Shared mechanisms support controlled retrieval from semantic and episodic memory: Evidence from semantic aphasia

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Abstract

Semantic cognition is supported by at least two interactive components: semantic representations and control mechanisms that shape retrieval to suit the circumstances. Semantic and episodic memory draw on largely distinguishable stores, yet it is unclear whether controlled retrieval from these representational systems is supported by shared mechanisms. Patients with semantic aphasia (SA) show heteromodal semantic control deficits following stroke to left inferior frontal gyrus (LIFG), an area implicated in semantic processing plus the control of memory and language. However, episodic memory has not been examined in these patients and although the role of LIFG in semantics is well-established, neuroimaging cannot ascertain whether this area is directly implicated in episodic control or if its activation reflects semantic processing elicited by the stimuli. Neuropsychology can address this question, revealing whether this area is necessary for both domains. We found that: (i) SA patients showed difficulty discarding dominant yet irrelevant semantic links during semantic and episodic decisions. Similarly, recently encoded events promoted interference during retrieval from both domains. (ii) Deficits were multimodal (i.e. equivalent using words and pictures) in both domains and, in the episodic domain, memory was compromised even when semantic processing required by the stimuli was minimal. (iii) In both domains, deficits were ameliorated when cues reduced the need to internally constrain retrieval. These cues could involve semantic information, self-reference or spatial location, representations all thought to be unaffected by IFG lesions. (iv) Training focussed on promoting flexible retrieval of conceptual knowledge showed generalization to untrained semantic and episodic tasks in some individuals; in others repetition of specific associations gave rise to inflexible retrieval and overgeneralization of trained associations during episodic tasks. Although the neuroanatomical specificity of neuropsychology is limited, this thesis provides evidence that shared mechanisms support the controlled retrieval of episodic and semantic memory.

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The author

I obtained BSc and Msc degrees in Psychology at the Università di Pisa (Italy) in 2009 and 2012. There I developed an interest in clinical neuropsychology and memory. After some experience as an Assistant Neuropsychologist I decided to pursue a PhD and I moved to York in 2014.

Declarations

I declare that this thesis is a presentation of original work and I am the primary or sole author. This work has not previously been presented for an award at this or any other University. All sources are acknowledged as References. Part of the work in this thesis has been submitted/published in scientific journals in collaboration with others. Acknowledgements for contributions of each co-author are at the beginning of each chapter.

Chapter 2 is a published paper: *Shared processes resolve competition within and between episodic and semantic memory: Evidence from patients with LIFG lesions.* Stampacchia S, Thompson HE, Ball E, Nathaniel U, Hallam G, Smallwood J, Lambon Ralph M and Jefferies E, Cortex 2018

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Sara Stampacchia,
The author

I declare that this thesis is primarily the work of Sara Stampacchia. My contribution to the papers listed above was primarily editing and supervision of the research. Sara Stampacchia collected much of the data (the contribution of others to specific datasets is acknowledged at the start of each chapter). She also completed the analyses, took the primary role in designing neuropsychological assessments, and wrote the first draft of the manuscripts above. When I am named as co-author, this was due to my role of editing and supervision.

Prof. Elizabeth Jefferies,
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This thesis is dedicated to the memory of my grandmother Sara,
my cousin Davide,
and my beloved cat Nana.

CHAPTER 1

Literature Review

1. Overview

Convergent evidence suggests that the anterior temporal lobes (ATL) and the hippocampus are critical substrates for the representation of heteromodal semantic and episodic memory respectively (Eichenbaum, 2017; Lambon Ralph *et al.*, 2017). Neuropsychology has revealed that ATL atrophy is associated with degraded conceptual knowledge, yet largely intact memory for recent events (cf. semantic dementia, SD, Binney, Embleton, Jefferies, Parker, & Lambon Ralph, 2010). Conversely, damage to the hippocampus and associated medial temporal structures is thought to affect the capacity to encode and retrieve recent events, while leaving conceptual knowledge largely uncompromised (cf. anterograde amnesia, Nadel & Moscovitch, 1997). This double dissociation reflects distinct properties of the two memory systems. Conceptual knowledge is acquired and continuously updated over the life-span through the extraction of multimodal features across multiple experiences. These rich representations are thought to be organized in a web-like structure and activation spreads automatically between related concepts (i.e. the concept of APPLE can activate the concept of TREE, TART and so on..., Patterson, Nestor, & Rogers, 2007). Conversely, episodic memory captures the co-occurrence of objects and people in time and space, in order to form separated and unique memory engrams of events.

Although these representations may draw on separable neural substrates within the temporal lobes, there is strong interaction between them during both encoding and retrieval. In some circumstances the two memory systems can be mutually supportive, yet in others they may be in conflict with each other. For example, memories for events (e.g. the memory of your most recent BIRTHDAY PARTY) draw strongly on conceptual knowledge (e.g. CAKES are usually served in celebration of birthdays) and this can be helpful in retrieving details of the event but can also promote false memories (e.g. remembering that a birthday cake was served when actually it was not). Similarly, recent events (e.g. a VISIT TO THE BANK) might either sustain or imperil the efficient retrieval of semantic knowledge (e.g. understanding that bank refers to the edge of a lake), by altering the way that inputs are interpreted and the manner in which activation spreads between concepts.

In addition, an emerging consensus suggests that multiple neurocognitive processes underpin retrieval from both semantic and episodic memory stores. Neuropsychological studies have showed that storage and controlled retrieval deficits are dissociable in the semantic domain. Patients with SD have degraded semantic knowledge, whereas patients with semantic aphasia (SA) following cerebro-vascular accident (CVA) to fronto-temporo-parietal regions show deficits of semantic control in the face of intact semantic knowledge (Jefferies and Lambon Ralph, 2006). The neuroimaging literature also shows that distinct brain networks support automatic and controlled aspects of retrieval (Badre and Wagner, 2007; Jefferies, 2013; Noonan *et al.*, 2013; Barredo *et al.*, 2015; Lambon Ralph *et al.*, 2017). Memories of past events or elements of semantic knowledge can pop up into awareness apparently automatically when triggered by the context or existing thoughts. This type of processing is thought to be largely supported by a brain network that is activated at rest during task-unrelated thoughts, i.e. the so-called default-mode network (DMN, Buckner, Andrews-Hanna, & Schacter, 2008; Raichle et al., 2001). The DMN has relatively strong connectivity with the two memory systems, i.e. with ATL and hippocampus (Yeo *et al.*, 2011). In other circumstances, retrieval is an effortful process and may require control over retrieval and selection between competing memory representations. For example, control is thought to be required when contextual information has to be taken into account to disambiguate aspects of knowledge (e.g. “that jam was awful”, which could mean being stuck in traffic or nasty marmalade) or when interference from past events needs to be discarded (e.g. remembering where in the parking lot you left your car this morning, as opposed to most mornings). In both situations there is a need to shape the retrieval of activated memories to suit the circumstances. A formal ALE meta-analysis by Noonan, Jefferies, Visser, & Lambon Ralph (2013) shows that semantic control is underpinned by a network of fronto-temporoparietal areas encompassing left inferior frontal gyrus (LIFG), posterior RIFG, posterior middle temporal gyrus (pMTG), dorsal angular gyrus bordering IPS (dAG/IPS) and pre-supplementary motor area (pre-SMA). A parallel neuroimaging literature suggest that overlapping areas are recruited in episodic tasks tapping control (in particular LIFG, Badre & Wagner, 2007).

The neuroimaging literature has shown that LIFG is activated by tasks tapping control in both the episodic and semantic domains, and several accounts suggest that it plays an important role in controlled retrieval of memory (Thompson-Schill *et al.*, 1997; Badre *et al.*, 2005; Badre and Wagner, 2007; Barredo *et al.*, 2015). This research suggests that control processes may be shared across episodic and semantic tasks. However, neuroimaging is correlational and causal inferences cannot be drawn. Neuropsychology can enrich these neuroimaging findings by revealing brain areas that are crucial for control processes in both domains. This thesis aims to address whether control processes are shared across semantic and episodic memory by testing patients with well-documented semantic control deficits and LIFG lesions (patients with SA) using episodic memory tasks that also varied in their control demands. In Chapter 2, we examined whether SA patients showed parallel deficits in both domains using paired associates tasks. In Chapter 3 we further assessed their episodic memory using a different episodic memory paradigm tapping control processes (i.e. source memory). In Chapter 4, we examined whether training on a task that aimed to improve semantic control had equivalent effects in both semantic and episodic tasks that were untrained.

In the remainder of this chapter, the rationale for this thesis is described in the light of two separate literatures relevant to memory control, focused on semantic and episodic tasks. In section 1, the nature of dissociable deficits in semantic cognition will be reviewed, while sections 2 and 3 will focus on neuroimaging studies examining controlled retrieval from semantic and episodic memory, respectively. Section 4 will discuss the possibility of shared neurocognitive mechanisms of memory control and describe circumstances that may potentially alleviate the impact of deficient memory control. Section 5 will anticipate the content of each empirical chapter.

2. Dissociable deficits in semantic cognition

In order to accurately retrieve meaning and use it appropriately, we need at least two principal components: stored conceptual representations and control processes (cf. Controlled Semantic Cognition framework, CSC, Lambon Ralph et al., 2017). Semantic control is the mechanism that supervises the spread of activation between concepts and allows us to retrieve information in a goal-relevant manner (Jefferies, 2013). For example, the concept of NEWSPAPER is associated with a web of associated information: we know it is a publication containing news/articles/advertisements; that it is regularly distributed online or in print on a daily, weekly or monthly basis; we know where in our house we keep the old ones, etc. However, this information is mostly irrelevant if we need to get rid of a fly in the room in the absence of a fly swap (Corbett *et al.*, 2011). In circumstances such as this one, only a subset of the semantic features associated with the concept (in this case, its shape and sturdiness) are relevant for the task at hand. Semantic control is the process that allows us to shape retrieval from the web of semantic knowledge that we have acquired in our lifespan to suit the current requirements.

Some of the earliest evidence for the distinction between conceptual representations and control processes that act on these representations was provided by neuropsychology. Patient studies have shown a double dissociation between degradation of semantic representations in Semantic Dementia and 'deregulated' retrieval of conceptual information, despite largely intact knowledge, in Semantic Aphasia (Jefferies and Lambon Ralph, 2006; Rogers *et al.*, 2015). These studies are described below.

2.1. Degraded representations in Semantic Dementia

Semantic dementia is a progressive degenerative disorder associated with cerebral atrophy circumscribed to the ATLs (Snowden *et al.*, 1989). Patients with SD show progressive degradation of conceptual representations and their deficits correlate with the extent of bilateral atrophy and hypometabolism of the ventrolateral ATLs (Mummery *et al.*, 2000; Nestor *et al.*, 2006). These patients show multimodal loss of knowledge about items across tasks with different input modalities and control demands, e.g. knowledge about the item "DOG" is consistently lost when probed using naming, word-picture matching, sound-picture matching and semantic associative tasks (Bozeat *et al.*, 2000; Jefferies and Lambon Ralph, 2006). During picture naming, SD patients typically produce superordinate responses (from a hierarchically higher category, e.g. DOG → 'animal') and coordinate-categorical errors (from the same category, e.g. DOG → 'cat'), reflecting preserved knowledge about general categories and loss of specific concepts (Jefferies and Lambon Ralph, 2006). They show loss of knowledge about atypical exemplars first (e.g. they correctly include BUDGIE but not EMU in the category 'birds'), suggesting that boundaries between concepts have become degraded (Mayberry et al., 2011). In line with the idea that most frequently encountered items have stronger semantic representations, they show better preservation of frequent rather than infrequent items (e.g. HORSE vs. ZEBRA, Bozeat et al., 2000; Jefferies, Patterson, Jones, & Lambon Ralph, 2009). Finally, they are relatively insensitive to phonemic cues during picture naming (e.g. e.. el.. ele.. for ELEPHANT), showing evidence of loss of semantic knowledge rather than a difficulty of access (Jefferies *et al.*, 2008a). Collectively these findings reflect a gradual loss of semantic knowledge from specific to general.

2.1.1. The Anterior Temporal Lobes as heteromodal hub of semantic knowledge

The 'hub-and-spokes' model of semantic cognition (Rogers *et al.*, 2004; Patterson *et al.*, 2007; Lambon Ralph *et al.*, 2017) proposes that semantic knowledge is mediated by the ATLs (i.e. the 'hub' or 'convergence zone') and other neocortical regions (i.e. the 'spokes'), which code for modality-specific features (e.g. auditory, visual, praxis, function and valence). According to this model, semantic knowledge emerges through the extraction of heteromodal coherent conceptual knowledge (mediated by the 'hub') from the different modalities with which we can learn about the world (mediated by the 'spokes'). This theory was strongly motivated by the findings from patients with SD. These patients with bilateral ATL atrophy, yet intact "spoke" regions, show equivalent loss of semantic knowledge when tested using different input modalities.

Although the extent of the atrophy in patients with SD often encompasses the whole bilateral ATL region, more recent evidence has suggested graded functional specialization within the ATL, reflecting the long-range connectivity of ATL subdivisions with 'spoke' regions (Lambon Ralph *et al.*, 2017). Strong convergent evidence from (i) correlational studies between neuropsychological deficits and brain structural data from SD patients (Mummery *et al.*, 2000; Nestor *et al.*, 2006), (ii) neuroscientific data from rTMS, distortion corrected fMRI and diffusion weighted imaging in healthy individuals (Binney et al., 2010; Binney, Parker, & Lambon Ralph, 2012; Visser & Lambon Ralph, 2011; Visser, Jefferies, Embleton, & Lambon Ralph, 2012) and (iii) electrophysiological recordings from humans (Abel *et al.*, 2015) suggest that the ventrolateral portion of the ATLs is crucial for heteromodal semantic representations, as it responds to semantic tasks irrespective of modality of presentation or stimulus category. By contrast, medial ATL shows a stronger response to visual and concrete stimuli (Hoffman, Binney, & Lambon Ralph, 2015; Visser et al., 2012); superior ATL shows a preference for auditory, spoken and abstract stimuli (Hoffman *et al.*, 2015) and dorso-polar ATL is sensitive to abstract social stimuli (Zahn *et al.*, 2007).

The 'hub and spoke' is not the sole model of semantic cognition and its neural basis. Alternative accounts have largely been inspired by observation of category-specific variation of semantic performance in various neurological patients (see Mahon & Caramazza, 2009 for a review). Lesions extending beyond ventral ATL have been associated with semantic deficits circumscribed to specific semantic categories: a classical example is the loss of knowledge of living but not man-made objects and vice versa (Humphreys & Riddoch, 2003). As anticipated above, the 'hub and spokes' model suggests that selective damage to spoke regions results in category-specific deficits (Lambon Ralph *et al.*, 2017). Similarly, the 'distributed domain-specific' account postulates that semantic knowledge is captured by patterns of connectivity across cortical regions responsible for domain-specific processing (e.g. sensory, motor, affective, conceptual; Mahon & Caramazza, 2011). Others have suggested that different semantic categories are underpinned by separable areas during input as opposed to output modalities and that conceptual knowledge results from multimodal integration in the so called ‘convergence zones’ (Damasio *et al.*, 1996). Similarly to the ‘hub and spoke model’, both accounts recognize the necessity of integration from sensory-motor inputs however, in contrast to the ‘hub and spoke’, this role is not attributed to ventral ATL, but instead to distributed cortical areas and/or patterns of connectivity (Lambon Ralph *et al.*, 2017). These models however do not explain the category-independent semantic deficits showed by SD patients with ATL lesions. The ATL has often been overlooked in fMRI studies; its anatomical location gives rise to strong magnetic susceptibility artefacts associated with signal loss and distortion (Visser, Jefferies, & Ralph, 2009), and one possibility is that this has resulted in reduced attention to this area in most fMRI studies informing these theories.

2.2. Semantic control deficits in Semantic Aphasia

The term ‘semantic aphasia’ was first coined by Head (1926) and later used by Luria (1973) to describe a subtype of patients with heterogenous aphasic symptomatology who showed difficulties in manipulating and using symbolic knowledge in verbal and non-verbal contexts. Later, Warrington (1996;1983) and colleagues introduced the distinction between *storage* and *access* deficits to distinguish the qualitatively different semantic impairment exhibited, respectively, by patients with SD and aphasia following middle cerebral artery stroke. In the last decade, research has shown that these *access* deficits are associated with deficits of ‘semantic control’ and semantic cognition in patients with SA has been extensively studied by our group and others. Since 2006, when the first systematic case-series comparison between SA and SD patients was published (Jefferies and Lambon Ralph, 2006), 46 papers containing the term “semantic aphasia” in title/abstract/keywords were published in peer reviewed journals (source: https://www.scopus.com, July 2018). The following paragraphs aim to provide a neuropsychological characterization of semantic aphasia and summarize this literature.

SA patients following CVA to left fronto-parietal regions show evidence of intact conceptual knowledge in the face of difficulties in flexibly retrieving relevant knowledge that is well-suited to the context or task-demands, in both verbal and non-verbal domains. In contrast to patients with SD, SA patients (i) have inconsistent performance on the same concepts when these are probed with tasks using different input modalities or varying in control demands (Jefferies and Lambon Ralph, 2006), reflecting *access* rather than *storage* impairments as described by Warrington et al. (1996; 1983); (ii) their performance is not affected by the frequency, familiarity or typicality of items but rather by the task characteristics (Jefferies and Lambon Ralph, 2006; Rogers *et al.*, 2015); (iii) in naming tasks, they often produce associative errors from a different category (e.g. SQUIRREL → ‘nuts’; GLASS → ‘ice’; LORRY → ‘diesel’, Jefferies & Lambon Ralph, 2006), which reflect retrieval at a very specific level of the concept which is nevertheless irrelevant for the task; (iv) similarly their performance is negatively influenced by interference from strongly related distractors in forced alternative choices tasks (e.g. they choose DASH instead of POINT as synonym of DOT); (v) they are sensitive to external constraints such as cues and miscues; for example they are aided by phonological cues during naming (e.g. e.. el.. ele.. for ELEPHANT, Jefferies et al., 2008; Noonan et al., 2010; Soni et al., 2009) and sentences probing the relevant meanings of ambiguous words (e.g. "the bank is slippery" for the association BANK – RIVER), yet their performance is negatively influenced when the context probes the irrelevant interpretations (e.g. 'the bank is slippery' for the association BANK – MONEY; Noonan et al., 2010). In line with their intact semantic knowledge, they often correctly retrieve strong associative links (e.g. SALT – PEPPER) and dominant meanings of ambiguous words (e.g. BANK – MONEY), yet they fail to retrieve distant associations (e.g. SALT – GRAIN) and subordinate interpretations (e.g. BANK – RIVER, Noonan et al., 2010), perhaps reflecting the increased need to control the spread of activation of strong but irrelevant neighboring concepts during the retrieval of less dominant meanings or associations. Finally, SA patients have been shown to have difficulties across modalities. For example, they are unable to use conceptual knowledge flexibly to support non-canonical uses of everyday objects. When the canonical object required to perform a task is not available (e.g. "hammer" to bash a nail into the wall), they have difficulties selecting an available object (e.g. "brick") that could be used instead (Corbett *et al.*, 2011). Similarly, they are sensitive to semantically related distracting objects during naturalistic tests of everyday action and object use tasks (Corbett, Jefferies and Lambon Ralph, 2009; Corbett, Jefferies, Ehsan, *et al.*, 2009; Corbett *et al.*, 2011), they show deficits in resolving competition when making judgements about environmental sounds (Jefferies and Lambon Ralph, 2006), and in judgements of associations presented as pictures as well as words (Jefferies and Lambon Ralph, 2006).

These deficits reflect difficulties in semantic control rather than a loss of semantic knowledge per se and this is consistent with the fact that SA patients do not have damage to the ventral portion of ATL. SA follows left hemisphere stroke, often affecting the middle cerebral artery or more rarely the posterior cerebral artery. The ATLs receive a double blood supply from the anterior temporal cortical artery of the middle cerebral artery and the anterior temporal branch of the distal posterior cerebral artery (Borden, 2006; Conn, 2008). It is unusual for both these blood supplies to be affected by stroke (Conn, 2008). Additionally, stroke rarely affects both hemispheres. Consequently, the ATL semantic 'hub' region is relatively invulnerable to stroke. Instead, semantic deficits in stroke aphasia are associated with damage to left prefrontal and/or posterior-temporal regions (Hart and Gordon, 1990; Chertkow *et al.*, 1997; Berthier, 2001; Hillis *et al.*, 2001; Dronkers *et al.*, 2004). The role of those areas in semantic cognition is described in the following section.

3. Semantic control network: converging evidence from TMS and neuroimaging

SA patients often have large lesions, as well as disruption to underlying white matter tracts. Therefore, it is important to consider evidence from other sources to establish links between specific brain regions or networks and their functions. Convergent evidence from TMS and fMRI studies of healthy participants has implicated a distributed network of brain areas that largely overlap with areas lesioned in SA patients in semantic control. An ALE meta-analysis based on 53 studies (71 contrasts) comparing semantic tasks with high vs. low control demands showed recruitment of the same distributed network damaged in SA patients, including the whole of LIFG extending to left inferior frontal sulcus (IFS), posterior RIFG, pre-SMA, dAG/IPS and pMTG (Noonan et al., 2013). There is also some evidence for graded functional specialization within this network, which suggests that anterior fronto-temporal portions (including anterior LIFG and pMTG) have a specific role in semantic control, while more posterior fronto-parietal areas (i.e. posterior LIFG/IFS and dAG/IPS) play a role in domain-general executive control and contribute to semantic control along with the control of other aspects of cognition (Davey *et al.*, 2016; Lambon Ralph *et al.*, 2017). Below, this view is discussed in the light of the most recent findings.

3.1. Role of LIFG in semantic control

Recent literature suggests that LIFG is not specifically implicated in language processing, but more broadly in semantic cognition, in particular, in the controlled retrieval of semantic knowledge (Thompson-Schill *et al.*, 1997; Badre *et al.*, 2005) even during non-verbal semantic tasks (Krieger-Redwood *et al.*, 2015). Activation of this region is modulated by distractors presented at retrieval, the strength of association between items, by ambiguity and the type of feature-selection required (Badre, Poldrack, Paré-Blagoev, Insler, & Wagner, 2005; Thompson-Schill, D’Esposito, Aguirre, & Farah, 1997; Wagner, Paré-Blagoev, Clark, & Poldrack, 2001). With the spatial specificity of fMRI, several authors have proposed a graded functional specialization of LIFG. Anterior LIFG (ant-LIFG or pars orbitalis) preferentially activates during semantic processing of associative links between items, with higher activation during weak vs. strong association (such as CANDLE – HALO vs. CANDLE – FLAME; Badre et al., 2005). In this situation, semantic retrieval needs to be controlled, in the sense that non-dominant aspects of meaning need to be the focus, but there are no explicit instructions that specify what the focus of retrieval should be – conceptual information itself specifies how semantic retrieval should be shaped to suit the context. In contrast, mid to posterior aspects of LIFG are recruited more generally in language tasks and are associated with conceptual retrieval that is tailored to an explicit goal, provided by the task instructions. For example, this portion of LIFG shows increased activation in semantic tasks that require participants to link words on the basis of their colour (e.g. TAR – COAL) or shape (Badre *et al.*, 2005). Posterior LIFG (post-LIFG or pars opercularis) bordering inferior frontal sulcus (IFS) is also less specific to semantic control; it is recruited during phonological tasks (such as syllable counting, Gold & Buckner, 2002; Poldrack et al., 1999), and the inferior frontal junction and IFS are implicated in domain-general cognitive control (e.g., Duncan, 2010). This graded functional distinction is also related to the organisation of distributed brain networks. While anterior-to-mid portions of LIFG form part of both the semantic control network (Noonan *et al.*, 2013) and default mode network (DMN, Yeo et al., 2011), showing functional coupling to pMTG during semantic control, more posterior portions extending to IFS and beyond form part of a network of areas thought to support domain-general executive control (i.e. the multiple demand network, MDN; Duncan, 2010).

3.2. Role of pMTG in semantic control

LIFG is not the only brain region implicated in semantic cognition; it participates in a large-scale distributed network (i.e. semantic control network; Noonan et al., 2013) and is functionally coupled with pMTG (and other regions in this network) during tasks tapping semantic control (Whitney, Jefferies, *et al.*, 2011; Davey *et al.*, 2016). There is however controversy in the literature about the role of pMTG in semantic cognition. Some studies have suggested that pMTG is necessary for capturing thematic (i.e. link between APPLE and WORM) as opposed to taxonomic (i.e. APPLE and PEAR) relationships (Schwartz et al., 2011) and have proposed that - similarly to ATL – pMTG along with AG constitutes a hub of semantic knowledge, extracting relationships between concepts rather than feature similarity. However, these findings are also compatible with a role of pMTG in semantic control. If, as advanced by the 'hub and spoke' model, the semantic hub is responsible for converting common features of experiences into context-invariant concepts, semantic units are likely to be organized on the basis of shared features and properties (Rogers *et al.*, 2004; Lambon Ralph *et al.*, 2017). Associations such as those between APPLE and WORM, which do not share features or properties, may require control especially when these semantic units are most distantly associated in the representational system (Hoffman *et al.*, 2018). In line with this view, Davey et al. (2015) showed that inhibitory TMS to pMTG disrupts the retrieval of weak but not strong thematic relationships. Other accounts propose that this area stores information about tool and action semantics since it is activated for words referring to actions (e.g. sawing; Martin, 2007) and fMRI evidence suggests that overlapping yet partially distinct portions of this area support both semantic control and action understanding (Davey, Rueschemeyer, *et al.*, 2015). In support of its role in semantic control, inhibitory TMS produces equivalent disruptive effects over LIFG and pMTG during judgements about weakly associated words (e.g. SALT – GRAIN), yet this stimulation has no effect for trials with high associative strength and therefore reduced control demands (SALT – PEPPER; Whitney et al. 2012). Although the parallel role of pMTG in semantic cognition and action understanding still represents a puzzle, this evidence suggests that anterior LIFG and pMTG are not critically engaged during more automatic patterns of semantic processing (such as retrieval of strong semantic associations), yet they are both recruited when control demands are high. Their engagement appears to promote appropriate aspects of meaning for the current context (Lambon Ralph *et al.*, 2017).

3.3. Parietal contributions to semantic cognition

IPS forms part of the semantic control network (Noonan *et al.*, 2013), however its contribution to controlled retrieval cannot be considered specific to semantics. Indeed, IPS (along with IFS and pre-central gyrus) is a core part of the MDN network (Duncan, 2010). In line with this, rTMS stimulation to IPS disrupts semantic *and* non-semantic tasks, such as the Navon letter search task (Whitney *et al.*, 2012). Dorsal AG/IPS (extending to superior parietal lobule) is involved in other executive demanding tasks, e.g., top-down attention, numerical calculation, tool-praxis, phonological decisions (for a meta-analysis see Humphreys & Lambon Ralph, 2015). Dorsal AG/IPS is therefore likely to be recruited during difficult semantic tasks tapping control, supporting broad executive demands and goal-directed behaviour necessary for these semantic decisions.

Angular gyrus seems to play a functionally distinct role. While dAG is recruited in difficult semantic decisions along with IPS, mid-AG forms a core part of the DMN (Yeo *et al.*, 2011), i.e. shows deactivation relative to rest during demanding tasks. A recent meta-analysis has showed that mid-AG deactivates also during ‘automatic’ semantic retrieval tasks, such as retrieving meaning of concrete words; in contrast, the area is activated during sentence-level processing, episodic tasks and number fact retrieval (Humphreys & Lambon Ralph, 2015). Inhibitory TMS stimulation to mid-AG impairs retrieval of strong semantic links while leaving unaffected weak semantic associations (Davey, Cornelissen, *et al.*, 2015). This evidence suggests that mid-AG a) is *not* necessary for semantic control, b) has a more domain-general role in cognition, c) that its polarity of activation reflects differences in task requirements (Humphreys & Lambon Ralph, 2015; Humphreys & Lambon Ralph, 2017).

A recent proposal suggests that AG may act as a buffer that track context over time (Hoffman et al. 2018). As anticipated above, AG is activated during sentences but not during single word comprehension (Humphreys & Lambon Ralph, 2015) and the two tasks differ in that the first requires information about existing contexts to be kept active. In Hoffman et al. (2018), neural networks were trained to link ambiguous words (e.g. BANK – CASHIER) among irrelevant options when contextual cues were available (e.g. ECONOMICS) as opposed to when they were not (mimicking the ambiguity task tested on SA patients by Noonan et al., 2010). The model was able to select the correct response irrespective of availability of cues when controlled retrieval processes were ‘available’ (i.e. when the model was trained to seek the activation state that fitted the response options and the level of noise at the response selection stage was kept normal). On the contrary, when controlled retrieval processes were ‘*not* available’ the model showed strong reliance on the contextual cues layer (mirroring the cueing effect showed by patients with SA; Noonan et al., 2010). This result first confirms that controlled retrieval processes are distinct from those hypothetically attributed to AG, i.e. context buffering. In addition and in line with Humphreys & Lambon Ralph (2015), this context layer in the model was necessary only when cues were provided, but not during processing of single words out of context. The authors hypothesised that in order to maintain sensitivity to prior context this layer would need to activate the representation of the context (i.e. the cue) over a longer time-scale than the semantic hub. Crucially, this hypothesis is consistent with fMRI evidence showing that AG activates over a longer time-scale as compared to sensory-motor areas while watching movies or listening to stories (Hasson *et al.*, 2008; Lerner *et al.*, 2011; Tylén *et al.*, 2015).

3.4. Are there separable neurocognitive components for domain-general executive control and semantic control?

As anticipated in the previous paragraphs, several lines of evidence suggest that domain-general executive processing (supported by the MDN; Duncan, 2010; Fedorenko, Duncan, & Kanwisher, 2013) can be distinguished from semantic control (underpinned by the semantic control network; Noonan et al., 2013). It has been proposed that the anterior portion of the semantic control network (including anterior LIFG and pMTG) plays a specific role in semantic control, whereas more posterior portions (LIFG/IFS and dAG/IPS) are implicated in executive control more broadly (Davey *et al.*, 2016; Lambon Ralph *et al.*, 2017). Inhibitory TMS to anterior LIFG and pMTG disrupts semantic tasks taxing control, while leaving automatic semantic retrieval as well as non-semantic executive tasks unaffected (i.e. Navon task; Whitney, Kirk, O'Sullivan, Lambon Ralph, & Jefferies, 2011). As mentioned above, rTMS to IPS elicits equivalent disruption of semantic and non-semantic executively-demanding tasks (Whitney *et al.*, 2012). Resting state and white matter tract connectivity studies have shown that anterior LIFG and pMTG are functionally and structurally connected with each other and with ventrolateral portions of ATL, yet posterior regions of LIFG bordering IFS do not show these patterns of connectivity (Binney et al., 2012; Davey et al., 2016; Jackson, Hoffman, Pobric, & Lambon Ralph, 2016). LIFG and pMTG do not form part of the MDN (Duncan, 2010), yet they activate during tasks unrelated thoughts (i.e. they are part of the DMN, Yeo et al., 2011). These two networks are anticorrelated at rest, although they need to cooperate during semantic and episodic memory tasks (Murphy *et al.*, 2018). Davey and colleagues (2016) have proposed that since both areas lie at the anatomical nexus between MDN and DMN they could play a crucial role in integrating *external* goal-oriented executively-demanding aspects of cognition (supported by MDN) and processing supported by DMN, by shaping the retrieval of *internal* representations.

4. Controlled retrieval of episodic memory

The automatic and controlled retrieval of episodic memoranda is also thought to rely on distinct neurocognitive processes, in common with current theories of semantic cognition. Automatic retrieval of episodic content usually happens when memories are strong in the representational system, such as when an external cue (e.g. a smell in the environment) or internal cue (e.g. an emotional state), automatically trigger their re-instatement. However, sometimes retrieving a particular episode requires the allocation of additional control and effortful search. For example, control may be important when there is interference between similar episodic memories (such as when we struggle to remember where we left the car in the car park in the morning) or when an event is not strong in the representational system (e.g. when we are trying to remember a distant memory). In this paragraph we will present convergent evidence from neuropsychology and neuroimaging supporting this distinction.

4.1. Dissociable episodic memory deficits

Neuropsychological studies point to qualitative differences in patients with amnesia following circumscribed medial temporal lobe (MTL) and prefrontal lesions. Patients with selective hippocampal lesions can show little evidence of retaining recently encoded events and their episodic performance is relatively unaffected by manipulations of control, for example the availability of interfering memories (Incisa Della Rocchetta and Milner, 1993). In contrast, patients with prefrontal lesions are impaired at episodic memory tasks that tax control demands (Blumenfeld and Ranganath, 2007). For example, they show susceptibility to recently encoded events that create proactive interference (Incisa Della Rocchetta and Milner, 1993; Gershberg and Shimamura, 1995; Shimamura *et al.*, 1995). They are also impaired in unconstrained tasks such as the free recall of episodic memories, but their performance is improved when provided with semantic and phonological cues or encoding/retrieval strategies (Incisa Della Rocchetta and Milner, 1993; Mangels *et al.*, 1996). Finally, they show normal memory for item recognition (Mangels *et al.*, 1996), but impaired memory when they have to retrieve the context in which that item was presented (i.e. source memory; Janowsky, Shimamura, & Squire, 1989). This suggests that the distinction between degraded representations and deregulated retrieval (Jefferies & Lambon Ralph, 2006) may hold also for the episodic domain.

4.2. Modulations of control demand

The retrieval of episodic memories is associated with a network of brain areas that largely overlaps with the semantic control network. In particular, LIFG has been associated with control over episodic memories (see Badre & Wagner, 2007 for a review, Barredo et al., 2015; Dobbins, Foley, Schacter, & Wagner, 2002; Han, O’Connor, Eslick, & Dobbins, 2012; Wimber, Rutschmann, Greenlee, & Bäuml, 2009), whereas parietal cortex is thought to contribute to retrieval via allocation of domain-general top-down resources as well as integration of contextual features (Bonnici *et al.*, 2016; Sestieri *et al.*, 2017; Hoffman *et al.*, 2018). As in the semantic domain, memory control has been manipulated in episodic tasks using several methods. For example, cognitive controlled demands are considered to be high: (i) when recent events create interference (i.e., proactive interference; Anderson & Neely, 1996); (ii) or when existing knowledge create competition with the target memory (i.e. false memories, Roediger & McDermott, 1995); (iii) when the to-be-retrieved memory trace is weak, as opposed to strong and vivid in the representational system (measured as number of encoding experiences or confidence associated with retrieval; Barredo et al., 2015; Hayes, Buchler, Stokes, Kragel, & Cabeza, 2011; Squire, Wixted, & Clark, 2007); (iv) during recall of contextual features of the event as opposed to the sense of familiarity with the encountered item (i.e. recollection vs. familiarity; Badre & Wagner, 2007); (v) during suppression of unwanted memories (i.e. think/no think paradigms, Anderson & Green, 2001). In the following paragraphs, findings using these paradigms tapping episodic control are discussed.

4.2.1. Interference resolution

Interference can be defined as competition among items that share the same retrieval cue (Anderson & Neely, 1996). This competition is thought to be resolved through the application of control processes that select target representations and dampen down distractors. In the semantic domain, competition is accrued by neighbouring concepts within the semantic system. For example, patients with SA show interference from semantically related concepts during naming tasks (for nuts → squirrel; Jefferies & Lambon Ralph, 2006). In episodic memory, competition can be generated by events with overlapping features which however occurred at different time points (Anderson & Neely, 1996). For example, retrieving where we left the car in the morning can be prone to interference from similar events that happened on different occasions. Interference resolution has been investigated using AB/AC paradigms, recent-negative tasks and retrieval induced forgetting.

In AB/AC paradigms, participants are first trained with the association between item A and item B. A little later, item A is paired with item C. Subsequently, both pairs are tested for retrieval. In healthy participants, retrieval of AC pairs is prone to interference from the previous AB association (Anderson & Neely, 1996). fMRI studies using different variants of this paradigm have showed increased LIFG recruitment during AC relative to AB trials at both encoding and retrieval (Henson *et al.*, 2002; Zeithamova and Preston, 2010). Similarly, patients with prefrontal lesions show additional memory impairment for the second pair when compared to healthy controls (Shimamura *et al.*, 1995).

Similarly to AB/AC paradigms, recent-negative paradigms manipulate the presence of interfering memories during the recognition of encoded item-lists. A lure-item presented in a previous trial (a recent negative) is likely to create errors and/or increase response times compared with when lure items were not presented in the previous trial (Monsell, 1978). This proactive interference effect is thought to occur because the items have overlapping features given that the recent negative is also recently familiar, along with the target. Several studies have implicated mid-LIFG during item recognition of recent vs. non recent trials (Jonides *et al.*, 1998; D'Esposito *et al.*, 1999; Postle and Brush, 2004; Badre and Wagner, 2005).

Interference during retrieval can be reduced by weakening competing representations – for example, through repeatedly practiced retrieval of selected target items. This phenomenon is called "retrieval induced forgetting" (RIF; Anderson, Bjork, & Bjork, 1994). In fMRI studies, retrieval of practiced, as opposed to non-practiced, targets is associated with reduced activation in fronto-parietal control regions -including LIFG (Kuhl *et al.*, 2007; Wimber *et al.*, 2009).

