org/10.1037/xge0000291.

Itkes, O., & Kron, A. (2019). Affective and semantic representations of valence: A conceptual framework. *Emotion Review, 11*(4), 283-293. https://doi.org/10.1177/1754073919868759.

Itkes, O., & Mashal, N. (2016). Processing negative valence of word pairs that include a positive word. *Cognition and Emotion, 30*(6), 1180-1187. https://doi.org/10.1080/02699931.2015.1039934.

Ito, T. A., Cacioppo, J. T., & Lang, P. J. (1998). Eliciting affect using the International Affective Picture System: Trajectories through evaluative space. *Personality and Social Psychology Bulletin, 24,* 855–879. https://doi.org/10.1177/0146167298248006.

Izard, C. E. (1992). Basic emotions, relations among emotions, and emotion-cognition relations. *Psychological Review, 99*(3), 561–565. https://doi.org/10.1037/0033-295X.99.3.561.

Izard, C. E. (1994). Innate and universal facial expressions: Evidence from developmental and cross-cultural research. *Psychological Bulletin, 115*(2), 288–299. https://doi.org/10.1037/0033-2909.115.2.288.

Jackson, R. L. (2021). The neural correlates of semantic control revisited. *NeuroImage, 224,* 117444. https://doi.org/10.1016/j.neuroimage.2020.117444.

Jackson, R. L., Hoffman, P., Pobric, G., & Lambon Ralph, M. A. (2016). The semantic network at work and rest: Differential connectivity of anterior temporal lobe subregions. *The Journal of Neuroscience, 36*(5), 1490-1501. https://doi.org/10.1523/JNEUROSCI.2999-15.2016

Jackson, R. L., Rogers, T. T., & Lambon Ralph, M. A. (2021). Reverse-engineering the cortical architecture for controlled semantic cognition. *Nature Human Behaviour, 5,* 774-786. https://doi.org/10.1038/s41562-020-01034-z.

James, W. (1884). What is an emotion? *Mind, 9*(34), 188-205.

Jastorff, J., De Winter, F., Van den Stock, J., Vandenberghe, R., Giese, M. A., & Vandenbulcke, M. (2016). Functional dissociation between anterior temporal lobe and inferior frontal gyrus in the processing of dynamic body expressions: Insights from behavioral variant frontotemporal dementia. *Human Brain Mapping, 37,* 4472-4486. https://doi.org/10.1002/hbm.23322.

Jefferies, E. (2013). The neural basis of semantic cognition: Converging evidence from neuropsychology, neuroimaging and TMS. *Cortex, 49,* 611-625. https://doi.org/10.1016/j.cortex.2012.10.008.

Jefferies, E., & Lambon Ralph, M. A. (2006). Semantic impairment in stroke aphasia versus semantic dementia: A case-series comparison. *Brain, 129,* 2132-2147. https://doi.org/10.1093/brain/awl153.

Jefferies, E., Patterson, K., Jones, R. W., & Lambon Ralph, M. A. (2009). Comprehension of concrete and abstract words in semantic dementia. *Neuropsychology, 23,* 492-499. https://doi.org/10.1037/a0015452.

Jefferies, E., Patterson, K., & Lambon Ralph, M. A. (2008). Deficits of knowledge versus executive control in semantic cognition: Insights from cued naming. *Neuropsychologia, 46,* 649-658. https://doi.org/10.1016/j.neuropsychologia.2007.09.007.

Jefferies, E., Thompson, H., Cornelissen, P., & Smallwood, J. (2019). The neurocognitive basis of knowledge about object identity and events: Dissociations reflect opposing effects of semantic coherence and control. *Philosophical Transactions of the Royal Society B, 375,* 20190300. https://doi.org/10.1098/rstb.2019.0300.

Jenkinson, M., Beckmann, C. F., Behrens, T. E., Woolrich, M. W., & Smith, S. M. (2012). FSL. *NeuroImage, 62,* 782-790. https://doi.org/10.1016/j.neuroimage.2011.09.015.

Jenkinson, M., & Smith, S. (2001). A global optimisation method for robust affine registration of brain images. *Medical Image Analysis, 5,* 143-156. https://doi.org/10.1016/S1361-8415(01)00036-6.

Johnson, N. F., Gold, B. T., Brown, C. A., Anggelis, E. F., Bailey, A. L., Clasey, J. L., & Powell, D. K. (2017). Endothelial function is associated with white matter microstructure and executive function in older adults. *Frontiers in Aging Neuroscience, 9*(255). https://doi.org/10.3389/fnagi.2017.00255.

Jokinen, H., Ryberg, C., Kalska, H., Ylikoski, R., Rostrup, E., Stegmann, M. B., Waldemar, G., Madureira, S., Ferro, J. M., van Straaten, E. C., Scheltens, P., Barkhof, F., Fazekas, F., Schmidt, R., Carlucci, G., Pantoni, L., Inzitari, D., Erkinjuntti, T., & LADIS group. (2007). Corpus callosum atrophy is associated with mental slowing and executive deficits in subjects with age-related white matter hyperintensities: The LADIS Study. *Journal of Neurology, Neurosurgery, and Psychiatry, 78*(5), 491-496. https://doi.org/10.1136/jnnp.2006.096792.

Juechems, K., Balaguer, J., Ruz, M., & Summerfield, C. (2017). Ventromedial prefrontal cortex encodes a latent estimate of cumulative reward. *Neuron, 93,* 705-714. https://doi.org/10.1016/j.neuron.2016.12.038.

Juran, S. A., Lundström, J. N., Geigant, M., Kumlien, E., Fredrikson, M., Åhs, F., & Olsson, M. J. (2016). Unilateral resection of the anterior medial temporal lobe impairs odor identification and valence perception. *Frontiers in Psychology, 6,* 2015. https://doi.org/10.3389/fpsyg.2015.02015.

Kajić, I., Schröder, T., Stewart, T. C., & Thagard, P. (2019). The semantic pointer theory of emotion: Integrating physiology, appraisal, and construction. *Cognitive Systems Research, 58,* 35-53. https://doi.org/10.1016/j.cogsys.2019.04.007.

Kang, C., Wang, Z., Surina, A., & Lü, W. (2014). Immediate emotion-enhanced memory dependent on arousal and valence: The role of automatic and controlled processing. *Acia Psychologia, 150,* 153-160. https://doi.org/10.1016/j.actpsy.2014.05.008.

Kay, J., Lesser, R., & Coltheart, M. (1992). *Psycholinguistic assessments of language processing in aphasia (PALPA)*. Hove (UK): Lawrence Erlbaum Associates.

Kendrick, L. T., Robson, H., & Meteyard, L. (2019). Executive control in frontal lesion aphasia: Does verbal load matter? *Neuropsychologia, 133,* 107178. https://doi.org/10.1016/j.neuropsychologia.2019.107178.

Kensinger, E. A., & Schacter, D. L. (2006). Processing emotional pictures and words: Effects of valence and arousal. *Cognitive, Affective, & Behavioral Neuroscience, 6*(2), 110-126. https://doi.org/10.3758/CABN.6.2.110.

Kerschensteiner, M., Poeck, K., & Brunner, E. (1972). The fluency-non fluency dimension in the classification of aphasic speech. *Cortex, 8*(2), 233-247. https://doi.org/10.1016/S0010-9452(72)80021-2.

Kiss, G. R., Armstrong, C., Milroy, R., & Piper, J. (1973) An associative thesaurus of English and its computer analysis. In A. J. Aitken, R. W. Bailey, & N. Hamilton-Smith. (Eds.), *The Computer and Literary Studies*. Edinburgh: University Press.

Klein, S. B. (2012). Self, memory, and the self-reference effect: an examination of conceptual and methodological issues. *Personality and Social Psychology Review, 16*(3), 283-300. https://doi.org/10.1177/1088868311434214.

Kohn, N., Eickhoff, S. B., Scheller, M., Laird, A. R., Fox, P. T., & Habel, U. (2014). Neural network of cognitive emotion regulation – an ALE meta-analysis and MACM analysis. *NeuroImage, 87*, 345-355. https://doi.org/10.1016/j.neuroimage.2013.11.001.

Kouneiher, F., Charron, S., & Koechlin, E. (2009). Motivation and cognitive control in the human prefrontal cortex. *Nature Neuroscience, 12*(7), 939-945. https://doi.org/10.1038/nn.2321.

Kousta, S.-T., Vigliocco, G., Vinson, D. P., Andrews, M., & Del Campo, E. (2011). The representation of abstract words: Why emotion matters. *Journal of Experimental Psychology: General, 140*(1), 14–34. https://doi.org/10.1037/a0021446.

Krieger-Redwood, K., & Jefferies, E. (2014). TMS interferes with lexical-semantic retrieval in left inferior frontal gyrus and posterior middle temporal gyrus: Evidence from cyclical picture naming. *Neuropsychologia, 64*, 24-32. https://doi.org/10.1016/j.neuropsychologia.2014.09.014.

Krieger-Redwood, K., Steward, A., Gao, Z., Wang, X., Halai, A., Smallwood, J., & Jefferies, E. (2022). Creativity in verbal associations is linked to semantic control. *Cerebral Cortex*, bhac405. https://doi.org/10.1093/cercor/bhac405.

Krieger-Redwood, K., Teige, C., Davey, J., Hymers, M., & Jefferies, E. (2015). Conceptual control across modalities: Graded specialisation for pictures and words in inferior frontal and posterior temporal cortex. *Neuropsychologia, 76*, 92-107. https://doi.org/10.1016/j.neuropsychologia.2015.02.030.