4.2.2. False memories

Other sets of representation can compete with episodic memory, such as semantic knowledge eliciting false memories. Episodic memory often interacts with semantic memory at encoding and retrieval (Tulving, 2002) and semantic similarities between encoded items can impair recollection and generate false memories (Roediger, Balota, & Watson, 2001). False memories are a common experience in everyday life. When you are in the kitchen trying to remember what is missing on the dining table, you might pick a FORK while the missing cutlery was actually a KNIFE. What makes these combinations particularly vulnerable to memory errors is the semantic proximity between the encoded items (e.g. a KNIFE) and the critical lure (e.g. a FORK). In the Deese–Roediger McDermott (DRM) paradigm (Roediger & McDermott, 1995), designed to investigate this phenomenon, participants encode a set of items belonging to the same semantic category and have to distinguish them from semantically related lures during retrieval. False and true memories activate similar areas of fronto-parietal cortex, potentially reflecting the need for monitoring and control in both situations, although only true memories were mediated by neural activity in the hippocampus (Dennis, Bowman, & Turney, 2015). The direct comparison between false and true memories revealed activation in PFC, including LIFG, and parietal regions (Dennis, Johnson, & Peterson, 2014; Garoff-Eaton, Kensinger, & Schacter, 2007). The false memory effect can be explained within the "spreading activation theory of memory" (Anderson, 1988), which posits that activation automatically spreads between interconnected representations. This effect is increased when memories share semantic features – and executive processes are necessary to overcome the competition that this creates (Anderson, 1988).

4.2.3. Source vs. item memory

The way in which episodic memory is probed can also influence control demands. Episodic retrieval depends on two distinctive but graded processes: recollection and familiarity (cf. dual-process theory; Buchler, Light, & Reder, 2008; Jacoby, 1991; Mandler, 1980; Yonelinas, 2002). Recollection of a complete experience, including the spatial-temporal context in which an item was encountered, is thought to rely to a greater extent on controlled retrieval since there is often a need to resolve competition between similar sources and/or reinstate information that was only weakly encoded (Dobbins *et al.*, 2002; Badre and Wagner, 2007; Barredo *et al.*, 2015). In contrast, familiarity involves seeing an item and deciding if it was presented before: this type of memory does not involve retrieving the context in which the item was presented (Mandler, 1980). Familiarity, as opposed to recollection is therefore less dependent on controlled retrieval. These processes have been compared experimentally using source judgements (for recollection) and item recognition (for familiarity). fMRI studies contrasting source vs. item memory consistently report prefrontal activation, including within LIFG (Cabeza *et al.*, 2003; Dobbins *et al.*, 2003; Dobbins and Wagner, 2005; Hayes *et al.*, 2011), as well as parietal activation (Daselaar, Fleck & Cabeza, 2006; Dobbins et al., 2003; Yonelinas, 2005). In line with the view that source memory requires competition resolution, Badre & Wagner (2005) pointed to a functional overlap in mid-LIFG between activation elicited by interference resolution (using recent negative paradigm) and source memory vs. item memory.

Control differences between source and item memory might explain the differential engagement of LIFG but are unlikely to explain the recruitment of parietal cortex. Several studies report greater ventral parietal activation (supramarginal/angular gyrus, SMG/AG and temporo-parietal junction, TPJ) during source memory and greater dorsal parietal recruitment during item memory (Wheeler and Buckner, 2003; Yonelinas *et al.*, 2005; Daselaar *et al.*, 2006). Source memory might place stronger demands on contextual integration which is thought to involve AG (Hoffman *et al.*, 2018). This idea also fits with emerging evidence that the DMN, including AG, is not task negative, as it is activated in harder conceptual judgements involving memory (Murphy *et al.*, 2018) and the retrieval of rich and multimodal episodes (Bonnici *et al.*, 2016).

4.2.4. Weak vs. strong memories

The processes supporting episodic retrieval can also be distinguished on the basis of the strength of signal associated with the retrieved memory (cf. strength theory; Squire et al., 2007). Recovering a weak memory trace is thought to demand greater cognitive control, since the relevant information will be less accessible and may also have to compete with other representations that are stronger but not currently relevant (Barredo *et al.*, 2015). Accordingly, activation of LIFG has been reported in a study comparing the retrieval of memories classified as weak (as they were only presented once during encoding) vs. stronger (since the items were presented several times; Barredo et al., 2015). This study also revealed functional coupling between anterior LIFG and medial-temporal structures during retrieval of weakly encoded memory traces.

4.2.5. High vs. low confidence memories

Episodic memories have also been classified as weak or strong on the basis of the subjective level of confidence associated with their recollection (Squire, Wixted, & Clark, 2007). However, confidence is unlikely to be directly correlated with memory control requirements. In fact, confidence ratings are more likely to reflect two other possible processes: a) the degree of detailed reinstatement and vividness associated with the memory trace and b) the extent to which top-down mechanisms are necessary to access the memory trace (Cabeza *et al.*, 2008). The contrast of high vs. low confidence activates more ventral regions (i.e. SMG and AG extending to TPJ), whereas low vs. high-confidence episodic decisions activate IPS and superior frontal lobule (see Cabeza, Ciaramelli, Olson, & Moscovitch, 2009 for a meta-analysis; Hayes et al., 2011). Patients with parietal lesions show normal free-recall of autobiographical memories, yet remembered material is impoverished in content and lacking in details compared to healthy controls (Berryhill *et al.*, 2007).

As already discussed, dorsal parietal cortex has been implicated in top-down executive domain-general processing (Humphreys, Hoffman, Visser, Binney, & Lambon Ralph, 2015; Humphreys &

Lambon Ralph, 2015; 2017). Dorsal portions of parietal cortex may come into play when the memory trace is not vivid (such as during low confidence memory decisions; Cabeza et al., 2008; Hayes et al., 2011), and domain general executive mechanisms are necessary to allocate top-down resources to controlled retrieval. fMRI studies have shown that IPS is activated until the episodic decision is made, probably reflecting manipulation of retrieved information according to task requirements (Sestieri *et al.*, 2011, 2017). On the contrary, AG which forms part of the DMN (Yeo *et al.*, 2011), is activated when episodic memory traces are fully recollected, vivid (such as during high confidence memory decisions) and rich in perceptual and/or emotional details (see Hoffman et al., 2018; Ramanan, Piguet, & Irish, 2017 for a proposed role of AG in context integration). In addition, AG is only transiently activated during episodic recollection (Sestieri *et al.*, 2011) and its activity has been suggested to reflect accumulation and online maintenance of retrieved episodic contextual features (Vilberg and Rugg, 2008; Shimamura, 2011).

4.2.6. Suppression of unwanted memories

Memories can be naturally forgotten, yet in other circumstances their retrieval is intentionally inhibited by active ‘suppression’ (e.g. during traumatic experiences). Memory inhibition has been extensively studied by Anderson and colleagues using the ‘think/no-think’ paradigm. Participants learn a list of item-pairs (e.g. ORDEAL – ROACH), and then undergo a further study-phase in which they are instructed either to think about the learnt associations (think) or to exert active inhibition (no-think) over retrieval of the associated item. Active inhibition strategies might involve deliberately focussing on visual features of the cue to block thoughts about the associated item. Active suppression hinders retrieval of the target item (e.g. ROACH) when probed by the trained cue (e.g. ORDEAL) and also when probed by untrained but semantically related cues (e.g. INSECT; Anderson & Green, 2001). This has been interpreted as successful inhibition of unwanted memories and their associations.

In fMRI, suppression of unwanted memories elicits activation of bilateral yet predominately right prefrontal cortex (including dorsolateral and IFG) and top-down inhibition of hippocampal activity (Anderson, Bunce, & Barbas, 2016; Anderson et al., 2004; Benoit, Hulbert, Huddleston, & Anderson, 2015). Therefore, while the activation elicited by the think/no-think task might overlap to some degree with other aspects of episodic memory control, the deliberate suppression of memory clearly also recruits other neurocognitive processes which are right-lateralized. Similar right-lateralized prefrontal activation is associated with the inhibition of motor responses (e.g. go/no-go tasks; Aron, Robbins, & Poldrack, 2004). A recent study adapting a go/no-go task so that it was based on semantic decisions found similar right-lateralized prefrontal activation (Gonzalez Alam *et al.*, 2018) and no involvement of left-lateralized semantic control regions as defined by Noonan et al. (2013). Consequently, it is not the case that all difficult semantic and episodic tasks give rise to maximal activation in left IFG. This hemispheric distinction can potentially be explained in terms of qualitative differences in the neurocognitive demands elicited by controlled retrieval and inhibition. In go/no-go as well as think/no-think paradigms, control is exerted on cognitive-behavioural responses elicited by certain inputs (i.e. switch behaviour when you see stimulus x – withhold button press or think about perceptual details rather than memory associations). This requirement to switch is specified *externally*: i.e., do not press for a particular category; focus on the typeface and not memory associations for a particular cue word. In contrast, controlled retrieval processes shape memory based on *intrinsic* characteristics that are not externally specified (e.g. memory items with similar features must be avoided; weak but relevant information must be brought to the fore, and the features of these memories themselves determine how control should be applied). Moreover, externally-specified inhibition tasks activate regions implicated in cognitive control across domains (i.e. MDN; Duncan, 2010) which, as already discussed, are thought to be partially distinct from memory control regions (Noonan *et al.*, 2013; Davey *et al.*, 2016; Lambon Ralph *et al.*, 2017).

4.2.7. Subsequent memory effect

LIFG shows stronger engagement during the encoding of items that are going to be better retrieved later. Kirchhoff et al. (2000) reported increased activation in anterior and mid-LIFG during encoding of words and pictures that were correctly remembered later during retrieval. This *subsequent memory effect* could reflect activity at the time of encoding which is focussing on forming task-relevant links and dampening down the retrieval of strong but irrelevant associations to the items being encoded. For example, in paired-associate memory, if BASKET-DOG need to be encoded, recruitment of LIFG might be important for linking these distantly associated items, as opposed to other possible associations that are semantically linked (such as BASKET – PICNIC or DOG – BONE) or previously encoded (such as BASKET – CANDLE), which might otherwise be retrieved. This suggests two hypothetical roles of LIFG during episodic retrieval: (i) its contribution could be linked to the retrieval of semantic information that supports episodic encoding, i.e. the meaning of items, or (ii) it might play a parallel role in supporting controlled retrieval from both episodic and semantic memory, given that both semantic and episodic relationships between items can create competition and this needs to be resolved in both types of tasks. This has caused some controversy in the literature. For example, fMRI evidence by Han et al. (2012) support the view that this area is recruited for processing meaning and, only *indirectly,* to support episodic retrieval. However, neuroimaging has limitations in addressing this issue given that it is correlational and not causal (see discussion in section 4.2). Investigating episodic memory in patients with semantic control deficits and LIFG lesions is one way of investigating the necessity of this brain area for shared controlled retrieval processes.

5. Controlled retrieval: shared neurocognitive mechanisms in semantic and episodic memory

The evidence discussed above raises the possibility that shared cognitive and neural mechanisms support the controlled retrieval of both semantic and episodic memory representations. In both domains, control is necessary to resolve competition between interfering representations. Competing representations can be within the same memory system (episodic; semantic) as the target; for example, when semantic retrieval is disrupted by semantically-related distractors, or when proactive interference from a previously-encoded association disrupts episodic memory. Competition might also occur across memory systems, for example, when semantic information elicits episodic false memories, and recent experiences (miscues) create competition with a target semantic representation. Similar control processes might also be employed to retrieve memory representations which are non-dominant in the representational system – because they are distantly associated concepts (in semantics) or weakly encoded/not readily available at retrieval (in the episodic domain). The neuroimaging data presented in previous sections suggest that these processes are supported by areas within inferior fronto-temporal and intraparietal cortex, although it is unclear where these controlled retrieval networks overlap across episodic and semantic tasks. Here we summarize the evidence presented above and discuss reasons why LIFG, and no other areas within the memory retrieval network, is the focus of interest of this thesis. We then discuss the possibility that LIFG plays a role in control that is *specific* to memory across domains and consider alternative views. Finally, circumstances that reduce control demands across memory domains will be considered.

5.1. Neurocognitive mechanisms of memory control

As discussed above, parietal cortex activates during memory retrieval but is unlikely to provide a direct contribution to memory control. Its dorsal portion has been implicated in top-down executive processing across tasks, including semantic and episodic retrieval (Humphreys & Lambon Ralph, 2015), whereas its ventral portion is thought to contribute to memory retrieval by supporting integration of multimodal contextual features (Bonnici *et al.*, 2016; Hoffman *et al.*, 2018). However, there are still puzzles concerning the differential roles of parietal cortex in memory retrieval across domains. For example, no studies to date have directly explored the differential contribution of fronto-temporal vs. parietal regions to episodic control in a similar way to semantics (i.e. using TMS, cf. Davey et al., 2015; Whitney, Kirk, et al., 2011). In addition, the opposite polarity of activation within AG for semantic (negative – i.e., deactivation relative to rest) and episodic (positive activation relative to rest) decisions is still to be understood (Humphreys et al., 2015). Finally, SMG and TPJ are activated during episodic retrieval but they are not activated by semantic tasks; some propose that their activation could reflect processing of perceptual features of events (Hutchinson *et al.*, 2009; Cabeza *et al.*, 2011).

The distinctive characteristics of memory control - i.e. the process of resolving competition between active memory representations to suit the current context - is more likely to be attributable to other areas of the brain, e.g. LIFG and potentially pMTG. In contrast to LIFG, pMTG is not consistently activated in studies of interference resolution in the episodic domain (however see Dobbins & Wagner, 2005; Han, O'Connor, Eslick, & Dobbins, 2012; Wimber et al., 2009) and it is therefore sensible to first focus on areas whose activation is consistently found in both domains.

LIFG has been implicated in the cognitive control of memory across domains (Badre and Wagner, 2005, 2007; Barredo *et al.*, 2015). The anterior-to-mid portion of LIFG is not recruited in domain-general executive demanding tasks (i.e. is not part of the MDN; Duncan, 2010) yet it activates during task-unrelated thoughts (i.e. forms part of the DMN; Yeo et al., 2011) and semantic and episodic control (Badre and Wagner, 2007; Noonan *et al.*, 2013). MDN and DMN need to cooperate to support controlled cognition (Vatansever *et al.*, 2015; Krieger-Redwood *et al.*, 2016; De Caso *et al.*, 2017; Murphy *et al.*, 2018) and it is possible that LIFG plays a *specific* role in the control of memory, supporting competition resolution among *internally* activated representations, irrespective of the memory domain (Badre and Wagner, 2007).

5.2. Does LIFG plays a *direct* or *indirect* role in episodic memory control?

Many episodic tasks use meaningful and/or verbal stimuli and this raises uncertainty about the role of LIFG in memory control. For example, increased LIFG activation when distractors are available (e.g. Badre & Wagner, 2005) does not imply that this area is needed to resolve competition, but could instead be necessary for processing the meaning of distractors. It is therefore unclear whether LIFG is mainly implicated in semantic processing (i.e. only *indirectly* recruited to support episodic retrieval) or if it plays a parallel role in both domains (i.e. *directly* implicated in memory control).

Dobbins & Wagner (2005) sought to determine whether LIFG responses during episodic retrieval reflected semantic processing. They compared the recollection of conceptual sources (i.e. whether a living/non-living or pleasant/unpleasant judgement was made at encoding) with perceptual sources (whether the item appeared in large/small size at encoding) and observed a double dissociation. The anterior portion of LIFG and pMTG were active during recollection of conceptual details whereas the right IFG and bilateral occipitotemporal cortex were more active for perceptual trials. In contrast, the magnitude of left mid-LIFG activation did not reliably differ between semantic and non-semantic (perceptual) source trials and this activation was greater during both perceptual and conceptual source retrieval relative to item recognition. In this study, pictures of meaningful stimuli (i.e. drum or fly) were used. Han et al. (2012) compared source recollection (i.e. having made a complexity or pleasantness judgment at encoding) of meaningful vs. non-meaningful material (i.e. kaleidoscopic scrambling). They found that the involvement of LIFG, both mid and anterior portions, was selectively related to the processing of meaningful memoranda, yet not activated during retrieval of non-meaningful material.

Collectively these results could suggest that LIFG may play a preferential role in semantic processing, playing only an *indirect* role in episodic retrieval. However, these conclusions have some crucial limitations. First, Dobbins & Wagner (2005) report mid-LIFG activation for the contrast of source vs. item memory during non-semantic source decision (i.e. dimension judgments) for highly concrete items (i.e. pictures of concrete objects), i.e. when semantic elaboration is at a minimum. Moreover, the non-meaningful materials used in Han et al. (2012) are unlikely to initiate the spread of activation that is a peculiar characteristic of episodic memory in natural contexts (Anderson, 1988) and this could explain the lack of activation of LIFG. Neuropsychological studies can be useful for determining whether this area is necessary for semantic elaboration and yet is not required for episodic competition resolution where semantic elaboration is minimal.

5.3. Circumstances that reduce control demands

In the previous paragraphs, circumstances in which memory-control demands are high have been discussed. However, it is also worth considering circumstances where control demands are diminished in order to address if this can alleviate memory control deficits.

5.3.1. Semantic knowledge

We already addressed how competition between semantic representations can generate detrimental effects on episodic memory, i.e. false memories. However, this is not always the case. For example, cues promoting semantic categorization (e.g. grouping items into meaningful categories at encoding) have been showed to alleviate episodic deficits in patients with frontal lesions (Incisa Della Rocchetta and Milner, 1993). Similarly episodic memory performance is augmented in healthy individuals when supported by semantic processing (Craik and Tulving, 1975); for example word-pairs are better remembered when semantically linked (i.e. BEACH – SUN vs. BEACH – LEAVES). Also, new information is better remembered when it is congruent with existing knowledge and schemas (van Kesteren *et al.*, 2014). Semantic elaboration is thought to give rise to level of processing effects, i.e. better memory for deep vs. shallow processed material (Craik and Lockhart, 1972) and it can be promoted by areas implicated in automatic semantic cognition (e.g. ATLs and mPFC, Binder, Desai, Graves, & Conant, 2009). Semantic links at encoding might reduce control demands during encoding (since in the absence of a pre-existing link, controlled retrieval processes may need to be employed to focus on a connection that can be generated to support episodic memory). Studies suggest that schema-dependent retrieval is mediated by medial prefrontal cortex (mPFC; van Kesteren et al., 2013; Van Kesteren et al., 2012) within the DMN, as opposed to areas in lateral PFC implicated in cognitive control.

5.3.2. Self-referential processing

In episodic memory, an extensive literature shows that processing items in a self-relevant manner has beneficial effects on memory retrieval, yielding a memory advantage compared to semantic processing and other encoding strategies (Symons and Johnson, 1997). Self-reference effect has been found using various type of stimuli, including personality-trait adjectives, nouns, words, geometrical shapes, faces (Sui *et al.*, 2012; Sui and Humphreys, 2015) and within numerous memory tasks, including source memory in healthy young (Serbun *et al.*, 2011) and older adults (Hamami *et al.*, 2011) and items assigned to the self through ownership (Cunningham *et al.*, 2008). Self-reference effects elicit activation of mPFC in neuroimaging studies (Kelley *et al.*, 2002; Macrae *et al.*, 2004), and are disrupted following lesions to this area (Philippi *et al.*, 2011). As noted above, mPFC also activates for schema-dependent memories and this is consistent with the idea that the self acts as a “superordinate schema” that facilitates memory for personal information (Rogers et al., 1977).

Medial PFC lies within the DMN and self-reference effects are associated with increased functional connectivity within DMN (De Caso *et al.*, 2017). As already mentioned, recent work has demonstrated that connectivity between DMN and MDN is important for controlled cognition (Vatansever *et al.*, 2015; Krieger-Redwood *et al.*, 2016; De Caso *et al.*, 2017; Murphy *et al.*, 2018). Self-reference effect is likely to occur even in circumstances where memory control is impaired, by means of intact DMN regions and their connectivity with areas supporting domain-general controlled cognition, i.e. MDN regions.

5.3.3. Spatial cues

Tulving first proposed that successful episodic retrieval is highly dependent on the specific cues available at encoding, and the extent to which they are also available at retrieval (cf. theory of encoding specificity; Tulving & Thomson, 1973). Episodic memory is constituted by temporally dated and spatially located events, which allows the separation of otherwise similar experiences. At retrieval, temporal features are necessarily different from those at encoding which makes the memory harder to retrieve; however, if the spatial context of encoding matches that of retrieval, the re-instatement of events is facilitated (such as when you go back to your home-town or to a place you visited on holiday). In line with this hypothesis, several studies have shown memory benefits when the spatial context of encoding and retrieval are similar (Robin and Moscovitch, 2014; Smith *et al.*, 2014). Medial temporal structures (i.e. hippocampus and entorhinal cortex) that support episodic memory have been associated with spatial representations. Studies have shown that the firing pattern of some of the cells within these areas provide information about one’s current position and orientation (Hartley, Lever, Burgess, & O'Keefe, 2014; Moser, Kropff, & Moser, 2008). It is conceivable that when the same spatial cues are present at encoding and retrieval, access to episodic memory (underpinned by the same medio-temporal structures) is facilitated.

Semantic knowledge, self-referential and spatial processing are underpinned by different regions, all of them overlapping with the DMN. This network is typically intact in SA patients with semantic control deficits and these types of processing could therefore alleviate memory control deficits in this patient group.

6. Introduction to thesis

Deficits of controlled retrieval in semantic and episodic memory have largely been studied separately; for example, in patients with SA and deregulated semantic retrieval, episodic retrieval has barely if ever been explored. Likewise, in patients with amnesia following prefrontal lesions, who show a strong sensitivity to cues and interference during episodic retrieval, tests of semantic memory have not differentiated between degraded representations (not expected) and semantic control (which might be impaired). Although neuroimaging studies suggest the potential for shared processes across semantic and episodic tasks, there is uncertainty as to whether the common patterns of activation are crucial for resolving both semantic and episodic competition, or if activation results from common task characteristics (such as the fact that words are typically presented in both cases). Consequently, it is unclear whether LIFG is primarily recruited to subserve semantic elaboration of episodic material, as opposed to memory control. A way to resolve this controversy would be to establish whether this area is necessary to resolve competition both i) *within* memory systems, i.e. semantic competition in semantic tasks and episodic competition in episodic tasks and ii) *between* memory systems, i.e. semantic competition in episodic tasks and episodic competition in semantic tasks. In addition, it is of key interest to explore whether those difficulties emerge when memory is tested for multimodal stimuli (verbal vs. non-verbal) and in conditions where semantic elaboration is at minimum.

Since patients with SA have lesions affecting areas implicated in both semantic and episodic control, such as LIFG (Badre and Wagner, 2007; Jefferies, 2013; Noonan *et al.*, 2013; Lambon Ralph *et al.*, 2017), they represent an ideal population for testing these claims. The second chapter will characterise the nature of episodic memory in patients with SA for the first time, using paired associates tasks to see if episodic memory performance resembles the pattern found for semantic cognition. If controlled retrieval processes are shared, we hypothesise that SA patients with LIFG lesions may show: (i) equivalent deficits in verbal and non-verbal domains, (ii) improved performance using techniques that reduce control demands such as cueing; (iii) an increase in false memories relative to controls – due to impaired control of irrelevant semantic associations; (iv) more interference from existing episodic memories; (v) equivalent difficulties in discarding both semantic and episodic representations when not relevant for the task.

Chapter 3 further assesses the multimodal nature of episodic deficits using non-verbal tasks comparing source vs. item memory, given that this contrast recruits LIFG in fMRI studies. During source memory tasks there is a need to resolve competition between at least two possible sources, whereas during item memory the item acts as cue and therefore the need for internal constraint is reduced. We expected the patients to show (i) impaired source memory in the face of spared item memory, (ii) better source memory in circumstances where the competition between possible sources is reduced by the presence of spatial cues, congruency with existing knowledge and self-referential processing; (iii) equivalent deficits when the sources are rich in meaning as opposed to when they require minimal semantic processing.

Finally, in Chapter 4, we will assess whether patients can *benefit* from neurobehavioral training that targets semantic control processes and consider whether this effect generalizes to both semantic and episodic memory tasks.

7. Notes to the reader

Patients' samples slightly differ in each Chapter, but most patients have been tested across the three studies. Patients' ID is kept constant across chapter, e.g. P1 is the same participant in Chapter 2, 3 and 4.

CHAPTER 2

Shared processes resolve competition within and between episodic and semantic memory: Evidence from patients with LIFG lesions

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Abstract

Semantic cognition is supported by two interactive components: semantic representations and mechanisms that regulate retrieval (cf. ‘semantic control’). Neuropsychological studies have revealed a clear dissociation between semantic and episodic memory. This study explores if the same dissociation holds for control processes that act on episodic and semantic memory, or whether both types of long-term memory are supported by the same executive mechanisms. We addressed this question in a case-series of semantic aphasic patients who had difficulty retrieving both verbal and non-verbal conceptual information in an appropriate fashion following infarcts to left inferior frontal gyrus (LIFG). We observed parallel deficits in semantic and episodic memory: (i) the patients’ difficulties extended beyond verbal materials to include picture tasks in both domains; (ii) both types of retrieval benefitted from cues designed to reduce the need for internal constraint; (iii) there was little impairment of both semantic and episodic tasks when control demands were minimised; (iv) there were similar effects of distractors across tasks. Episodic retrieval was highly susceptible to false memories elicited by semantically-related distractors, and confidence was inappropriately high in these circumstances. Semantic judgements were also prone to contamination from recent events. These findings demonstrate that patients with deregulated semantic cognition have comparable deficits in episodic retrieval. The results are consistent with a role for LIFG in resolving competition within both episodic and semantic memory, and also in biasing cognition towards task-relevant memory stores when episodic and semantic representations do not promote the same response.

Key words: episodic memory; semantic memory; controlled retrieval; LIFG; stroke aphasia.

1. Introduction

Neuropsychological studies provide compelling evidence for the existence of separable episodic and semantic memory stores. Patients with semantic dementia have progressive yet selective degeneration of conceptual knowledge across all tasks and input modalities, which correlates with the degree of atrophy in the anterior ventrolateral temporal lobes (Mummery *et al.*, 2000; Butler *et al.*, 2009), yet their memory for recent episodic events is largely intact (Graham and Hodges, 1997; Graham *et al.*, 1997, 2000, 2003). In contrast, anterograde amnesia is characterised by poor encoding and retrieval of specific events as opposed to factual information, following damage to the hippocampus and associated structures in the medial temporal lobes (Nadel and Moscovitch, 1997; Vargha-Khadem *et al.*, 1997; Nestor *et al.*, 2006). These findings suggest that anterior ventrolateral temporal cortex supports conceptual generalisation across experiences, while hippocampus promotes pattern separation for recently-encoded episodes (McClelland *et al.*, 1995; Kumaran and McClelland, 2012).

Studies also point to the existence of contrastive types of semantic deficit. The term “semantic aphasia” was first coined by Head (1926) to describe patients showing difficulties in shaping and manipulating knowledge to serve symbolic processing - in the presence of heterogenous language impairments - rather than loss of semantic knowledge per se. In line with Head’s clinical description, studies have shown that, unlike the degraded knowledge in semantic dementia, patients with semantic aphasia (SA) show deregulated semantic cognition across different tasks and input modalities following left frontoparietal stroke (Jefferies and Lambon Ralph, 2006; Jefferies *et al.*, 2008a; Rogers *et al.*, 2015). SA patients show inconsistent semantic performance when the same concepts are tested under different control demands, as well as sensitivity to cues and miscues that constrain retrieval or increase the availability of irrelevant knowledge (Jefferies *et al.*, 2008a; Noonan *et al.*, 2010; Corbett *et al.*, 2011). They have difficulty retrieving non-dominant aspects of knowledge and dealing with competition from strong yet irrelevant semantic distractors during semantic retrieval (Noonan *et al.*, 2010; Almaghyuli *et al.*, 2012). These problems extend beyond language, to affect sound, picture and action understanding (Corbett, Jefferies and Lambon Ralph, 2009; Corbett, Jefferies, Ehsan, *et al.*, 2009; Corbett *et al.*, 2011; Gardner *et al.*, 2012; Thompson *et al.*, 2015a). Collectively this evidence shows that SA patients have multimodal deficits of semantic control, i.e. they find it difficult to flexibly retrieve and shape semantic knowledge to suit the task or circumstances and show impairment when there is a need to resolve competition between different meanings or features of concepts. The distinction between semantic dementia and patients with SA supports a component process account, in which semantic cognition emerges from interactions between transmodal conceptual representations and control processes (Controlled Semantic Cognition Framework; Jefferies, 2013; Lambon Ralph *et al.*, 2017).

This proposal is also pertinent to understanding differences in episodic memory deficits in amnesia (see Blumenfeld and Ranganath, 2007 for a review). In contrast to patients with circumscribed medial temporal lobe injury (such as HM, Scoville and Milner, 1957), patients with additional prefrontal involvement show better cued than free recall (Incisa Della Rocchetta and Milner, 1993; Mangels *et al.*, 1996) and disproportionate difficulty in retrieving word-pairs previously associated with other targets, reflecting a failure to overcome proactive interference (Shimamura *et al.*, 1995). In both semantic and episodic tasks, bringing to mind unusual associations, or task-relevant knowledge in the face of strong competition, might involve promoting specific aspects representations and suppressing irrelevant dominant information (Anderson, 1988; Badre and Wagner, 2007; Whitney, Kirk, *et al.*, 2011). The similarity of these theoretical accounts fuels interest in whether they have a shared or distinct neural basis.

Functional neuroimaging studies suggest that overlapping networks are important for the control of episodic and semantic memory (see Figure 1A). Left inferior frontal gyrus (LIFG) has a well-established role in the control of episodic memory: it shows a stronger response in the retrieval of weakly vs. strongly-encoded memories (Hayes *et al.*, 2011; Barredo *et al.*, 2015) and is engaged by interference resolution (Badre and Wagner, 2005; Wimber *et al.*, 2009). Likewise, this region shows increased activation in semantic retrieval for ambiguous words, weak associations or strong distracters (for a meta-analysis, see Noonan, Jefferies, Visser, & Lambon Ralph, 2013; also Badre & Wagner, 2005, 2007; Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997). Controlled retrieval from episodic and semantic memory partially overlaps with "multiple-demand regions" that are engaged for difficult tasks across multiple domains; however, anterior LIFG lies outside this network and appears to specifically support the control of memory (Badre *et al.*, 2005; Nelson *et al.*, 2009; Davey *et al.*, 2016). In line with this proposal, inhibitory transcranial magnetic stimulation to LIFG disrupts control-demanding semantic judgements but not more automatic aspects of semantic retrieval or demanding non-semantic judgements (Gough *et al.*, 2005; Hoffman *et al.*, 2010; Whitney, Kirk, *et al.*, 2011; Krieger-Redwood and Jefferies, 2014; Hallam *et al.*, 2016).

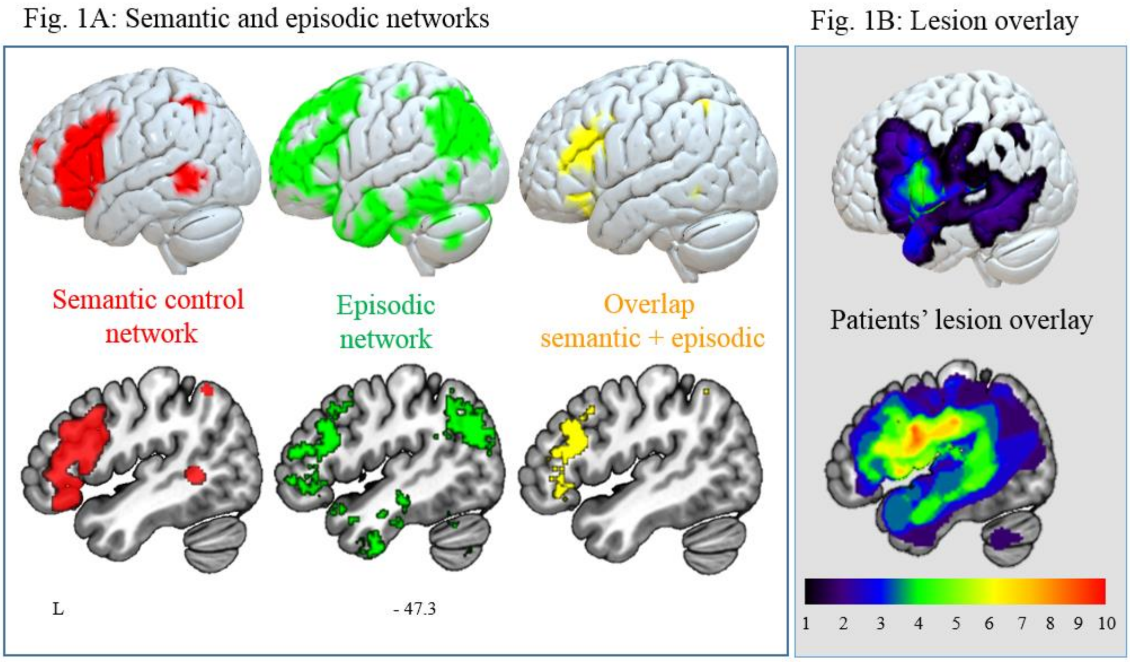


Fig. 1A: Semantic and episodic networks

Fig. 1B: Lesion overlay

Figure 1: Brain networks implicated in semantic and episodic retrieval overlap with patients' lesions. (A) Semantic control network (red, from Noonan et al., 2013, adapted by Humphreys and Lambon Ralph, 2014), episodic memory network (green, from Neurosynth; a meta-analysis of 393 studies containing the term "episodic"), the overlap of the two networks (yellow). Rendered views are displayed using Surfice (https://www.nitrc.org/projects/surfice/); sagittal views using MRIcroGL (http://www.cabiatl.com/mricrogl/). The overlap mask included only one cluster of a minimum of 50 voxels which corresponded to mid-to-post LIFG, pars triangularis extending to pars opercularis and middle frontal gyrus (MNI -48, 24, 24). (B) Lesion overlay of the sample of SA patients included in the study. Patients' brains compared to aged-matched controls. Grey matter, white matter and CSF were segmented and changes from the healthy control brains were highlighted as 'lesion' using automated methods (Seghier *et al.*, 2008). Colour bar indicates amount of overlap from 1 to 10 patients.

Despite these similarities, few studies have directly compared manipulations of difficulty across episodic and semantic judgements. It is unclear whether LIFG contributes to episodic memory indirectly by regulating conceptual retrieval or whether LIFG is crucial for regulating retrieval from both memory stores. Neuropsychology can help to resolve this theoretical uncertainty by establishing if damage to LIFG gives rise to symmetrical deficits of episodic and semantic memory. Semantic and episodic representations often mutually support retrieval: to understand the semantic link between items like DOG and BEACH, we can bring to mind specific episodes in which these items co-occurred (Westmacott and Moscovitch, 2003; Westmacott *et al.*, 2004). Similarly, in event memory, we draw on semantic representations of related episodes to support encoding and retrieval, giving rise to "levels of processing effects" (Anderson, 1981; DeWitt *et al.*, 2012). We therefore need the capacity to select a response from one or other system, depending on the task demands. The inappropriate application of semantic information in an episodic context can give rise to false memories (Roediger, Balota, & Watson, 2001; Roediger & McDermott, 1995) and the engagement of LIFG might help to avoid these errors (Garoff-Eaton *et al.*, 2007; Kim and Cabeza, 2007; Dennis *et al.*, 2014).

In this study, we examined chronic post-stroke patients with SA and well-documented deficits of semantic control following LIFG lesions. To date, there has been little research on episodic memory in aphasia, including SA. We therefore investigated whether SA patients would show episodic deficits resembling their semantic impairment – namely, multimodal difficulties across verbal and non-verbal tasks, and sensitivity to cues that reduce the requirement for internally-constrained retrieval. We assessed whether semantic control impairment would elicit 'false episodic memories'. In addition, to establish if semantic deficits directly underpin poor episodic memory or, alternatively, whether LIFG is critical for memory control across domains, we considered whether LIFG lesions would elicit 'false semantic associations' when semantic retrieval is preceded by task-irrelevant episodic encoding. Patients with multimodal semantic deficits following infarcts within LIFG may have difficulty resolving competition between episodic and semantic memory and their responses might reflect task-irrelevant memory representations, if LIFG plays a general role in regulating retrieval from both systems.

2. Participants

2.1. Patients

The study was approved by the local ethical committee and informed consent was obtained. Ten participants [six females; M(SD): Age = 62.8 (11.2); Age left education: 16.4 (1.2); years since CVA: 8.9 (5.6)] with chronic stroke aphasia from a left-hemisphere CVA were recruited from communication groups in Yorkshire, UK. Demographic details are provided in Table 1. On the basis of their aphasic symptomatology they could be classified as follows: two Global; two Mixed Transcortical; five Transcortical Sensory/Anomic; one Broca. In line with the inclusion criteria adopted by Jefferies and Lambon Ralph (2006), patients were selected to show difficulties accessing semantic knowledge in both verbal and non-verbal tasks.

We previously found that such multimodal semantic deficits in stroke aphasia reflect difficulties with controlled access to semantic information (Corbett, Jefferies, Ehsan, *et al.*, 2009; Noonan *et al.*, 2010; Corbett *et al.*, 2011; Gardner *et al.*, 2012; Thompson *et al.*, 2015a), and this pattern was reproduced in this sample (see Background Neuropsychological Testing). All the patients showed greater difficulty on semantic tasks when control demands were high. In line with our previous results, we expected patients to show (i) a strong influence of word ambiguity, with poorer performance for subordinate meanings (assessed using the Ambiguity task below); (ii) strong effects of cueing and miscuing (in the Ambiguity task); (iii) poor inhibition of strong competitors (assessed using the Synonym judgment task with distractors); (iv) difficulty accessing non-canonical functions and uses of objects (assessed using the Object Use task). We also expected inconsistent performance – at the group level – on semantic tasks probing the same concepts with different control demands (assessed using the Cambridge semantic battery).