Kristinsson, S., Zhang, W., Rorden, C., Newman-Norlund, R., Basilakos, A., Bonilha, L., Yourganov, G., Xiao, F., Hillis, A., & Fridriksson, J. (2021). Machine learning-based multimodal prediction of language outcomes in chronic aphasia. *Human Brain Mapping, 42*(6), 1682-1698. https://doi.org/10.1002/hbm.25321.

Kropf, E., Syan, S. K., Minuzzi, L., & Frey, B. N. (2019). From anatomy to function: The role of the somatosensory cortex in emotional regulation. *Brazilian Journal of Psychiatry, 41*(3), 261-269. http://doi.org/10.1590/1516-4446-2018-0183.

Kuhnke, P., Chapman, C. A., Cheung, V. K. M., Turker, S., Graessner, A., Martin, S., Williams, K. A., & Hartwigsen, G. (2022). The role of the angular gyrus in semantic cognition: A synthesis of five functional neuroimaging studies. *Brain Structure and Function*. https://doi.org/10.1007/s00429-022-02493-y.

Kumfor, F., Ibañez, A., Hutchings, R., Hazelton, J. L., Hodges, J. R., & Piguet, O. (2018). Beyond the face: How context modulates emotion processing in frontotemporal dementia subtypes. *Brain*, *141*, 1172-1185. https://doi.org/10.1093/brain/awy002.

Kundu, P., Brenowitz, N. D., Voon, V., Worbe, Y., Vértes, P. E., Inati, S. J., Saad, Z. S., Bandettini, P. A., & Bullmore, E. T. (2013). Integrated strategy for improving functional connectivity mapping using multiecho fMRI. *PNAS*, *110*, 16187-16192. https://doi.org/10.1073/pnas.1301725110.

Kundu, P., Inati, S. J., Evans, J. W., Luh, W. M., & Bandettini, P. A. (2011). Differentiating BOLD and non-BOLD signals in fMRI time series using multi-echo EPI. *NeuroImage*, *60*, 1759-1770. https://doi.org/10.1016/j.neuroimage.2011.12.028.

Kuznetsova, A., Brockhoff, P. B., & Christensen, R. H. B. (2017). lmerTest package: Tests in linear mixed effects models. *Journal of Statistical Software*, *82*(13), 1-26. https://doi.org/10.18637/jss.v082.i13.

Lambon Ralph, M. A., Jefferies, E., Patterson, K., & Rogers, T. T. (2017). The neural and computational bases of semantic cognition. *Nature Reviews Neuroscience*, *18*(1), 42-55. https://doi.org/10.1038/nrn.2016.150.

Lambon Ralph, M. A., Sage, K., Jones, R. W., & Mayberry, E. J. (2010). Coherent concepts are computed in the anterior temporal lobes. *Proceedings of the National Academy of Sciences of the United States of America*, *107*, 2717-2722. https://doi.org/10.1073/pnas.0907307107.

Landauer, T. K., & Dumais, S. T. (1997). A solution to Plato's problem: The latent semantic analysis theory of acquisition, induction, and representation of knowledge. *Psychological Review*, *104*(2), 211–240. https://doi.org/10.1037/0033-295X.104.2.211.

Landers, R. N. (2014). Developing a theory of gamified learning: linking serious games and gamification of learning. *Simulation & Gaming*, *45*(6), 752-768. https://doi.org/10.1177/1046878114563660.

Lang, P. J. (1994). The varieties of emotional experience: A meditation on James-Lange theory. *Psychological Review*, *101*(2), 211–221. https://doi.org/10.1037/0033-295X.101.2.211.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (2008). *International affective picture system (IAPS): Affective ratings of pictures and instruction manual. Technical Report A-8*. University of Florida, Gainesville, FL.

Lang, P. J., Greenwald, M. K., Bradley, M. M., & Hamm, A. O. (1993). Looking at pictures: Affective, facial, visceral and behavioral reactions. *Psychophysiology*, *30*, 261-273. https://doi.org/10.1111/j.1469-8986.1993.tb03352.x.

Langen, C. D., Cremers, L. G. M., de Groot, M., White, T., Ikram, M. A., Niessen, W. J., & Vernooij, M. W. (2018). Disconnection due to white matter hyperintensities is associated with lower cognitive scores. *NeuroImage*, *183*, 745-756. https://doi.org/10.1016/j.neuroimage.2018.08.037.

Lanzoni, L., Ravasio, D., Thompson, H., Vatansever, D., Margulies, D., Smallwood, J., & Jefferies, E. (2020). The role of default mode network in semantic cue integration. *NeuroImage, 219,* 117019. https://doi.org/10.1016/j.neuroimage.2020.117019.

Lanzoni, L., Thompson, H., Beintari, D., Berwick, K., Demnitz-King, H., Raspin, H., Taha, M., Stampacchia, S., Smallwood, J., & Jefferies, E. (2019). Emotion and location cues bias conceptual retrieval in people with deficient semantic control. *Neuropsychologia, 131,* 294-305. https://doi.org/10.1016/j.neuropsychologia.2019.05.030.

Larsen, K., Petersen, J. H., Budtz-Jørgensen, E., & Endahl, L. (2000). Interpreting parameters in the logistic regression model with random effects. *Biometrics, 56*(3), 909-914. https://doi.org/10.1111/j.0006-341x.2000.00909.x.

Laures, J., Odell, K., & Coe, C. (2003). Arousal and auditory vigilance in individuals with aphasia during a linguistic and nonlinguistic task. *Aphasiology, 17*(12), 1133-1152. https://doi.org/10.1080/02687030344000436.

Lee, S., Parthasarathi, T., & Kable, J. W. (2021). The ventral and dorsal default mode networks are dissociably modulated by the vividness and valence of imagined events. *Journal of Neuroscience, 41*(24), 5243-5250. https://doi.org/10.1523/JNEUROSCI.1273-20.2021.

Lee, M. H., Smyser, C. D., & Shimony, J. S. (2013). Resting-state fMRI: a review of methods and clinical applications. *American Journal of Neuroradiology, 34*(10), 1866-1872. https://doi.org/10.3174/ajnr.A3263.

Lenth, R. (2020). *Emmeans: Estimated Marginal Means, aka Least-Squares Means*. R package version 1.5.2-1. https://CRAN.R-project.org/package=emmeans.

Leung, J. H., Purdy, S. C., Tippett, L. J., & Leão, S. H. S. (2017). Affective speech prosody perception and production in stroke patients with left-hemispheric damage and healthy controls. *Brain & Language, 166,* 19-28. https://doi.org/10.1016/j.bandl.2016.12.001.

Lin, A., Adolphs, R., & Rangel, A. (2012). Social and monetary reward learning engage overlapping neural substrates. *SCAN, 7,* 274-281. https://doi.org/10.1093/scan/nsr006.

Lindquist, K. A. (2017). The role of language in emotion: existing evidence and future directions. *Current Opinion in Psychology, 17,* 135-139. https://doi.org/10.1016/j.copsyc.2017.07.006.

Lindquist, K. A., Barrett, L. F., Bliss-Moreau, E., & Russell, J. A. (2006). Language and the perception of emotion. *Emotion, 6*(1), 125-138. https://doi.org/10.1037/1528-3542.6.1.125.

Lindquist, K. A., Gendron, M., Barrett, L. F., & Dickerson, B. C. (2014). Emotion perception, but not affect perception, is impaired with semantic memory loss. *Emotion, 14*(2), 375-387. https://doi.org/10.1037/a0035293.

Lindquist, K. A., Gendron, M., & Satpute, A. B. (2016). Language and emotion: Putting words into feelings and feelings into words. In L. F. Barrett, M. Lewis, & J. M. Haviland-Jones (Eds.). *Handbook of emotions* (4th ed., pp. 579-594). New York, NY: Guildford Press.

Lindquist, K. A., Satpute, A. B., & Gendron, M. (2015). Does language do more than communicate emotion? *Current Directions in Psychological Science, 24*(2), 99-108. https://doi.org/10.1177/0963721414553440.

Lindquist, K. A., Satpute, A. B., Wager, T. D., Weber, J., & Barrett, L. F. (2016). The brain basis of positive and negative affect: Evidence from a meta-analysis of the human neuroimaging literature. *Cerebral Cortex, 26,* 1910-1922. https://doi.org/10.1093/cercor/bhv001.

Lowe, M. J., Dzemidzic, M., Lurito, J. T., Mathews, V. P., Phillips, M. D. (2000). Correlations in low-frequency BOLD fluctuations reflect cortico-cortical connections. *NeuroImage, 12,* 582-587. https://doi.org/10.1006/nimg.2000.0654.

Lüdecke, D. (2018). ggeffects: Tidy Data Frames of Marginal Effects from Regression Models. *Journal of Open Source Software, 3*(26), 772. https://doi.org/10.21105/joss.00772.

Madan, C. R. (2017). Motivated cognition: Effects of reward, emotion, and other motivational factors across a variety of cognitive domains. *Collabra: Psychology, 3*(1), 24. https://doi.org/10.1525/collabra.111.

Mahon, B. Z., & Caramazza, A. (2011). What drives the organization of object knowledge in the brain? *Trends in Cognitive Sciences, 15*(3), 97-103. https://doi.org/10.1016/j.tics.2011.01.004.

Mancuso, L., Cavuoti-Cabanillas, S., Liloia, D., Manuello, J., Buzi, G., Cauda, F., & Costa, T. (2022). Tasks activating the default mode network map multiple functional systems. *Brain Structure and Function, 227,* 1711-1734. https://doi.org/10.1007/s00429-022-02467-0.