Table 1. Demographics

Patient ID	Age	Gender	Education*	Years since CVA	Type of Aphasia
P1	60	F	18	6	Global
P2	77	M	15	6	Mixed Transcortical
P3	59	F	16	8	Global
P4	66	M	15	23	Mixed Transcortical
P5	58	F	18	6	Transcortical Sensory/Anomic
P6	57	M	18	13	Transcortical Sensory
P7	65	M	16	6	Broca
P8	70	F	16	10	Transcortical Sensory/Anomic
P9	77	F	16	4	Anomic
P10	39	F	16	7	Transcortical Sensory/Anomic
Mean	62.8	6/10	16.4	8.9	
SD	11.2	females	1.2	5.6	

Table 1 Legend: * Age left education, CVA: Cerebrovascular accident

2.2. Lesion analysis

We used an automated method for identifying lesioned tissue: grey matter, white matter and CSF were segmented and changes from the healthy control brains were highlighted as ‘lesion’ (Seghier *et al.*, 2008). A lesion map generated using this approach is shown in Figure 1. In addition, we manually assessed lesions of individual patients by tracing MRI scans onto standardized templates (Damasio and Damasio, 1989). All ten patients had lesions affecting posterior LIFG (see Figure 1B and Table 2); in seven cases, this damage extended to mid-to-anterior LIFG. Some lesions extended to inferior parietal and/or posterior temporal regions, with less overlap between cases in these additional regions. Three patients (P1, P3, P7) showed some degree of damage in the ATL. However, ventral ATL, which has been implicated in conceptual representation across modalities (Binney *et al.*, 2012; Visser *et al.*, 2012), was intact in all ten cases. This region is supplied by both the anterior temporal cortical artery of the middle cerebral artery and the anterior temporal branch of the distal posterior cerebral artery, reducing its vulnerability to stroke (Phan *et al.*, 2005; Borden, 2006; Conn, 2008). The hippocampus was also intact. Figure 1B provides a lesion overlay for the patient group, showing common lesions in regions of LIFG implicated in semantic control and episodic retrieval in neuroimaging studies of healthy participants.

2.3. Controls

Performance was compared for patients and healthy controls (N = 10 to 15, across different studies). None of the controls had a history of psychiatric or neurological disorder. They were matched to the patients on age and years of education ($p > 0.06$ across all comparisons).

Table 2. Patients' lesions analysis

		Fronto-lateral							Medial				Parieto - temporal									
Patient ID	**Lesion size***	SMA/PMC	FP	DLPFC		ant-IFG	mid-IFG	post-IFG	vm-PFC	dm-PFC	ACC	PCC	SMG	AnG	pMTG	STG	MTG	ITG	FuG	TP	PHG	Hpc
												Brodmann Areas										
		6	10	9	46	47	45	44	10	9	24/32/33	23/31	40	39	37	22	21	20	36	38	28	28
P1	12	1		1	1		1	1					2	1	1	2				1		
P2	15	2		2		2	2	2					1			2						
P3	15	2		2		2	1	2					2	1	2	2	2	1				
P4	8	2						1					1		2							
P5	15	2						2				2	2	1	1							
P6	7	1					1	2			1	1	1	1	1							
P7	14	2				2	1	2			1	1	1	1	1	2	1					
P9	4	1						1							1	1	1					
P10	9	0					1	2								2						

Table 2 Legend: MRI scans were manually traced onto Damasio templates. Lesion size* was calculated as % template damaged. For areas not comprehensively characterized by Damasio templates, analyses were combined with manual analysis of the structural scan with the help of a trained radiographer. Quantification of lesion: 2 = complete destruction/serious damage to cortical grey matter; 1 = partial destruction/mild damage to cortical grey matter; empty = intact. Anatomical abbreviations: SMA/PMC: of Supplementary Motor Area/ Premotor Cortex; FP: Frontal Pole; DLPFC: Dorsolateral Prefrontal Cortex; ant-IFG: Inferior Frontal Gyrus, pars orbitalis; mid-IFG: Inferior Frontal Gyrus, pars triangularis; post-IFG: Inferior Frontal Gyrus, pars opercularis; SMG: Supramarginal Gyrus; AnG: Angular Gyrus; pMTG: posterior Middle Temporal Gyrus; STG: Superior Temporal Gyrus; MTG: Middle Temporal Gyrus; ITG: Inferior Temporal Gyrus; FuG: Fusiform Gyrus; TP: Temporal Pole; PHG: Parahippocampal Gyrus; Hpc: Hippocampus.

3. Background neuropsychological testing

3.1. Non-semantic tests

Data for individual patients is shown in Table 3. The “cookie theft” picture description (Goodglass and Kaplan, 1983) revealed non-fluent speech in half of the patients. Word repetition (PALPA 9; Kay, Lesser, & Coltheart M., 1992) was also impaired in five patients out of ten. Executive/attentional impairment was seen in seven of the ten patients (see Table 3), across four tasks: Elevator Counting with and without distraction from the Test of Everyday Attention (Robertson *et al.*, 1994); Ravens Coloured Progressive Matrices (RCPM; Raven, 1962); Brixton Spatial Rule Attainment task (Burgess and Shallice, 1997) and Trail Making Test A & B (Reitan, 1958). This is in line with previous studies which found that deregulated semantic cognition correlated with executive dysfunction in stroke aphasia (Jefferies and Lambon Ralph, 2006; Noonan *et al.*, 2010). Digit span was impaired in all patients, while 7 out of 10 had spatial spans in the normal range. The patients showed normal performance in the Face Recognition task from the Wechsler Memory Scale (WMS-III, Wechsler, 1997), which has minimal control demands. This confirms they were not amnesic. In contrast, the Verbal Paired Associates test from WMS-III was impaired (see below).

Table 3. Non-semantic background tests: individual scores

Test	Max	Controls Mean (SD)	Patients Mean	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10
Non-semantic language tests													
PALPA 9 real word repetition (total)	80	73a	60	NA	**71**	**42**	75	78	79	**1**	NT	74	77
Category Fluency (8)	-	62a	27.8	NA	26	**15**	**26**	**14**	**26**	NA	**4**	80	**57**
Letter Fluency (F, A, S)	-	18a	6	NA	2	**2**	**6**	**3**	**6**	NA	**3**	**16**	**9**
Cookie theft (words/minute)	-	-	24.85	0	18	9	12	60	37	0	21.5	54	37
Executive and spatial processing													
TEA: counting without distraction	7	4.2a	5.14	**4**	5	6	5	**4**	NT	7	7	5	7
TEA: counting with distraction	10	2.6a	2	**2**	3	**1**	**1**	**2**	NT	7	3	**2**	6
Raven's coloured matrices (total)	36	32.9 (2.41)	28.3	31	29	31	**24**	**19**	30	34	31	**21**	33
Brixton spatial anticipation (correct)	54	28a	23.44	**21**	**7**	**18**	**26**	**24**	**23**	31	NT	31	30
Trail Making Test A (correct)	24	24a	23.1	**19**	**22**	**23**	24	24	**23**	24	24	24	24
Trail Making Test B (correct)	23	17a	14.4	**2**	23	**16**	**12**	**1**	**5**	23	21	19	22
Visuospatial processing													
VOSP dot counting	10	8a	9.33	**7**	10	10	9	10	10	8	NT	10	10
VOSP position discrimination	20	18a	17.56	19	20	**4**	19	**17**	20	19	NT	20	20
VOSP number location	10	7a	8.88	8	10	**5**	10	10	10	10	NT	**5**	8
VOSP cube analysis	10	6a	8.13	8	9	**4**	**4**	7	9	10	NT	10	8

Wechsler Memory Scale													
Digit Span Forward	9	6.82 (0.64)	3.5	**0***	**5**	**4**	**2**	6	**4**	**2***	**5**	**3**	**4**
Digit Span Backward	8	5.6 (0.97)	1.5	**0***	**2**	**2**	**0**	**2**	**0**	NA	**3**	NT	**3**
Spatial Span Forward	19	10(3)b	6.8	10	5	10	6	5	**3**	6	7	7	9
Spatial Span Backward	19	10(3)b	7.1	8	**2**	10	6	**3**	**3**	9	10	10	10
Face Recognition Immediate	19	10(3)b	10.7	9	10	12	14	**17**	13	10	7	9	6
Face Recognition Delayed	19	10(3)b	12	8	13	11	11	18	13	15	13	8	10

Table 3 Legend: Scores are number of correct. a= Normal cut-off; b=WMS Age adjusted scaled score (SD); Bold underlined numbers denotes impaired scores (less than two standard deviations below mean); NT = unavailable for testing; NA = testing was not attempted because patients were non-fluent; TEA = Test of Everyday Attention; VOSP = Visual Object and Space Processing battery. Digit Span: participants were required to immediately retrieve numbers sequences of increased length, in forwards or backwards order. * = For non-fluent patients we used a paper with numbers wrote down during recall. Patients were instructed to point to each number in the same sequence in which was vocally presented by the experimenter. The sheet was not available during the presentation of numbers to avoid the use of spatial strategy for retaining the sequence in working memory. Face Recognition: participants were asked to remember 24 unfamiliar faces, presented one at time. Memory was tested immediately and following a delay of 25-35 minutes (delayed condition); participants identified 24 target faces amongst 48 stimuli, responding either “yes” or “no” to each face.

3.2. Cambridge semantic battery

This assesses semantic retrieval for a set of 64 items across tasks (Bozeat *et al.*, 2000; Adlam *et al.*, 2010), including picture naming, word-picture matching, verbal and pictorial semantic associations (Camel and Cactus Test, CCT). In line with their varying language output impairment, patients showed large variability during picture naming [percentage correct M(SD) = 63.3 (37.6)]. In contrast, performance was uniformly at ceiling in word-picture matching [M(SD) = 95.9 (5.5)]. When secondary associations between concepts were to be retrieved on the CCT – i.e. control demands were higher – performance was lower with no differences across modalities [words M(SD) = 78.3 (16.3); pictures M(SD) = 77.7 (13.6)]. Individual test scores are provided in Table 4. Pairwise correlations between the six combinations of these four tasks revealed a correlation across word and picture association judgements [r = 0.63, p = .05]. The word and picture trials were probing the same association and therefore had highly correlated control demands. All other pairwise correlations were not significant [p ≥ 0.08]. This replicates the findings of Jefferies & Lambon Ralph (2006), who showed correlations across modalities within the same task (when control demands remained constant) but not between tasks with different controlled retrieval requirements.

3.3. Tests of semantic control

In line with the original use of the term “semantic aphasia” by Henry Head (1926) and the findings of Jefferies & Lambon Ralph (2006), the patients in this study had deficits affecting the appropriate use of concepts presented as words and objects. We presented three tasks that manipulated the control demands of verbal and non-verbal semantic judgements. See Figure 2 for group-level results and Table 4 for individual data.

3.3.1. Ambiguity task

Semantic judgements (60 items) probed the dominant (MONEY) and subordinate (RIVER) meanings of ambiguous words (e.g., BANK). These semantic decisions were preceded by no cue, or by a sentence that primed the relevant meaning (cue condition e.g., for MONEY, I WENT TO SEE THE BANK MANAGER) or irrelevant interpretation (miscue condition e.g., THE BANK WAS SLIPPERY; Fig. 2A), from Noonan et al., 2010. There were four response options on each trial. All the patients were below the normal cut-off in all conditions. Every individual patient showed better comprehension for dominant than for subordinate interpretations [no cue condition percentage correct: dominant M (SD): 81.3 (9.9); subordinate M (SD) = 53.7 (12.4)]. In addition, every single patient showed additional impairment in accessing subordinate meaning following miscues rather than cues [percentage correct subordinate trials: miscues M (SD) = 45.0 (14.0); cues M (SD) = 73.7 (13.4)]. Patients’ performance was compared against controls using ANOVA, including dominance (dominant; subordinate), cueing (miscue; no cue;

cue) and group (SA patients vs. controls). There were main effects of dominance [F(1,16) = 86.23, p < .001] and cueing [F(2,15) = 17.38, p < .001] plus interactions of dominance by cueing [F(2,15) = 8.34, p = .004], dominance by group [F(1,16) = 52.86, p = .001], cueing by group [F(2,15) = 14.81, p < .001] and the three-way interaction [F(2,15) = 6.00, p = .012; control data from Noonan et al., 2010; Fig. 2A].

3.3.2. Synonym judgment task

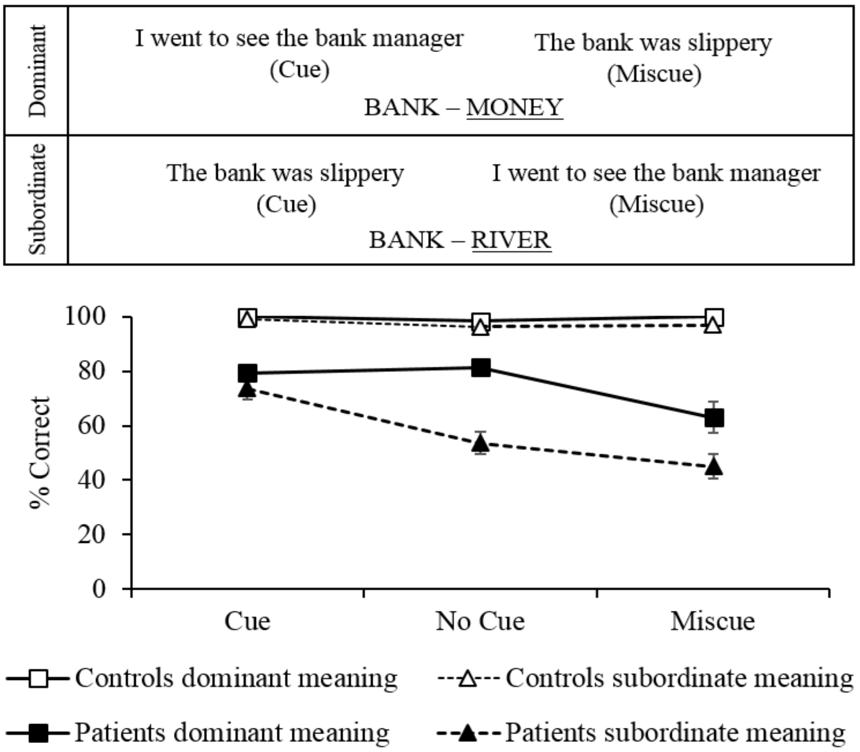
We tested synonym judgement with strong or weak distractors (84 trials), from Samson, Connolly, & Humphreys, 2007; e.g., DOT with POINT [target], presented with DASH [strong distractor] or LEG [weak distractor; Fig. 2B]. There were three response options per trial. Accuracy was below the cut-off for all patients and poorer when semantically-related but irrelevant distractors were presented [percentage correct: weak M (SD): 67.7 (11.4); strong M (SD): 45.8 (13.5)]. Patients' performance was compared against controls using a 2 by 2 mixed ANOVA [main effect of condition: F(1,15) = 10.19, p = .006; group interaction: F(1,15) = 20.81, p <.001; Fig. 2B; control data from Samson et al., 2007].

3.3.3. Object use task

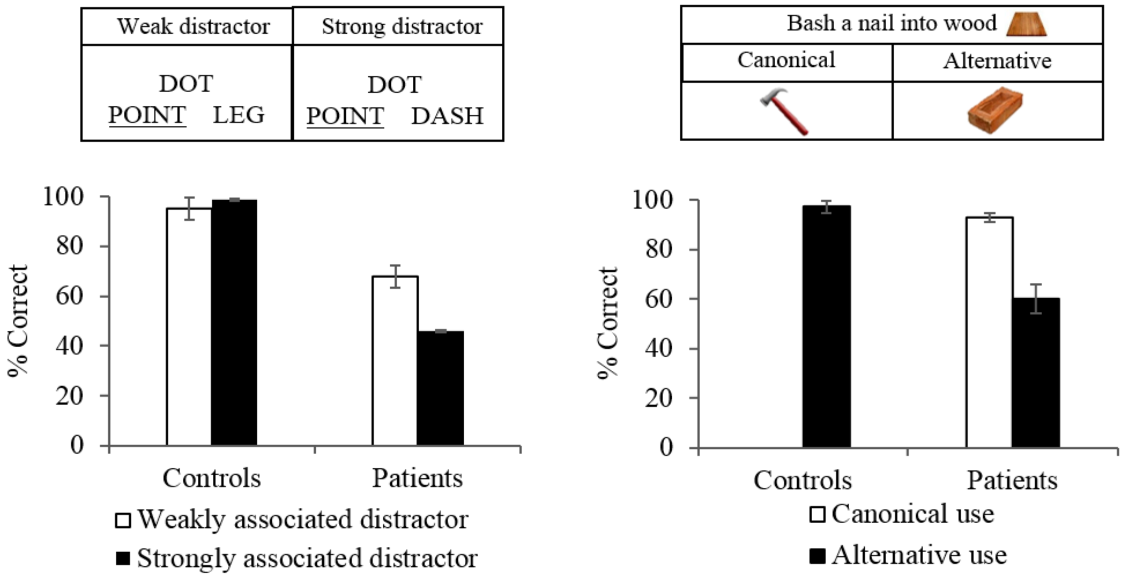
The object use task (74 items), from Corbett et al., (2011), involved selecting an object to accomplish a task (e.g., bash a nail into wood), with all items represented as photographs. The target was either a canonical tool, normally used to complete the task (e.g., HAMMER), or an alternative non-canonical option (e.g., BRICK), presented among a set of five unsuitable distractors. All patients were poorer at selecting non-canonical than canonical targets [percentage correct: canonical M (SD) = 92.7 (7.9); alternative M (SD) = 60 (19); t(9) = 8.34, p < .001] and almost all were impaired compared to controls [t(16) = -5.47, p < .001, see Fig. 2C; control data from Corbett et al., 2011 and not collected for the canonical condition given near-ceiling performance]. One single patient (P5) was not below the normal cut-off in the non-canonical condition, however this patient was impaired at the pictorial version of the CCT.

The SA group showed strong sensitivity to all these control manipulations (Figure 2) – i.e., more impaired comprehension of subordinate than dominant interpretations of ambiguous words; sensitivity to cues and miscues; better comprehension with weak than strong distractors and better retrieval of canonical than alternative object use. A composite score reflecting each patient's deficits in semantic cognition was derived from the Camel and Cactus Test and the three semantic control tasks described above using factor analysis. Patients are ordered by this composite score in the graphs and tables below.

In the next section, we examined whether our participants with deregulated semantic retrieval would show parallel deficits of episodic memory, including benefits of cues designed to constrain retrieval in both domains.



A) Ambiguity task



B) Synonym judgment task

C) Object use task

Figure 2. Tests manipulating semantic control. (A): Ambiguity task, from Noonan et al., (2010). (B): Synonym judgement task, from Samson et al., (2007). (C): Object use task, from Corbett et al., (2011). Error bars show SE of mean.

Table 4. Semantic background tests: individual scores

Test	Max	Control Mean (SD)	Patient Mean	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10
Cambridge Semantic Battery													
Picture Naming	64	59a	40.5	**1**	61	**19**	**50**	60	**50**	**3**	**43**	**56**	62
Word-Picture Matching	64	62.7a	61.4	63	62	**60**	64	**62**	**62**	**52**	63	64	**62**
Word CCT	64	60.7 (2.06)	50.1	**39**	**43**	**29**	**53**	59	**52**	57	**48**	61	60
Picture CCT	64	58.9 (3.1)	49.7	**31**	**44**	**45**	56	**45**	57	54	**51**	53	61
Ambiguity task													
Miscued dominant	30	30 (0)	18.9	**12**	**13**	**13**	**14**	**20**	**19**	**21**	**27**	**24**	**26**
Miscued subordinate	30	29 (1.20)	13.5	**7**	**10**	**14**	**8**	**10**	**15**	**18**	**16**	**18**	**19**
No cue dominant	30	29.5 (0.54)	24.4	**22**	**18**	**24**	**22**	**24**	**26**	**27**	**25**	**28**	**28**
No cue subordinate	30	28.9(0.64)	16.1	**11**	**9**	**14**	**14**	**19**	**17**	**19**	**18**	**21**	**19**
Cued dominant	30	30 (0)	23.8	**23**	**21**	**19**	**22**	**24**	**23**	**23**	**27**	**27**	**29**
Cued subordinate	30	29.75 (0.46)	22.1	**25**	**14**	**20**	**18**	**19**	**28**	**24**	**25**	**23**	**25**
Synonym with distractors													
Strong	42	39.87 (2.23)	19.2	**15**	**12**	**13**	**20**	**21**	**23**	**30**	NT	**22**	**17**
Weak	42	41.50 (0.53)	28.4	**25**	**23**	**29**	**24**	**27**	**30**	**31**	NT	**28**	**39**
Object use													
Alternative	37	33.67a	22.2	**14**	**13**	**14**	**21**	34	**22**	**22**	**27**	**26**	**29**
Canonical	37	NA	34.3	32	31	29	35	37	35	33	37	37	37

Table 4 Legend: Scores are number of correct; a = normal cut-off, NT = unavailable for testing, Bold underlined numbers denotes impaired scores (less than two standard deviation below mean). NA: not available

4. Verbal paired associate recall with cueing

4.1. Method

In a Verbal Paired Associates task (WMS-III, Wechsler, 1997), participants learned eight pairs of unrelated words (e.g., BANK-CARTOON). These were presented aurally four times, in a different order each time. Participants then attempted to recall the associate aloud from the probe. When there was no correct response, participants were given progressive phonological cues (i.e. the target's initial phonemes, one at a time) to reduce the need for internal constraints on episodic recall, e.g., "c.. ca.. car.. cart.. cartoo..". Progressive phonological cues have already been shown to benefit semantic retrieval in SA (Jefferies *et al.*, 2008a; Soni *et al.*, 2009; Noonan *et al.*, 2010). The task was administered to eight patients; two with poor speech production were not tested (P1 and P7).

4.2. Results

4.2.1. Accuracy

In the no-cue condition, patients' accuracy was significantly lower than controls [t(21) = 5.12; p < .001]. Both patients and controls benefited from phonemic cueing [F(1,21) = 148.87, p < .001], but patients showed a stronger cueing effect than controls [cueing by group interaction: F(1,21) = 20.81, p < .001; Fig. 3]. In an individual analysis, every patient showed a significant improvement in performance after cueing [McNemar p < .001].

4.2.2. Error analysis

Errors in the no cue condition were assigned to one of five categories: semantically-related to probe/target; interference (probe or target from a different pair); perseveration (repeating an inaccurate response given on a previous trial); phonologically-related to probe (sharing at least one phoneme in the correct position); unrelated. Omissions were disregarded. Four patients (P2 = 62%, P3 = 25%, P4 = 43%, P6 = 24%) produced semantically-related words in response to the probe (e.g., STAR-LADDER → "star-heaven"; ELEPHANT-GLASS – "elephant-giraffe"). There were insufficient numbers of errors for statistical analysis, especially amongst control participants (although this pattern is explored in alternative-forced-choice recognition tasks below).

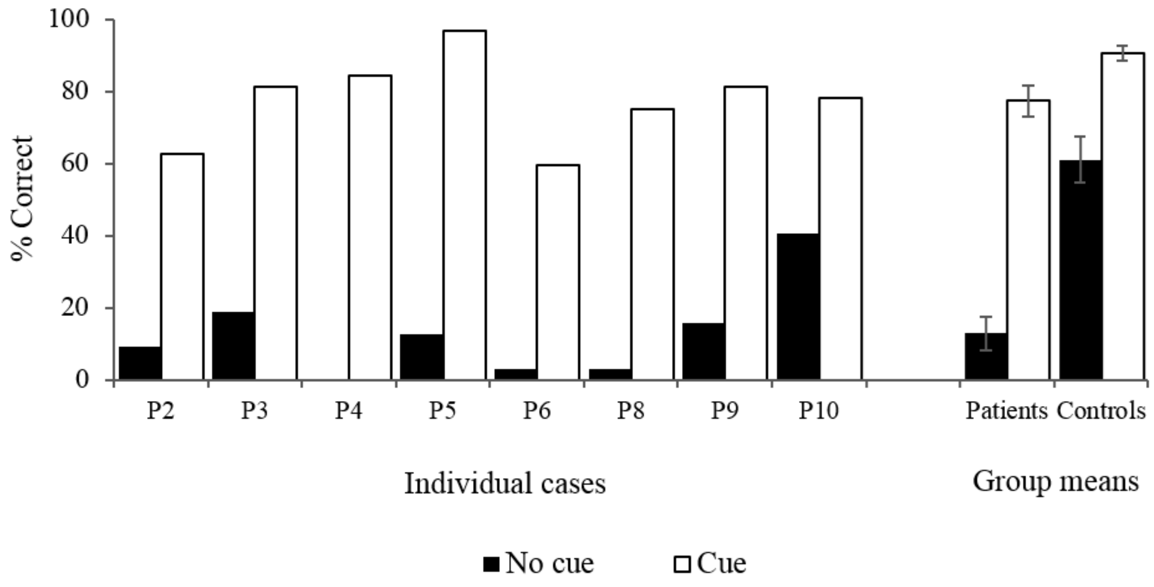


Figure 3. Verbal paired associate recall with phonological cueing (adapted from WMS-III, Wechsler, 1997). Error bars show SE of mean.

5. Paired associate recognition tasks

5.1. Rationale

As some patients had impaired speech production, the experiments below examined recognition. Experiment 1 manipulated the semantic relatedness of the probe and target words, the strength of episodic encoding, and the presence or absence of semantic distractors designed to elicit false episodic memories. Experiment 2 followed a similar structure but all of the words were semantically unrelated, to establish if episodic recognition was impaired relative to controls even when the role of meaning in encoding and retrieval was minimised. Experiment 3 presented pictures, not words, to establish if the multimodal nature of the semantic deficit would extend to episodic memory. We also asked participants to rate how confident they were in each decision on a scale from one (not confident at all) to seven (very confident).

5.2. Method

5.2.1. Experiment 1

Participants tried to remember which two words were presented together as a pair. There were two manipulations during the learning phase, relatedness and episodic strength. Word-pairs were either semantically related or unrelated; they were also repeated five times or only once (see Fig. 4A and Appendix Table 1 for list of stimuli). Each probe word was paired with both a related and an unrelated target in separate lists, allowing us to examine interference errors. Latent Semantic Analysis (LSA; Laham & Steinhart, 1998) established stronger associations for related vs. unrelated trials [Related M (SD) = 0.32 (0.15) vs. Unrelated M (SD) = 0.09 (0.08); t(31) = 8.02, p < .001]. There were no LSA differences between other conditions [t(15) < 1].

In each encoding block, eight word-pairs were presented consecutively on a screen using E-Prime 2.0. Probes and targets were initially presented individually for 1000ms and then the word-pair appeared on the screen for 3000ms. The words were read aloud by the researcher. Immediately after encoding, participants performed a recognition task in which they were asked to select the word previously presented with the probe, from amongst four response options. On each trial, there was a novel semantic distractor related to the probe (SEM); an episodic distractor that was a target on a different trial (EP); and a semantic-episodic distractor that was both semantically related to the probe and a target for another probe (SEM+EP). LSA showed that semantically-related distractors were more associated to the probe than episodic distractors [SEM vs. EP: t(30) = 7.80, p < .001; SEM+EP vs. EP: t(63) = 10.28, p = .001]. The targets and different distractor types were matched for frequency, length and imageability [t < 1, p > .31]. Patients indicated their choice by pointing. The order of recognition trials was randomised for each participant. There were 8 word pairs per learning list, and 8 lists presented in a counterbalanced order across participants, providing 64 trials for analysis. To ensure that patients comprehended the instructions, the task was preceded by practice trials testing memory for four words pairs. When the response was wrong, the correct answer was provided, and the practice procedure was repeated until the participant showed complete understanding. In Experiments 2 and 3 this was not necessary since patients were already familiar with the task. Patients' showed insight about their accuracy in all three experiments (see confidence analysis in section 5.3.6), confirming understanding of task instructions.

5.2.2. Experiment 2

In a subsequent experiment, we used the same task structure but eliminated semantic links between the stimuli, using LSA scores of 0.5 or below [See Appendix Table 2 for list of stimuli]. Targets and distractors were matched to the items presented in Experiment 1 for frequency (using CELEX, Max Planck Institute for Psycholinguistics, 2001) and letter length [t ≤ 1.14, p ≥ .162].

5.2.3. Experiment 3

In a non-verbal episodic memory task, we presented black-and-white line drawings of items during the training phase (mostly from Snodgrass & Vanderwart, 1980) and coloured photographs of the same objects for recognition. These images were as dissimilar as possible to prevent participants from relying on perceptual matching to identify the target. We again manipulated semantic relatedness (related, unrelated) and episodic encoding strength (pairs presented once or five times). Items on semantically-related trials were drawn from the same semantic category (e.g., APPLE-ORANGE). Other aspects of the procedure followed the description for Experiment 1 (see Fig. 4A for design and Appendix Table 3 for list of stimuli).

5.3. Results

Descriptive statistics are provided in Table 5.

5.3.1. Effects of relatedness and episodic strength on verbal recognition accuracy

Figure 4C shows the key results. Patients showed poorer performance than controls in verbal recognition overall [Experiment 1: t(21) = 5.45, p < .001; Experiment 2: t(11.6) = 8.0; p < .001]. In Experiment 1, ANOVA was used to examine the effects of group, semantic relatedness (related vs. unrelated probe-target pairs) and episodic strength (episodic encoding weak vs. strong). This revealed main effects of semantic relatedness [F(1,21) = 49.63, p < .001] and episodic strength [F(1,21) = 7.80, p = .011]. There was a significant interaction between group and semantic relatedness [F(1,21) = 16.62, p = .001; Fig. 4A]: patients derived a larger benefit from the availability of pre-existing semantic links at encoding [patients: t(9) = 5.93, p > .001; controls: t(12) = 2.94, p = .024, Bonferroni-corrected], perhaps because they were less able than controls to find a way to link unrelated pairs during encoding. There was also a near-significant interaction between relatedness, episodic strength and group [F(1,21) = 4.26, p = .052]. Neither patients nor controls showed an effect of episodic strength in the unrelated condition [although the contrast approached significance for controls: t(12) = 2.48, p = .060; patients: t < 1, Bonferroni corrected for two comparisons]. In the related condition, controls showed better accuracy on episodic strong vs. weak trials [t(12) = 3.64, p = .009], while the patients remained insensitive to this manipulation [t(9) = 2.05, p = .140, Bonferroni corrected for two comparisons]. Moreover, episodic strength had no effect across groups in Experiment 2, when all of the trials were unrelated [main effect and interaction, F ≤ 2.7].

5.3.2. Effects of presentation modality on accuracy

Figure 4E shows key results. In Experiment 3, which employed pictures, patients were again less accurate than controls [t(21) = 6.19; p < .001]. In contrast to Experiment 1, there was no main effect of relatedness on picture recognition [F(1,21) = 2.46, p = .132], and no relatedness by group interaction [F < 1]. There was a main effect of episodic strength [F(1,21) = 24.08, p < .001], which did not differ across the groups [F < 1]. An analysis of modality (pictures in Experiment 3 vs. words in Experiment 1) and group (patients and controls) found main effects of group [better performance for controls, F (1,21) = 46.04, p <.001] and modality [better performance for pictures, F(1,21) = 4.63, p = .043] but no interaction [F < 1], indicating a multimodal deficit of comparable severity for words and pictures.

5.3.4. Semantic error analysis

Since SA patients have difficulty controlling semantic retrieval to suit the task demands (Noonan et al., 2010), they may find it difficult to ignore semantic connections that are irrelevant for episodic memory (e.g. the distractor TEACHER for the encoded pair "SCHOOL-CAKE"). We examined whether the patients were more likely than controls to choose semantically-related responses using ANOVA to compare related and unrelated trials, separately for each experiment and error type (expressed as a percentages of incorrect trials per condition). In Experiment 1 employing words, SEM errors (i.e., related in meaning but not previously presented) were the only error type selected more often by the patients [F(1,21) = 14.79, p = .001, Fig. 4D]. This pattern was not observed in Experiment 3 employing pictures [for SEM errors, there were no main effects of group and no interaction, F ≤ 2.41, p > .135]. It might be easier to reject novel distractor pictures – even those which are semantically-related – given the richness and distinctiveness of these stimuli.

5.3.5. Proactive interference and perseveration errors

Proactive interference errors were coded when the correct response from a previous list was repeated (e.g. 1st list: PARTY-CHILDREN → "party-children"; 2nd list: PARTY-BASKET → "party-children"), while perseveration errors were scored when the same incorrect response occurred across two lists (e.g., 1st list: PARTY-CHILDREN → "party-balloon"; 2nd list: PARTY-BASKET → "party-balloon"). These errors were expressed as a percentage of incorrect trials in which the error was possible. In Experiment 1, patients made more proactive interference errors [t(21) = 4.02, p = .001] and perseverations [t(12.6) = 2.90, p = .011] than controls. All perseverations were semantically related to the probe. Similarly, in Experiment 2 employing unrelated words, patients made more proactive interference errors than controls [t(21) = 5.08; p < .001] but there were few perseverations in both groups and no group difference [t ≤ 1], consistent with the semantic origin of these errors in Experiment 1. In Experiment 3, when items were presented as pictures, there was no difference across groups in the rate of proactive interference [t(12.64) = 1.64, p = .125] and perseveration errors [t(9) = 2.17, p = .058].

5.3.6. Confidence ratings

We used Linear Mixed Effects Models to examine the effects of trial-by-trial accuracy as well as experimental factors on confidence ratings, and to overcome missing data (i.e., controls without incorrect trials or patients without correct trials in particular conditions). Main effects and interaction terms were retained only if they improved the model fit. Allowing random intercepts per participant improved model fit in all analyses [$\chi^2(1) \geq 3.84$, p ≤ .05]. Key results are displayed in Figure 4F with additional details in the Supplementary Materials. Interactions with group were interpreted by conducting separate multilevel models for patients and controls.

In the final model for Experiment 1 [-2LL = 4009.91], confidence ratings were predicted by response accuracy [F(1, 1451) = 88.07, p < .001]; relatedness of response [F(1, 1451) = 34.65, p < .001], episodic strength [F(1, 1449) = 23.30, p < .001], group [F(1, 24) = 7.76, p = 0.010] and the interaction between group and relatedness [F (1, 1451) = 4.6, p = 0.032]. Patients had disproportionately higher confidence in their episodic memory when they selected a semantically-related item [b = .27, F(1, 631) = 24.98, p < .001; Fig. 4F] relative to the controls [b = .13, F(1, 791) = 9.09, p = .003]. In Experiment 2, all probe-target pairs were semantically-unrelated; therefore, this experiment was not suited to investigating confidence for semantically-driven false memories. In Experiment 3 (episodic picture task), confidence did not show an interaction between group and relatedness of the response (there was a four-way interaction), while confidence in Experiment 4 (described below) did not show any interactions with group (see Supplementary Materials sections 9.1. and 9.2.). Analyses of the patient group confirmed that confidence was predicted by accuracy in all four experiments [Experiment 1: F(1,630) = 40.17,p < .001; Experiment 2: F(1,631) = 55.26, p < .001; Experiment 3: F(1,631) = 50.49, p < .001; Experiment 4: F(1,1150) = 44.9, p < .001], indicating that these participants were able to produce meaningful confidence ratings.

5.3.7. Summary

Semantic links between probes and target at encoding supported episodic memory for the patients (Experiment 1 and 2), whereas the presence of semantic distractors and previously encoded memories (i.e. proactive interference) at retrieval elicited a disproportionate number of false episodic memories and perseverations (Experiment 1 and 2). Episodic deficits also arose when non-verbal material was used (Experiment 3) and patients were disproportionately confident when their response was congruent with existing semantic knowledge (Experiment 1).

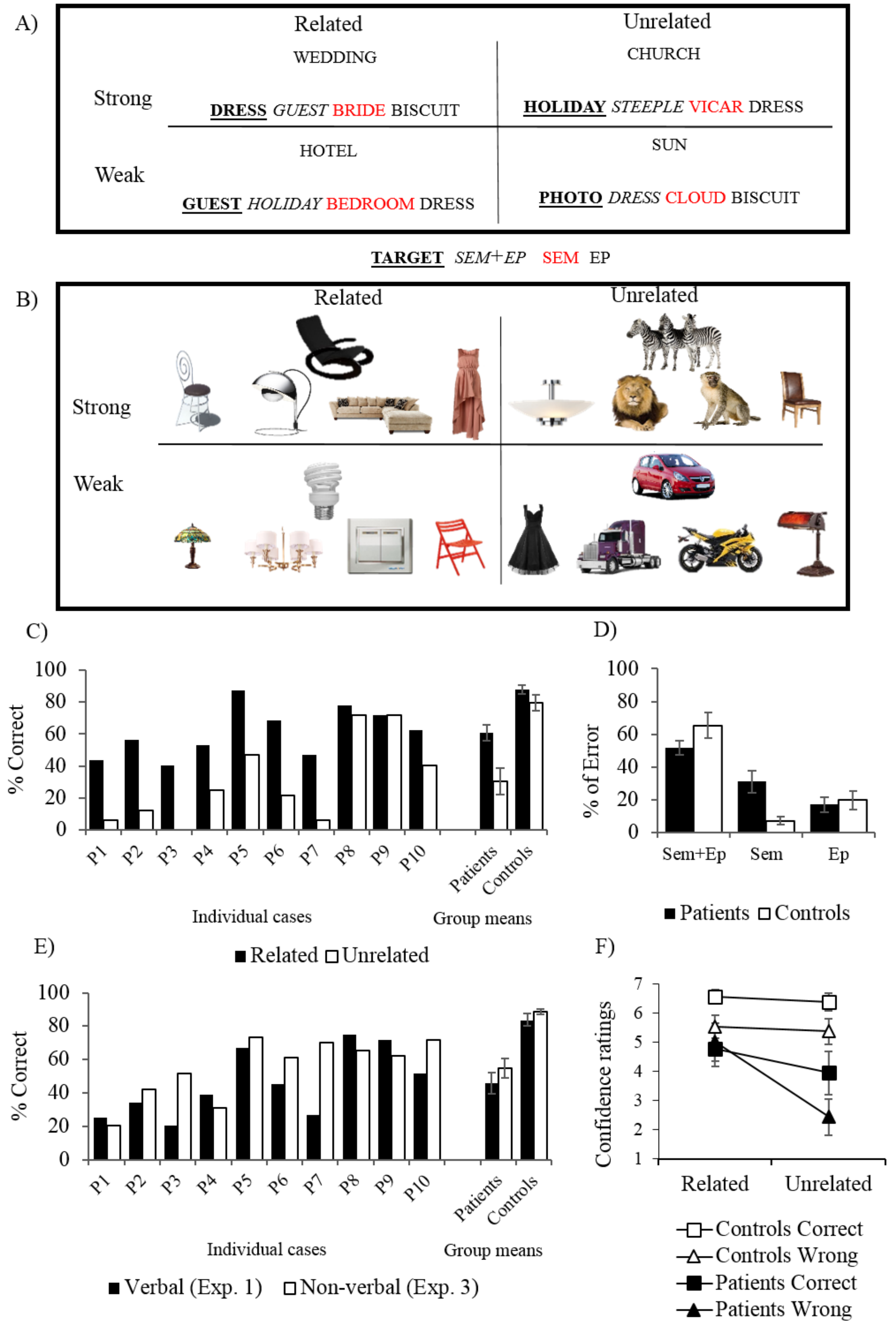


Figure 4. Paired associate recognition tasks and key results. A) Experiment 1 (words). B) Experiment 3 (pictures). Related and Unrelated conditions: probe paired with a semantically related or unrelated target at encoding. Strong trials: repeated 5 times at encoding; Weak trials: presented only once at encoding. Response options: Target – item paired with the probe at encoding; SEM distractor –

novel and semantically related to the probe; SEM+EP distractor – semantically related to the probe and a target word for another probe; EP distactor – target on a different trial but not semantically related to the probe. Response options are displayed in the same order in both tasks. C) Effect of relatedness on accuracy in Experiment 1; D) Errors in Experiment 1; E) Modality effect: Experiment 1 vs. 3. F) Confidence analysis for Experiment 1: relatedness by accuracy by group. Error bars show SE of mean.

Table 5. Experiment 1, 2, 3 and 4: descriptive statistics accuracy and error type

	Experiment 1		Experiment 2		Experiment 3		Experiment 4*	
	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls
	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)
Accuracy %								
Correct	45.6 (20.1)	83.7 (13.3)	52.1 (15.3)	93.4 (6.6)	55 (18.3)	88.7 (6.5)	61.3 (11)	90.4 (3.9)
Related	60.9 (15.5)	87.7 (9.8)	-	-	54.1 (17.5)	85.3 (11.4)	64.6 (13.3)	94.1 (5.0)
Unrelated	30.3 (26.5)	79.6 (17.6)	-	-	55.9 (21.2)	92.1 (6.2)	58 (8.9)	86.7 (4.8)
Episodic strong/trained*	47.2 (24.8)	88.7 (10.9)	54.1 (16.7)	95 (6.5)	59.7 (19.7)	93.3 (4.9)	54 (13.8)	90.9 (5.3)
Episodic weak/untrained*	44.1 (17.3)	78.6 (16.5)	50 (17.3)	91.8 (7.7)	50.3 (17.8)	84.1 (9.8)	68.6 (11.3)	89.8 (4.2)
Errors %								
Related trials SEM/ Trained trials EPI*	37.3 (27.7)	8.4 (13.5)	-	-	22.4 (13.7)	10.5 (16)	42.3 (12.6)	38.7 (10.7)
Unrelated trials SEM/ Untrained trials UNR1*	27.9 (18.5)	5.7 (10)	-	-	13.6 (18.8)	27.4 (39.5)	25.3 (6.9)	46.5 (16)
Related trials SEMEP/ Trained trials FAM*	58.8 (30.3)	76.5 (32)	-	-	61.9 (21.2)	85.8 (20.9)	11.4 (6.2)	2.4 (5.6)
Unrelated trials SEMEP/ Untrained trials UNR2*	47.7 (16.2)	30.9 (34.9)	-	-	43.9 (23)	22.3 (30.9)	9.4 (5.2)	6.5 (10.2)
Related trials EP/ Trained trials UNR 3*	3.9 (5.9)	7.4 (14.8)	-	-	15.7 (10.5)	3.6 (8.9)	5.6 (5.8)	3.5 (5.9)

Unrelated trials EP/ Untrained trials UNR 3*	24.4 (22.4)	21.1 (28.1)	-	-	42.5 (28)	42.6 (39.2)	6 (3.4)	2.4 (4.4)
Proactive interferences	40.7 (15.3)	17.1 (12.9)	33.3 (14.5)	8.3 (9)	19.9 (18)	9.6 (9.24)	-	-
Perseverations	31.9 (27.1)	3.8 (13.9)	19.3 (22.4)	7.7 (27.7)	14.6 (21.3)	0 (0)	-	-

Table 5 Legend. Scores are % of correct. For Exp. 1, 2, 3: Related and Unrelated = probe paired with a semantically related/unrelated target at encoding; Strong = repeated 5 times at encoding; Weak = presented only once at encoding; SEM = novel and semantically related to the probe; SEM+EP = semantically related to the probe and target word for another probe; EP = target on a different trial but not semantically related to the probe. For Exp. 4: Related and Unrelated = EPI/UNR1 distractors semantically related or unrelated with target; Trained = probe episodically-associated with episodic distractor during episodic training; Untrained = probe not presented during episodic training; EPI = episodic distractor associated with the probe during episodic training; FAM = associated with a different probe during episodic training; UNR1, 2, 3 = novel unrelated distractors.

6. Effects of episodic distractors on semantic decisions

6.1. Rationale

In the episodic memory tasks above, the patients relied more than controls on semantic links between probes and targets and they were vulnerable to false memories that reflected difficulties resolving competition between episodic and semantic representations. Next we established whether the patients' difficulties reflected a failure to control semantic retrieval specifically, or if there were parallel deficits in supressing irrelevant episodic links when making semantic judgements. Unrelated items were paired to create episodic associations, and participants subsequently made semantic judgements to these items. On some trials, the probe and target had been previously presented as a pair, while on others, the probe was episodically-linked to a distractor. One participant (P8) was unable to take part in Experiment 4.

6.2. Method

Experiment 4 included two phases: *episodic training* and *semantic judgments*. During *episodic training,* participants pressed the arrow keys to indicate the location of an item on the screen, relative to another in the centre. In each session, there were four pairs of semantically-unrelated pictures presented consecutively; verbal labels were displayed underneath each picture and read aloud by the examiner. To check that the pairs had been encoded, participants were asked to recognize the episodic target alongside an unrelated foil (2AFC: e.g. "Was TEA presented with MONEY or DRESS?"). They were tested on three separate trials, employing different foils, both immediately and after a filled delay of twenty minutes. All participants were correct on both immediate and delayed recognition in at least two out of three trials.

The *semantic judgment* task (Fig. 5A) immediately followed delayed recognition. There were eight probe words, including the four probes trained in the episodic training phase, plus four new and untrained ones. Each probe was presented on four different trials, with different semantically-related targets, producing a total of 32 trials. In half of the trials, the target was presented alongside a distractor that had been episodically-associated with the probe. In the other trials, none of the distractors had been presented in the episodic training phase. Additionally, in half the trials, this critical distractor was semantically-related to the target [LSA: M(SD) = 0.34 (0.2); e.g., MONEY with BAG] but not the probe [LSA: M(SD) = 0.1 (0.1) MONEY with TEA]. Consequently, the target might accrue activation from both the semantic link with the probe and the primed distractor. In the other trials, there was no semantic association between the target and the distractor [LSA: M(SD) = 0.08 (0.09); e.g., MONEY with LEAVES).

The target was presented alongside three distractors. On trials with episodic training, these were the episodic distractor, a familiar distractor that was associated with a different probe during episodic training and a novel unrelated distractor. On trials without episodic training, all distractors were unrelated [LSA: M(SD) = 0.08 (0.08)]. The stimuli are provided in Appendix Table 4. The response options were presented visually and read aloud to the patients, who indicated their choice by pointing. This entire procedure was repeated on four different lists on separate sessions, providing 128 trials for analysis. Untrained trials on one list became trained trials in another, ensuring that differences between conditions could only be explained in terms of the effects of training. The order of trials and lists were randomized across participants. Prior to the semantic judgment task, participants were warned of the different task requirements and explicitly instructed and reminded over the course of the task to select words “related in meaning”. To ensure understanding of task instructions, the actual task was preceded in all sessions by two semantic judgment practice trials and explicit feedback were provided (a green tick as opposed to a red cross, when correct vs. incorrect). Participants were always correct in the practice trials and showed insight about their accuracy (see Supplementary Materials section 9.2. for confidence analysis) suggesting they understood the task instructions.

6.3. Results

Descriptive statistics are provided in Table 5.

6.3.1. Effect of episodic training on semantic judgments

Fig. 5B shows the key results. ANOVA examining the effects of episodic training, target-distractor relatedness and group revealed a main effect of episodic training [F(1,17) = 9.89, p = .006] and an episodic training by group interaction [F(1,17) = 13.32, p = .002]. There were fewer correct responses for episodically-trained trials in patients but not controls [patients: t(8) = - 3.56, p = .014: controls: t < 1; Bonferroni corrected, Fig. 5B]. There was also a main effect of relatedness [F(1,17) = 29.24, p < 0.001] showing that both groups were more accurate when the target was semantically related to a distractor.

6.3.2. Episodic error analysis

We compared selection of the episodic distractor on trials with episodic training with the matched unrelated distractor on trials without episodic training, with errors expressed as a percentage of incorrect trials. Key results are reported in Fig. 5C. There was a main effect of group [F(1,17) = 7.33, p = .015 and a significant interaction of error type by group [F(1,17) = 7.55, p = .014]: patients were more likely to choose the episodic distractor following training [patients: t(8) = 3.86, p = .01; controls: t(9) = -1.04, p = 0.6, Bonferroni corrected, see Fig. 5C].

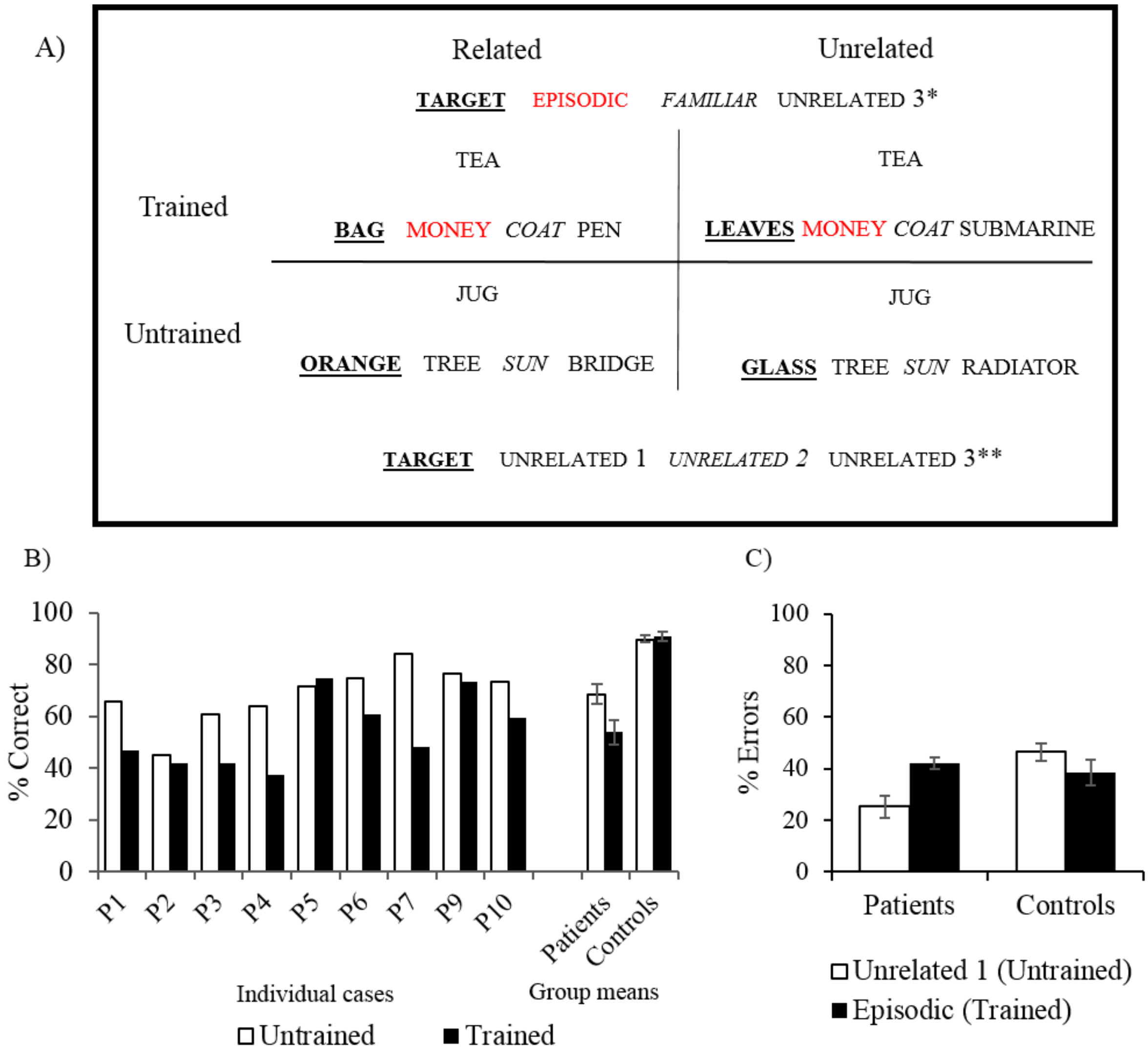


Figure 5. Experiment 4 (semantic judgement task with and without episodic distractors): design and key results. A) Experiment 4 design. Trained trials: probe associated with episodic distractor during training phase; Untrained trials: probe not presented during episodic training; Related trials: episodic distractor semantically related to target; Unrelated trials: episodic distractor unrelated to target. Response options: Target – semantically associated with probe; Episodic (trained trials only) – associated with the probe during episodic training; Familiar (trained trials only): associated with a different probe during episodic training; Unrelated: novel unrelated distractors (all distractors were unrelated in untrained trials). B) Effect of episodic training on semantic judgement. C) Percentage of errors that were episodically-associated with the probe, relative to selection of matched distractors on untrained trials. Error bars show SE of mean.

7. Correlation between semantic and episodic performance

The semantic control composite score (see above) and an episodic composite score derived from overall accuracy in Experiments 1, 2 and 3 were highly correlated [r = .736, p = .015, Fig. 6A]. Similarly, there was a strong correlation between the number of semantic and episodic errors [from Experiment 1 and 4 respectively, r = .729, p = .026, Fig. 6B]. This suggests that semantic control difficulties are highly associated with episodic memory performance, as is the capacity to avoid errors driven by both irrelevant episodic and semantic information.

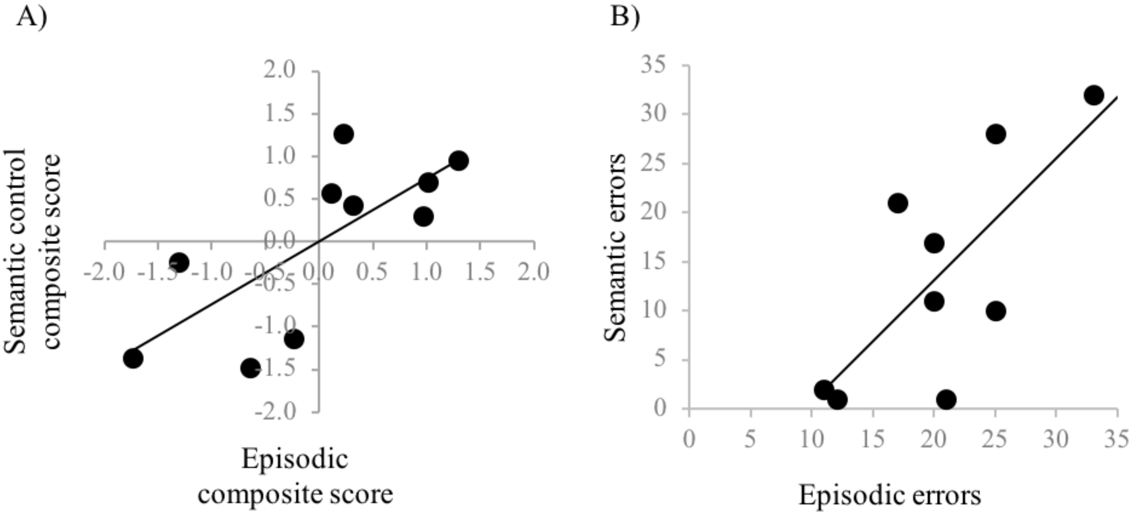


Figure 6. Correlations between semantic and episodic performance

8. Discussion

This study investigated deficits of episodic memory in patients with multimodal semantic impairment following stroke aphasia (cf. SA). These individuals have deficient executive control over semantic information, as opposed to a loss of conceptual knowledge, following lesions in frontal and/or temporoparietal regions (Jefferies and Lambon Ralph, 2006; Noonan *et al.*, 2010; Thompson *et al.*, 2015a). In the current sample, the lesion overlay was focussed on LIFG, a key region for semantic control, and all patients had damage to this region. While past studies of these patients have focussed exclusively on deficits in semantic tasks, we might expect parallel deficits in episodic memory since functional neuroimaging studies have implicated LIFG in controlled retrieval across both semantic and episodic tasks. In line with this hypothesis, we found patients had difficulty retrieving information in a flexible fashion appropriate to the circumstances in both episodic and semantic tasks. In the semantic domain, the patients struggled to understand non-dominant interpretations of ambiguous words as well as non-canonical uses of objects presented as pictures (cf. Corbett et al., 2011; Noonan et al., 2010). In the episodic domain, the patients were impaired at paired-associate learning tasks, particularly when the target was presented alongside a recent item from another trial or a distractor that was strongly-related to the probe, causing interference. Like the semantic deficit, this impairment of episodic memory was multimodal, affecting paired-associate tasks presented using words or pictures, supporting the view that shared control processes interact with heteromodal episodic and semantic representations in the hippocampus and anterior temporal lobes.

The patients relied on well-established semantic links during episodic encoding. They had difficulty forming associations 'on the fly' between words that were not already related – and consequently, their semantic control deficit increased rather than reduced their reliance on semantic information in episodic tasks. Their episodic retrieval was inappropriately driven by semantic connections, leading to the intrusion of irrelevant information (i.e., false recognition of semantically-related distracters). This resembles the pattern for semantic judgements; patients also had difficulty correctly identifying synonyms when the target word was presented alongside a strong associate that acted as a distracter (e.g., PIECE with SLICE and CAKE). Patients' confidence in their episodic memory was strongly driven by the semantic relationship between the response and probe, suggesting they had difficulty appropriately focussing on the strength of task-relevant as opposed to irrelevant information to evaluate their memory. This impairment is likely to have a significant impact on everyday functioning, since patients have difficulty separating strong semantic signals from representations of past events.

The patients also showed increased proactive interference, suggesting they had weak inhibition over competing episodic memories. This pattern would be expected if the same neurocognitive mechanisms support episodic and semantic selection. To confirm this interpretation, we demonstrated that presenting pairs of unrelated words to create episodic associations generated interference during subsequent semantic judgements involving the same items. The patients' difficulties did not simply reflect the impaired application of semantic knowledge to promote successful episodic encoding and retrieval. Instead, they had difficulty regulating activation in *both* memory systems and generating appropriate cognitive states when these two sets of memory representations were in conflict. The patients also showed similar effects of cueing on episodic and semantic retrieval. Episodic memory was improved by the provision of progressive phonological cues indicating that the patients were able to encode and retain information in episodic memory, yet they had difficulty focussing retrieval on *relevant* information when the task was relatively unconstrained. Similar effects of semantic cueing have been observed in picture naming (Jefferies *et al.*, 2008a; Soni *et al.*, 2009) and comprehension tasks (Noonan *et al.*, 2010), including in the current patients. In sum, our findings suggest that shared mechanisms are responsible for focussing cognition on currently-relevant memory representations, especially in the face of competition from strongly-encoded yet irrelevant information, in both episodic and semantic tasks. This necessity to constrain retrieval is reduced when the task provides strong cues to retrieval that reduce competition and the need to internally shape retrieval.

Our findings have important implications for neuroscientific accounts of memory retrieval. Most neuroimaging and neuropsychological studies to date have examined manipulations of either episodic *or* semantic tasks, and have not directly compared effects of control demands across these domains. This study therefore provides new insights into how these representations interact in ways that both support and impair performance. Distinct heteromodal LTM representations supporting generalised and unique aspects of experience are thought to lie in adjacent regions of ventral ATL and hippocampus (McClelland *et al.*, 1995; O'Reilly *et al.*, 2014), and these sources of semantic and episodic information are likely to be highly interactive. Learning benefits from existing knowledge that is coherent with new experiences (Bartlett, 1932; Craik and Tulving, 1975; Van Kesteren *et al.*, 2012). Also, intact semantic knowledge can support episodic memory in amnesic patients with selective hippocampal lesions (Verfaellie *et al.*, 2000) and new episodic learning is influenced by degraded semantic knowledge in semantic dementia (Mayberry *et al.*, 2011). The activation of conceptual representations at the point of retrieval can then give rise to competition between these systems. The patients relied to a greater extent than the healthy controls on semantic representations to aid episodic learning, presumably because control processes are critical to establish new links that are unsupported by past experience. By the same token, the patients were vulnerable to false memories driven by irrelevant semantic associations, presumably because control processes also play a critical role in selecting memory representations to suit the current demands of the task. Irrespective of the type of memory, the patients were overly influenced by the most dominant, activated form of information (episodic or semantic).

In addition, while neuroimaging studies of healthy volunteers have demonstrated a role for LIFG in executive aspects of both semantic and episodic tasks (in separate studies), the current work adds weight to the view that LIFG plays a *critical* role in memory control across domains, since neuropsychological studies are causal and not correlational. The neuroimaging findings of Badre and colleagues have linked distinct regions of LIFG to (i) controlled retrieval and (ii) post-retrieval selection, across semantic and episodic memory tasks (Badre and Wagner, 2007; Barredo *et al.*, 2015). Mid-to-posterior LIFG, damaged in every patient in our sample, is thought to contribute to the resolution of competition between activated representations in both episodic and semantic judgements (Badre & Wagner, 2005, 2007; Barredo et al., 2015) and this region also makes a crucial contribution to lexical selection and phonological tasks (Poldrack *et al.*, 1999; Gold and Buckner, 2002; Hirshorn and Thompson-Schill, 2006). LIFG is known to be engaged in situations in which recently-activated information is irrelevant to the current task, such as in the recent negatives paradigm (Jonides *et al.*, 1998; Badre and Wagner, 2005). The effect of distracters and cues in episodic and semantic memory tasks, and the frequency of perseverations and interference errors, can be explained in terms of a deficit in selecting relevant semantic and episodic representations. Mid-to-anterior parts of LIFG are proposed to have a more specific role in memory retrieval, assisting with the recovery of weakly-encoded semantic and episodic information (Barredo *et al.*, 2015). There is less clear-cut evidence of this deficit: although we manipulated episodic encoding strength, the patients showed a smaller effect of this variable than the controls, at least when semantic relationships were also available at encoding.

However, the patients' large lesions do not allow us to separately examine the contributions of anterior and posterior aspects of LIFG.

Most neuroimaging and neuropsychological studies of memory control have employed verbal stimuli (but see Turriziani *et al.*, 2010; Krieger-Redwood *et al.*, 2015): the current work is therefore also important in demonstrating that shared neurocognitive processes support memory control for *non-verbal* episodic and semantic tasks (Corbett *et al.*, 2011; Krieger-Redwood and Jefferies, 2014; Thompson *et al.*, 2015a). These results are explicable within a framework in which modality-general control processes (drawing on LIFG and other temporo-parietal regions) interact with heteromodal representations captured within ATL (a key hub for semantic representations) and hippocampus (the episodic 'store'). However, differences between the verbal and non-verbal tasks (e.g., in the effect of semantic encoding and distraction) also place constraints on this theoretical framework. While the verbal episodic memory task showed a strong positive effect of semantic relatedness at encoding, and significant disruption from semantically-related distracters, the picture-based task showed neither of these effects. One possibility is that semantic-episodic interactions are stronger for verbal tasks, in line with the proposal that pictures gain privileged access to the hippocampus via the ventral visual stream (Graham *et al.*, 2010; Baddeley and Hitch, 2017). As a consequence, both the positive and negative consequences of semantic involvement in paired associate learning may be greater for verbal stimuli.

8.1. Limitations and future directions

Our past work has pointed to roles for both posterior middle temporal gyrus (pMTG) and dorsal angular gyrus (dAG) in semantic control (Noonan *et al.*, 2013). The contribution of these regions to controlled episodic retrieval is yet to be established, but would be predicted given the large-scale distributed network that LIFG participates in. Both pMTG and dAG are commonly damaged in patients with aphasia following left hemisphere strokes, although unlike LIFG, these regions were not universally affected in the current sample. Although our data support the hypothesis of a critical role of LIFG in memory control (Badre and Wagner, 2007; Barredo *et al.*, 2015), the current study cannot provide incontrovertible evidence that LIFG – and no other sites – within MCA-territory infarcts support controlled retrieval from episodic and semantic memory. Future studies could address this issue by comparing episodic performance after LIFG and other lesions (either in clinical groups or through the use of inhibitory TMS). In the current study we have shown that patients with LIFG lesions have difficulty controlling competition within and between episodic and semantic memory. Our focus is on shared components at the cognitive level, and the extent to which this pattern extends to patients with left hemisphere stroke outside IFG remains debatable.

We have previously shown a double dissociation in semantic cognition between patients with SA and people with semantic dementia (Jefferies and Lambon Ralph, 2006). SA patients show impaired control over semantic retrieval, while semantic dementia is linked to degraded conceptual knowledge.

It would be useful to confirm there is a similar double dissociation in episodic memory between SA and patients with hippocampal lesions, who might be expected to have impaired episodic memory yet intact memory control processes. Future studies could also test if stroke survivors who have a cognitive profile not compatible with SA - such as those with relatively specific phonological deficits – show intact retrieval of episodic memories.

8.2. Conclusions

We observed similar control deficits in episodic and semantic tasks in our patient sample with LIFG lesions. These results support the hypothesis that common control processes across episodic and semantic memory focus retrieval on currently-relevant representations, especially in the face of competition from strongly-encoded yet irrelevant information. There were parallel effects of strong competitors and cueing, plus a multi-modal deficit in both semantic and episodic memory. The patients experienced false episodic memories driven by the inappropriate retrieval of semantic associations and, similarly, recent experience inappropriately influenced the patients' semantic judgements. This indicates that episodic representations of recent events and semantic representations of common elements of experience are both utilised to support episodic and semantic judgements. Control processes normally play a crucial role in allowing us to weight these sources of information to suit the circumstances.

Acknowledgments

This manuscript is dedicated to the memory of one special patient who sadly passed away in the course of this study. We are indebted to the patients, their carers, and the control participants for their generous assistance with this study. Woody Chao, Dominic Arnold and Sioned Thomas assisted with the collection of control data.

Funding

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Supplementary Materials

9. Supplementary analyses of confidence in Experiments 3 and 4

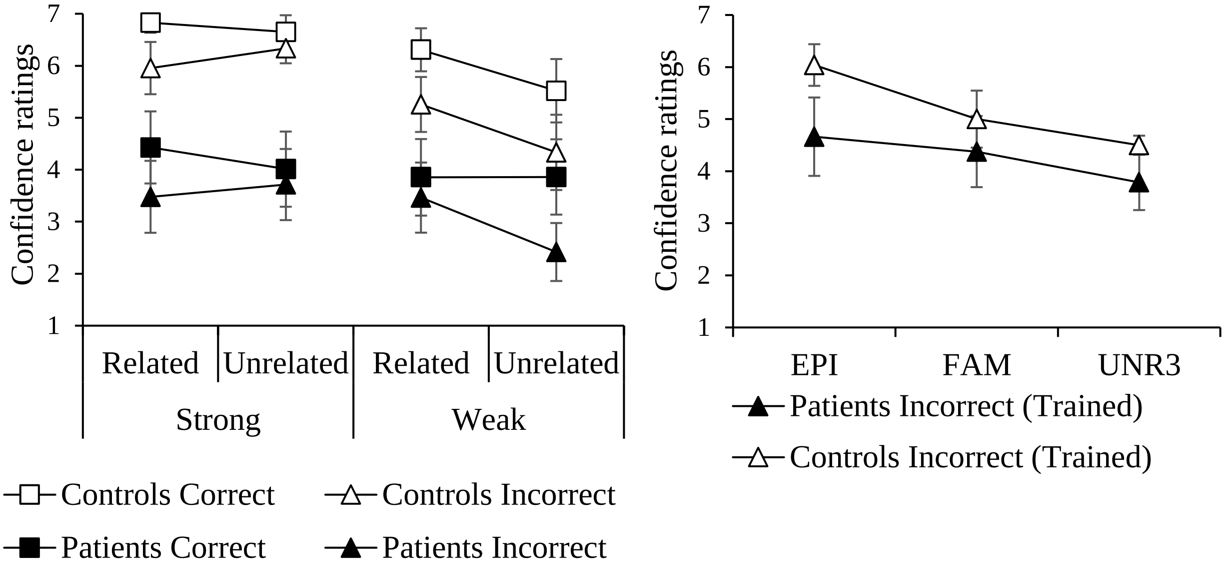
9.1. Experiment 3 (episodic memory for pictures)

The final model [-2LL = 5150.26] revealed that confidence was predicted by accuracy [F(1, 1451) = 69.85, p < .001], group [F(1, 1012) = 358.67, p < .001], relatedness of response [F(1, 1448) = 30.63 , p < .001] and episodic strength [F(1, 1448) = 76.28, p < .001]. There was an interaction of episodic strength by group [F(1, 1448) = 9.67, p = .002] and a four-way interaction of these factors [F(1, 1448) = 6.38, p = .012]. The effect of episodic strength was larger in the control group [patients: b = .19, F(1, 630.01) = 15.83, p < .001; controls: b = .43, F(1, 819.27) = 68.20 p < .001]. We investigated the four-way interaction by examining the effect of accuracy and relatedness in strong and weak trials separately for both groups. During strong trials, confidence ratings were predicted by accuracy in both groups [patients: b = 0.33, F(1, 308) = 18.13, p <.001; controls: b = .26, F(1, 412) = 4.87, p = .028]; additionally patients' confidence was higher for semantically-related responses [b = .11, F(1,308) = 5.33, p = .022] but this effect was not found for controls [b = -.05, F < 1]. During weak trials, confidence ratings were predicted by accuracy in both groups [patients: b = .38, F(1, 308) = 27.88, p = .001; controls: b = .48, F(1, 410) = 11.76, p = .001] and by the relatedness of the response in both groups [patients: b = .15, F (1,307) = 4.72, b = .030; controls: b = .34, F (1,408) = 5.87, p = .016; see Supplementary Figure 1]. For both strong and weak trials there was no relatedness by accuracy interaction in both groups [F ≤ 1.7; p ≥ .220].

9.2. Experiment 4 (semantic memory with episodic distractors)

In Experiment 4, episodically-trained distractors were present on half the trials; therefore it was not possible to examine the effect of the main experimental manipulations and the presence of episodic distractors in a single analysis. Consequently, we ran two analyses. The first examined confidence ratings as a function of response accuracy, group, episodic training and semantic relatedness of the target and distractor. The final model [-2LL = 7993.43] included only main effects of accuracy and group. Controls were more confident than patients [b = - .59, F(1, 19.05) = 5.62, p = .028] and both groups were more confident during correct vs. incorrect trials [main effect of accuracy: b = .42, F(1, 2414) = 174.67, p < .001].

In the second model we explored confidence ratings as function of type of error. This model examined incorrect and trained trials only, looking at effects of error type (EPI, FAM vs. UNR3), group and target-distractor relatedness. The final model [-2LL = 1094.72] included the main effects of type of error and group. Controls were more confident than patients [main effect of group: b = - .74, F(1, 19.90) = 4.76, p = .041] and both groups were more confident when the episodic distractor was selected [main effect of error type: b = -.39, F (1, 309.19) = 16.41, p <.001, Supplementary Fig. 1B]. However, there was no interaction between these factors.



Supplementary Figure 1. Confidence ratings Experiment 3 (A) and 4 (B). Error bars show SE of mean.

CHAPTER 3

Control the source: Source memory for semantic, spatial and self-related items in patients with LIFG lesions

Acknowledgments:

This chapter was submitted to a peer-reviewed journal on 13/09/2018. Elizabeth Jefferies and the author developed the experimental design and the main ideas in this manuscript. Suzanne Pegg, Glyn Hallam, Jonathan Smallwood, Matthew Lambon Ralph and Hannah Thompson provided important input to experimental design and the writing of the manuscript. Stimuli and data collection were carried out by the author, Suzanne Pegg, Sioned Thomas and Glyn Hallam.

Abstract

Patients with multimodal semantic deficits following stroke (‘semantic aphasia’) have largely intact knowledge, yet difficulty controlling conceptual retrieval to suit the circumstances. Although conceptual representations are thought to be largely distinct from episodic representations of recent events, controlled retrieval processes may overlap across semantic and episodic memory domains. We investigated this possibility by examining item familiarity and source memory for recent events in semantic aphasia following infarcts affecting left inferior frontal gyrus. We tested the hypothesis that the nature of impairment in episodic judgements reflects the need for control over retrieval: item familiarity might be relatively intact, given it is driven by strong cues (re-presentation of the item), while source recollection might be more impaired since this task involves resolving competition between several potential sources. This pattern was observed most strongly when the degree of competition between sources was higher, i.e. when non-meaningful sources had similar perceptual features, and existing knowledge was incongruent with the source. In contrast, when (i) spatial location acted as a strong cue for retrieval; (ii) existing knowledge was congruent with episodic memory and (iii) distinctiveness of sources was increased by means of self-referential processing, source memory reached normal levels. These findings confirm the association between deregulated control of semantic and episodic memory in patients with semantic aphasia and delineate circumstances that ameliorate or aggravate these deficits.

1. Introduction

The retrieval of episodic memory is thought to result from an interplay between stored representations and control processes (Levy and Anderson, 2002; Badre and Wagner, 2007). A similar interaction between conceptual representations and control processes is thought to be critical in semantic cognition (cf. Controlled Semantic Cognition framework, Jefferies, 2013; Lambon Ralph, Jefferies, Patterson, & Rogers, 2017). Moreover, while *representations* of conceptual and episodic memory are thought to be distinct, as reflected by clear neuropsychological dissociations (Vargha-Khadem *et al.*, 1997; Verfaellie *et al.*, 2000; Manns *et al.*, 2003; McKinnon *et al.*, 2006; Nestor *et al.*, 2006), control processes that support the capacity to focus retrieval on currently-relevant memory representations may be shared across episodic and semantic tasks (Rajah and McIntosh, 2005; Badre and Wagner, 2007; Burianova and Grady, 2007; Burianova *et al.*, 2010). This prediction emerges from neuroimaging studies of healthy participants that reveal activation in similar brain areas (including left inferior frontal gyrus, LIFG) during both semantic and episodic retrieval (Badre and Wagner, 2007; Burianova and Grady, 2007). However, few (if any) neuropsychological studies have examined semantic and episodic tasks in the same participants, and neuroimaging studies that have observed overlapping patterns of activation in LIFG are unable to determine if this region is necessary for performance on both of these tasks. Studies of the retrieval deficits of patients with LIFG lesions are especially useful in this context.