Marcus, D. S., Fotenos, A. F., Csernansky, J. G., Morris, J. C., & Buckner, R. L. (2010). Open access series of imaging studies: Longitudinal MRI data in nondemented and demented older adults. *Journal of Cognitive Neuroscience, 22*(12), 2677-2684. https://doi.org/10.1162/jocn.2009.21407.

Margulies, D. S., Ghosh, S. S., Goulas, A., Falkiewicz, M., Huntenburg, J. M., Langs, G., Bezgin, G., Eickhoff, S. B., Castellanos, F. X., Petrides, M., Jefferies, E., & Smallwood, J. (2016). Situating the default-mode network along a principal gradient of macroscale cortical organization. *PNAS, 113*(44), 12574-12579. https://doi.org/10.1073/pnas.1608282113.

Marino Dávolos, J., Arias, J. C., & Jefferies, E. (2020). Linking individual differences in semantic cognition to white matter microstructure. *Neuropsychologia, 141,* 107438. https://doi.org/10.1016/j.neuropsychologia.2020.107438.

Martin, A. (2016). GRAPES – Grounding representations in action, perception, and emotion systems: How object properties and categories are represented in the human brain. *Psychonomic Bulletin & Review, 23,* 979–990. https://doi.org/10.3758/s13423-015-0842-3.

Martin, A., & Fedio, P. (1983). Word production and comprehension in Alzheimer's disease: The breakdown of semantic knowledge. *Brain and Language, 19,* 124-141. https://doi.org/10.1016/0093-934X(83)90059-7.

Mas-Herrero, E., Sescousse, G., Cools, R., & Marco-Pallarés, J. (2019). The contribution of striatal pseudo-reward prediction errors to value-based decision-making. *NeuroImage, 193,* 67-74. https://doi.org/10.1016/j.neuroimage.2019.02.052.

Mckeown, B., Strawson, W. H., Wang, H-T., Karapanagiotidis, T., Vos de Wael, R., Benkarim, O., Turnbull, A., Margulies, D., Jefferies, E., McCall, C., Bernhardt, B., & Smallwood, J. (2020). The relationship between individual variation in macroscale functional gradients and distinct aspects of ongoing thought. *NeuroImage, 220,* 117072. https://doi.org/10.1016/j.neuroimage.2020.117072.

Meersmans, K., Bruffaerts, R., Jamoulle, T., Liuzzi, A. G., De Dyne, S., Storms, G., Dupont, P., & Vandenberghe, R. (2020). Representation of associative and affective semantic similarity of abstract words in the lateral temporal perisylvian language regions. *NeuroImage, 217,* 116892. https://doi.org/10.1016/j.neuroimage.2020.116892.

Mekler, E. D., Brühlmann, F., Tuch, A. N., & Opwis, K. (2017). Towards understanding the effects of individual gamification elements on intrinsic motivation and performance. *Computers in Human Behavior, 71,* 525-534. https://doi.org/10.1016/j.chb.2015.08.048.

Messina, I., Bianco, S., Sambin, M., & Viviani, R. (2015). Executive and semantic processes in reappraisal of negative stimuli: Insights from a meta-analysis of neuroimaging studies. *Frontiers in Psychology, 6,* 956. https://doi.org/10.3389/fpsyg.2015.00956.

Meteyard, L., Rodriguez Cuadrado, S., Bahrami, B., & Vigliocco, G. (2012). Coming of age: A review of embodiment and the neuroscience of semantics. *Cortex, 48,* 788-804. https://doi.org/10.1016/j.cortex.2010.11.002.

Mikolov, T., Chen, K., Corrado, G., & Dean, J. (2013). *Efficient estimation of word representations in vector space*. arXiv. arXiv:1310.4546v1.

Miller, L. A., Hsieh, S., Lah, S., Savage, S., Hodges, J. R., & Piguet, O. (2012). One size does not fit all: Face emotion processing impairments in semantic dementia, behavioural-variant frontotemporal dementia and Alzheimer's disease are mediated by distinct cognitive deficits. *Behavioural Neurology, 25,* 53-60. https://doi.org/10.1155/2012/683052.

Montefinese, M., Hallam, G., Stampacchia, S., Thompson, H. E., & Jefferies, E. (2020). Deficits of semantic control disproportionately affect low-relevance conceptual features: Evidence from semantic aphasia. *Aphasiology, 35*(11), 1448-1462. https://doi.org/10.1080/02687038.2020.1814950.

Morawetz, C., Bode, S., Baudewig, J., & Heekeren, H. R. (2017). Effective amygdala-prefrontal connectivity predicts individual differences in successful emotion regulation. *Social Cognitive & Affective Neuroscience, 12*(4), 569-585. https://doi.org/10.1093/scan/nsw169.

Mori, A., Okamoto, Y., Okada, G., Takagaki, K., Takamura, M., Jinnin, R., Ichikawa, N., Yamamura, T., Yokoyama, S., Shiota, S., Yoshino, A., Miyake, Y., Okamoto, Y., Matsumoto, M., Matsumoto, K., & Yamawaki, S. (2018). Effects of behavioural activation on the neural circuit related to intrinsic motivation. *BJPsych Open, 4*, 317-323. https://doi.org/10.1192/bjo.2018.40.

Moscovitch, M., Rosenbaum, R. S., Gilboa, A., Addis, D. R., Westmacott, R., Grady, C., McAndrews, M. P., Levine, B., Black, S., Wincour, G., & Nadel, L. (2005). Functional neuroanatomy of remote episodic, semantic and spatial memory: A unified account based on multiple trace theory. *Journal of Anatomy, 207*(1), 35-66. https://doi.org/10.1111/j.1469-7580.2005.00421.x.

Mummery, C. J., Patterson, K., Price, C. J., Ashburner, J., Frackowiak, R. S., & Hodges, J. R. (2000). A voxel-based morphometry study of semantic dementia: relationship between temporal lobe atrophy and semantic memory. *Annals of Neurology, 47*(1), 36-45. https://doi.org/10.1002/1531-8249(200001)47:1<36::AID-ANA8>3.0.CO;2-L.

Murphy, C., Jefferies, E., Rueschemeyer, S-A., Sormaz, M., Wang, H., Margulies, D. S., & Smallwood, J. (2018). Distant from input: Evidence of regions within the default mode network supporting perceptually-decoupled and conceptually-guided cognition. *NeuroImage, 171,* 393-401. https://doi.org/10.1016/j.neuroimage.2018.01.017.

Murphy, C., Poerio, G., Sormaz, M., Wang, H., Vatansever, D., Allen, M., Margulies, D. S., Jefferies, E., & Smallwood, J. (2019). Hello, is that me you are looking for? A re-examination of the role of the DMN in social and self relevant aspects of off-task thought. *PLoS ONE, 14*(11), e0216182. https://doi.org/10.1371/journal.pone.0216182.

Murphy, C., Rueschemeyer, S.-A., Watson, D., Karapanagiotidis, T., Smallwood, J., & Jefferies, E. (2017). Fractionating the anterior temporal lobe: MVPA reveals differential responses to input and conceptual modality. *NeuroImage, 147,* 19-31. https://doi.org/10.1016/j.neuroimage.2016.11.067.

Niendam, T. A., Laird, A. R., Ray, K. L., Dean, Y. M., Glahn, D. C., & Carter, C. S. (2012). Meta-analytic evidence for a superordinate cognitive control network subserving diverse executive functions. *Cognitive, Affective, & Behavioral Neuroscience, 12,* 241-268. https://doi.org/10.3758/s13415-011-0083-5.

Nook, E. C., Lindquist, K. A., & Zaki, J. (2015). A new look at emotion perception: Concepts speed and shape facial emotion recognition. *Emotion, 15*(5), 569-578. https://doi.org/10.1037/a0039166.

Noonan, K. A, Jefferies, E., Corbett, F., & Lambon Ralph, M. A. (2010). Elucidating the nature of deregulated semantic cognition in semantic aphasia: Evidence for the roles of prefrontal and temporo-parietal cortices. *Journal of Cognitive Neuroscience, 22*(7), 1597-1613. https://doi.org/10.1162/jocn.2009.21289.

Noonan, K. A., Jefferies, E., Visser, M., & Lambon Ralph, M. A. (2013). Going beyond inferior prefrontal involvement in semantic control: Evidence for the additional contribution of dorsal angular gyrus and

posterior middle temporal cortex. *Journal of Cognitive Neuroscience, 25*(11), 1824-1850. https://doi.org/10.1162/jocn_a_00442.

Northoff, G., & Hayes, D. J. (2011). Is our self nothing but reward? *Biological Psychiatry, 69(11)*, 1019-1025. https://doi.org/10.1016/j.biopsych.2010.12.014.

Notebaert, W., & Braem, S. (2015). Parsing the effects of reward on cognitive control. In T. S. Braver (Ed.), *Motivation and Cognitive Control* (pp. 105-122). New York, NY: Routledge.

Nugiel, T., Alm, K. H., & Olson, I. R. (2016). Individual differences in white matter macrostructure predict semantic control. *Cognitive, Affective, & Behavioral Neuroscience, 16,* 1003-1016. https://doi.org/10.3758/s13415-016-0448-x.

Ochsner, K. N., Knierim, K., Ludlow, D. H., Hanelin, J., Ramachandran, T., Glover, G., & Mackey, S. C. (2004). Reflecting upon feelings: An fMRI study of neural systems supporting the attribution of emotion to self and other. *Journal of Cognitive Neuroscience, 16*(10), 1746-1772. https://doi.org/10.1162/0898929042947829.