In a recent study, we investigated whether stroke aphasia patients with multimodal semantic impairment (i.e., semantic aphasia, SA) exhibited parallel deficits in semantic and episodic memory following infarcts in LIFG (Stampacchia *et al.*, 2018). In line with preservation of ventrolateral portions of the anterior temporal lobes (ATL, see Fig, 1C) – a brain region which has been suggested to act as heteromodal hub of semantic knowledge (Binney, Embleton, Jefferies, Parker, & Lambon Ralph, 2010; Lambon Ralph *et al*., 2017; Visser, Jefferies, Embleton, & Lambon Ralph, 2012) – SA patients have largely intact conceptual knowledge but difficulty flexibly retrieving relevant information to suit the circumstances. These patients show inconsistent performance across tasks probing the same concepts but with differing control demands (Jefferies and Lambon Ralph, 2006). They are particularly impaired in understanding the subordinate meanings of words and non-canonical uses of objects (Noonan *et al.*, 2010; Corbett *et al.*, 2011); they are sensitive to cues/miscues that direct or misdirect retrieval, and fail to inhibit strong yet irrelevant semantic distractors (Jefferies *et al.*, 2008b; Soni *et al.*, 2009; Noonan *et al.*, 2010; Corbett *et al.*, 2011). These deficits are thought to reflect poor semantic control, i.e. the capacity to flexibly shape conceptual retrieval in an appropriate way. Accordingly, patients' lesions encompass areas known to support semantic control (according to a neuroimaging meta-analysis by Noonan, Jefferies, Visser, & Lambon Ralph, 2013, see Fig. 1A and 1B). This pattern of semantic impairment is qualitatively distinct from the degraded conceptual knowledge seen in semantic dementia (SD) following atrophy within ventral ATL, as SD patients show a high degree of consistency in which items are comprehended across tasks with differing demands (Jefferies and Lambon Ralph, 2006; Jefferies *et al.*, 2008b). Stampacchia *et al*. (2018) found that SA patients showed many of the hallmarks of deregulated retrieval in episodic as well as semantic decisions, using paired-associate tasks. Episodic judgements showed a benefit of cues that reduced the need to internally constrain retrieval. SA patients were vulnerable to strong but irrelevant semantic associates and previously-encoded associations-giving rise to false memories and proactive interference errors – and their episodic deficits were multimodal, affecting both word and picture tasks. These findings suggest that shared mechanisms underpin controlled retrieval from both semantic and episodic memory. However, Stampacchia *et al.* (2018) found some differences between verbal and non-verbal paired-associate learning tasks (e.g. reduced vulnerability to semantic and episodic interference for the picture-based episodic memory task) and it is unclear if this reflected modality-differences in memory control or task characteristics (it might be easier to reject picture distractors given the richness and distinctiveness of these stimuli). In the current study, we investigated: a) whether the episodic deficits found in SA would extend to other paradigms tapping episodic memory control; b) the multimodal nature of these deficits, using picture-based tasks; c) circumstances that could ameliorate or aggravate episodic deficits in SA.

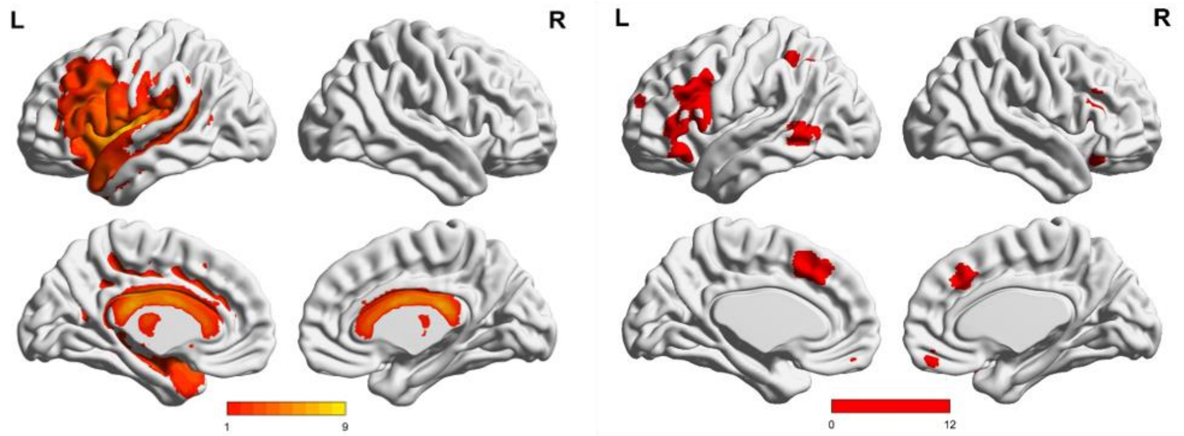
We assessed whether the degree of episodic impairment in patients with SA varies across different types of memory judgement tapping item and source memory. In item memory, participants decide whether an item was previously encountered by means of an old/new response. In contrast, source memory tasks require participants to retrieve the circumstances in which an item was encoded – for example, the time, spatial context or task in which it was previously encountered. Ageing and neuropsychological studies show dissociations between item and source memory. Damage to medial-temporal structures affects both types of memory judgements (Gold *et al.*, 2006; Dede *et al.*, 2013), while frontal lobe damage is associated with source memory impairment and minimal or no item memory deficits (Schacter, 1987; Janowsky *et al.*, 1989). Likewise, source memory declines in old age, while item memory does not change (Chalfonte and Johnson, 1996; Naveh-Benjamin, 2000).

Functional neuroimaging studies show that source memory engages medial-temporal structures (Ross and Slotnick, 2008) – but also a network of areas associated with controlled memory retrieval, including LIFG (Dobbins *et al.*, 2002; Dobbins and Wagner, 2005; Hayes *et al.*, 2011; Han *et al.*, 2012). LIFG, which is thought to resolve competition between competing memories (Badre and Wagner, 2007), is more necessary in source memory compared to item memory for several reasons: (i) In item recognition, presentation of the item acts as a strong external cue reducing competition between memories; (ii) During source memory tasks, there are typically two or more alternative source options for each item, giving rise to competition. Differences in the nature of the sources – i.e., their distinctiveness and/or compatibility with previous knowledge or experience – should influence the degree of control required and the likelihood of potential source memory failures.

In this study, we compared item and source memory in a case-series of SA patients with deregulated semantic retrieval following infarcts that affected left lateral prefrontal cortex including

LIFG. We predicted that source memory would show significant impairment in this group, but item memory would be largely unaffected. We also expected source memory deficits to be ameliorated by the presentation of strong cues that distinguished between otherwise confusable sources, but worsened in circumstances that increase competition between sources. The degree of competition was manipulated in three ways. (i) First, we expected spatial location to act as a strong cue for retrieval (Robin and Moscovitch, 2014; Smith *et al.*, 2014), since the network supporting spatial representations is largely intact in patients with SA (see Fig. 1D). A match in spatial location between encoding and retrieval should reduce the demands on controlled retrieval, since it provides a potent cue to separate sources. (ii) We also expected better performance when existing knowledge was congruent with episodic memory. Previous research has demonstrated semantic cueing improves comprehension of ambiguous words in SA (Noonan *et al.*, 2010; Corbett *et al.*, 2011). Here we expected patients to show reduced source memory impairment when sources were congruent with pre-existing knowledge. Conversely, source memory deficits should be magnified when a source competes with existing knowledge (e.g., when a CARROT was located in a CLOTHES SHOP, not a GREENGROCER). (iii) Finally, we expected deficits to be reduced when the distinctiveness of sources was increased by means of self-referential processing. Self-referenced items are typically better recalled because they are more meaningful and distinctive (Dulas *et al.*, 2011; Hamami *et al.*, 2011; Rosa and Gutchess, 2011; Serbun *et al.*, 2011; Durbin *et al.*, 2017) – and this might reduce competition between sources. Self-reference effects have been linked to regions including medial prefrontal cortex (Kelley *et al.*, 2002; Macrae *et al.*, 2004; De Caso *et al.*, 2017; Wong *et al.*, 2017) that are largely intact in semantic aphasia. In summary, this study examined whether patients with semantic aphasia have an episodic memory deficit that is linked to poor control over memory retrieval beyond the semantic and language domain, using non-verbal source memory tasks, and investigated factors that ameliorate or aggravate these deficits.

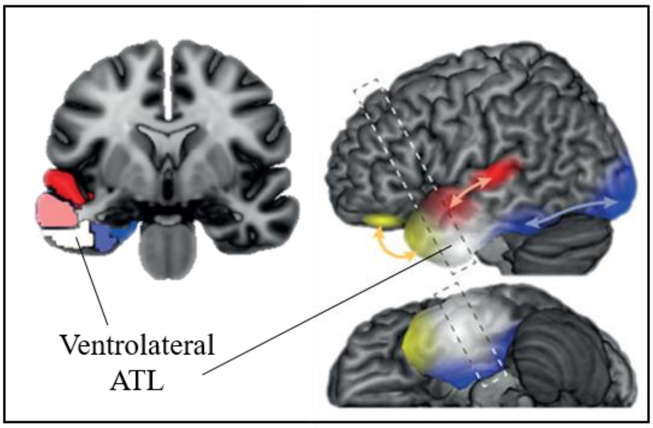
Damage to semantic control network



A Patients' lesion overlay

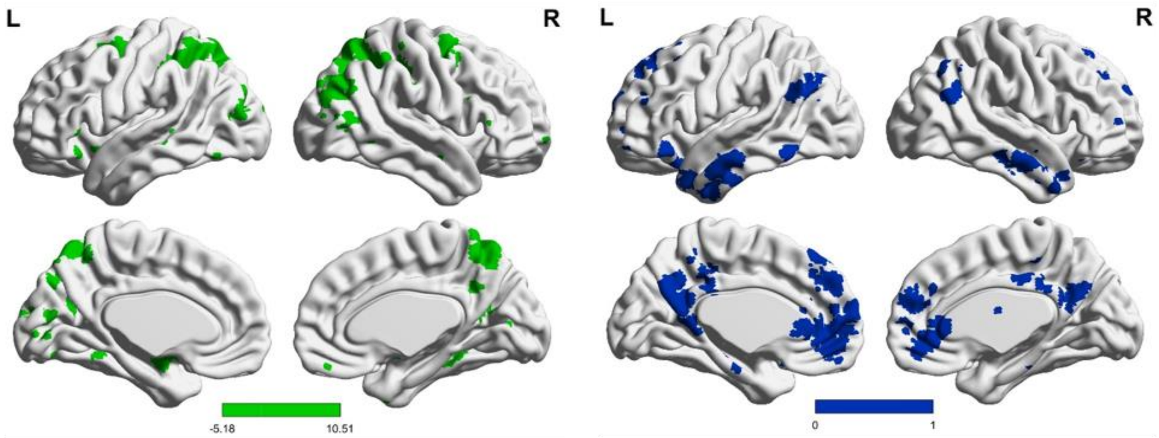
B Semantic control network

Preservation of ventral ATL implicated in semantic representations



C Heteromodal semantic hub

Preservation of spatial and self-relevant processes



D "Spatial" network

E "Self-reference" network

Figure 1. Patient lesions and overlap with functional networks of semantic control, semantic, spatial and self- representations. A) Lesion overlay of the sample of SA patients included in the study.

Patients' brains compared to aged-matched controls. Grey matter, white matter and CSF were segmented and changes from the healthy control brains were highlighted as 'lesion' using automated methods (Seghier et al., 2008). Colour bar indicates amount of overlap from 1 to 9 patients. B) Semantic control network from Noonan et al. (2013), adapted by Humphreys and Lambon Ralph (2015). C) Neuroanatomical sketch of the graded division within ATL in lateral and coronal cross-section views, adapted from Lambon Ralph et al. (2017) with permission. ATL subregions respond differentially to input sources: valence (yellow), audition (red) and vision (blue), while ventrolateral ATL (white) is equally engaged by all input types. It is proposed that ventrolateral ATL constitutes a heteromodal hub for semantic representation. D) Spatial network generated using Neurosynth: a meta-analysis of 1157 studies containing the term "spatial". E) Self-reference network generated using Neurosynth: a meta-analysis of 127 studies containing the term "self-referential". A, B, D and E were visualized with the BrainNet Viewer (Xia, Wang, & He, 2013, http://www.nitrc.org/projects/bnv/).

2. Participants

2.1 Patients

Nine participants [5 female; mean age = 63 years (SD = 11.5); mean education leaving age = 16.4 years (SD = 1.2); mean years since CVA = 8.8 (SD = 5.9)] with chronic stroke aphasia from left-hemisphere CVA were recruited from communication groups in Yorkshire, UK. On the basis of their aphasic symptomatology they could be classified as follows: two Global; two Mixed Transcortical; four Transcortical Sensory/Anomic; one Broca. One patient (P4) withdrew from the study and took part in Experiments 1 and 2 only. Individual data are provided in Table 1.

2.1.1. Inclusion criteria

In line with the original use of the term "semantic aphasia" by Henry Head (1926) and the inclusion criteria proposed by Jefferies & Lambon Ralph, (2006), the patients in this study had deficits affecting the appropriate use of concepts presented as words and objects when control demands were high. In addition to verbal semantic problems, they were impaired on at least one non-verbal task (see section 3.2). In common with previous SA samples, the patients showed strong effects of semantic control manipulations across tasks (details below). Individual patient data and task descriptions are provided in section 3.2.

Table 1. Demographics

Patient ID	Age	Gender	Education*	Years since CVA	Type of Aphasia
P1	60	F	18	6	Global
P2	77	M	15	6	Mixed Transcortical
P3	59	F	16	8	Global
P4	66	M	15	23	Mixed Transcortical
P5	58	F	18	6	Transcortical Sensory/Anomic
P6	57	M	18	13	Transcortical Sensory
P7	65	M	16	6	Broca
P9	77	F	16	4	Anomic
P10	39	F	16	7	Transcortical Sensory/Anomic
Mean	62	6/9 females	16.4	8.8	
SD	11.5		1.2	5.9	

Table 1 Legend: Age left education, CVA: cerebrovascular accident.

2.1.3. Lesion analysis

MRI scans were traced onto standardized templates (Damasio and Damasio, 1989) and lesion identification was manually performed (see Table 2 and Fig. 1A for lesion overlay). All nine patients had lesions affecting left posterior LIFG; in seven cases this damage extended to mid-to-anterior LIFG. Parietal regions (supramarginal gyrus and/or angular gyrus) were also affected in 7 cases out of 9, and pMTG was affected in all but two cases. While there was some damage to ATL in 3 patients (P1, P2, P4), the ventral portion of ATL, which has been implicated in conceptual representation across modalities (Binney, Parker and Lambon Ralph, 2012; Visser *et al.*, 2012), was intact in all cases. This region is supplied by both the anterior temporal cortical artery of the middle cerebral artery and the anterior temporal branch of the distal posterior cerebral artery, reducing its vulnerability to stroke (Phan *et al.*, 2005; Borden, 2006; Conn, 2008). The hippocampus and parahippocampal gyrus were intact in all patients and medial PFC was also spared, although cingulate cortex was affected in two patients (P6 and P7).

2.2. Controls

Ten controls [7 females; age = 70.8 years (SD = 7.5); education leaving age = 18.1 (SD = 12.8)] took part in the study. None of the controls had a history of psychiatric or neurological disorder. They were matched to the patients on age [t(17) = -1.77, p = .095] and years of education [t(12.7) = -1.71, p = .111].

Table 2. Patients' lesion analysis

Patient ID	Lesion size*	Fronto-lateral							Medial				Parieto - temporal									
		SMA/PMC	FP	DLPFC		ant-IFG	mid-IFG	post-IFG	vm-PFC	dm-PFC	ACC	PCC	SMG	AnG	pMTG	STG	MTG	ITG	FuG	TP	PHG	Hpc
		BA	BA	BA	BA	BA	BA	BA	BA	BA	BA	BA	BA	BA	BA	BA	BA	BA	BA	BA	BA	BA
		6	10	9	46	47	45	44	10	9	24 32 33	23 31	40	39	37	22	21	20	36	38	28	28
P1	12	1		1	1		1	1					2	1	1	2				1		
P2	15	2		2		2	2	2					1			2						
P3	15	2		2		2	1	2					2	1	2	2	2	1				
P4	8	2						1					1		2							
P5	15	2						2				2	2	1	1							
P6	7	1					1	2			1	1	1	1	1							
P7	14	2				2	1	2			1	1	1	1	1	2	1					
P9	4	1						1							1	1	1					
P10	9	0					1	2								2						

Table 2 Legend: MRI scans were manually traced onto Damasio templates. Lesion size* was calculated as % template damaged. For areas not comprehensively characterized by Damasio templates, analyses were combined with manual analysis of the structural scan with the help of a trained radiographer. Quantification of lesion: 2 = complete destruction/serious damage to cortical grey matter; 1 = partial destruction/mild damage to cortical grey matter; empty = intact. Anatomical abbreviations: SMA/PMC: Supplementary Motor Area/ Premotor Cortex; FP: Frontal Pole; DLPFC: Dorsolateral Prefrontal Cortex; ant-IFG: Inferior Frontal Gyrus, pars orbitalis; mid-IFG: Inferior Frontal Gyrus, pars triangularis; post-IFG: Inferior Frontal Gyrus, pars opercularis; vmPFC: Ventromedial Prefrontal Cortex; dmPFC: Dorsomedial Prefrontal Cortex; ACC: Anterior Cingulate Cortex; PCC: Posterior Cingulate Cortex; SMG: Supramarginal Gyrus; AnG: Angular Gyrus; pMTG: posterior Middle Temporal Gyrus; STG: Superior Temporal Gyrus; MTG: Middle Temporal Gyrus; ITG: Inferior Temporal Gyrus; FuG: Fusiform Gyrus; TP: Temporal Pole; PHG: Parahippocampal Gyrus; Hpc: Hippocampus.

3. Background neuropsychology

3.1. Non-semantic tests

Data for individual patients are shown in Table 3. The “cookie theft” picture description (Goodglass and Kaplan, 1983) revealed non-fluent speech in half of the patients. Word repetition (PALPA 9; Kay, Lesser and Coltheart M., 1992) was also impaired in four patients out of nine. Executive/attentional impairment was seen in seven of the nine patients across four tasks: Elevator Counting with and without distraction from the Test of Everyday Attention (Robertson *et al.*, 1994); Ravens Coloured Progressive Matrices (RCPM; Raven, 1962); Brixton Spatial Rule Attainment task (Burgess and Shallice, 1997) and Trail Making Test A & B (Reitan, 1958). This is in line with previous studies which found that deregulated semantic cognition was associated with executive dysfunction in stroke aphasia (Jefferies and Lambon Ralph, 2006; Noonan *et al.*, 2010; Thompson *et al.*, 2018). Digit Span was impaired in all patients, while six out of nine had spatial spans in the normal range. The patients showed normal performance in the Face Recognition task from the Wechsler Memory Scale (WMS-III, Wechsler, 1997) which has minimal control demands, confirming they were not amnesic.

Table 3. Non-semantic background tests: individual scores

Test	Max	Controls Mean (SD)	Patients Mean	P1	P2	P3	P4	P5	P6	P7	P9	P10
Non-semantic language tests												
PALPA 9 real word repetition (total)	80	73a	62.1	NA	**71**	**42**	75	78	79	**1**	74	77
Category Fluency (8)	-	62a	38.4	NA	26	**15**	**26**	**14**	**26**	NA	80	**57**
Letter Fluency (F, A, S)	-	18a	7.2	NA	2	**2**	**6**	**3**	**6**	NA	**16**	**9**
Cookie theft (words/minute)	-	-	25.2	0	18	9	12	60	37	0	54	37
Executive and spatial processing												
TEA: counting without distraction	7	4.2a	4.8	**4**	5	6	5	**4**	NT	7	5	7
TEA: counting with distraction	10	2.6a	1.8	**2**	3	**1**	**1**	**2**	NT	7	**2**	6
Raven's coloured matrices (total)	36	32.9 (2.41)	28.0	31	29	31	**24**	**19**	30	34	**21**	33
Brixton spatial anticipation (correct)	54	28a	23.4	**21**	**7**	**18**	**26**	**24**	**23**	31	31	30
Trail Making Test A (correct)	24	24a	23.0	**19**	**22**	**23**	24	24	**23**	24	24	24
Trail Making Test B (correct)	23	17a	13.7	**2**	23	**16**	**12**	**1**	**5**	23	19	22
Visuospatial processing												
VOSP dot counting	10	8a	9.3	**7**	10	10	9	10	10	8	10	10
VOSP position discrimination	20	18a	17.6	19	20	**4**	19	**17**	20	19	20	20
VOSP number location	10	7a	8.9	8	10	**5**	10	10	10	10	**5**	8
VOSP cube analysis	10	6a	8.1	8	9	**4**	**4**	7	9	10	10	8
Wechsler Memory Scale												
Digit Span Forward	9	6.82 (0.64)	4.0	**0***	**5**	**4**	**2**	6	**4**	**2***	**3**	**4**
Digit Span Backward	8	5.6 (0.97)	1.5	**0***	**2**	**2**	**0**	**2**	**0**	NA	NT	**3**
Spatial Span Forward	19	10(3)b	6.8	10	5	10	6	5	**3**	6	7	9

Spatial Span Backward	19	10(3)b	6.8	8	**2**	10	6	**3**	**3**	9	10	10
Face Recognition Immediate	19	10(3)b	11.1	9	10	12	14	17	13	10	9	6
Face Recognition Delayed	19	10(3)b	11.9	8	13	11	11	18	13	15	8	10

Table 3 Legend: Scores are number of correct. a= Normal cut-off; b=WMS Age adjusted scaled score (SD); Bold underlined numbers denotes impaired scores (less than two standard deviations below mean); NT = unavailable for testing; NA = testing was not attempted because patients were non-fluent; TEA = Test of Everyday Attention; VOSP = Visual Object and Space Processing battery. Digit Span: participants were required to immediately retrieve numbers sequences of increased length, in forwards or backwards order. * = For non-fluent patients we used a paper with numbers wrote down during recall. Patients were instructed to point to each number in the same sequence in which was vocally presented by the experimenter. The sheet was not available during the presentation of numbers to avoid the use of spatial strategy for retaining the sequence in working memory. Face Recognition: participants were asked to remember 24 unfamiliar faces, presented one at time. Memory was tested immediately and following a delay of 25-35 minutes (delayed condition); participants identified 24 target faces amongst 48 stimuli, responding either “yes” or “no” to each face.

3.2. Cambridge semantic battery

This assesses semantic retrieval for a set of 64 items across tasks (Bozeat *et al.*, 2000; Adlam *et al.*, 2010), including picture naming, word-picture matching, and verbal and pictorial semantic associations (Camel and Cactus Test, CCT). Patients showed large variability in picture naming, reflecting additional phonological deficits in some cases [percentage correct M(SD) = 62.8% (39.5)]. In contrast, performance was uniformly at ceiling in word-picture matching [M(SD) = 95.7% (5.7)], indicating intact comprehension in tasks with minimal control demands. On the CCT, when associations between concepts had to be retrieved and control demands were higher, there was greater impairment, with no differences across modalities [words M(SD) = 78.6% (17.2); pictures M(SD) = 77.4% (14.4)]. Individual test scores are provided in Table 4. Pairwise correlations across the six combinations of these four tasks revealed no significant associations between tasks [$p \geq 0.11$]. Only when tasks had the same control demands across different modalities - i.e. during word and picture association judgements – did this correlation approach significance [$r = 0.64$, $p = .066$]. This is in line with the findings of Jefferies & Lambon Ralph, (2006), who found consistent performance across modalities within the same task (when control demands remained constant) but not between tasks with different controlled retrieval requirements.

3.2. Tests of semantic control

Three tasks manipulated the control demands of verbal and non-verbal semantic judgements (see Table 4 for individual data; previously reported by Stampacchia *et al.*, 2018).

3.3.1. Ambiguity task

Semantic judgements (60 items) probed the dominant (MONEY) and subordinate (RIVER) meanings of ambiguous words (e.g., BANK). These decisions were presented without cues or preceded by a sentence that primed the relevant interpretation for that trial (cue condition: e.g., for MONEY, I WENT TO SEE THE BANK MANAGER) or the irrelevant interpretation (miscue condition: e.g., THE BANK WAS SLIPPERY). There were four response options on each trial. Further details are available from Noonan *et al.* (2010). All the patients were below the normal cut-off in all conditions. Every individual patient showed better comprehension for dominant than for subordinate interpretations [no cue condition percentage correct: dominant M (SD): 81.1 (11.1); subordinate M (SD) = 53.0 (13.7)]. In addition, every single patient showed additional impairment in accessing subordinate meaning following miscues rather than cues [percentage correct subordinate trials: miscues M (SD) = 44.1 (15.3); cues M (SD) = 72.6 (14.5)]. In a 2 (dominant vs. subordinate) by 3 (cue, no cue, miscue) by 2 (patients, controls) ANOVA, there were main effects of dominance [$F(1,15) = 80.22$, $p < .001$] and cueing [$F(2,14) = 18.39$, $p < .001$] plus interactions of dominance by cueing [$F(2,14) = 7.28$, $p = .007$], dominance by group [F(1,15) = 48.35, p < .001], cueing by group [F(2,14) = 18.19, p < .001] and the three-way interaction [F(2,14) = 5.61, p = .016; control data from Noonan *et al*., 2010].

3.3.2. Synonym judgment task

We presented a synonym judgement task (84 trials) from Samson *et al.* (2007). Trials included strong or weak distractors; e.g., DOT with POINT [target], presented with DASH [strong distractor] or LEG [weak distractor]. There were three response options per trial. Accuracy was below the cut-off for all patients and poorer when semantically-related but irrelevant distractors were presented [percentage correct: weak distractors M (SD): 67.7 (11.4); strong distractors M (SD): 45.8 (13.5)]. In a 2 (strong/ weak distractors) by 2 (patients, controls) ANOVA, there was a main effect of condition: F(1,15) = 10.19, p = .006 and an interaction with group: F(1,15) = 20.81, p <.001 (control data from Samson *et al.*, 2007).

3.3.3. Object use task

An object use task (74 items) involved selecting an object to accomplish a goal (e.g., BASH A NAIL INTO WOOD), with all items represented as photographs, from Corbett *et al.* (2011). The target was either the canonical tool, normally used to complete the task (e.g., HAMMER), or a non-canonical option that could be used instead (e.g., BRICK), presented among a set of five unsuitable distractors. All patients were poorer at selecting non-canonical targets [percentage correct: canonical M (SD) = 91.9 (7.9); alternative M (SD) = 58.6 (19.5); t(8) = 7.72, p < .001] and impaired compared to controls [t(8.4) = 5.87, p < .001; control data from Corbett *et al.* (2011), and not collected for the canonical condition given near-ceiling performance]. One single patient (P5) was not below the normal cut-off in the non-canonical condition; however this case was impaired at the pictorial version of the CCT and consequently still showed evidence of a multimodal deficit.

Table 4. Semantic background tests: individual scores

Test	Max	Control Mean (SD)	Patient Mean	P1	P2	P3	P4	P5	P6	P7	P9	P10
Cambridge Semantic Battery												
Picture Naming	64	59a	40.2	**1**	61	**19**	**50**	60	**50**	**3**	**56**	62
Word-Picture Matching	64	62.7a	61.2	63	62	**60**	64	**62**	**62**	**52**	64	**62**
Word CCT	64	60.7 (2.06)	50.3	**39**	**43**	**29**	**53**	59	**52**	57	61	60
Picture CCT	64	58.9 (3.1)	49.6	**31**	**44**	**45**	56	**45**	57	54	53	61
Ambiguity task												
Miscued dominant	30	30 (0)	18.0	**12**	**13**	**13**	**14**	**20**	**19**	**21**	**24**	**26**
Miscued subordinate	30	29 (1.20)	13.2	**7**	**10**	**14**	**8**	**10**	**15**	**18**	**18**	**19**
No cue dominant	30	29.5 (0.54)	24.3	**22**	**18**	**24**	**22**	**24**	**26**	**27**	**28**	**28**
No cue subordinate	30	28.9(0.64)	15.9	**11**	**9**	**14**	**14**	**19**	**17**	**19**	**21**	**19**
Cued dominant	30	30 (0)	23.4	**23**	**21**	**19**	**22**	**24**	**23**	**23**	**27**	**29**
Cued subordinate	30	29.75 (0.46)	21.8	**25**	**14**	**20**	**18**	**19**	**28**	**24**	**23**	**25**
Synonym with distractors												
Strong	42	39.87 (2.23)	19.2	**15**	**12**	**13**	**20**	**21**	**23**	**30**	**22**	**17**
Weak	42	41.50 (0.53)	28.4	**25**	**23**	**29**	**24**	**27**	**30**	**31**	**28**	**39**
Object use												
Alternative	37	33.67a	21.7	**14**	**13**	**14**	**21**	34	**22**	**22**	**26**	**29**
Canonical	37	NA	34.0	32	31	29	35	37	35	33	37	37

Table 4 Legend: Scores are number of correct; a = normal cut-off, NT = unavailable for testing, Bold underlined numbers denotes impaired scores (less than two standard deviation below mean); NA = not available.

4. Source memory: Methods overview

4.1. Overview of experiments

Experiment 1a examined the role of a spatial cue in ameliorating source memory deficits in SA. During an encoding phase, photos of everyday objects were placed in different coloured boxes. During recollection, participants were asked to decide whether they had seen each item (familiarity judgement). When they recognised items as 'old', they were asked which box it had been placed in (source judgement). In the recollection phase, items and sources (i.e., photographs of the coloured boxes) were shown on a computer screen. In Experiment 1a, the boxes were presented in different positions on the screen. In Experiment 1b, the boxes were in the same spatial location as at encoding. In Experiment 2, we retained the spatial cues and examined source memory trials that were congruent or incongruent with knowledge. The stimuli were items that would be purchased in specific shops (e.g., fruits and vegetables and bakery products), presented in a semantically-congruent source (a CARROT in a box labelled GREENGROCER) or a semantically-incongruent source (e.g., CARROT in the BAKERY). We next manipulated the meaningfulness/distinctiveness of the sources using self-reference paradigms. In the encoding phase of Experiment 3, the participant and tester each had a basket, and shopping items were 'won' by either person and placed into these baskets. We then assessed item and source memory for self- and other-related items (retaining spatial location as a valid cue). Experiment 4 assessed the memory advantage for self-related items using a classic verbal self-reference paradigm. Personality trait-adjectives were either encoded to reference to the self or an acquainted other (i.e. the Queen) or shallow processed (i.e. judgment about font, e.g. "case" condition); source and item memory were then assessed.

4.2. Scoring and analysis

Item and source accuracy were scored using a discrimination index Pr (Snodgrass and Corwin, 1988). This index was preferred to standard measures of accuracy (e.g. percentage correct) because it controls for guessing in the item familiarity task; however, unlike other metrics, like d', it allowed a direct comparison between item and source memory in Experiments 1-3. Pr was scored as: a) the difference of hits minus false alarms, for item memory; b) the difference between correct and incorrect responses divided by the number of hits, for source memory. Pr varied between 1 and -1, with chance being 0 for 2AFC tasks (Experiments 1-3) and -0.33 for 3AFC (source memory decisions in Experiment 4). In Experiments 1-3, ANOVAs was used to assess effects of memory type (item vs. source) and encoding condition (e.g. congruent vs. incongruent) by group (patients vs. controls). In Experiment 4, since the number of response options in item memory (two: yes and no) and source memory (three: case vs. self vs. other) were no longer comparable, separate ANOVAs were computed for source and item memory, examining encoding condition (i.e. self vs. other vs. case) by group.

5. The effect of spatial location source memory (Experiments 1a and 1b)

5.1. Rationale

Spatial location is a potent contextual cue for episodic recollection. In Experiment 1a, the location of the boxes at encoding was not maintained on the screen during recollection, while in Experiment 1b, the boxes were always presented on the left or right-hand side, during both encoding and retrieval. We expected source memory to be more impaired than item familiarity in SA patients, especially in the absence of spatial cues.

5.2. Method

5.2.1. Procedure

A schematic of the task is shown in Fig. 2A. Participants were instructed to try to remember a series of shopping items and whether they were placed in a blue or a red box in front of them. During encoding, a set of 40 shopping items, shown as coloured photographs on 14.5-by-10cm laminated cards, were each presented for around 3 seconds, named by the experimenter and placed in one of the boxes. Items were split 50/50 between boxes and the allocation of items to sources was randomized between participants. During a retrieval phase immediately afterwards, coloured pictures of the 40 targets and 20 distractors were presented individually on a laptop screen using E-prime 2.0. Items were randomly assigned to target/distractors between participants. In Experiment 1a (without spatial cues), the position of the boxes on the screen (left vs. right) was alternated on every trial, such that the location of the target was not systematically related to the location of the source at encoding. In Experiment 1b (with spatial cues), the layout of the boxes on the screen preserved the spatial layout at encoding. For each item, participants were instructed to indicate (i) whether the item had been presented previously (selecting “yes” or “no”) and (ii) only for familiar items, which box they had been placed in (selecting the blue or red box). This procedure was repeated twice in the no spatial cue condition, and three times in the cue spatial condition, in separate sessions, using different stimuli. This difference is due to participants’ reduced availability during testing of Experiment 1a.

5.2.2. Stimuli

In Experiment 1a (without spatial cues), the stimulus set comprised of 120 items commonly found in supermarkets, drawn from the following categories: drinks, tinned and canned products, general household and toiletries. In Experiment 1b (spatial cue condition), we used a set of 180 items, including the above categories, plus fruit and vegetable and bakery products. Below, we present an omnibus analysis across all items and conditions. An analysis of data using only the items presented across the two experiments revealed a similar pattern of results (see below). The list of stimuli is provided in Appendix Tables 1a and 1b.

5.3. Results

We performed a two-way mixed ANOVA, including memory type (item, source), spatial cueing (spatial cue present/ absent) and group (patients, controls) as factors. Interactions were explored using separate ANOVAs for patients and controls. Accuracy was lower for the patients [main effect of group: F(1,16) = 7.57, p = .014] and for source memory [main effect of memory type: F(1,16) = 28.16, p < .001]. There was a memory type by group interaction [F(1,16) = 8.23, p = .011] revealing source memory impairment for patients only [main effect of memory type for patients: F(1,7) = 23.45, p = .002; and for controls: F(1,9) = 4.29, p = .068, Fig. 2D]. There was a main effect of spatial cueing [F (1,16) = 25.87, p < .001]; performance was improved if location was a valid cue. This effect interacted with group [spatial cueing by group interaction: F(1.16) = 11.25, p = .004], revealing greater benefit from spatial cue for the patients [main effect of spatial cue patients: F(1,7) = 16.87, p = .005; controls: F(1,9) = 5.63, p = .042]. There were also interactions of spatial cue by memory type [F (1,16) = 6.59, p = .021] and memory type by spatial cueing by group [F (1,16) = 8.94, p = .009]. The effect of spatial cueing was greater during source than item memory, but only for the patients [memory type by spatial cueing interaction for patients: F(1,7) = 9.22, p = .019; and for controls: F(1,9) = .167, p = .693]. With the exception of one single case (P9), all patients showed poorer source memory when the spatial cue was unavailable (Fig. 2C). [1]

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[1] An additional two-way mixed ANOVA was performed using only trials overlapping in both Experiment 1a and 1b. Patients showed preserved item memory and impaired source memory [memory type by group interaction: F(1,16) = 30.37, p < .001] and less impaired performance on trials where spatial cues were available [spatial cue by group: F(1,16) = 13.97, p = .002] especially for source memory [although the three way interaction did not reach significance: F(1,16) = 1.031, p = .325]. There was also a main effect spatial cueing [F(1,16) = 11.08, p = .004] and memory type [F(1,16) = 52.01, p < .001].

5.4. Summary of Experiment 1

Patients selected to show controlled retrieval deficits in semantic cognition also showed poor source recollection in episodic memory, especially in the absence of strong spatial cues that helped to disambiguate the sources.