Ogawa, S., Menon, R. S., Tank, D. W., Kim, S. G., Merkle, H., Ellermann, J. M., & Ugurbil, K. (1993). Functional brain mapping by blood oxygenation level-dependent contrast magnetic resonance imaging. A comparison of signal characteristics with a biophysical model. *Biophysical Journal, 64*(3), 803-812. https://doi.org/10.1016/S0006-3495(93)81441-3.

Olman, C. A., Davachi, L., & Inati, S. (2009). Distortion and signal loss in medial temporal lobe. *PLOS ONE, 4*(12), e8160. https://doi.org/10.1371/journal.pone.0008160.

Ortony, A., & Turner, T. J. (1990). What's basic about basic emotions? *Psychological Review, 97*(3), 315-331. https://doi.org/10.1037/0033-295x.97.3.315.

Osborne-Crowley, K., Wilson, E., De Blasio, F., Wearne, T., Rushby, J., & McDonald, S. (2019). Preserved rapid conceptual processing of emotional expressions despite reduced neuropsychological performance following traumatic brain injury. *Neuropsychology, 33*(6), 872-882. https://doi.org/10.1037/neu0000545.

Osborne-Crowley, K., Wilson, E., De Blasio, F., Wearne, T., Rushby, J., & McDonald, S. (2020). Empathy for people with similar experiences: Can the perception-action model explain empathy impairments after traumatic brain injury? *Journal of Clinical and Experimental Neuropsychology, 42*(1), 28-41. https://doi.org/10.1080/13803395.2019.1662375.

Otto, A. R., & Vassena, E. (2021). It's all relative: Reward-induced cognitive control modulation depends on context. *Journal of Experimental Psychology: General, 150*(2), 306-313. https://doi.org/10.1037/xge0000842.

Padmala, S., & Pessoa, L. (2011). Reward reduces conflict by enhancing attentional control and biasing visual cortical processing. *Journal of Cognitive Neuroscience, 23*(11), 3419-3432. https://doi.org/10.1162/jocn_a_00011.

Padmanabhan, J. L., Cooke, D., Joutsa, J., Siddiqi, S. H., Ferguson, M., Darby, R. R., Soussand, L., Horn, A., Kim, N. Y., Voss, J. L., Naidech, A. M., Brodtmann, A., Egorova, N., Gozzi, S., Phan, T. G., Corbetta, M., Grafman, J., & Fox, M. D. (2019). A human depression circuit derived from focal brain lesions. *Biological Psychiatry, 86*(10), 749-758. https://doi.org/10.1016/j.biopsych.2019.07.023.

Parro, C., Dixon, M. L., & Christoff, K. (2018). The neural basis of motivational influences on cognitive control. *Human Brain Mapping, 39*(12), 5097-5111. https://doi.org/10.1002/hbm.24348.

Patterson, K., Nestor, P. J., & Rogers, T. T. (2007). Where do you know what you know? The representation of semantic knowledge in the human brain. *Nature Reviews Neuroscience, 8*(12), 976-987. https://doi.org/10.1038/nrn2277.

Pauligk, S., Kotz, S. A., & Kanske, P. (2019). Differential impact of emotion on semantic processing of abstract and concrete words: ERP and fMRI evidence. *Scientific Reports, 9,* 14439. https://doi.org/10.1038/s41598-019-50755-3.

Peirce, J. W., Gray, J. R., Simpson, S., MacAskill, M. R., Höchenberger, R., Sogo, H., Kastman, E., & Lindeløv, J. (2019). PsychoPy2: experiments in behavior made easy. *Behavior Research Methods, 51,* 195-203. https://doi.org/10.3758/s13428-018-01193-y.

Pereira, F., Gershman, S., Ritter, S., & Botvinick, M. (2016). A comparative evaluation of off-the-shelf distributed semantic representations for modelling behavioural data. *Cognitive Neuropsychology, 33*(3-4), 175-190. https://doi.org/10.1080/02643294.2016.1176907.

Phan, T. G., Fong, A. C., Donnan, G. A., & Reutens, D. C. (2007). Digital map of posterior cerebral artery infarcts associated with posterior cerebral artery trunk and branch occlusion. *Stroke, 38,* 1805-1811. https://doi.org/10.1161/STROKEAHA.106.477000.

Perry, R. J., Graham, A., Williams, G., Rosen, H., Erzinçlioglu, S., Weiner, M., Miller, B., & Hodges, J. (2006). Patterns of frontal lobe atrophy in frontotemporal dementia: A volumetric MRI study. *Dementia and Geriatric Cognitive Disorders, 22*(4), 278-287. https://doi.org/10.1159/000095128.

Pini, L., Salvalaggio, A., De Filippo De Grazia, M., Zorzi, M., Thiebaut De Schotten, M., & Corbetta, M. (2021). A novel stroke lesion network mapping approach: Improved accuracy yet still low deficit prediction. *Brain Communications, 3*(4), fcab259. https://doi.org/10.1093/braincomms/fcab259.

Poldrack, R. A. (2007) Region of interest analysis for fMRI. *Social Cognitive and Affective Neuroscience, 2*(1), 67-70. https://doi.org/10.1093/scan/nsm006.

Ponari, M., Norbury, C. F., & Vigliocco, G. (2018). Acquisition of abstract concepts is influenced by emotional valence. *Developmental Science, 21,* e12549. https://doi.org/10.1111/desc.12549.

Ponari, M., Norbury, C. F., & Vigliocco, G. (2020). The role of emotional valence in learning novel abstract concepts. *Developmental Psychology, 56*(10), 1855-1865. http://doi.org/10.1037/dev0001091.

Preston, S. D. (2007). A perception-action model for empathy. In T. F. D. Farrow (Ed.), *Empathy in mental illness* (pp. 428–447). Cambridge: Cambridge University Press.

Preston, S. D., & Stansfield, R. B. (2008). I know how you feel: Task-irrelevant facial expressions are spontaneously processed at a semantic level. *Cognitive, Affective, & Behavioral Neuroscience, 8*(1), 54-64. https://doi.org/10.3758/cabn.8.1.54.

Price, A. R., Bonner, M. F., Peelle, J. E., & Grossman, M. (2015). Converging evidence for the neuroanatomic basis of combinatorial semantics in the angular gyrus. *The Journal of Neuroscience, 35*(7), 3276-3284. https://doi.org/10.1523/JNEUROSCI.3446-14.2015.

Price, A. R., Peelle, J. R., Bonner, M. F., Grossman, M., & Hamilton, R. H. (2016). Causal evidence for a mechanism of semantic integration in the angular gyrus as revealed by high-definition transcranial direct current stimulation. *The Journal of Neuroscience, 36*(13), 3829-3838. https://doi.org/10.1523/JNEUROSCI.3120-15.2016.

Pulvermüller, F. (2005). Brain mechanisms linking language and action. *Nature Reviews Neuroscience, 6,* 576-582. https://doi.org/10.1038/nrn1706.

Pulvermüller, F. (2013). How neurons make meaning: brain mechanisms for embodied and abstract-symbolic semantics. *Trends in Cognitive Sciences, 17*(9), 458-470. https://doi.org/10.1016/j.tics.2013.06.004.

Pylkkänen, L. (2019). The neural basis of combinatory syntax and semantics. *Science, 366,* 62-66. https://doi.org/10.1126/science.aax0050.

R Core Team (2020). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing, Vienna, Austria. URL: https://www.R-project.org/.

Raichle, M. E. (2015). The brain's default mode network. *Annual Review of Neuroscience, 38,* 433-447. https://doi.org/10.1146/annurev-neuro-071013-014030.

Raven, J. (1962). Coloured progressive matrices sets A, AB, B. London: H.K. Lewis.

Reilly, J., Peele, J. E., Garcia, A., & Crutch, S. J. (2016). Linking somatic and symbolic representation in semantic memory: The dynamic multilevel reactivation framework. *Psychonomic Bulletin & Review, 23,* 1002-1014. https://doi.org/10.3758/s13423-015-0824-5.

Reitan, R. M. (1958). Validity of the trail making test as an indicator of organic brain damage. *Perceptual and Motor Skills, 8,* 271-276. https://doi.org/10.2466/pms.1958.8.3.271.

Renoult, L., Irish, M., Moscovitch, M., & Rugg, M. D. (2019). From knowing to remembering: the semantic-episodic distinction. *Trends in Cognitive Sciences, 23*(12), 1041-1057. https://doi.org/10.1016/j.tics.2019.09.008.

Riberto, M., Pobric, G., & Talmi, D. (2019). The emotional facet of subjective and neural indices of similarity. *Brain Topography, 32,* 956-964. https://doi.org/10.1007/s10548-019-00743-7.

Rice, G. E., Caswell, H., Moore, P., Hoffman, P., & Lambon Ralph, M. A. (2017). The effects of left versus right anterior temporal lobe resection on semantic processing of words, objects, and faces. *Journal of the Neurological Sciences, 381,* 684. https://doi.org/10.1016/j.jns.2017.08.1924.

Rice, G. E., Caswell, H., Moore, P., Hoffman, P., & Lambon Ralph, M. A. (2018). The roles of left versus right anterior temporal lobes in semantic memory: A neuropsychological comparison of postsurgical temporal lobe epilepsy patients. *Cerebral Cortex, 28*(4), 1487-1501. https://doi.org/10.1093/cercor/bhx362.

Rice, G. E., Lambon Ralph, M. A., Hoffman, P. (2015). The roles of left versus right anterior temporal lobes in conceptual knowledge: An ALE meta-analysis of 97 functional neuroimaging studies. *Cerebral Cortex, 25*(11), 4734–4791. https://doi.org/10.1093/cercor/bhv024.

Rizio, A. A., & Diaz, M. T. (2016). Language, aging, and cognition: Frontal aslant tract and superior longitudinal fasciculus contribute to working memory performance in older adults. *Neuroreport, 27*(9), 689-693. https://doi.org/10.1097/WNR.0000000000000597.

Robertson, D., Davidoff, J., & Braisby, N. (1999). Similarity and categorisation: Neuropsychological evidence for a dissociation in explicit categorisation tasks. *Cognition, 71,* 1-42. http://dx.doi.org/10.1016/S0010-0277(99)00013-X.

Robertson, L. C., Knight, R. T., Rafal, R., & Shimamura, A. P. (1993). Cognitive neuropsychology is more than single-case studies. *Journal of Experimental Psychology, 19*(3), 710-717. https://doi.org/10.1037/0278-7393.19.3.710.

Robertson, I., Ward, T., Ridgeway, V., & Nimmo-Smith, I. (1994). *The test of everyday attention*. London: Thames Valley Test Company.

Rochat, L., Van der Linden, M., Renaud, O., Epiney, J., Michel, P., Sztajzel, R., Spierer, L., & Annoni, J. (2013). Poor reward sensitivity and apathy after stroke: Implication of basal ganglia. *Neurology, 81*(19), 1674-1680. https://doi.org/10.1212/01.wnl.0000435290.49598.1d.

Röer, J. P., Bell, R., & Buchner, A. (2013). Self-relevance increases the irrelevant sound effect: Attentional disruption by one's own name. *Journal of Cognitive Psychology, 25*(8), 925-931. https://doi.org/10.1080/20445911.2013.828063.

Rogers, T. T., Cox, C. R., Lu, Q., Shimotake, A., Kikuchi, T., Kunieda, T., Miyamoto, S., Takahashi, R., Ikeda, A., Matsumoto, R., & Lambon Ralph, M. A. (2021). Evidence for a deep, distributed and dynamic code for animacy in human ventral anterior temporal cortex. *eLife, 10,* e66276. https://doi.org/10.7554/eLife.66276.

Rogers, B. P., Morgan, V. L., Newton, A. T., & Gore, J. C. (2007). Assessing functional connectivity in the human brain by fMRI. *Magnetic Resonance Imaging, 25*(10), 1347-1357. https://doi.org/10.1016/j.mri.2007.03.007.

Rogers, T. T., Patterson, K., Jefferies, E., & Lambon Ralph, M. A. (2015). Disorders of representation and control in semantic cognition: Effects of familiarity, typicality, and specificity. *Neuropsychologia, 76,* 220-239. https://doi.org/10.1016/j.neuropsychologia.2015.04.015.

Rojkova, K., Volle, E., Urbanski, M., Humbert, F., Dell'Acqua, F., & Thiebaut de Schotten, M. (2016). Atlasing the frontal lobe connections and their variability due to age and education: A spherical deconvolution tractography study. *Brain Structure and Function, 221*(3), 1751-1766. https://doi.org/10.1007/s00429-015-1001-3.

Romani, C., Thomas, L., Olson, A., & Lander, L. (2019). Playing a team game improves word production in poststroke aphasia. *Aphasiology*, *33*(3), 253-288. https://doi.org/10.1080/02687038.2018.1548205.

Rosen, H. J., Gorno-Tempini, M. L., Goldman, W. P., Perry, R. J., Schuff, N., Weiner, M., Feiwell, R., Kramer, J. H., & Miller, B. L. (2002). Patterns of brain atrophy in frontotemporal dementia and semantic dementia. *Neurology*, *58*(2), 198-208. https://doi.org/10.1212/WNL.58.2.198.

Ross, E. D., Thompson, R. D., & Yenkosky, J. (1997). Lateralization of affective prosody in brain and the callosal integration of hemispheric language functions. *Brain and Language, 56,* 27-54. https://doi.org/10.1006/brln.1997.1731.

Rotaru, A. S., & Vigliocco, G. (2019). Modelling semantics by integrating linguistic, visual and affective information. In A. K. Goel, C. M. Seifert, and C. Freska (Eds.). *Proceedings of the 41st Annual Meeting of the Cognitive Science Society (CogSci 2019)* (pp. 2681-2687). Montreal, Canada, Cognitive Science Society. https://libguides.jcu.edu.au/apa/articles/conference-papers.

Rotaru, A. S., Vigliocco, G., & Frank, S. L. (2018). Modeling the structure and dynamics of semantic processing. *Cognitive Science, 42,* 2890-2917. https://doi.org/10.1111/cogs.12690.

Ryan, R. M., & Deci, E. L. (2000). Intrinsic and extrinsic motivations: classic definitions and new directions. *Contemporary Educational Psychology, 25,* 54-67. https://doi.org/10.1006/ceps.1999.1020.

Sabatinelli, D., Fortune, E. E., Li, Q., Siddiqui, A., Krafft, C., Oliver, W. T., Beck, S., & Jeffries, J. (2011). Emotional perception: Meta-analyses of face and natural scene processing. *NeuroImage, 54,* 2524-2533. https://doi.org/10.1016/j.neuroimage.2010.10.011.

Salvalaggio, A., De Filippo De Grazia, M., Pini, L., Thiebaut De Schotten, M., Zorzi, M., & Corbetta, M. (2021b). Reply: Lesion network mapping predicts post-stroke behavioural deficits and improves localization. *Brain*, *144*(4), e36. https://doi.org/10.1093/brain/awab004.

Salvalaggio, A., De Filippo De Grazia, M., Zorzi, M., Thiebaut de Schotten, M., & Corbetta, M. (2020). Post-stroke deficit prediction from lesion and indirect structural and functional disconnection. *Brain, 143*(7), 2173-2188. https://doi.org/10.1093/brain/awaa156.

Salvalaggio, A., Pini, L., De Filippo De Grazia, M., Thiebaut De Schotten, M., Zorzi, M., & Corbetta, M. (2021a). Reply: Lesion network mapping: Where do we go from here? *Brain*, *144*(1), e6. https://doi.org/10.1093/brain/awaa351.

Samson, D., Connolly, C., & Humphreys, G. W. (2007). When “happy” means “sad”: Neuropsychological evidence for the right prefrontal cortex contribution to executive semantic processing. *Neuropsychologia, 45,* 896-904. https://doi.org/10.1016/j.neuropsychologia.2006.08.023.

Saragosa, N. M., & Silvers, J. A. (2022). The neural bases of emotion regulation within a process model framework. *Encyclopedia of Behavioral Neuroscience, 2*(3), 439-444. https://doi.org/10.1016/B978-0-12-819641-0.00072-4.

Sato, T., Uchida, G., Lescroart, M. D., Kitazono, J., Okada, M., & Tanifuji, M. (2013). Object representation in inferior temporal cortex is organized hierarchically in a mosaic-like structure. *Journal of Neuroscience, 33*(42), 16642-16656. https://doi.org/10.1523/JNEUROSCI.5557-12.2013.

Satpute, A. B., & Lindquist, K. A. (2019). The default mode network's role in discrete emotion. *Trends in Cognitive Sciences, 23*(10), 851-862. https://doi.org/10.1016/j.tics.2019.07.003.

Satterthwaite, T. D., Ciric, R., Roalf, D. R., Davatzikos, C., Bassett, D. S., & Wolf, D. H. (2019). Motion artifact in studies of functional connectivity: Characteristics and mitigation strategies. *Human Brain Mapping, 40,* 2033-2051. https://doi.org/10.1002/hbm.23665.

Sauter, D. A. (2018). Is there a role for language in emotion perception? *Emotion Review, 10*(2), 111-115. https://doi.org/10.1177/1754073917693924.

Schachter, S. & Singer, J. E. (1962). Cognitive, social, and physiological determinants of emotional state. *Psychological Review, 69,* 379–399. https://doi.org/10.1037/h0046234.

Schaefer, A., Kong, R., Gordon, E. M., Laumann, T. O., Zuo, X., Holmes, A. J., Eickhoff, S. B., & Yeo, B. T. T. (2018). Local-global parcellation of the human cerebral cortex from intrinsic functional connectivity MRI. *Cerebral Cortex, 28,* 3095-3114. https://doi.org/10.1093/cercor/bhx179.

Schulte, T., & Müller-Oehring, E. M. (2010). Contribution of callosal connections to the interhemispheric integration of visuomotor and cognitive processes. *Neuropsychology Review, 20,* 174-190. https://doi.org/10.1007/s11065-010-9130-1.

Schwartz, M. F., Kimberg, D. Y., Walker, G. M., Brecher, A., Faseyitan, O. K., Dell, G. S., Mirman, D., & Coslett, H. B. (2011). Neuroanatomical dissociation for taxonomic and thematic knowledge in the human brain. *PNAS, 108*(2), 8520-8524. https://doi.org/10.1073/pnas.1014935108.

Scott, G. G., Keitel, A., Becirspahic, M., Yao, B., & Sereno, S. C. (2019). The Glasgow Norms: Ratings of 5,500 words on nine scales. *Behavior Research Methods, 51,* 1258-1270. https://doi.org/10.3758/s13428-018-1099-3.