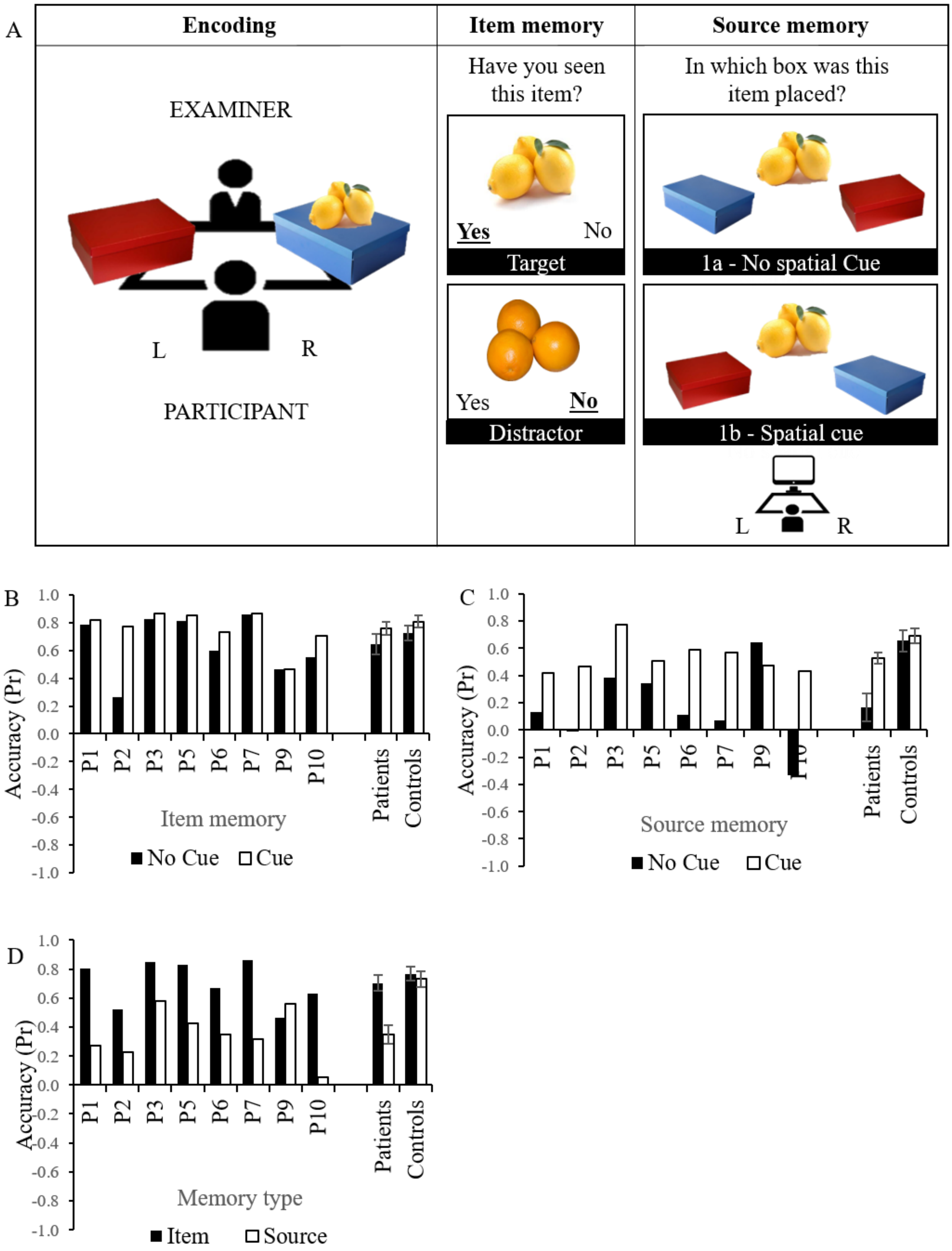

Figure 2: Experiment 1 design and results. A) Schematic of encoding, item and source memory phases of Experiments 1a and 1b. L = participant's left-hand side, R = participant's right-hand side. Both target items (previously presented) and distractors (semantically-related items) were presented during item memory decisions. For items judged as familiar, source memory was tested. During source memory decisions, in Experiment 1a, boxes were randomly allocated to the L or R hand-side, preventing participants from relying on the spatial location at encoding; in Experiment 1b, the position of the boxes at encoding and at retrieval was the same. B) Item memory accuracy during Experiments 1a (No Cue) and 1b (Cue). C) Source memory accuracy during Experiments 1a (No Cue) and 1b (Cue). D) Item and source memory accuracy collapsed across Experiments 1a and 1b. Accuracy is expressed using a discrimination index Pr, with 0 being chance level. Error bars show SE of mean.

6. The effect of meaning in source memory (Experiment 2)

6.1. Rationale

We presented shopping items within 'shops' that were semantically-congruent or incongruent with the category of the item (e.g., fruit and vegetable items were placed either in the GREENGROCER or the BAKERY). We anticipated that patients would have greater problems than control participants in retrieving sources that conflicted with background knowledge.

6.2. Method

A schematic of the task is shown in Fig. 3A. Participants were instructed to try to remember a series of shopping items, allocated to one of two shops, represented by boxes labelled with coloured pictures of the store. Participants were warned that items would not be necessarily allocated to the store in which they are usually found (e.g. CARROTS could be placed into the BAKERY). During encoding, participants were shown a set of 40 shopping items pictures, which were placed in either the congruent or the incongruent shop (20 items per condition). During a retrieval phase, administered immediately afterwards, these target items plus 20 distractors were presented individually on a laptop: participants decided a) whether each item had been presented previously; and b) which shop these familiar items had been placed in. The procedure was repeated twice on separate sessions, so that there were 40 + 40 congruent, incongruent targets and 40 distractors in the analysis. Experiment 2 used the same items as Experiment 1a, and items were randomly assigned to conditions prior to testing each participant. List of stimuli is provided in Appendix Tables 1a and 1b. All other details of the procedures at encoding and retrieval are as described for Experiment 1.

6.3. Results

We examined the effects of memory type (item, source), semantic congruency (congruent incongruent) and group (patients, controls). Interactions were explored using separate ANOVAs for patients and controls. There was no significant difference in overall accuracy across groups [F(1,16) = 3.65, p = .074]. Both groups were less accurate during source than item memory [F(1,16) = 25.30, p < .001]. There was a memory type by group interaction [F(1,16) = 5.96, p = .027], revealing greater impairment for source vs. item memory for the patients [main effect of memory type patients: F(1,7) = 16.03, p = .005; controls: F(1,9) = 6.75, p = .029, Fig. 3D]. There was also a main effect of congruency [F(1,16) = 11.04, p = .004], which interacted with group [F(1,16) = 6.56, p = .021]: only patients had higher accuracy for congruent vs. incongruent trials [main effect of congruency patients: F(1,7) = 8.09, p = .025; controls: F(1,9) = 1.16, p = .310]. There were also interactions of congruency by memory type [F(1,16) = 10.82, p = .005] and congruency by memory type by group [F(1,16) = 5.11, p = .038]. The effect of congruency was greater during source than item memory, but only for the patients [congruency by memory type interaction for patients: F(1,7) = 7.06, p = .033; and for controls F(1,9) = 2.37, p = .158]. This effect of congruency is shown for item memory in Fig. 3B and for source memory in Fig. 3C. All patients but P3 showed poorer source than item memory and higher accuracy during congruent than incongruent source memory trials (Fig. 3C & 3D). Patients who were semantically more impaired (towards the left-hand side of the graph) systematically chose the wrong source in the incongruent condition (i.e. they assigned items to congruent sources, e.g. CARROT in the GREENGROCER) more often than chance (i.e., accuracy was below 0).

6.4. Summary of Experiment 2

Patients with semantic control deficits and PFC lesions were vulnerable to interference from semantic knowledge that was incongruent with recent experience in judgements of episodic memory. This effect was seen strongly in measures of source memory but did not affect recognition of the items themselves. Patients with semantic aphasia are thought to have difficulty controlling competition from strong conceptual representations that are not relevant to the task being performed. Here, they may have failed to control competition between episodic representations of recent events and semantic representations of object meaning when these two sets of representations were in conflict.

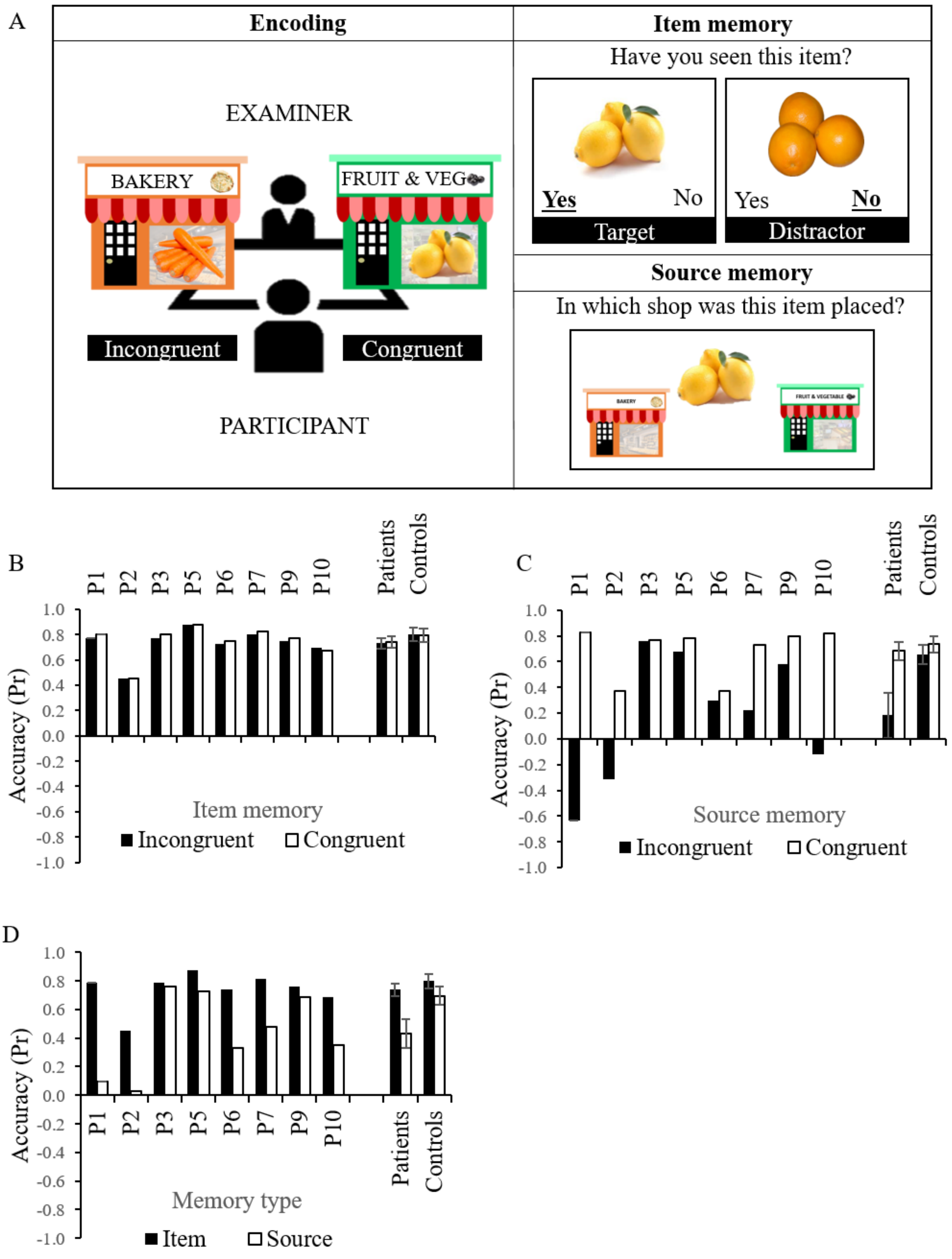

Figure 3: Experiment 2 design and results. A) Schematic of encoding, item and source memory phases of Experiment 2. At encoding, items were either allocated to sources congruent or incongruent with existing semantic knowledge. Both target items (previously presented) and distractors

(semantically-related items) were presented during item memory decisions. For items judged as familiar, source memory was tested. B) Item memory accuracy for congruent and incongruent trials. C) Source memory accuracy for congruent and incongruent trials. D) Item and source memory accuracy collapsed across congruent and incongruent trials. Accuracy is expressed using a discrimination index Pr, with 0 being chance level. Error bars show SE of mean.

7. The effect of self-referential processing on source memory (Experiments 3 and 4)

7.1 Rationale

Self-referential processing is thought to increase the salience and distinctiveness of memories and might therefore decrease the control demands necessary to distinguish between competing sources. However, the effect of self-referential processing on source memory has not been previously explored in patients with semantic control deficits, who have damage to lateral but not medial prefrontal cortex. We expected the patients to show normal self-reference effects (better memory for self-processed items) and, therefore, a higher performance overall, reducing the difference between item and source memory. In Experiment 3, we instructed participants to remember objects assigned either to themselves or the researcher, using photographs of shopping items as in the experiments above, and tested item familiarity and source memory. This task has been previously shown to promote self-referential processing (Cunningham *et al.*, 2008, 2011) and to be associated with medial prefrontal cortex activation (Turk *et al.*, 2011). In Experiment 4, we used a classical self-reference paradigm in which participants were asked to decide whether a personality-trait adjective described themselves or the Queen, or was presented in upper or lower-case letters (focussing attention on surface features of the word). We then performed a surprise memory task including item and source memory decisions.

7.2. Experiment 3: Method

A schematic of the procedure is shown in Fig. 4A. The task was similar to Experiments 1 and 2, except that the items were placed in two shopping baskets, given to the participant and the researcher. Participants were asked to imagine that they or the researcher had won these items and to try to remember who had received each prize. This experiment used the same items as Experiment 2 (list of stimuli is provided in Appendix Tables 1a and 1b). All other details of the procedure are as described above.

7.3. Experiment 3: Results

We examined the results using a two-way mixed ANOVA looking at memory type (item/ source memory), referent (other, self) and group (patients, controls). Patients and controls did not differ in term of overall accuracy [F(1,17) = 2.35, p = .144] and both groups were less accurate during source than item memory [F(1,17) = 12.38, p = .003], with no interaction between memory type and group [F(1,17) = 2.95, p = .104, Fig 4D]. There was also a main effect of referent [F(1,17) = 7.32, p = .015], which did not interact with group [F(1,17) = 0.00, p = .989] or memory type [F(1,17) = 1.70, p = .210]. The three-way interaction of memory type by referent by group was not significant [F(1,17) = 0.06, p = .804]. These results demonstrate a normal self-reference effect in the patients (Fig. 4C).

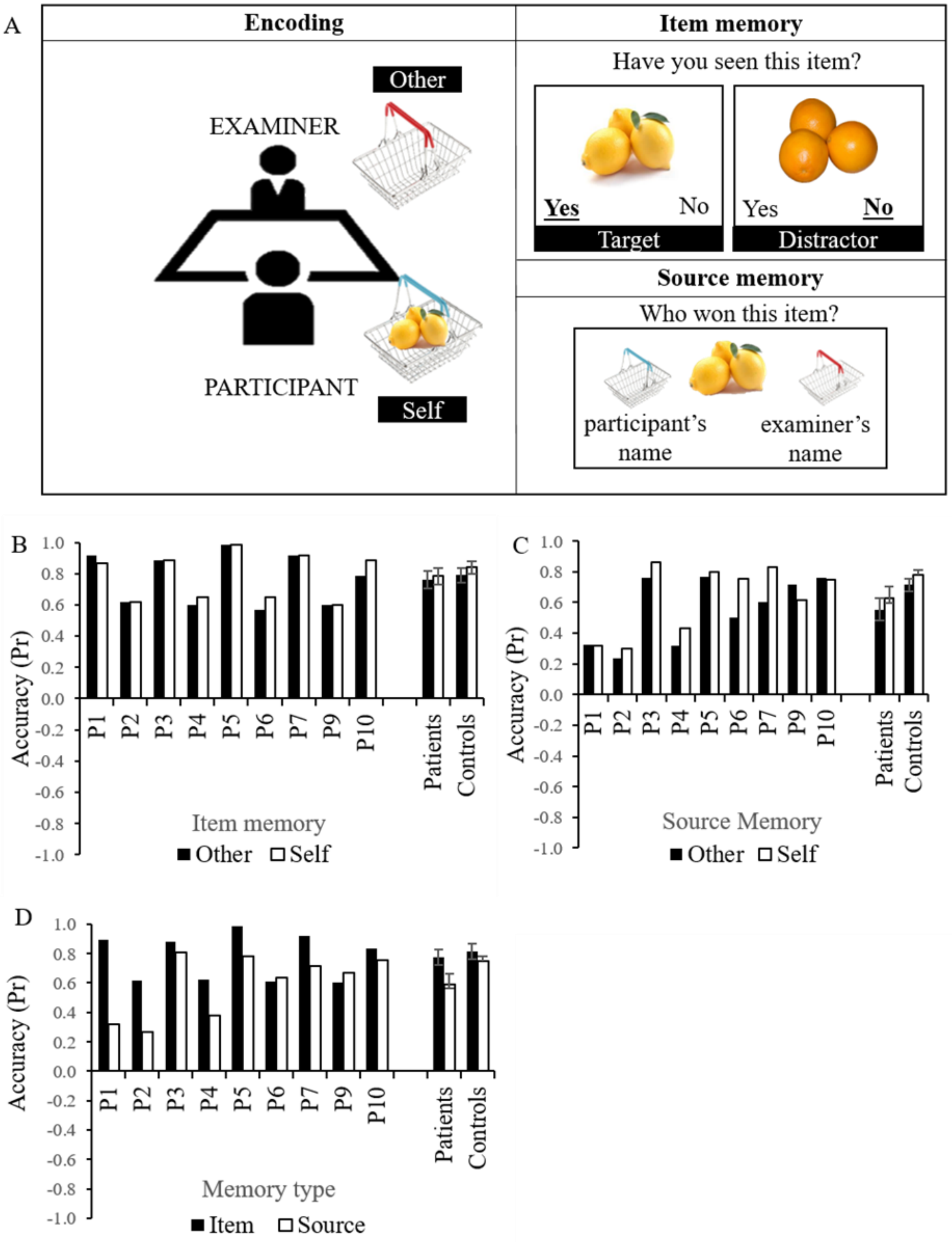

Figure 4: Experiment 3 design and results. A) Schematic of encoding, item and source memory phases of Experiment 3. At encoding items were either placed into the participant's (self) or the examiner's (other) shopping basket. Both target items (previously presented) and distractors (semantically-related items) were presented during item memory decisions. For items judged as

familiar, source memory was tested; the participant's and examiner's first names were displayed on screen under the correspondent shopping baskets. B) Item memory accuracy for self and other trials. C) Source memory accuracy for self and other trials. D) Item and source memory accuracy collapsed across self and other trials. Accuracy is expressed using a discrimination index Pr, with 0 being chance level. Error bar show SE of mean.

7.4. Experiment 4: Method

A schematic of the design procedure is shown in Fig. 5A. During encoding, participants were presented with a list of 60 personality-trait adjectives, read aloud and displayed individually on the screen using E-prime 2.0. Adjectives were allocated to three different encoding conditions, presented in separate blocks of 20 items. During the "SELF" and "OTHER" conditions, participants decided whether the adjectives described themselves or the Queen, providing a "yes" or "no" response; during the "CASE" condition, they indicated whether the word was displayed in lower or uppercase letters. Items remained on screen until a response was provided. Participants were not aware at this stage that memory would be tested later. During retrieval immediately afterwards, 60 targets and 60 distractors were presented individually on the screen. Participants decided (i) whether each adjective had been presented previously, by saying "yes" or "no" and (ii) which condition each familiar item had been presented in (by pointing to labels reading "you", "queen", "case").

The words were selected from a database of 555 personality-trait adjectives rated for likeability and meaningfulness (Anderson, 1968). They were selected to have neutral valence (likeability from 201 and 401, on a scale from 0 to 600) and high frequency according to SUBLEX (Van Heuven *et al.*, 2014). Selected adjectives were split into two lists matched for likeability, meaningfulness, length and frequency [$t < 1$, $p \geq .352$] one used as targets and one as distractors for all participants. The assignment of targets to encoding conditions (i.e. self vs. other vs. case) and the order of presentation during encoding was counterbalanced across participants using a Latin square design. A list of stimuli is provided in Appendix Table 2. In order to match visual similarity across conditions, half of the adjectives were presented in upper and lower-case letters during encoding (and in lower case letters during retrieval). Items were presented in a random order.

7.5. Experiment 4: Results

ANOVA was used to examine encoding condition (case, other, self) by group (patient, control), for the item and source memory measures separately. Patients showed poorer item memory relative to controls [main effect of group: $F(1, 17) = 11.29$, $p = .004$]. There was a main effect of encoding condition [$F(2,34) = 25.67$, $p < .001$], and the interaction with group approached significance [$F(2,34) = 2.92$, $p = .067$]. Group level contrasts revealed that self-referenced adjectives were better remembered when compared to the case condition in both groups [patients: F(1,8) = 8.88, p = .018, controls: F(1,9) = 52.35, p < .001]; controls also showed a benefit for other vs. case-referenced adjectives [patients: F < 1; controls: F(1,9) = 23.14, p < .001, see Fig. 5B]. Source memory was impaired in the patients relative to controls [main effect of group: F(1,17) = 13.57, p = .002]. There was a main effect of encoding condition [F(2,34) = 4.09, p = .025] and no interaction with group [F < 1]. Contrasts revealed that both self and other-referenced adjectives were better remembered than case [self vs. case: F(1,17) = 6.42, p = .021; other vs. case: F(1,17) = 4.39, p = .051, see Fig. 5C].

7.6. Summary of Experiments 3 and 4

In Experiment 3, SA patients showed normal self-reference effects. When sources were self-relevant, they no longer showed source memory deficits, relative to item memory. In Experiment 4, patients again showed the normal benefits of self-referential processing on memory. Self-referential adjectives were better remembered than adjectives relating to someone else, or more shallowly processed words.

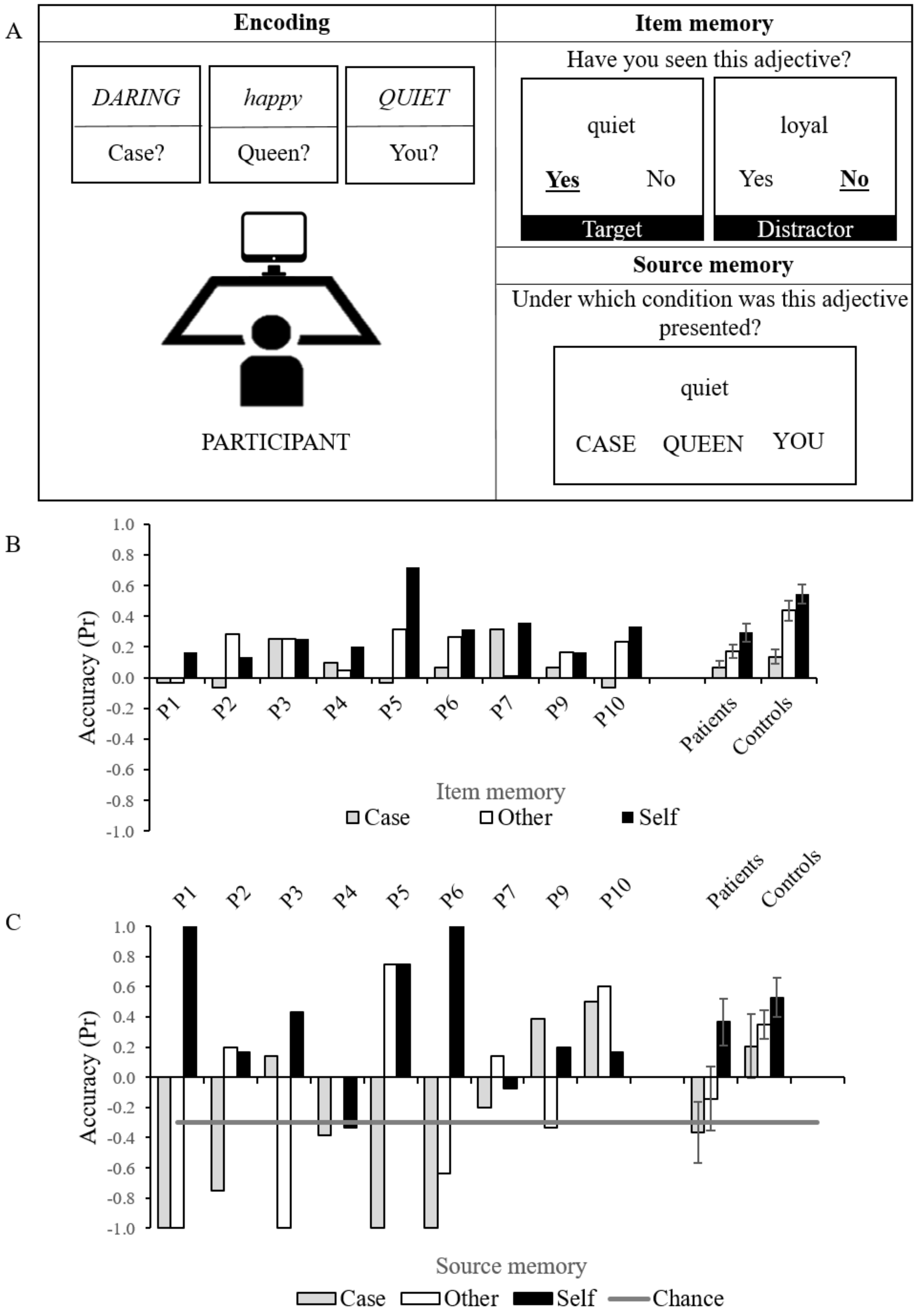

Figure 5. Experiment 4: design and results. A) Schematic of encoding, item and source memory phases of Experiment 4. At encoding participant were asked whether adjective described them (self),

the Queen (other) or were displayed in upper or lower case (case). Both target items (previously presented) and distractors (semantically-related items) were presented during item memory decisions. For adjectives judged as familiar, source memory was tested. B) Item memory accuracy for self, other and case trials. C) Source memory accuracy for self, other and case trials. D) Item and source memory accuracy collapsed across self, other and case trials. Accuracy is expressed using a discrimination index Pr, with chance level being 0 for item memory and -.033 for source memory. Error bar show SE of mean.

8. Discussion

We investigated item familiarity and source memory in a sample of semantic aphasia patients who had semantic control deficits and lesions of LIFG, to examine the possibility of parallel impairments of episodic and semantic memory characterised by difficulties overcoming competition from strong but irrelevant representations and a failure to control retrieval in line with the requirements of the task. In particular, we considered whether these individuals would show poor source memory in the context of relatively normal judgements of item familiarity, given that source memory is thought to draw on control processes that resolve competition between similar sources. We also examined whether the source memory impairment reflected the availability of spatial cues at retrieval (Experiment 1), consistency with pre-existing conceptual representations (Experiment 2) and the degree to which the sources were differentiated by means of self-referential processing (Experiments 3 and 4). In this way, the study delineates the circumstances in which retrieval from episodic memory requires control and provides support for a theoretical account in which shared memory control processes shape retrieval from both episodic and semantic memory.

We found that the magnitude of the source memory impairment was related to factors influencing the degree of competition between similar sources. Patients were more impaired at source memory judgements when sources were retrieved in the absence of spatial cues (Experiment 1). Spatial representations may provide a means of differentiating highly similar sources in episodic memory. The patients also showed greater source memory impairment when shopping items were paired with semantically incongruent sources (i.e., CARROTS in the BAKERY as opposed to GREENGROCER; Experiment 2). During congruent trials, source memory reached normal levels in the patients, but in incongruent trials, patients had difficulty disregarding task-irrelevant semantic associations, suggesting a lack of flexibility in the application of existing knowledge to episodic memory. Finally, the memory impairment for photographs of objects was eliminated when the distinctiveness or importance of the source was increased by means of self-referential processing at encoding (Experiment 3). In Experiment 4, using personality trait adjectives, item and source memory were equally impaired in the patients relative to controls, perhaps reflecting the higher language demands of this task. Nevertheless, the patients showed a normal difference between shallow encoding (decisions about upper/lowercase letters) and deep encoding (decisions about SELF or THE QUEEN), suggesting that both meaning-based and self-referential processes were used by patients to separate sources. In patients with SA, representations of space, meaning and self are all thought to be largely intact, while control over retrieval is impaired (see Fig. 1). Consequently, all three of these representational frameworks can differentiate potentially-confusable sources, reducing competition between memories.

This study supports the hypothesis that shared neurocognitive mechanisms support the controlled retrieval of semantic and episodic memories, extending the findings of a previous study, which employed paired-associate tasks in SA patients with LIFG lesions (Stampacchia *et al.*, 2018). The current work shows that similar deficits of episodic memory are observed in aphasia patients with deregulated semantic cognition, even in highly non-verbal tasks. We found several important parallels between the source memory deficits documented here and the semantic impairment previously described for these patients. These are discussed in turn below:

Multimodal impairment: Although patients with SA have aphasia consequent on left-hemisphere stroke, they have controlled retrieval deficits that affect both verbal and non-verbal tasks. In the semantic domain, patients with SA show equivalent deficits in accessing associations presented using words and pictures (CCT, Jefferies & Lambon Ralph, 2006) and they have difficulty retrieving non-canonical uses of objects presented as pictures (Corbett *et al.*, 2011), showing that their semantic control deficits are multimodal. Whilst our previous study (Stampacchia *et al.*, 2018) provided evidence of episodic memory deficits on largely *verbal* paired associate tasks in SA, the current study showed that these deficits extended to inherently *non-verbal* source memory tasks, which involved the formation and retrieval of associations between pictures of objects and coloured boxes, shops or people. The multimodal nature of the controlled retrieval deficit in SA, across both semantic and episodic memory tasks, supports the view that shared memory control processes interact with heteromodal semantic and episodic memory representations, which are formed within brain regions such as the ventral ATL and the hippocampus. Both of these brain regions, implicated in semantic and episodic memory respectively, are thought to integrate a wide range of features across modalities, allowing the formation of representations of heteromodal events and concepts (Eichenbaum, 2017; Lambon Ralph *et al.*, 2017).

Sensitivity to cues that constrain retrieval: In semantic memory, patients with SA are highly sensitive to cues that direct retrieval towards relevant features and associations; for example, relevant sentences enable them to access the non-dominant meanings of ambiguous words (Noonan *et al.*, 2010), and pictures of the common recipients of tools (e.g., PAPER for SCISSORS, or a NAIL for HAMMER) facilitate the production of appropriate actions (Corbett *et al.*, 2011). In a similar way, we found that non-verbal contextual cues (i.e. spatial location, Experiment 1b) acted as potent cues in source memory judgements. It appears that in both episodic and semantic memory judgements, SA patients have greater difficulties than healthy controls when the pattern of retrieval required by the task is relatively unconstrained by the information provided, and therefore the need for internally-generated constraint is higher.

Difficulty resolving competition: Previous research has shown that conceptual retrieval in patients with SA is disrupted by semantic distractors that create competition with target concepts (Noonan *et al.*, 2010; Thompson *et al.*, 2018). Similarly, in this study, SA patients' capacity to recall the correct source for a recently-presented item was impaired when semantic knowledge was in conflict with episodic memory (Experiment 2): this semantic congruency effect is likely to reflect competition between the two memory systems. Similarly, Stampacchia *et al.* (2018) showed that paired-associate learning was vulnerable to semantic distractors that elicited false memories in SA patients. The patients were also more vulnerable than control participants to proactive interference (e.g. competition within episodic memory). Our observation that self-reference could alleviate the patients' episodic control deficits (Experiments 3 and 4) might be explained in a similar way – self-related representations are highly distinctive and potentially more resistant to competition from non-self-related representations.

All of the patients in the current sample had damage affecting LIFG. This brain region shows greater activation during control-demanding semantic tasks, such as when dominant yet irrelevant representations need to be suppressed or when there are many distractors (Badre *et al.*, 2005; Noonan *et al.*, 2013; Krieger-Redwood and Jefferies, 2014; Krieger-Redwood *et al.*, 2015). A parallel neuroimaging literature has linked LIFG, close to the peak overlap in our patient group, to competition resolution in episodic memory tasks (Badre and Wagner, 2005; Dobbins and Wagner, 2005; Kuhl *et al.*, 2007). For example, a classifier trained on the cortical patterns evoked by target and competitor memories in a retrieval induced forgetting paradigm found that pattern suppression for competitors was linked to greater activity in this area (Wimber *et al.*, 2015). The contrast between source and item memory also reveals LIFG activation (Dobbins *et al.*, 2002; Dobbins and Wagner, 2005; Han *et al.*, 2012; Barredo *et al.*, 2015). These findings are highly consistent with a role for LIFG in resolving competition during both episodic and semantic decisions (Badre and Wagner, 2007; Burianova and Grady, 2007; Burianova *et al.*, 2010; Barredo *et al.*, 2015), in line with our results.

The neuropsychological evidence provided in the current study complements this neuroimaging research, since it suggests that LIFG is likely to play a *necessary* role in the control of both semantic and episodic retrieval. In contrast, the activation of LIFG in episodic memory is considered by some researchers to reflect the importance of semantic or linguistic processing in episodic tasks (e.g., Han *et al.*, 2012); as such, LIFG might not make a necessary or critical contribution to controlled episodic retrieval. In contrast with this view, our results showed that a non-verbal source memory task was impaired in patients with LIFG lesions, not only when there was competition between episodic memory and existing knowledge (Experiment 2), but also when non-meaningful sources competed strongly (Experiment 1a). Although our patient sample had relatively large left hemisphere lesions, extending beyond the area of overlap in LIFG, inhibitory transcranial magnetic stimulation (TMS) studies of healthy volunteers provide a test of the causal role of specific brain regions with higher spatial resolution. This research supports the view that LIFG plays an essential role in controlled semantic retrieval (Hoffman *et al.*, 2010; Whitney, Kirk, *et al.*, 2011; Whitney *et al.*, 2012; Krieger-Redwood and Jefferies, 2014). Future TMS research could test the clear prediction emerging from the current work that inhibitory stimulation to LIFG should disrupt controlled retrieval from episodic as well as semantic memory.

Our findings also reveal circumstances in which there is a reduced need for control processes to resolve competition in memory. These effects can be related to the pattern of brain injury in the SA group. The patients' lesions encompass areas involved in semantic control (Fig. 1A and 1B). In contrast, ventrolateral ATL implicated in heteromodal semantic representation (Fig. 1C) and regions thought to support spatial and self-referential processing (Fig. 1D and 1E) are preserved. In line with this, the patients showed intact source memory when episodic memory was congruent with existing knowledge, and when spatial and self-related cues were available. The hippocampus and surrounding cortex are thought to support the integration of spatio-temporal features to form unique event memories (see Eichenbaum, 2017 for a recent review). Since these medial-temporal structures are intact in SA patients, the features of events are likely to be bound together relatively normally by hippocampal networks at encoding. At retrieval, distinguishing between similar sources (i.e. the process of pattern separation) may require additional control when events share spatial-temporal features, i.e. they occur within a narrow time window and in similar locations (as in our experiments). Existing semantic representations can facilitate pattern separation when episodic memories are congruent with existing knowledge or schemas (i.e. in Experiment 2, Gilboa & Marlatte, 2017): when sources are non-meaningful (such as in Experiment 1), this process is more prone to error. Additionally, the availability during retrieval of the egocentric spatial configuration present at encoding can act as a potent cue, as it can facilitate the re-instatement of the remaining features of the event memory from its spatial location. Intracranial recordings show that neurons in the hippocampus and entorhinal cortex track spatial configurations (for a review see Moser, Kropff, & Moser, 2008). When these hippocampal-encoded spatial representations are activated by the external environment, the need to control source retrieval using fronto-parietal regions (including LIFG) may be diminished. As such, rTMS to LIFG in healthy individuals disrupts retrieval of abstract words – requiring competition resolution between multiple meanings – only in the absence of contextual cues (Hoffman *et al.*, 2010). Finally, the patients have intact medial cortical structures (Fig. 1A) implicated in self-referential processing (Fig. 1E, De Caso *et al., 2017;* Macrae *et al.*, 2004; Philippi, Duff, Denburg, Tranel and Rudrauf, 2011). Self-reference promotes memory in healthy participants (Symons and Johnson, 1997; Hamami *et al.*, 2011; Serbun *et al.*, 2011) and was also beneficial for the SA patients (Experiments 3 and 4). Self-referential processing is likely to reduce competition between memory sources in several ways (see Humphreys and Sui, 2015 for a general discussion). Self-related stimuli have higher salience (see Sui, Liu, Mevorach, & Humphreys, 2015) and higher intrinsic reward when compared with items with no self-relevance (see Sui, He, & Humphreys, 2012). Self-reference is thought to promote the binding of items and sources, even in the face of amnesic and semantic impairment (Sui and Humphreys, 2013). By this view, self-reference acts a form of "integrative glue" that affects coupling between self-representational regions (i.e. ventromedial PFC) and regions implicated in processing of external stimuli and memory (see Sui & Humphreys, 2015 for a review). This would reduce competition between sources with overlapping surface features, ameliorating the effects of control deficits in SA patients.

In conclusion, this study supports the hypothesis that source memory is impaired in SA patients with lesions to LIFG; they had difficulty suppressing irrelevant information when this competed with the correct source, and often failed to resolve competition between sources that lacked distinctiveness. Conversely, self-referential processing, semantic congruency and spatial processing are sustained by intact structures including midline regions such as medial prefrontal cortex (Macrae *et al.*, 2004; Philippi *et al.*, 2011; De Caso *et al.*, 2017), ventral ATL (Binney *et al.*, 2010; Visser and Lambon Ralph, 2011; Visser *et al.*, 2012) and hippocampus (Bird and Burgess, 2008; Eichenbaum, 2017). Representations provided by these structures may provide a means of distinguishing between similar sources and therefore compensate for the impaired role of prefrontal cortex in resolving competition during retrieval. This study also has clinical implications, showing that self-reference, spatial processing and semantic congruency may facilitate the accurate retrieval of episodic memories in patients with memory control deficits.

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CHAPTER 4

Training flexible conceptual retrieval in Semantic Aphasia

Acknowledgements:

A version of this chapter is being prepared for publication. The version for publishing includes additional neuroimaging data that were not collected/analysed by the author and therefore not included in this thesis. Data collection for the current chapter was by Glyn Hallam and the author. Stimuli for the training task with and without feedback were developed by Hannah Thompson, James Davey, Elizabeth Jefferies, Glyn Hallam and the author. The project was funded by Stroke Association (TSA/12/02) grant awarded to Elizabeth Jefferies and Matt Lambon Ralph. We are indebted to the patients and their carers for their generous assistance with this study.