Shao, X., Mckeown, B., Karapanagiotidis, T., Vos de Wael, R., Margulies, D. S., Bernhardt, B., Smallwood, J., Krieger-Redwood, K., & Jefferies, E. (2022). Individual differences in gradients of intrinsic connectivity within the semantic network relate to distinct aspects of semantic cognition. *Cortex, 150,* 48-60. https://doi.org/10.1016/j.cortex.2022.01.019.

Shallice, T. (1988). *From Neuropsychology to mental structure.* Cambridge: Cambridge University Press. https://doi.org/10.1017/CBO9780511526817.

Shashidhara, S., & Erez, Y. (2019). Reward motivation modulates representation of behaviorally-relevant information across the frontoparietal cortex. *bioRxiv.* https://doi.org/10.1101/609537.

Shashidhara, S., Mitchell, D. J., Erez, Y., & Duncan, J. (2019). Progressive recruitment of the frontoparietal multiple-demand system with increased task complexity, time pressure, and reward. *Journal of Cognitive Neuroscience, 31*(11), 1617-1630. https://doi.org/10.1162/jocn_a_01440.

Sheldon, S., Fenerci, C., & Gurguryan, L. (2019). A neurocognitive perspective on the forms and functions of autobiographical memory retrieval. *Frontiers in Systems Neuroscience, 13*(4), 1-6. https://doi.org/10.3389/fnsys.2019.00004.

Sheldon, S., & Levine, B. (2016). The role of the hippocampus in memory and mental construction. *Annals of the New York Academy of Sciences, 1369*(1), 76-92. https://doi.org/10.1111/nyas.13006.

Sierpowska, J., Gabarrós, A., Fernández-Coello, A., Camins, À., Castañer., S., Juncadella., M., François., C., & Rodríguez-Fornells, A. (2019). White-matter pathways and semantic processing: intrasurgical and lesion-symptom mapping evidence. *NeuroImage: Clinical, 22*, 101704. https://doi.org/10.1016/j.nicl.2019.101704.

Small, D. M., Gitelman, D., Simmons, K., Bloise, S. M., Parrish, T., & Mesulam, M. M. (2005). Monetary incentives enhance processing in brain regions mediating top-down control of attention. *Cerebral Cortex, 15*, 1855-1865. https://doi.org/10.1093/cercor/bhi063.

Smallwood, J., Bernhardt, B. C., Leech, R., Bzdok, D., Jefferies, E., & Margulies, D. S. (2021). The default mode network in cognition: A topographical perspective. *Nature Reviews Neuroscience.* https://doi.org/10.1038/s41583-021-00474-4.

Smith, S. M., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E. J., Johansen-Berg, H., Bannister, P. R., De Luca, M., Drobnjak, I., Flitney, D. E., Niazy, R., Saunders, J., Vickers, J., Zhang, Y., De Stefano, N., Brady, J. M., & Matthews, P. M. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *NeuroImage, 23*(S1), 208-219. https://doi.org/10.1016/j.neuroimage.2004.07.051.

Smith, S. M., & Nichols, T. E. (2009). Threshold-free cluster enhancement: Addressing problems of smoothing, threshold dependence and localisation in cluster inference. *NeuroImage, 44*(1), 83-98. https://doi.org/10.1016/j.neuroimage.2008.03.061.

Snodgrass, J. G., & Corwin, J. (1988). Pragmatics of measuring recognition memory: Applications to dementia and amnesia. *Journal of Experimental Psychology: General, 117*(1), 34-50. https://doi.org/10.1037//0096-3445.117.1.34.

Souter, N. E., Lindquist, K. A., & Jefferies, E. (2021). Impaired emotion perception and categorization in semantic aphasia. *Neuropsychologia, 162*, 108052. https://doi.org/10.1016/j.neuropsychologia.2021.108052.

Souter, N. E., Reddy, A., Walker, J., Marino Dávolos, J., & Jefferies, E. (2022). How do valence and meaning interact? The contribution of semantic control. PsyArXiv. https://doi.org/10.31234/osf.io/vte82.

Souter, N. E., Stampacchia, S., Hallam, G., Thompson, H., Smallwood, J., & Jefferies, E. (2022). Motivated semantic control: Exploring the effects of extrinsic reward and self-reference on semantic retrieval in semantic aphasia. *Journal of Neuropsychology, 16*(2), 407-433. https://doi.org/10.1111/jnp.12272.

Souter, N., Wang, X., Thompson, H., Krieger-Redwood, K., Halai, A. D., Lambon Ralph, M. A., Thiebaut de Schotten, M., & Jefferies, E. (2022). Mapping lesion, structural disconnection, and functional disconnection to symptoms in semantic aphasia. *Brain Structure and Function, 227*, 3043-3061. https://doi.org/10.1007/s00429-022-02526-6.

Soutschek, A., & Tobler, P. N. (2018). Motivation for the greater good: neural mechanisms of overcoming costs. *Current Opinion in Behavioral Sciences, 22*, 96-105. https://doi.org/10.1016/j.cobeha.2018.01.025.

Spiers, H. J., Love, B. C., Le Pelley, M. E., Gibb, C. E., & Murphy, R. A. (2017). Anterior temporal lobe tracks the formation of prejudice. *Journal of Cognitive Neuroscience, 29*(3), 530-544. https://doi.org/10.1162/jocn_a_01056.

Spitz, G., Maller, J. J., O'Sullivan, R., & Ponsford, J. L. (2013). White matter integrity following traumatic brain injury: The association with severity of injury and cognitive functioning. *Brain Topography, 26*(4), 648-660. https://doi.org/10.1007/s10548-013-0283-0.

Spreng, R. N., Sepulcre, J., Turner, G. R., Stevens, W. D., & Schacter, D. L. (2013). Intrinsic architecture underlying the relations among the default, dorsal attention, and frontoparietal control networks of the human brain. *Journal of Cognitive Neuroscience, 25*(1), 74-86. https://doi.org/10.1162/jocn_a_00281.

Stampacchia, S., Hallam, G. P., Thompson, H. E., Nathaniel, U., Lanzoni, L., Smallwood, J., Lambon Ralph, M. A., & Jefferies, E. (2021). Training flexible conceptual retrieval in post-stroke aphasia. *Neuropsychological Rehabilitation, 32*(7), 1429-1455. https://doi.org/10.1080/09602011.2021.1895847.

Stampacchia, S., Pegg, S., Hallam, G., Smallwood, J., Lambon Ralph, M. A., Thompson, H., & Jefferies, E. (2019). Control the source: Source memory for semantic, spatial and self-related items in patients with LIFG lesions. *Cortex, 119*, 165-183. https://doi.org/10.1016/j.cortex.2019.04.014.

Stampacchia, S., Thompson, H. E., Ball, E., Nathaniel, U., Hallam, G., Smallwood, J., Lambon Ralph, M. A., & Jefferies, E. (2018). Shared processes resolve competition within and between episodic and semantic memory: Evidence from patients with LIFG lesions. *Cortex, 108*, 127-143. https://doi.org/10.1016/j.cortex.2018.07.007.

Stephan, K. E., Harrison, L. M., Penny, W. D., & Friston, K. J. (2004). Biophysical models of fMRI responses. *Current Opinion in Neurobiology, 14*(5), 629-635. https://doi.org/10.1016/j.conb.2004.08.006.

Stevenson, R. A., Mikels, J. A., & James, T. W. (2007). Characterization of the affective norms for English words by discrete emotional categories. *Behavior Research Methods, 39*(4), 1020-1024. https://doi.org/10.3758/BF03192999.

Stoodley, C. J., & Schmahmann, J. D. (2009). Functional topography in the human cerebellum: A meta-analysis of neuroimaging studies. *NeuroImage, 44*(2), 489-501. https://doi.org/10.1016/j.neuroimage.2008.08.039.

Sui, J., He, X., & Humphreys, G. W. (2012). Perceptual effects of social salience: Evidence from self-prioritization effects on perceptual matching. *Journal of Experimental Psychology: Human Perception and Performance, 38*(5), 1105–1117. https://doi.org/10.1037/a0029792.

Sui, J., & Humphreys, G. W. (2013). Self-referential processing is distinct from semantic elaboration: Evidence from long-term memory effects in a patient with amnesia and semantic impairments. *Neuropsychologia, 51,* 2663-2673. https://doi.org/10.1016/j.neuropsychologia.2013.07.025.

Sui, J., & Humphreys, G. W. (2015a). The interaction between self-bias and reward: evidence for common and distinct processes. *The Quarterly Journal of Experimental Psychology, 68*(10), 1952-1964. https://doi.org/10.1080/17470218.2015.1023207.

Sui, J., & Humphreys, G. W. (2015b). The integrative self: how self-reference integrates perception and memory. *Trends in Cognitive Sciences, 19*(2), 719-727. https://doi.org/10.1016/j.tics.2015.08.015.

Swirsky, L. T., & Spaniol, J. (2019). Cognitive and motivational selectivity in healthy aging. *WIREs Cognitive Science,* e1512. https://doi.org/10.1002/wcs.1512.

Talmi, D., & McGarry, L. M. (2012). Accounting for immediate emotional memory enhancement. *Journal of Memory and Language, 66*(1), 93-108. https://doi.org/10.1016/j.jml.2011.07.009.

Tamir, D. I., & Mitchell, J. P. (2012). Disclosing information about the self is intrinsically rewarding. *PNAS, 109*(21), 8038-8043. https://doi.org/10.1073/pnas.120212910.

Teige, C., Cornelissen, P. L., Mollo, G., Gonzalez Alam, T. R. D. J., McCarty, K., Smallwood, J., & Jefferies, E. (2019). Dissociations in semantic cognition: Oscillatory evidence for opposing effects of semantic control and type of semantic relation in anterior and posterior temporal cortex. *Cortex, 120,* 308-325. https://doi.org/10.1016/j.cortex.2019.07.002.