Abstract

Therapy for comprehension deficits in aphasia typically focusses on strengthening links between conceptual representations and their lexical-articulatory forms. However, these approaches show little generalization to untrained items. Moreover, research has shown that semantic deficits in aphasia can affect both verbal and non-verbal tasks, particularly in patients with deregulated retrieval as opposed to degraded knowledge. This study therefore aimed to facilitate conceptual retrieval in a sample of such patients with semantic aphasia (SA) by training the retrieval of both strong and weak semantic associations and providing explicit feedback. We examined whether the effect of training generalized to measures of both episodic and semantic memory, given that SA patients have parallel deficits of controlled retrieval in both memory domains. In the training task, there was improvement with practice, particularly for trained items. An untrained task tapping semantic control using pictorial stimuli (Camel and Cactus Test) also improved. Episodic tasks showed no overall improvement after training. However, at the individual level we found that two patients (P2 and P6) had higher accuracy and made fewer semantic errors in a paired-associative episodic memory task after training. P2 also showed generalization to untrained items within the semantic training task, consistent with improved control over memory retrieval across domains. In addition, P1 who showed the strongest improvement on the trained semantic associations but failed to generalise this improvement across untrained items, showed poorer episodic memory performance when these semantic associations were presented as distractors. Together, these results suggest that semantic training can be beneficial in patients with SA but that, in some individuals, repetition of specific associations can give rise to relatively inflexible retrieval and overgeneralization of those trained associations. Future research should seek to understand which patients are most likely to benefit from this type of training.

1. Introduction

Research has shown that comprehension deficits arise in at least three ways, and these might benefit from different types of intervention. First, patients with stroke aphasia often have difficulty accessing conceptual meaning from language, while understanding is relatively good for pictures – as in pure word deafness and Wernicke's aphasia (Robson *et al.*, 2012; Thompson *et al.*, 2015b). Understanding the meaning of visual objects can also be specifically disrupted after posterior cerebral artery infarcts (Roberts *et al.*, 2013). These patients are likely to benefit from compensatory strategies maximising use of preserved input pathways. Other individuals have heteromodal semantic impairment, affecting both verbal and non-verbal stimuli. This pattern can reflect two qualitatively different impairments. Atrophy of the anterior temporal lobes (seen in semantic dementia, SD) leads to progressive degradation of semantic knowledge. SD patients show loss of specific and less familiar items first and consistent performance across different tasks probing the same concepts (Jefferies and Lambon Ralph, 2006; Mayberry *et al.*, 2011). These patients show some benefits in training studies focussed on relearning conceptual distinctions as long as the training is continued, potentially reflecting the fact that the anterior temporal lobes can continue to learn even as they are degrading (Heredia *et al.*, 2009; Mayberry *et al.*, 2011; Savage *et al.*, 2013).

Heteromodal semantic impairment does not always reflect degraded knowledge, however. Work by our group and others (Thompson-Schill, 2003; Jefferies and Lambon Ralph, 2006; Jefferies, 2013; Lambon Ralph *et al.*, 2017) shows that semantic deficits can also reflect difficulty constraining retrieval such that it is appropriate to the context or task. We have referred to this pattern as "semantic aphasia" (SA), since it affects both verbal and non-verbal manipulations of semantic knowledge, including picture matching and object use (Corbett, Jefferies and Lambon Ralph, 2009; Corbett, Jefferies, Ehsan, *et al.*, 2009; Corbett *et al.*, 2011). SA patients are thought to have impaired semantic control processes, which 'shape' conceptual retrieval following damage to left inferior frontal and/or posterior temporal regions. This causes greater impairment when non-dominant information needs to be retrieved, or when strong distractors need inhibiting. There has been little attempt to design training or rehabilitation strategies for these patients, although we might expect that approaches that provide practice in retrieving a range of different kinds of association (including non-dominant aspects of knowledge) might be most successful in promoting flexible patterns of semantic cognition.

The capacity to control mental activity in a flexible fashion, to suit the changing demands of a task, is highly relevant to communication and comprehension. Executive control is often impaired in people with aphasia, especially in those with more significant impairment (Glosser and Goodglass, 1990; Purdy, 2002) and preserved executive control is thought to be necessary for strong recovery of language after stroke (Geranmayeh *et al.*, 2017). The fMRI response to language stimuli in aphasia resembles the response evoked by hard-to-comprehend material in healthy controls (Brownsett *et al.*, 2014) and the activation of regions that support cognitive control (i.e. multi-demand network) seems to predictive of recovery in this population (Geranmayeh *et al.*, 2014, 2017). Semantic control areas, activated by the contrast of hard and easy semantic judgements in healthy participants (Thompson-Schill *et al.*, 1997; Badre and Wagner, 2007; Noonan *et al.*, 2013), lie adjacent to, and partially overlap with, multiple demand regions (Duncan, 2010; Davey *et al.*, 2016). It is possible that recruitment of multiple demand regions during semantic tasks can compensate, at least partially, deficits stemming from damage in semantic control network. Cognitive training might benefit many people with aphasia if it can strengthen engagement of control mechanisms within language and semantic tasks. Studies addressed to other clinical populations (i.e. traumatic brain injury) have already showed that cognitive control training is more effective than knowledge-based training (Vas *et al.*, 2016) and promotes increased connectivity in multi-demand regions (Han *et al.*, 2018). This suggests that this approach could be worthwhile in aphasia. Moreover, an approach with special focus on semantic flexibility in SA has not been evaluated previously.

Many training studies in aphasia have targeted naming deficits (Kiran and Bassetto, 2008). These studies tend to show a clear benefit for items that are trained multiple times, but weaker generalisation to untrained items (Marshall *et al.*, 1990; Davis and Pring, 1991; Pring *et al.*, 1993). This suggests that such training strengthens lexical-articulatory forms, or the links between conceptual representations and perceptual features that are activated by the picture. Efforts to support semantic processing at the single item level in aphasia have been largely unsuccessful in people with semantic deficits (e.g., Van Hees *et al.*, 2013). Few investigations have attempted to ameliorate these comprehension problems – perhaps because, as it has been noted previously, comprehension deficits in aphasia are often accompanied by broader deficits (e.g., Purdy, 2002; Jefferies and Lambon Ralph, 2006; Baldo *et al.*, 2015; Thompson *et al.*, 2018). People with poor cognitive control respond less well to conventional speech and language therapy (Fillingham, Sage and Lambon Ralph, 2005; Fillingham, Sage and Ralph, 2005; Fillingham *et al.*, 2006; for a systematic literature review see Simic *et al.*, 2017). This might be because such individuals are less good at allocating and maintaining attention to the training task, and/or because their primary difficulty is not weakness in any specific type of language/conceptual representation that can be overcome through practice. In fact, massed practice at retrieving the same specific meanings or associations is arguably unhelpful in people with deregulated semantic cognition, since successful comprehension requires flexibility – i.e., understanding the world around us requires different responses at different times, depending on the context. Therefore, a more successful approach might involve helping patients to access a wide range of different associations, some relatively strong and some weaker, depending on the semantic decision to be made.

In this study, we trained the retrieval of diverse types of association to improve comprehension in patients with SA. Although we examined SA patients in this study, our approach might be applicable to any groups with deregulated semantic retrieval, in which heteromodal comprehension is impaired as a consequence of poor control (such as patients with lesions in semantic control key areas following non-stroke aetiologies). Volunteers were asked to decide which word was associated with a probe word, and the associations to be retrieved ranged in their associative strength from weak to strong. On each trial, the participants were helped to understand the relevant association through the provision of feedback and a linking photograph that captured the relevant association in a concrete way. We presented novel training items within each session, to encourage flexibility, but a subset of the items were also repeated across time points. In this way, we could look at the extent to which any training effect generalised to untrained items.

Chapters 2 and 3 of this thesis demonstrated parallel impairment of semantic and episodic memory in SA patients. These individuals failed to discard strong but irrelevant semantic associations when performing episodic memory decisions (generating false memories). In a similar fashion, they had difficulty ignoring recently-presented episodic links when making semantic decisions. As in the semantic domain, deficits in episodic memory were increased in tasks with higher control demands, including paired associative tasks with strong distractors (see Chapter 2) and source memory tasks (see Chapter 3). These deficits were diminished when the requirement to constrain retrieval was reduced through the provision of different types of cues – phonological, spatial and self-referential (see Chapter 2 and 3). Collectively, this evidence suggests that both semantic and episodic deficits stem from difficulty constraining retrieval to suit the current context or goal. This leads to two hypotheses about the effect of semantic training on episodic memory in this study. First, for individual patients who showed positive effects of semantic training that generalised to untrained items (consistent with improved flexibility and control over retrieval), we would expect greater capacity to resolve competition between existing memories also in the context of episodic retrieval. This was tested using a paired-associates task (i.e. Experiment 1, Chapter 2). Secondly, for individuals who learned specific associations without generalisation (a pattern *not* consistent with improved control over retrieval), we might expect episodic memory to be disrupted when these strengthened semantic links were presented as distractors. This is because such patients should have particular difficulty avoiding semantic distractors in episodic tasks, especially when these have been reinforced by repeated recent retrieval.

2. Participants

Eleven patients were recruited from local stroke and communication support groups in Yorkshire, UK (7 females, mean age = 61, SD = 11). Patients were selected to show multimodal semantic impairment and sensitivity to controlled retrieval demands in both verbal and non-verbal semantic tests (tests from Noonan *et al*., 2010 and Corbett *et al*., 2011) and were therefore similar to cases with SA previously described (e.g. Jefferies and Lambon Ralph, 2006). All patients and control participants gave written informed consent as approved by the local Research Ethics Committee. All the patients had chronic aphasia arising from a cerebrovascular accident affecting left prefrontal cortex (typically along with other regions) at least two years before the study. None of the patients were undergoing a structured course of individual or group therapy for treatment of comprehension deficits during the course of the study, though some patients were completing computerised self-guided naming therapies such as React2. The patients had a range of other language impairments (e.g., deficits in repetition and fluency of speech), although their comprehension problems could not be entirely accounted for in these terms. The patients therefore spanned several ‘classical’ diagnostic categories including transcortical sensory aphasia, Broca’s and global aphasia. Demographic details and aphasia classification are reported in Table 1.

3. Background neuropsychological assessment

3.1. Non-semantic tests

To characterise language processing, we examined word repetition (Test 9 from PALPA, Psycholinguistic Assessments of Language Processing in Aphasia; Kay *et al.*, 1992) and words per minute on the Cookie Theft picture description task (BDAE; Goodglass and Kaplan, 1983). Four patients showed severe impairment of repetition, while one had milder impairment. Three of these four individuals were also unable to produce speech in the Cookie Theft picture description task, and three additional cases showed reduced speech fluency. We assessed executive function and non-verbal reasoning with Raven’s progressive coloured matrices test (Raven, 1962) and Brixton rule attainment test (Burgess and Shallice, 1997). Eight of the group showed deficits on at least one of these assessments, in line with previous studies which found that deregulated semantic cognition correlated with executive dysfunction in stroke aphasia (Jefferies and Lambon Ralph, 2006; Noonan *et al.*, 2010; Thompson *et al.*, 2018). Individual scores are reported in Table 1.

Table 1. Demographics, non-semantic background task and aphasia classification

			P1	P2	P3	P4	P6	P12	P7	P5	P9	P10	P11
Age			61	78	60	67	58	48	66	59	78	40	57
Sex			F	M	F	M	M	F	M	F	F	F	F
Years since CVA			7	7	9	24	14	4	7	7	5	8	8
							Non-semantic background tasks						
Test	Max	Cut-off											
Category fluency (mean per cat.)	-	8	**0**	**7**	**5**	**4**	**7**	**0**	**0**	14	17	17	15
Cookie theft (words/minute)	-	-	0	18	9	12	37	0	0	60	54	37	38
PALPA 9, real word repetition	16	14	**0**	14	**12**	15	16	**0**	**2**	16	15	16	**6**
Forward digit span	-	5	**0**	**4**	**2**	5	**4**	**0**	**0**	6	5	5	6
Raven's coloured matrices	36	28	31	29	31	**24**	**30**	**32**	**34**	**19**	**21**	**33**	**33**
Brixton (correct)	54	28	**21**	**7**	**18**	**26**	**23**	**6**	31	**24**	31	30	39
							Aphasia classification						
Fluency			Non-fl	Mid	Non-fl	Mid	Fluent	Non-fl	Non-fl	Fluent	Fluent	Fluent	Fluent
Comprehension			Poor	Poor	Poor	Mid	Mid	Mid	Poor	Mid	Good	Mid	Good
Repetition			Poor	Good	Mid	Good	Good	Poor	Poor	Good	Good	Good	Mid
Naming			Poor	Good	Poor	Good	Good	Mid	Poor	Good	Good	Good	Poor
			Global	MTA	Global	MTA	TSA	Broca's	Broca's	TSA /Anomic	Anomic	TSA/ Anomic	Anomic

Table 1 Legend: Scores are number of correct, unless specified. CVA: Cerebrovascular accident. NT = unavailable for testing, Bold underlined numbers denotes impaired scores (below cut-off). MTA: Mixed Transcortical Aphasia; TSA: Transcortical Sensory Aphasia.

3.2. Cambridge semantic battery

This assesses semantic retrieval for a set of 64 items across tasks (Bozeat *et al.*, 2000; Adlam *et al.*, 2010), including picture naming, word-picture matching, verbal and pictorial semantic associations (Camel and Cactus Test, CCT). Word-picture matching involved an array of ten semantically-related items, while the association judgements required a probe to be matched with one of four response options, presented as either pictures or words (in written form and also spoken aloud by the researcher). In line with their varying language output impairment, patients showed large variability during picture naming [percentage correct M(SD) = 58 (40.3)]. In contrast, performance was uniformly at ceiling in word-picture matching [M(SD) = 95.9 (5.2)]. When secondary associations between concepts were to be retrieved – i.e. on the CCT – and control demands were therefore higher, performance was lower with no differences across modalities [words M(SD) = 79.4 (15.7); pictures M(SD) = 80.4 (14.5)]. Individual test scores are provided in Table 2. All but one of the patients (P10) showed some impairment on this standard semantic battery.

3.3. Tests of semantic control

Four tasks manipulated control demands. All of the patients were below the normal cut-off on both verbal tasks (ambiguity task; synonym judgement tasks) and non-verbal judgements (object use; CCT pictures from the Cambridge Semantic Battery). Individual scores are reported in Table 2.

3.3.1. Ambiguity task

This probed the dominant (MONEY) and subordinate (RIVER) meanings of ambiguous words (e.g., BANK) in a four alternative-forced-choice task (Noonan *et al.*, 2010). On some trials, there were sentence cues (e.g., for MONEY, I WENT TO SEE THE BANK MANAGER) or miscues that related to the irrelevant interpretation (e.g., THE BANK WAS SLIPPERY). All the patients were below the normal cut-off in all conditions. Every patient showed better comprehension of dominant [percentage correct M(SD) = 82.7 (10.5)] than for subordinate [M(SD) = 54.8 (13.3)] interpretations, and better performance for subordinate trials following correct cues [M(SD) = 72.6 (14.5)] than miscues [M(SD) = 44.1 (15.3)] (with the exception of P12 and P11 who were not tested with cues and miscues). Excluding those two cases, a mixed ANOVA examining the effects of dominance (subordinate and dominant) and cueing (no cue, cue and miscue) by group (patients vs. controls from Noonan *et al.*, 2010) showed main effects of dominance [F(1,15) = 80.22, p < .001] and cueing [F(2,30) = 28.32, p < .001] plus interactions for dominance by cueing [F(2,30) = 9.51, p = .001], dominance by group [F(1,15) = 48.35, p < .001] and cueing by group [F(2,30) = 24.25, p < .001]. The three-way interaction [dominance by cueing by group [F(2,30) = 7.77, p = .002] reflected greater difficulty with subordinate meanings when no cues or miscues were provided. A supplementary ANOVA including all cases and omitting the cueing factor showed the same effects of dominance [main effect: F(1,17) = 166.30, p < .001; interaction with group: F(1,17) = 123.23, p < .001].

3.3.2. Object use task

This task required patients to select an object to accomplish a task (e.g., bash a nail into wood), with all items represented as photographs (Corbett *et al.*, 2011). The target was either a canonical tool, normally used to complete the task (e.g., HAMMER), or an alternative non-canonical option (e.g., BRICK), presented among a set of five unsuitable distractors, requiring suppression of the irrelevant yet dominant use of the object. All of the patients (except P5, who was below the normal range for the picture CCT test) were more impaired at selecting non-canonical targets [canonical M(SD) = 92.4 (7.5) vs. alternative M(SD) = 61.7 (19.4); t(10) = 7.70, p <.001]. As a group, they showed poorer performance for non-canonical targets than controls [who were not asked to select the canonical use due to ceiling effects): t(10.6) = 5.99, p < .001 (control data from Corbett *et al*. 2011).

3.3.3. Synonym tasks

(ii) Frequency effects in 96-item synonym judgement (Jefferies *et al.*, 2009): In this task, administered to all patients but P12, a probe word was presented with three response options. The words on each trial varied in lexical frequency and imageability (full task details in Jefferies *et al.*, 2009). Patients with semantic aphasia, in common with those with “access” impairment, typically do not show sensitivity to frequency (Warrington and Cipolotti, 1996; Jefferies *et al.*, 2007; Hoffman *et al.*, 2011; Thompson *et al.*, 2015b), unlike semantic dementia patients with “storage” impairment (Jefferies *et al.*, 2009). Three patients out of eleven showed slightly higher performance during high frequency trials (P2, P9, P10); one patient (P3) performed better for low frequency trials. The majority of patients (six) showed no frequency effect, in line with expectations. We compared our SA sample with the SD patients from Jefferies *et al*. (2009). ANOVA revealed a frequency by group interaction [F(1,20) = 35.46, p < .001] as well as the main effect of frequency [F(1,20) = 45.84, p < .001]. The SA patients showed no difference between high frequency trials [percentage correct M(SD) = 75.8(10.1)] and low frequency trials [M(SD) = 74.8(11)], unlike the SD patients.

(iii) 84-item synonym judgment task with strong and weak distractors (Samson *et al.*, 2007; Noonan *et al.*, 2010): Synonyms were presented alongside strong and weak associates as distractors; e.g., DOT with POINT [target], presented with DASH [strong distractor] or LEG [weak distractor]. Performance was below normal cut-off for all patients in trials with strong distractors; P12 was not tested and P7 showed no sensitivity to strong distractors. All the remaining cases showed poorer performance when semantic distractors were presented. ANOVA looking at distractor strength (related vs. unrelated) and group (patients vs. controls, with control data from Samson *et al.*, 2007) revealed that accuracy was poorer for the patients when semantically-related but irrelevant distractors were presented [main effect of distractor strength: F(1,16) = 6.29, p = .023 and distractor strength by group interaction: F(1,16) = 14.22, p = .002].

In summary, the SA patients were impaired at retrieving non-dominant aspects of meaning across verbal and non-verbal tasks, like previous samples (Corbett *et al*., 2011; Jefferies & Lambon Ralph, 2006; Noonan *et al*., 2010). A composite score reflecting each patient's overall semantic control abilities was derived from the Camel and Cactus Tests, Object use and the Ambiguity task without cues (i.e. the semantic control tests that were administered to all participants) using factor analysis. Patients are ordered by this composite score in the graphs and tables below.

Table 2. Background semantic tasks: individual scores

Semantic background tasks

Test	Max	Cut-off	P1	P2	P3	P4	P6	P11	P7	P5	P9	P10	P12
Cambridge Semantic Battery													
Picture naming	64	59	**1**	61	**19**	**50**	**50**	**0**	**3**	60	**56**	62	**46**
Word-Picture matching	64	62	63	62	**60**	64	62	**61**	**52**	62	64	62	63
Word CCT	64	56	**39**	**43**	**29**	**53**	**52**	**50**	57	59	61	60	56
Picture CCT	64	52	**31**	**44**	**45**	56	57	59	54	**45**	53	61	61
Ambiguity task													
Miscued dominant	30	30	**12**	**13**	**13**	**14**	**19**	NT	**21**	**20**	**24**	**26**	NT
Miscued subordinate	30	28	**7**	**10**	**14**	**8**	**15**	NT	**18**	**10**	**18**	**19**	NT
No cue dominant	30	28	**22**	**18**	**24**	**22**	**26**	**27**	**27**	**24**	**28**	**28**	**27**
No cue subordinate	30	28	**11**	**9**	**14**	**14**	**17**	**17**	**19**	**19**	**21**	**19**	**21**
Cued dominant	30	30	**23**	**21**	**19**	**22**	**23**	NT	**23**	**24**	**27**	**29**	NT
Cued subordinate	30	29	**25**	**14**	**20**	**18**	**28**	NT	**24**	**19**	**23**	**25**	NT
Synonym task (96 items)													
High frequency	48	42	**27**	**33**	**32**	**37**	**38**	NT	**39**	**34**	**41**	43	**40**
Low frequency	48	44	**30**	**25**	**39**	**37**	**38**	NT	**42**	**32**	**37**	**38**	**41**
Synonym task with distractors (84 items)													
Strong	42	40	**15**	**12**	**13**	**20**	**23**	NT	**30**	**21**	**22**	**17**	**38**
Weak	42	35	**25**	**23**	**29**	**24**	**30**	NT	**31**	**27**	**28**	**39**	36

Object use													
Alternative	37	34	**14**	**13**	**14**	**21**	**22**	**24**	**22**	34	**26**	**29**	***32***
Canonical	37	-	**32**	**31**	**29**	**35**	**35**	**33**	**33**	37	37	37	*37*

Table 2 Legend: Scores are number of correct, unless specified. Legend: NT = unavailable for testing, Bold underlined numbers denotes impaired scores (below cut-off).

4. Methods

4.1. Overview of experiments

Patients were trained using a semantic associative task, administered in six consecutive sessions across two weeks. We examined training effects by looking at performance (i) over the course of training and (ii) on a semantic associative task – with the same design of the training task but without feedback – administered before and after training. In both cases, generalization effects were examined by looking at performance for untrained/novel trials (e.g. presented only once over the course of training) as opposed to repeatedly trained trials. (iii) Before and shortly after the training period, we also administered tasks tapping semantic and episodic control to assess generalization beyond the training paradigm.

4.2. Analyses overview

Repeated-measures ANOVA and 2-tailed paired samples t-tests were used to assess training effects and experimental manipulations (e.g. to compare trained vs. novel items, and to assess the effect of associative semantic strength) at the group level. Individual performance was analysed using McNemar tests when the same trials were tested at different time points (such as for repeatedly trained trials tested during first vs. last session of the training task). When different trials were presented before and after training (such as for novel trials of the training task) chi-square or Fisher's exact tests were used.

5. Training Paradigm

5.1. Training task: Procedure

Participants performed a three-alternative-forced-choice semantic association task. Three words appeared on the bottom of the screen for three seconds, during which time they were read out aloud by the examiner, followed by a single probe word appearing at the top. Participants were required to point to one of the three words that had the closest semantic association with the probe word. There was no maximum time allowed for a response; participants were asked to guess if they were unsure. The examiner repeated the words again at the participant's request.

We manipulated the strength of association between the probe and target. Strong associations required little control over retrieval, since the dominant association for the probe corresponded to the target, while medium and weak associations required more control over semantic activation in order to focus retrieval on the relevant relationship and suppress stronger but currently irrelevant associations (cf. Badre and Wagner, 2005; Whitney *et al.*, 2011). The distractor words for each trial were related to the target to increase inhibitory demands. For example: TAXI – PHONE not E-MAIL or FAX (weak association); JELLY BEAN – NEWSAGENT not FLORIST or BUTCHER (medium-strength association); HEN – EGGS not MILK or CHEESECAKE (strong association). Forty trials were repeated in every session, whereas 25 novel trials were presented to test for generalisation. This gave 65 trials per session for analyses. Each training session started with 3 practice trials which were omitted from the analysis and lasted around 15-20 minutes. The order of the training sessions was counterbalanced across participants. The strength of association for each of these trials was matched across sessions (i.e. each session had the same overall level of difficulty). Associative strength was derived from Edinburgh Association Thesaurus (EAT; Kiss *et al.*, 1973). Approximately one third of the trials in both the repeated and novel conditions were strong, medium and weak associations (Strong M (SD) = 6.0 (0.3), 15 trials; Medium M (SD) = 4.8 (0.4); 15 trials; Weak M (SD) = 3.1 (0.5); 10 trials). The six training sessions were conducted over a 2-3 week period, with sessions separated by at least 24 hours. The task was presented using E-Prime 2.0 (Psychology Software Tools). The complete list of stimuli is provided in Appendix Table 1.

At the end of each trial, participants were provided with feedback as to whether they were correct or incorrect. This took the form of a green tick with the word “correct”, or a red cross with “incorrect”. An image was also displayed on the screen that reinforced the relevant semantic association. For example, for the association between PLANE and AIRCRAFT CARRIER, an image was displayed of a plane taking off from an aircraft carrier. These images were presented for both correct and incorrect trials. The feedback and summary picture were presented until the patient was ready to move onto the next trial. A verbal description was added to summarise the link between the target and probe if the picture was unclear to the patient.

5.2. Semantic association task without feedback: Procedure

Before and after training, participants performed a task with the same format as the training task, but without the provision of feedback and without the linking picture after each trial. As in the training task, associative strength between the probe and target was manipulated; this was matched across the pre- and post-training sessions. There were 82 trials: 24 were presented 1-to-6 times during training (i.e. trained) whereas 58 were not trained. List of trials is provided in Appendix Table 2. This procedure therefore assessed whether (i) there was an overall improvement in selecting the correct semantic associate among distractor following training and (ii) whether any improvement was restricted to trials that had been trained, or generalised to trials that had not been trained.

5.3. Training task: Results

Group level effects: See Figure 1 for key results and Supplementary Table 1 for descriptive statistics. A 6 (training sessions) by 2 (repeated vs. novel) by 3 (strong, medium and weak associations) ANOVA revealed an overall improvement across sessions [main effect of training session [F(5,50) = 4.1, p = .004] and higher accuracy for repeated as opposed to novel items [F(1,10) = 68.61, p < .001]. There was also a main effect of strength of association [F(2,20) = 32.57, p <.001], revealing higher accuracy for strong vs. medium vs. weak associations. There were also two interactions. There was a stronger training effect for repeated trials [training session by repetition: F(5,50) = 3.01, p = .018]. Follow-up tests comparing the first and last sessions showed that the trained items increased in accuracy [t(10) = 4.84, p = .001], while novel items did not [t(10) = .709, p = .494, Fig. 1]. In addition, repetition interacted with strength of association [F(2,20) = 11.01, p =.001]. This revealed that across all training sessions, strength of association had little effects on accuracy when trials were repeatedly trained [there was difference between strong vs. weak trials only: t (10) = 3.5, p = .036; Bonferroni corrected for six comparisons]. On the contrary, when trials were presented only once, patients' capacity to retrieve semantic links was much more strongly influenced by the associative strength between items [strong vs. weak [t(10) = 5.78, p = .001]; medium vs. weak [t(10) = 5.15, p = .002, Bonferroni corrected for six comparisons]. All other interactions were non-significant [F < 1.5].

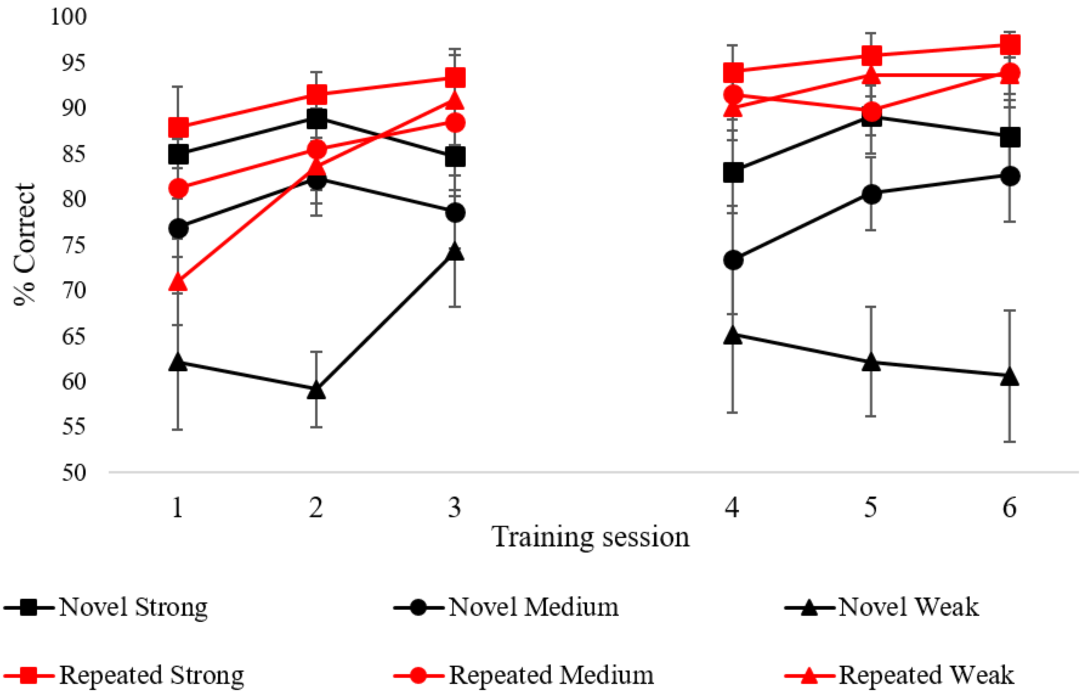

Figure 1. Training study, group level analysis. Training sessions by repetition (repeated, novel) by associative strength (strong, medium, weak). Error bars show SEM.

Individual analysis: See Figure 2 for key results and Table 3 for descriptive statistics. Effects of repetition and strength of association were examined separately in each individual patient to increase statistical power. For repeated trials, 3 patients (P1, P7 and P12) showed significant improvement from session 1 vs. session 6 [McNemar $p \leq .008$]. In all the other cases performance was higher in the last vs. first session of training, but this did not reach significance. For novel trials, only P2 showed a trend towards higher accuracy in the last vs. first session [χ2 (1) = 3.31, $p = .069$]. P1, P2 and P11 showed increased accuracy between first and last session for, respectively, strong [χ2(1) = 4.75, $p = .029$], medium [χ2(1) = 4.75, $p = .029$] and low [Fisher's exact test: $p = .037$] strength of association trials. No significant improvement was found for the all other patients [χ2 (1) < 3].

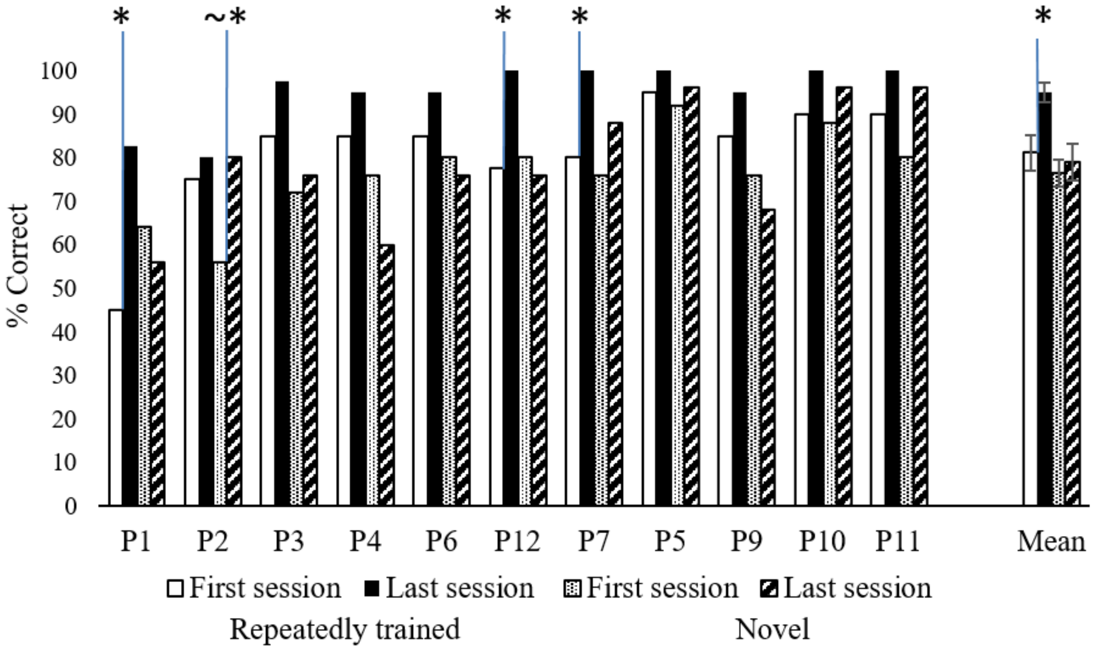

Figure 2. Training study, individual analysis. Training sessions (first vs. last) by repetition (repeated, novel). * = significant ($p < .05$) difference between conditions; ~* = difference between conditions approaching significance ($p \leq .07$). Error bars show SEM.

Table 3. Training task: descriptive statistics.

Session	1						2						3					
Training	Novel			Repeated			Novel			Repeated			Novel			Repeated		
Assoc. Strength	Strong	Medium	Weak	Strong	Medium	Weak	Strong	Medium	Weak	Strong	Medium	Weak	Strong	Medium	Weak	Strong	Medium	Weak
P1	66.7	70.0	50.0	46.7	46.7	40.0	77.8	60.0	66.7	86.7	80.0	60.0	66.7	70.0	50.0	73.3	66.7	50.0
P2	80.0	55.6	16.7	86.7	53.3	90.0	90.0	66.7	50.0	73.3	53.3	60.0	80.0	77.8	66.7	100	53.3	70.0
P3	77.8	80.0	50.0	93.3	80.0	80.0	90.0	77.8	33.3	86.7	73.3	90.0	66.7	60.0	33.3	80.0	86.7	100
P4	70.0	66.7	100	86.7	86.7	80.0	80.0	88.9	66.7	93.3	80.0	90.0	80.0	66.7	66.7	93.3	86.7	100
P6	90.0	77.8	66.7	93.3	86.7	70.0	90.0	100	66.7	93.3	73.3	90.0	100	66.7	83.3	80.0	93.3	90.0
P12	90.0	88.9	50.0	93.3	80.0	50.0	90.0	88.9	83.3	93.3	93.3	90.0	80.0	77.8	83.3	100	93.3	90.0
P7	100	70.0	50.0	80.0	80.0	80.0	100	66.7	50.0	86.7	93.3	70.0	88.9	90.0	100	100	100	100
P5	90.0	88.9	100	93.3	100	90.0	90.0	100	66.7	93.3	100	90.0	100	77.8	83.3	100	100	100
P9	70.0	77.8	83.3	100	80.0	70.0	80.0	77.8	50.0	100	93.3	90.0	80.0	77.8	100	100	93.3	100
P10	100	90.0	66.7	93.3	100	70.0	100	88.9	50.0	100	100	90.0	100	100	83.3	100	100	100
P11	100	80.0	50.0	100	100	60.0	90.0	88.9	66.7	100	100	100	88.9	100	66.7	100	100	100
Mean	84.9	76.9	62.1	87.9	81.2	70.9	88.9	82.2	59.1	91.5	85.5	83.6	84.6	78.6	74.2	93.3	88.5	90.9
SD	12.7	10.7	24.8	14.9	17.6	15.8	7.3	13.5	13.7	7.9	14.9	13.6	12.1	13.2	20.2	10.3	15.2	16.4

Session	4						5						6					
Training	Novel			Repeated			Novel			Repeated			Novel			Repeated		
Assoc. Strength	Strong	Medium	Weak	Strong	Medium	Weak	Strong	Medium	Weak	Strong	Medium	Weak	Strong	Medium	Weak	Strong	Medium	Weak
P1	55.6	90.0	33.3	73.3	86.7	70.0	60.0	55.6	66.7	73.3	80.0	80.0	66.7	50.0	50.0	93.3	80.0	70.0
P2	70.0	66.7	50.0	86.7	73.3	70.0	90.0	88.9	50.0	93.3	73.3	80.0	90.0	88.9	50.0	86.7	80.0	70.0
P3	88.9	60.0	33.3	100	86.7	100	100	60.0	66.7	100	86.7	100	100	80.0	33.3	100	93.3	100
P4	70.0	44.4	66.7	80.0	80.0	80.0	80.0	77.8	66.7	100	80.0	90.0	90.0	55.6	16.7	93.3	93.3	100
P6	80.0	100	100	100	100	90.0	90.0	77.8	50.0	100	93.3	100	70.0	77.8	83.3	93.3	100	90.0
P12	90.0	88.9	83.3	93.3	93.3	90.0	90.0	88.9	16.7	93.3	93.3	90.0	80.0	88.9	50.0	100	100	100
P7	100	50.0	66.7	100	100	100	100	80.0	83.3	100	93.3	100	88.9	90.0	83.3	100	100	100
P5	100	88.9	16.7	100	100	100	70.0	77.8	83.3	93.3	100	90.0	100	100	83.3	100	100	100
P9	70.0	77.8	100	100	86.7	100	100	100	66.7	100	86.7	100	70.0	77.8	50.0	100	86.7	100
P10	88.9	90.0	83.3	100	100	90.0	100	90.0	83.3	100	100	100	100	100	83.3	100	100	100
P11	100	50.0	83.3	100	100	100	100	90.0	50.0	100	100	100	100	100	83.3	100	100	100
Mean	83.0	73.3	65.2	93.9	91.5	90.0	89.1	80.6	62.1	95.8	89.7	93.6	86.9	82.6	60.6	97.0	93.9	93.6
SD	15.0	19.8	28.3	9.6	9.5	11.8	13.8	13.3	19.8	8.0	9.1	8.1	13.2	17.0	23.9	4.6	8.1	12.1

Table 3 Legend: Scores are percentages of correct response.