The tedana Community, Zaki, A., Bandettini, P. A., Bottenhorn, K. L., Caballero-Gaudes, C., Dowdle, L. T., DuPre, E., Gonzalez-Castillo, J., Handwerker, D., Heunis, S., Kundu, P., Laird, A. R., Markello, R., Markiewicz, C. J., Maullin-Sapey, T., Moia, S., Salo, T., Staden, I., Teves, J., Uruñuela, E., Vaziri-Pashkam, M., & Whitaker, K. (2021). ME-ICA/tedana: 0.0.11. *Zenodo.* https://doi.org/10.5281/zenodo.5541689.

Thiebaut de Schotten, M., Dell'Acqua, F., Forkel, S. J., Simmons, A., Vergani, F., Murphy, D. G., & Catani, M. (2011). A lateralized brain network for visuospatial attention. *Nature Neuroscience, 14*(10), 1245-1246. https://doi.org/10.1038/nn.2905.

Thiebaut de Schotten, M., Dell'Acqua, F., Ratiu, P., Leslie, A., Howells, H., Cabanis, E., Iba-Zizen, M. T., Plaisant, O., Simmons, A., Dronkers, N. F., Corkin, S., & Catani, M. (2015). From Phineas Gage and

Monsieur Leborgne to H.M.: Revisiting disconnection syndromes. *Cerebral Cortex, 25*(12), 4812-4827. https://doi.org/10.1093/cercor/bhv173.

Thiebaut de Schotten, M., Foulon, C., & Nachev, P. (2020). Brain disconnections link structural connectivity with function and behaviour. *Nature Communications, 11*, 5094. https://doi.org/10.1038/s41467-020-18920-9.

Thiebaut de Schotten, M., Tomaiuolo, F., Aiello, M., Merola, S., Silvetti, M., Lecce, F., Bartolomeo, P., & Doricchi, F. (2014). Damage to white matter pathways in subacute and chronic spatial neglect: A group study and 2 single-case studies with complete virtual "in vivo" tractography dissection. *Cerebral Cortex, 24*(3), 691-706. https://doi.org/10.1093/cercor/bhs351.

Thompson, H. E., Almaghyuli, A., Noonan, K. A., barak, O., Lambon Ralph, M. A., & Jefferies, E. (2018). The contribution of executive control to semantic cognition: Convergent evidence from semantic aphasia and executive dysfunction. *Journal of Neuropsychology, 12*, 312-340. https://doi.org/10.1111/jnp.12142.

Thompson, H., Davey, J., Hoffman, P., Hallam, G., Kosinski, R., Howkins, S., Wooffindin, E., Gabbitas, R., & Jefferies, E. (2017). Semantic control deficits impair understanding of thematic relationships more than object identity. *Neuropsychologia, 104*, 113-125. https://doi.org/10.1016/j.neuropsychologia.2017.08.013.

Thompson, H. E., Henshall, L., & Jefferies, E. (2016). The role of the right hemisphere in semantic control: A case-series comparison of right and left hemisphere stroke. *Neuropsychologia, 85*, 44-61. https://doi.org/10.1016/j.neuropsychologia.2016.02.030.

Thompson, H. E., Noonan, K. A., Halai, A. D., Hoffman, P., Stampacchia, S., Hallam, G., Rice, G. E., De Dios Perez, B., Lambon Ralph, M. A., & Jefferies, E. (2022). Damage to temporoparietal cortex is sufficient for impaired semantic control. *Cortex, 156*, 71-85. https://doi.org/10.1016/j.cortex.2022.05.022.

Thompson-Schill, S. L., D'Esposito, M., Aguirre, G. K., & Farah, M. J. (1997). Role of left inferior prefrontal cortex in retrieval of semantic knowledge: A reevaluation. *PNAS, 94*(26), 14792-14797. https://doi.org/10.1073/pnas.94.26.14792.

Toronov, V., Walker, S., Gupta, R., Choi, J. H., Gratton, E., Hueber, D., & Webb, A. (2003). The roles of changes in deoxyhemoglobin concentration and regional cerebral blood volume in the fMRI BOLD signal. *NeuroImage, 19*(4), 1521-1531. https://doi.org/10.1016/S1053-8119(03)00152-6.

Tracy, J. L., & Robins, R. W. (2008). The automaticity of emotion recognition. *Emotion, 8*(1), 81–95. https://doi.org/10.1037/1528-3542.8.1.81.

Umarova, R., & Thomalla, G. (2020). Indirect connectome-based prediction of post-stroke deficits: Prospects and limitations. *Brain, 143*(7), 1966-1970. https://doi.org/10.1093/brain/awaa186.

van den Berg, E., Nys, G. M. S., Brands, A. M. A., Ruis, C., van Zandvoort, M. J. E., & Kessels, R. P. C. (2009). The Brixton Spatial Anticipation Test as a test for executive function: Validity in patient

groups and norms for older adults. *Journal of the International Neuropsychological Society, 15,* 695-703. https://doi.org/10.1017/S1355617709990269.

van den Heuvel, M. P., & Pol, H. E. H. (2010). Exploring the brain network: A review on resting-state fMRI functional connectivity. *European Neuropsychopharmacology, 20*(8), 519-534. https://doi.org/10.1016/j.euroneuro.2010.03.008.

van der Meer, L., Costafreda, S., Aleman, A., & David, A. S. (2010). Self-reflection and the brain: A theoretical review and meta-analysis of neuroimaging studies with implications for schizophrenia. *Neuroscience & Biobehavioral Reviews, 34*(6), 935-946. https://doi.org/10.1016/j.neubiorev.2009.12.004.

Van Essen, D. C., Smith, S. M., Barch, D. M., Behrens, T. E., Yacoub, E., Ugurbil, K., & WU-Minn HCP Consortium. (2013). The WU-Minn Human Connectome Project: an overview. *NeuroImage, 80,* 62-79. https://doi.org/10.1016/j.neuroimage.2013.05.041.

Van Heuven, W. J. B., Mandera, P., Keuleers, E., & Brysbaert, M. (2014). Subtlex-UK: A new and improved word frequency database for British English. *Quarterly Journal of Experimental Psychology, 67,* 1176-1190. https://doi.org/10.1080/17470218.2013.850521.

Varela, F. J., Thompson, E., & Rosch, E. (1991). *The embodied mind: Cognitive science and human experience*. Cambridge, MA: MIT Press.

Vatansever, D., Bzdok, D., Wang, H-T., Mollo, G., Sormaz, M., Murphy, C., Karapanagiotidis, T., Smallwood, J., & Jefferies, E. (2017). Varieties of semantic cognition revealed through simultaneous decomposition of intrinsic brain connectivity and behaviour. *Neuroimage, 158,* 1-11. https://doi.org/10.1016/j.neuroimage.2017.06.067.

Vatansever, D., Manktelow, A. E., Sahakian, B. J., Menon, D. K., & Stamatakis, E. A. (2017). Angular default mode network connectivity across working memory load, *Human Brain Mapping, 38*(1), 41-52. https://doi.org/10.1002/hbm.23341.

Vatansever, D., Smallwood, J., & Jefferies, E. (2021). Varying demands for cognitive control reveals shared neural processes supporting semantic and episodic memory retrieval. *Nature Communications, 12,* 2134. https://doi.org/10.1038/s41467-021-22443-2.

Vigliocco, G., Kousta, S-T., Della Rosa, P. A., Vinson, D. P., Tettamanti, M., Devlin, J. T., & Cappa, S. F. (2014). The neural representation of abstract words: The role of emotion. *Cerebral Cortex, 24,* 1767-1777. https://doi.org/10.1093/cercor/bht025.

Vigliocco, G., Krason, A., Stoll, H., Monti, A., & Buxbaum, L. J. (2020). Multimodal comprehension in left hemisphere stroke patients. *Cortex, 133,* 309-327. https://doi.org/10.1016/j.cortex.2020.09.025.

Vigliocco, G., Meteyard, L., Andrews, M., & Kousta, S. (2009). Toward a theory of semantic representation. *Language and Cognition, 1-2,* 219-247. https://doi.org/10.1515/LANGCOG.2009.011.

Vinson, D., Ponari, M., & Vigliocco, G. (2014). How does emotional content affect lexical processing? *Cognition & Emotion, 28*(4), 737-746. https://doi.org/10.1080/02699931.2013.851068.

Visser, M., Jefferies, E., & Lambon Ralph, M. A. (2010). Semantic processing in the anterior temporal lobes: A meta-analysis of the functional neuroimaging literature. *Journal of Cognitive Neuroscience, 22*(6), 1083-1094. https://doi.org/10.1162/jocn.2009.21309.

Visser, M., & Lambon Ralph, M. A. (2011). Differential contributions of bilateral ventral anterior temporal lobe and left anterior superior temporal gyrus to semantic processes. *Journal of Cognitive Neuroscience, 23*(10), 3121–3131. https://doi.org/10.1162/jocn_a_00007.

Voineskos, A. N., Rajji, T. K., Lobaugh, N. J., Miranda, D., Shenton, M. E., Kennedy, J. L., Pollock, B. G., & Mulsant, B. H. (2012). Age-related decline in white matter tract integrity and cognitive performance: A DTI tractography and structural equation modeling study. *Neurobiology of Aging, 33,* 21-34. https://doi.org/10.1016/j.neurobiolaging.2010.02.009.

Von Der Heide, R. J., Skipper, L. M., Klobusicky, E., & Olson, I. R. (2013). Dissecting the uncinate fasciculus: Disorders, controversies and a hypothesis. *Brain, 136*(6), 1692-1707. https://doi.org/10.1093/brain/awt094.

Wang, R., Benner, T., Sorensen, A. G., & Wedeen, V. J. (2007). Diffusion toolkit: A software package for diffusion imaging data processing and tractography. *Proceedings of the International Society for Magnetic Resonance in Medicine, 15,* 3720.

Wang, X., Bernhardt, B. C., Karapanagiotidis, T., De Caso, I., Gonzalez Alam, T. R. D. J., Cotter, Z., Smallwood, J., & Jefferies, E. (2018). The structural basis of semantic control: Evidence from individual differences in cortical thickness. *NeuroImage, 181,* 480-489. https://doi.org/10.1016/j.neuroimage.2018.07.044.

Wang, X., Gao, Z., Smallwood, J., & Jefferies, E. (2021). Both default and multiple-demand regions represent semantic goal information. *Journal of Neuroscience, 41*(16), 3679-3691. https://doi.org/10.1523/JNEUROSCI.1782-20.2021.

Wang, X., Margulies, D. S., Smallwood, J., & Jefferies, E. (2020). A gradient from long-term memory to novel cognition: Transitions through default mode and executive cortex. *NeuroImage, 220,* 117074. https://doi.org/10.1016/j.neuroimage.2020.117074.

Wang, X., Wang, B., & Bi, Y. (2019). Close yet independent: Dissociation of social from valence and abstract semantic dimensions in the left anterior temporal lobe. *Human Brain Mapping, 40*(16), 4759-4776. https://doi.org/10.1002/hbm.24735.

Warriner, A. B., Kuperman, V., & Brysbaert, M. (2013). Norms of valence, arousal, and dominance for 13,915 English lemmas. *Behavior Research Methods, 45,* 1191-1207. https://doi.org/10.3758/s13428-012-0314-x.

Warrington, E. K., & James, M. (1991). *The Visual Object and Space Battery Perception*. Bury St Edmunds: Thames Valley Company.

Warrington, E. K., & Shallice, T. (1984). Category specific semantic impairments. *Brain, 107*(3), 829-853. https://doi.org/10.1093/brain/107.3.829.

Wechsler, D. (1997). *Wechsler memory scale (3rd ed.)*. San Antonio, TX: The Psychological Corporation.

Westbrook, A., van den Bosch, R., Määttä, J. I., Hofmans, L., Papadopetrak, D., Cools, R., & Frank, M. J. (2020). Dopamine promotes cognitive effort by biasing the benefits versus costs of cognitive work. *Science, 367*(6484), 1362-1366. https://doi.org/10.1126/science.aaz5891.

Whitfield-Gabrieli, S., & Nieto-Castanon, A. (2012). Conn: A functional connectivity toolbox for correlated and anticorrelated brain networks. *Brain Connectivity, 2*(3), 125-141. https://doi.org/10.1089/brain.2012.0073.

Whitney, C., Kirk, M., O'Sullivan, J., Lambon Ralph, M. A., & Jefferies, E. (2011). The neural organization of semantic control: TMS evidence for a distributed network in left inferior frontal and posterior middle temporal gyrus. *Cerebral Cortex, 21,* 1066-1075. https://doi.org/10.1093/cercor/bhq180.

Winkler, A. M., Ridgway, G. R., Webster, M. A., Smith, S. M., & Nichols, T. E. (2014). Permutation inference for the general linear model. *NeuroImage, 92,* 381-397. https://doi.org/10.1016/j.neuroimage.2014.01.060.

Woolrich, M. W., Jdabdi, S., Patenaude, B., Chappell, M., Manki, S., Behrens, T., Beckmann, C., Jenkinson, M., & Smith, S. M. (2009). Bayesian analysis of neuroimaging data in FSL. *NeuroImage, 45,* S173-S186. https://doi.org/10.1016/j.neuroimage.2008.10.055.

Wu, Y., Wang, J., Zhang, Y., Zheng, D., Zhang, J., Rong, M., Wu, H., Wang, Y., Zhou, K., & Jiang, T. (2016). The neuroanatomical basis for posterior superior parietal lobule control lateralization of visuospatial attention. *Frontiers in Neuroanatomy, 10,* 32. https://doi.org/10.3389/fnana.2016.00032.

Xia, M., Wang, J., & He, Y. (2013). BrainNet Viewer: A network visualization tool for human brain connectomics. *PLoS One, 8*(7), e68910. https://doi.org/10.1371/journal.pone.0068910.

Yarkoni, T., Poldrack, R., Nichols, T., Van Essen, D. C., & Wager, T. D. (2011). Large-scale automated synthesis of human functional neuroimaging data. *Nature Methods, 8*(8), 665-670. https://doi.org/10.1038/nmeth.1635.

Yee, D. M., Adams, S., Beck, A., & Braver, T. S. (2019). Age-related differences in motivational integration and cognitive control. *Cognitive, Affective, & Behavioral Neuroscience, 19,* 692-714. https://doi.org/10.3758/s13415-019-00713-3.

Yee, D. M., & Braver, T. S. (2018). Interactions of motivation and cognitive control. *Current Opinion in Behavioral Sciences, 19,* 83-90. https://doi.org/10.1016/j.cobeha.2017.11.009.

Yeo, B. T. T., Krienen, F. M., Sepulcre, J., Sabuncu, M. R., Lashkari, D., Hollinshead, M., Roffman, J. L., Smoller, J. W., Zöllei, L., Polimeni, J. R., Fischl, B., Liu, H., Buckner, R. L. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology, 106*(3), 1125-1165. https://doi.org/10.1152/jn.00338.2011.

Yin, S., Li, Y., & Chen, A. (2022). Functional coupling between frontoparietal control subnetworks bridges the default and dorsal attention networks. *Brain Structure and Function, 227,* 2243-2260. https://doi.org/10.1007/s00429-022-02517-7.

Zemack-Rugar, Y., Bettman, J. R., & Fitzsimons, G. J. (2007). The effects of nonconsciously priming emotion concepts on behavior. *Journal of Personality and Social Psychology, 93*(6), 927-939. https://doi.org/10.1037/0022-3514.93.6.927.

Zhang, M., Bernhardt, B. C., Wang, X., Varga, D., Krieger-Redwood, K., Royer, J., Rodríguez-Cruces, R., Vos de Wael, R., Margulies, D. S., Smallwood, J., & Jefferies, E. (2022). Perceptual coupling and decoupling of the default mode network during mind-wandering and reading. *eLife, 11,* e74011. https://doi.org/10.7554/eLife.74011.

Zhang, M., Nathaniel, U., Savill, N., Smallwood, J., & Jefferies, E. (2022). Intrinsic connectivity of left ventrolateral prefrontal cortex predicts individual differences in controlled semantic retrieval. *NeuroImage, 246,* 118760. https://doi.org/10.1016/j.neuroimage.2021.118760.

Zhang, M., Varga, D., Wang, X., Krieger-Redwood, K., Gouws, A., Smallwood, J., & Jefferies, E. (2021). Knowing what you need to know in advance: The neural processes underpinning flexible semantic retrieval of thematic and taxonomic relations. *NeuroImage, 224,* 117405. https://doi.org/10.1016/j.neuroimage.2020.117405.

Zhang, Q., Wang, H., Luo, C., Zhang, J., Jin, Z., & Li, L. (2019). The neural basis of semantic cognition in Mandarin Chinese: A combined fMRI and TMS study. *Human Brian Mapping, 40*(18), 5412-5423. https://doi.org/10.1002/hbm.24781.

Zhang, J., Wu, C., Meng, Y., & Yuan, Z. (2017). Different neural correlates of emotion-label words and emotion-laden words: An ERP study. *Frontiers in Human Neuroscience, 11,* 455. https://doi.org/10.3389/fnhum.2017.00455.

Zhao, X., Jia, L., & Maes, J. H. R. (2018). Effect of achievement motivation on cognitive control adaptations. *Journal of Cognitive Psychology, 30*(4), 453-465. https://doi.org/10.1080/20445911.2018.1467915.

Zhao, W., Li, Y., & Du, Y. (2021). TMS reveals dynamic interaction between inferior frontal gyrus and posterior middle temporal gyrus in gesture-speech semantic integration. *Journal of Neuroscience, 41*(50), 10356-10364. https://doi.org/10.1523/JNEUROSCI.1355-21.2021.

Zhou, P., Critchley, H., Garfinkel, S., & Gao, Y. (2021). The conceptualization of emotions across cultures: A model based on interoceptive neuroscience. *Neuroscience and Biobehavioral Reviews, 125,* 314-327. https://doi.org/10.1016/j.neubiorev.2021.02.023.

Zhuang, Q., Xu, L., Zhou, F., Yao, S., Zheng, X., Zhou, X., Li, J., Xu, X., Fu, M., Li, K., Vatansever, D., Kendrick, K. M., & Becker, B. (2021). Segregating domain-general from emotional context-specific inhibitory control systems - ventral striatum and orbitofrontal cortex serve as emotion-cognition integration hubs. *NeuroImage, 238,* 118269. https://doi.org/10.1016/j.neuroimage.2021.118269.

Zoom Video Communications Inc. (2016). *Security guide. Zoom Video Communications Inc.* Retrieved from https://d24cgw3uvb9a9h.cloudfront.net/static/81625/doc/Zoom-Security-White-Paper.pdf.