5.4. Semantic association task without feedback: Results

Group level effects: See Figure 3 for key results and Table 4 for descriptive statistics. A 2 (session: pre vs. post) by 2 (trained vs. untrained) by 3 (strong, medium and weak associations) ANOVA revealed main effects of session [F(1,10) = 17.61, p = .002], training [F(1,10) = 13.7, p = .004] and strength of association [F(2,20) = 3.75, p = .041]. An interaction of session by training [F(1,10) = 14.16, p = .004] reflected greater improvement for trained trials. Paired t-tests showed that there was an improvement in accuracy on trained items [t(10) = 3.65, p = .008, Bonferroni corrected for two comparisons] but no significant improvement on untrained items [t(10) = 1.56, p = .33, Bonferroni corrected for two comparisons]. There were also interactions of training by strength of association [F(2,20) = 4.64, p = .022] and a three-way interaction [training by strength of association by session: F(2,20) = 8.94, p = .002]. This showed some improvement after training even for untrained trials, but only for trials with high associative strength [t (10) = 3.17, p = .06, Bonferroni corrected for six comparisons], i.e. when control demands were minimal. No difference was found for medium associative strength and performance dropped for weak associative trials [but this was not significant: p = .33]. For trained trials, there was improvement after training for both strong and weak trials [nearly reaching significance for weak trials: t(10) = 3.01, p = .072, Bonferroni corrected for six comparisons].

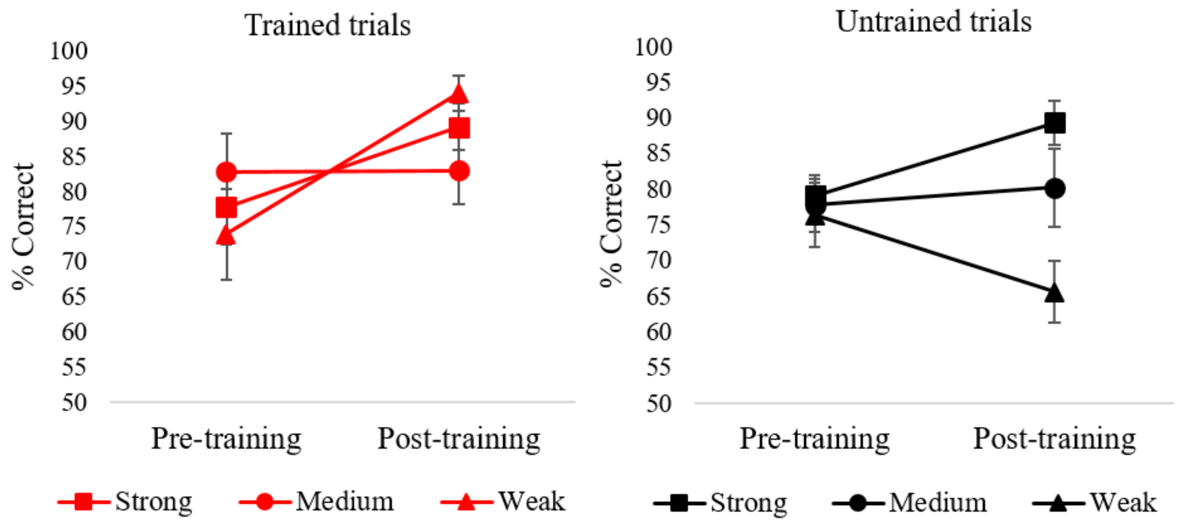

Figure 3. Semantic associative task without feedback, group level analysis. Session (pre vs. post) by training (trained, untrained) by associative strength (strong, medium, weak).
Error bars show SEM.

Individual analysis: Figure 4 shows key results. All patients (but P12 and P11) showed improvement after training for trained trials. This effect approached significance for P1 [χ2 (1) = 3.63, p = .057] and was non-significant in all other cases [χ^2 (1) < 3]. All patients showed little or no improvement for untrained trials [χ^2 (1) < 2]. P2, P5, P6 and P7 showed significantly higher accuracy after training for high strength of association trials [respectively: χ^2 (1) = 4.31, p = .038; Fisher's exact test: p = .026; χ^2 (1) = 3.72, p = .054: Fisher's exact test: p = .005]. No significant improvement was found for medium and low trials for the all the patients [χ^2 (1) < 2].

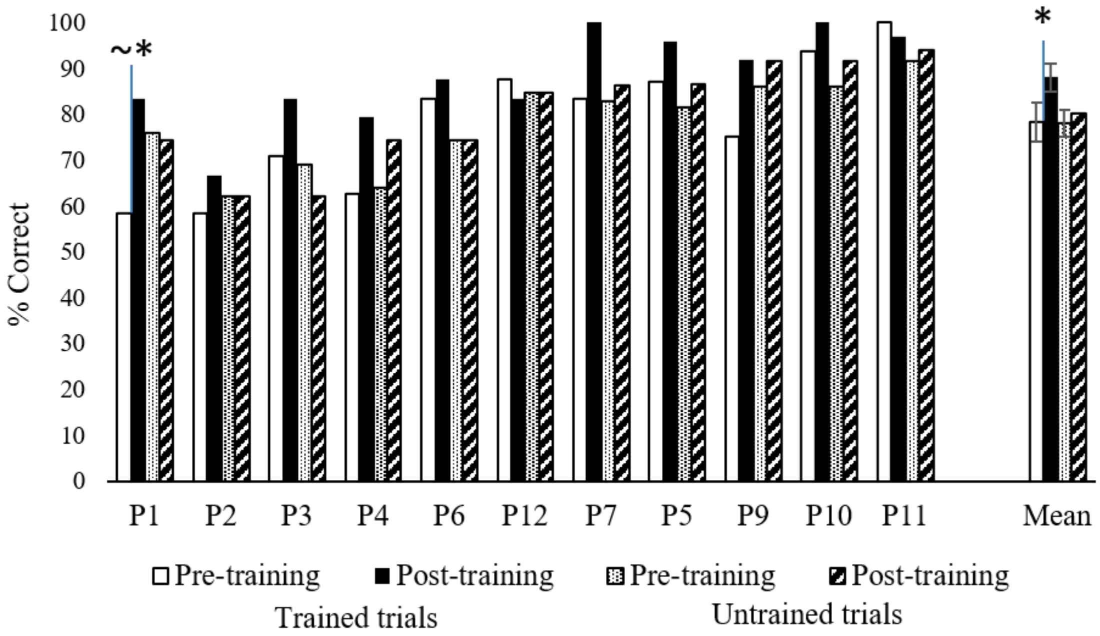

Figure 4: Semantic associative task without feedback, individual analysis. Session (pre vs. post) by training (trained, untrained). ~* = difference between conditions approaching significance ($p \leq .07$). Error bars show SEM.

Table 4. Semantic associative task without feedback: descriptive statistics

Session	Pre - training						Post - training					
Training	Untrained			Training			Untrained			Trained		
Assoc. strength	Strong	Medium	Weak	Strong	Medium	Weak	Strong	Medium	Weak	Strong	Medium	Weak
P1	86.4	81.8	50.0	100	55.6	50.0	81.8	72.7	64.3	77.8	77.8	100
P2	68.2	54.5	64.3	55.6	66.7	50.0	95.5	45.5	35.7	66.7	55.6	83.3
P3	65.2	66.7	78.6	75.0	80.0	50.0	68.2	59.1	57.1	88.9	66.7	100
P4	68.2	63.6	57.1	77.8	55.6	50.0	77.3	77.3	64.3	88.9	66.7	83.3
P6	75.0	66.7	81.3	57.1	92.3	100	86.4	63.6	71.4	100	77.8	83.3
P12	95.5	86.4	64.3	100	88.9	66.7	86.4	86.4	78.6	77.8	77.8	100
P7	78.3	85.7	85.7	62.5	100	83.3	100	90.9	57.1	100	100	100
P5	79.2	84.2	81.3	57.1	100	100	95.7	100	53.3	100	90.0	100
P9	81.0	88.2	91.7	80.0	71.4	75.0	95.5	95.5	78.6	88.9	100	83.3
P10	81.0	88.2	91.7	90.0	100	87.5	95.5	90.9	85.7	100	100	100
P11	91.7	88.9	93.8	100	100	100	100	100	75.0	91.7	100	100
Mean	79.0	77.7	76.3	77.7	82.8	73.9	89.3	80.2	65.6	89.1	82.9	93.9
SD	9.7	12.3	15.1	18.0	17.9	21.6	10.2	18.1	14.3	11.1	16.0	8.4

Table 4 Legend: scores are percentages of correct response

6. Semantic control tests

6.1. Procedure

A set of semantic assessments were repeated in the two weeks before and after training, to characterise any changes in performance over the training period. After training we retested the ambiguity task (dominant vs. subordinate without cues, for all patients but P12), the object-use task (for all patients but P12) and a subset of 26 of the harder Camel and Cactus Test trials. Individual analyses were performed on overall accuracy (without distinguishing conditions) to retain sufficient statistical power.

6.2. Results

(i) The 26-items CCT showed a significant increase in accuracy after training [t(10) = 3.04, p = .012; pre-training M(SD) = 70.3 (12.8); post-training M(SD) = 79.4 (9.9)]. This suggests that the group did show some generalisation of the training. Individual analyses showed that only patient (P3) significantly improved after training [McNemar: 4.17, p = .041]. However, all patients except P1, P12, P7 and P10 showed a positive change in accuracy (≥ + 7.7 % correct) after training. See Figure 5.

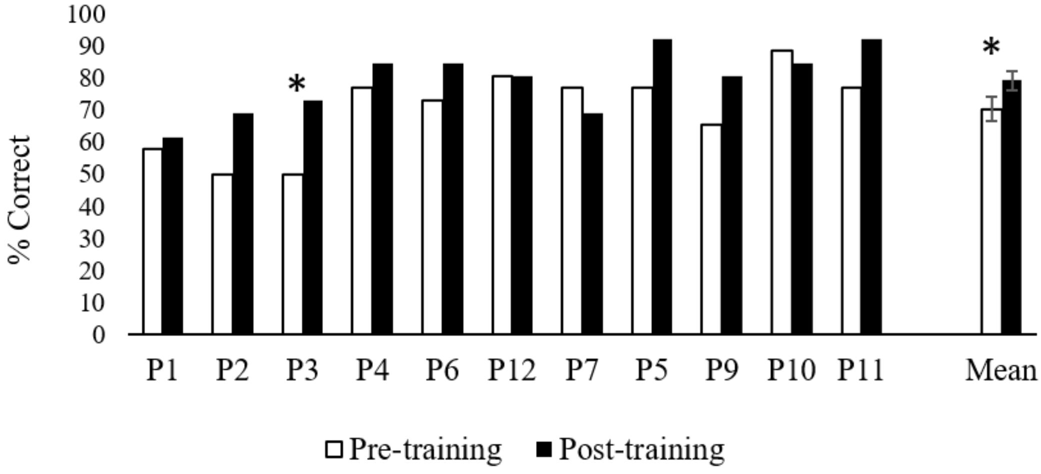

Figure 5. Camel and Cactus test pictures: effect of training.

* = significant (p < .05) improvement after training. Error bars show SEM.

(ii) For the ambiguity task, a 2-by-2 ANOVA looking at the effect of time (pre vs. post training) and dominance (dominant vs. subordinate meaning) revealed no change in accuracy over time [F < 1], lower accuracy for subordinate trials [main effect of dominance: F(1,9) = 32.61, p < .001] and no interaction [F < 1]. None of the patients showed a significant improvement pre vs. post accuracy [McNemar p > .180]. See Figure 6.

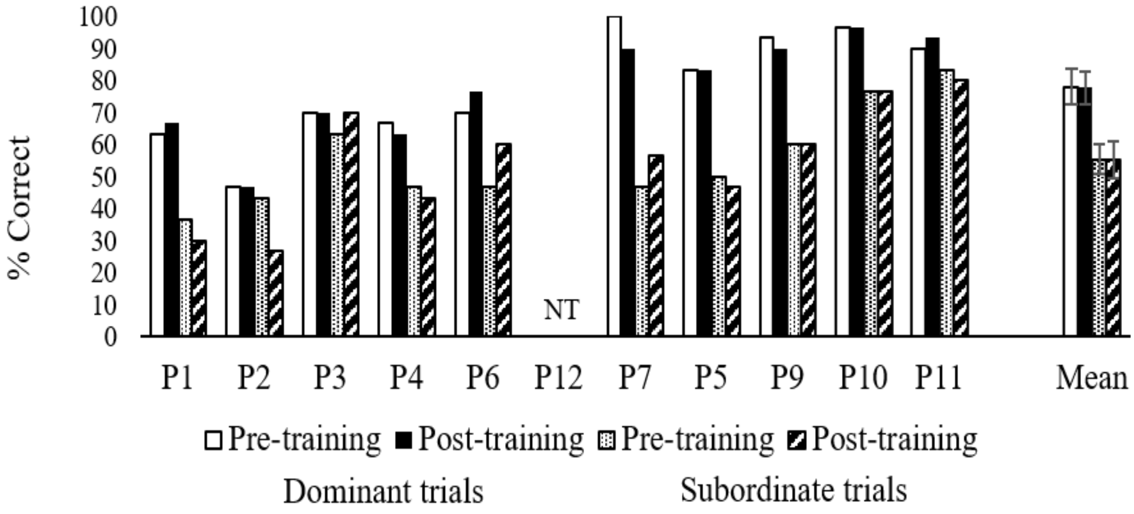

Figure 6. Ambiguity task: effect of training

. NT = not tested. Error bars show SEM.

(iii) The object use task also showed no change across pre- and post-training sessions [main effect of time: F < 1] and better accuracy for canonical vs. alternative use trials [F (1, 9) = 74.29, p < .001] with no interaction [F < 1]. One patient (P4) showed higher accuracy after training [McNemar: 5.50, p = .019]. See Figure 7.

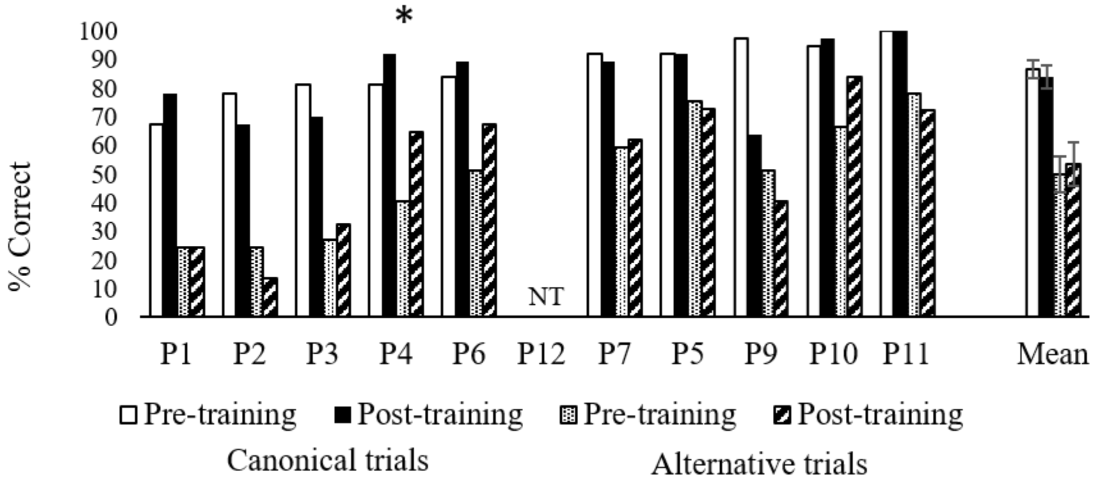

Figure 7. Object use task: effect of training.

* = significant ($p < .05$) improvement after training. NT = not tested. Error bars show SEM.

7. Episodic memory tests

Since the work presented in this thesis showed parallel deficits of controlled retrieval in semantic and episodic memory tasks in patients with SA, we also presented two paired-associate tests of episodic memory, both before and after training, to investigate whether improvements in controlled semantic retrieval after training (i.e., improvements in retrieval that generalise to untrained items or tasks) would similarly facilitate performance on measures of episodic retrieval. Moreover, since some patients fail to improve their control of retrieval with training, yet strengthen specific semantic associations that were trained repeatedly, we also asked whether, for more impaired patients, there was a cost to training, in circumstances in which trained semantic associations could act as strong competitors in episodic tasks.

7.1. Episodic Experiment 1: Procedure

This followed the design of Experiment 1 in Chapter 2 where this task elicited higher rates of semantically-driven false memories in patients with semantic control deficits. We examined whether training flexibility in semantic retrieval would increase episodic memory accuracy and reduce semantically-driven false memories. Participants were instructed to try to remember which two words were presented together as a pair. There were two manipulations during the learning phase, semantic relatedness and episodic strength. Word-pairs were either semantically related (e.g. WEDDING – DRESS) or unrelated (e.g. CHURCH – HOLIDAY); they were also repeated five times or only once (see Fig. 4A Chapter 2). In each encoding block, eight word-pairs were presented consecutively on a screen using E-Prime 2.0. Probes and targets were initially presented individually for 1000ms and then the word-pairs appeared on the screen for 3000ms. The researcher read all words aloud at the time of presentation. Immediately after encoding, participants performed a recognition task in which they were asked to select the word previously presented with the probe, from amongst four response options. On each trial, there was a novel semantic distractor related to the probe (SEM); an episodic distractor that was a target on a different trial (EP); and a semantic-episodic distractor that was both semantically related to the probe and a target for another probe (SEM+EP). Words were read aloud by the experimenter and patients indicated their choice by pointing. The order of recognition trials was randomised for each participant. There were eight-word pairs per learning list, and a total of eight lists. Each participant was randomly assigned to four out of the eight lists, two presented before training and two presented after training, providing sixteen trials for analysis at each time point. Stimuli slightly differed from those presented in Experiment 1 of Chapter 2, in order for each list to have both related and unrelated trials. A list of stimuli is provided in Appendix Table 3. This experiment was administered to six patients taking part in the training study (P1, P2, P3, P5, P6 and P9), all of whom had been tested previously (see Chapter 2).

7.2. Episodic Experiment 2: Procedure

In this paired-associate task, items were presented with semantic distractors that were trained to be semantically-linked to the probe word in the semantic training task. This determined the extent to which repeated practice in retrieving specific semantic links would elicit false memories for those specific associations. As in Episodic Experiment 1, participants were instructed to remember word-pairs. As before, they were presented five times or only once during the learning phase, but in this experiment, they were all semantically unrelated (e.g. BLUEBERRY – PORT) and probes were not re-presented with different targets in different phases of the experiment. During the recognition task, the target was presented alongside a medium or weakly-related item repeatedly paired with the probe during the six semantic training sessions (e.g. BLUEBERRY – PUNNET) and two unrelated distractors. There were eight word-pairs per learning list, and two lists. Each participant was tested on the same two lists, before and after training, providing sixteen trials for analysis at each time point. List order was randomised across participants. The complete list of stimuli is provided in Appendix Table 4. Other aspects of this task mirrored those detailed for Episodic Experiment 1. It was administered to the same participants as Episodic Experiment 1, plus P12.

7.3. Episodic Experiment 1: Results

Group level analysis: A 2 by 2 ANOVA looking at relatedness at encoding (related vs. unrelated) and time (pre vs. post training) replicated previous results: patients showed better accuracy for related trials [main effect of relatedness F(1,5) = 12.66, p = .016]; however there was no difference in accuracy before and after training [F(1,5) = 1.84, p = .233] and no interaction [F < 1]. Individual analyses were not performed on related and unrelated trials separately as there were insufficient numbers of trials. Results showed that P6's accuracy was significantly higher after training [χ^2 (1) = 6.15, p = .013], and this effect approached significance for P2 [Fisher's exact test: p = .083]; in both cases accuracy for unrelated trials was higher after training (see Fig. 8) and the number of semantic errors after training was numerically lower. Other patients did not show a change in accuracy [p ≥ .710] and there was no decrease in false memories.

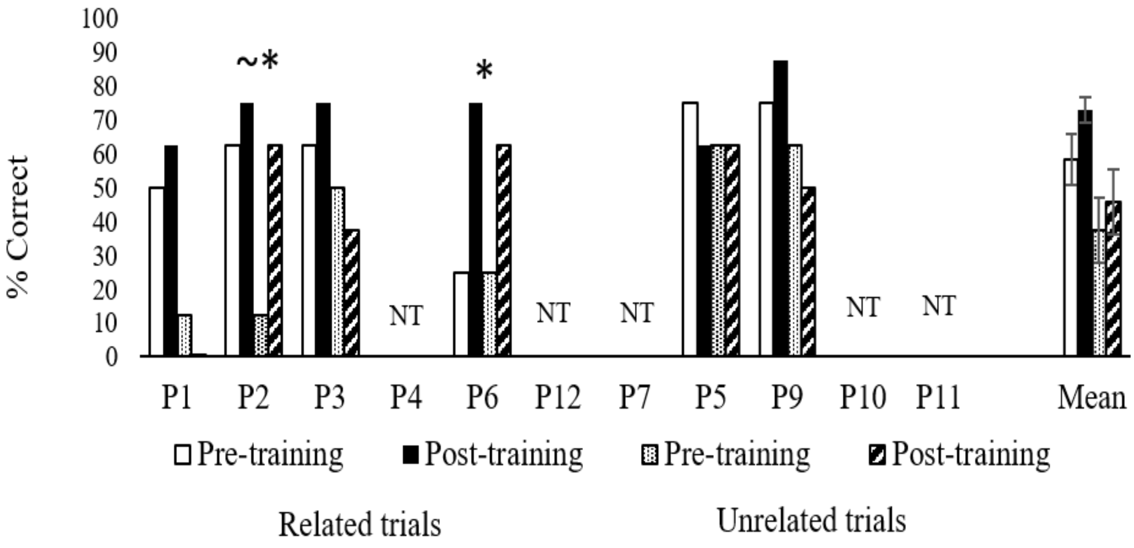

Figure 8. Episodic Experiment 1: effect of training.

NT = not tested; * = significant (p < .05) improvement after training; ~* = improvement after training approaching significance (p = .083). Error bars show SEM.

7.4. Episodic Experiment 2

There was no change in accuracy across the group following semantic training in Episodic Experiment 2 [t < 1]. We expected patients with strong training effects yet no generalisation to untrained items to have poorer episodic accuracy after training, since this task presented trained items as semantic distractors. One patient (P1) showed poorer performance post-training [McNemar = 7.11, p = .004]. All other patients showed no difference in accuracy.

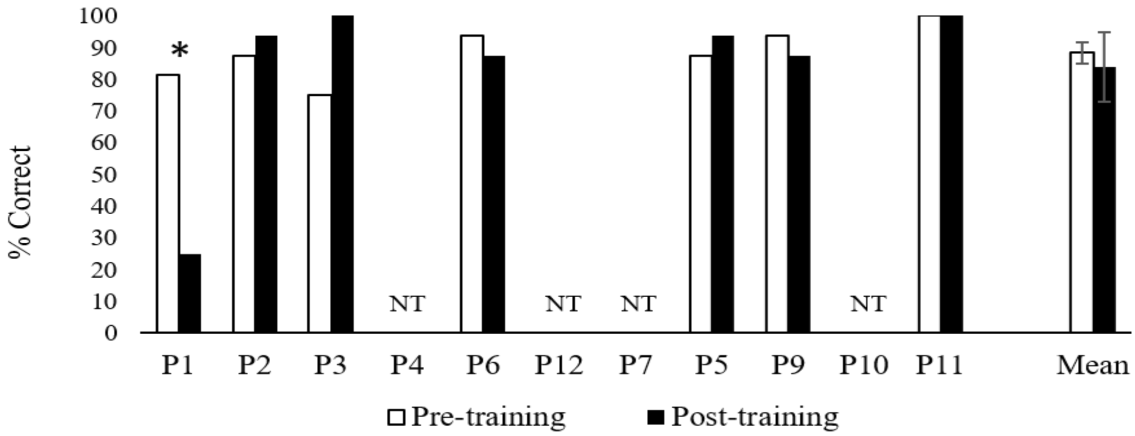

Figure 9: Episodic experiment 2: effect of training

NT = not tested; * = significant (p < .05) improvement after training; ~* = improvement after training approaching significance (p ≤ .083). Error bars show SEM.

8. Generalization of training effects among memory domains

Individual and group-level differences in accuracy before and after training (and for last vs. first session in the Training task) are summarized in Table 5. Out of the seven patients who took part in the study and were tested at baseline and after training for episodic memory, six showed signs of generalization on a non-trained semantic control task, i.e. improvement in CCT. In Episodic task 2, all six of these cases were either near ceiling (≥ 87.5 %) or showed a positive change after training. On Episodic task 1, two patients showed increased performance (P2, P6), one was not tested and the remaining three showed no improvement (i.e. P3, P5, P9).

Table 5. Training effects

	Training task		Semantic Associative task (no feedback)		Ambiguity Task		Object Use				
Patient ID	Repeated	Novel	Trained	Untrained	Dominant	Subordinate	Canonical	Alternative	CCT Pictures	Episodic 1	Episodic 2
P1	**37.5** ↑	-8	**25.0** ↑	-1.7	3.3	-6.7	10.8 ↑	0.0	3.8	0	**-56.25**
P2	5	**24** ↑	8.3↑	0.0	0.0	-16.7	-10.8	-10.8	19.2 ↑	**31.3** ↑	6.25 ↑
P3	12.5 ↑	4	12.5 ↑	-6.9	0.0	6.7 ↑	-10.8	5.4 ↑	**23.1** ↑	0	25 ↑
P6	10 ↑	-4	4.2	0.0	6.7 ↑	13.3 ↑	5.4 ↑	16.2 ↑	11.5 ↑	**43.8** ↑	-6.25 c
P5	5 c	4 c	8.7 ↑	5.1 ↑	0.0	-3.3	0.0 c	-2.7	15.4 ↑	-6.3	6.25 ↑
P9	10 ↑	-8	16.7 ↑	5.4 ↑	-3.3 c	0.0	-33.4	-10.8	15.4 ↑	0	-6.25 c
P11	10 ↑	16 ↑	-3.1 c	2.6 c	3.3 c	-3.3	0.0 c	-6.2	15.4 ↑	NT	0 c
P4	10 ↑	-16	16.7 ↑	10.3 ↑	-3.3	-3.3	10.8 ↑	**24.3** ↑	7.7 ↑	NT	NT
P12	**22.5** ↑	-4	-4.2	0.0	NT	NT	NT	NT	0.0	NT	NT
P7	**20** ↑	12 ↑	16.7 ↑	3.4	-10.0	10.0 ↑	-2.7 c	2.7	-7.7	NT	NT
P10	10 ↑	8 ↑ c	6.3 ↑c	5.4 ↑	0.0 c	0.0	2.6 c	17.1 ↑	-3.8	NT	NT
Mean	*	n.s.	*	n.s.	n.s.	n.s.	n.s.	n.s.	*	n.s.	n.s.

Table 5 Legend: scores show the difference between in percentages of correct responses between last vs. first session (for the Training Task) and post vs. pre-training (for the remaining task). Bold and underlined numbers denotes significant differences as per individual analysis reported in main text, whereas bold numbers denotes differences approaching significance. Baseline task = semantic associative task without feedback; CCT = Camel & Cactus; Episodic 1 = Paired associates task; Episodic 2 = Paired associates task with trained items; n.s. = non-significant; * = significant; NT = not tested; ↑ = performance higher after training, i.e. more than 5% correct; c = ceiling performance or near ceiling performance (≥ 87.5 %) before and after training.

9. Discussion

In a group of semantic aphasia (SA) with multimodal semantic deficits stemming from poor semantic control, we assessed the effects of a training task designed to encourage flexibility in the retrieval of semantic associations. We found improvement in the accessibility of semantic associations; however, this effect was more marked for items trained repeatedly. There was little evidence of generalisation of this training effect to novel items in the training task itself. Nevertheless, the group showed some generalisation because a similar yet untrained task involving the retrieval of semantic associations (Camel & Cactus Test) also improved with training.

Training often does not generalise to new items – for example, in picture naming therapies for participants with aphasia (Marshall *et al.*, 1990; Davis and Pring, 1991; Pring *et al.*, 1993). Training effects also typically fail to generalise to untrained tasks – for example, following protocols to increase cognitive control or working memory (Melby-Lervåg and Hulme, 2013). Our results are broadly consistent with this pattern. However, the group-level effect on one of our background semantic tasks (Camel & Cactus Test) is promising, suggesting this type of training might be more broadly beneficial. There is also some evidence that some individuals in our cases-series benefitted more than others: although our single-subject analyses had substantially-reduced statistical power relative to the group-level analyses, we found that one individual case showed an effect of the semantic training task on novel trials, while three individuals showed significant changes on trained trials. It might be that more intensive training over a longer period, with more sessions, or more trials per session, could produce a larger effect. In addition, it might be possible to optimise the training to encourage relevant patterns of retrieval across different contexts. For example, the word BANK could be trained on associations of its dominant (i.e. financial institution; e.g. BANK – MONEY, not MORNING, HEART or CHILD) or subordinate (i.e. edge of a lake/river; e.g. BANK – RIVER, not DRESS SONG or BIRTH) meanings on consecutive trials. This could promote flexible retrieval of conceptual knowledge according to the task requirement.

In line with the central focus of this thesis, the patients were also asked to complete tests of episodic memory before and after the semantic training. We hypothesised that there might be two distinct effects of semantic training, given the findings in Chapters 2 and 3. First, any patients who successfully generalised the effects of semantic training to new items were expected to have a greater capacity for controlled semantic retrieval. A current debate in the literature concerns whether the same neurocognitive processes underpin controlled retrieval for semantic and episodic representations. If these processes are indeed shared, patients who show improvements on novel semantic associations following the training protocol might also improve in their capacity to avoid semantic distractors during episodic memory judgements. Secondly, those patients who effectively learn about associations that are repeated many times during the training task but without generalising this learning to novel (untrained) semantic associations might have greater difficulty disregarding these same trained associations in episodic memory judgements.

Specific cases in this case-series provide some support for both of these views. First, P2 was the only patient to show an improvement in performance on the novel trials in the training task, and also showed the second biggest improvement in the Camel and Cactus test following training. This suggests that his capacity to control semantic retrieval was benefitted by the training protocol. Interestingly, the training also somewhat improved his performance on Episodic Experiment 1 (Paired Associate Learning without trained distractors; the difference between pre- and post-training performance approached significance). Consequently, his capacity to control both semantic and episodic retrieval may have increased. A second patient, P6, also showed improved performance on Episodic Experiment 1 following training. Although there was no evidence of generalisation of the semantic training to novel items for this case, P6 showed improvement for subordinate trials of the ambiguity task, alternative trials of the object use task and the Camel and Cactus test, all of which suggest generalisation. Both patients showed improvement on the unrelated episodic memory trials after training, perhaps because these trials taxed the capacity to generate novel associations between items that had to be linked episodically. This is in line with the notion that the training may have augmented control over conceptual retrieval in these cases. In addition, these two patients were the only ones out of six that were tested who showed a reduction in the numbers of semantically-related items chosen in the episodic memory task, consistent with the expected effects of improved control over memory retrieval.

There was also evidence that learning about specific associations without generalisation could disrupt episodic memory judgements when these same trained semantic items were presented as distractors. Three cases (P1, P7 and P12) showed a pattern of improved retrieval of trained associations without generalisation (P1 and P7 showed this pattern also in the semantic associative task without feedback). These cases also showed some of the smallest improvements on the Camel and Cactus test following training, confirming this lack of generalisation. One of these patients was subsequently tested on Episodic Experiment 2 (Paired Associate Learning with trained distractors; P1). This individual showed a sizable reduction in accuracy in this episodic memory test following the semantic training, because she tended to choose the trained distractor instead of the target. This demonstrates that semantic training in patients who show the hallmarks of poor semantic control can have a detrimental effect on performance when semantic information is competing with the relevant response. This patient was also the most impaired in the case-series, showed little improvement in the CCT and therefore likely to have the least flexible semantic retrieval across tasks.

In conclusion, patients with semantic control deficits may benefit from training tasks that encourage the retrieval of diverse types of semantic associations. There were clear individual differences in our sample, suggesting not all patients will be able to generalise the effects of training to untrained items or tasks. Our results confirm the need to develop more effective training protocols that target executive processes in patients with aphasia, since this kind of training is thought to be more likely to produce functionally-meaningful improvement (Vas *et al.*, 2016; Han *et al.*, 2018). This may be the case especially in people with semantic aphasia who have difficulty regulating their retrieval of conceptual information, yet little loss of semantic knowledge from long-term memory. Not enough is yet known about the optimisation of such cognitive training – for example, too much repetition of the same items might reduce mental flexibility, as these items become too dominant within the mental landscape. However, too little repetition might reduce the opportunity for patients to accurately retrieve diverse types of associations for themselves, and thereby acquire more effective retrieval strategies. Further work is also needed to establish the intensity of training required to maximise recovery and the role of individual variability on these parameters.

CHAPTER 5

Discussion chapter

1. Introduction and research themes

This thesis investigated whether patients with multimodal semantic control difficulties following stroke (cf. semantic aphasia; SA) showed parallel deficits in the episodic domain. This is an important research question because neuropsychological studies have demonstrated a dissociation between a) degraded semantic knowledge in the context of good memory for recent events (for example, in semantic dementia, SD) and b) deficient formation and retention of episodic memories, alongside preserved semantic performance (in amnesia; Graham and Hodges, 1997). However, more recently, it has been shown that multimodal semantic deficits can arise both as a result of loss of conceptual information and as a consequence of deregulated semantic retrieval (Jefferies and Lambon Ralph, 2006). Patients with SA have intact conceptual knowledge, yet they find it difficult to shape retrieval according to circumstances, following damage to left inferior frontal gyrus (LIFG) and/or other regions in the wider neural network associated with semantic control (Jefferies and Lambon Ralph, 2006; Gardner *et al.*, 2012; Noonan *et al.*, 2013). During semantic tasks, these patients show sensitivity to cues and miscues (Corbett *et al.*, 2008; Jefferies *et al.*, 2008b; Soni *et al.*, 2009; Noonan *et al.*, 2010) and they find it difficult to discard dominant aspects of knowledge which are not relevant for the task (Noonan *et al.*, 2010). These problems extend beyond language, to affect sound, picture and action understanding (Corbett, Jefferies and Lambon Ralph, 2009; Corbett, Jefferies, Ehsan, *et al.*, 2009), suggesting that semantic control processes interact with heteromodal semantic representations. This raises the question of whether controlled retrieval mechanisms also dissociate across semantic and episodic tasks, or alternatively if the neurocognitive processes that support controlled aspects of semantic cognition are also relevant for episodic retrieval. Functional neuroimaging studies have implicated overlapping areas (including left inferior frontal gyrus; LIFG; Badre and Wagner, 2007) in controlled retrieval across both semantic and episodic tasks; however, this pattern has been interpreted in a variety of ways and it is unclear if the LIFG activation seen during episodic judgements is necessary for good episodic as well as semantic retrieval (e.g. see Han, O'Connor, Eslick and Dobbins, 2012). In this context, neuropsychological research has clear theoretical as well as clinical and practical significance. Consequently, this thesis investigated whether SA patients showed parallel difficulties in episodic and semantic memory, to our knowledge for the first time. We used both paired-associate tasks and source memory paradigms which tap both verbal and non-verbal aspects of episodic memory.

We selected patients with aphasia following left-hemisphere stroke, who had multimodal semantic control deficits, in line with previous studies of SA (e.g. Jefferies and Lambon Ralph, 2006). Mid to posterior-LIFG was damaged in all cases. In Chapter 2 we compared semantic and episodic paired-associate tasks in order to investigate whether the patients exhibited parallel deficits in both memory domains, i.e. a) multimodal deficits affecting both verbal and non-verbal tasks; b) sensitivity to cues that reduce the need to internally-constrain retrieval, c) difficulties discarding dominant yet currently irrelevant representations within both semantic and episodic tasks (e.g., strongly-related semantic distractors related to the meaning of the probe or proactive interference from recently acquired episodic memories) and d) difficulty selecting semantic vs. episodic information in line with the demands of the task. Given that the patients' semantic deficits are thought to stem from difficulties regulating competition between active representations, in Chapter 3 we further investigated if patients' episodic memory was impaired in source memory tasks in which the degree of competition between sources was manipulated. Source memory is a form of episodic memory that strongly activates LIFG (Dobbins *et al.*, 2002; Hayes *et al.*, 2011; Han *et al.*, 2012) and this might reflect the need to control competition between alternative sources. The sources were either meaningful or non-meaningful and they were perceptually similar or incongruent with existing knowledge (creating high competition) or more distinct with regards to spatial and self-referential processing (reducing competition). In the final empirical chapter (Chapter 4), we investigated the consequences of these findings for neuro-rehabilitation. We trained patients using a task focussed on promoting the flexible retrieval of conceptual knowledge and tested the effects of this training for both semantic cognition and episodic memory tasks. We were interested in whether improvements in controlled semantic retrieval would generalize to episodic retrieval, and also whether individuals who failed to generalise the effects of practising specific semantic associations to new items would find these items more distracting when attempting to recall episodic associations.

The findings help to separate several accounts of the contribution of LIFG to memory. Neuroimaging studies have suggested at least three putative roles of LIFG: a) LIFG may have a largely exclusive role in verbal semantic processing and/or language control (e.g. see Hirshorn and Thompson-Schill, 2006); b) LIFG may primarily support heteromodal semantic processing and it is recruited during episodic memory tasks to resolve competition between concepts associated with events (e.g. see Han *et al.*, 2012); or alternatively, c) LIFG resolves competition both within memory systems and between episodic and semantic representations (e.g. see Badre and Wagner, 2007). Investigations comparing episodic recall in verbal and non-verbal tasks addressed the first of these accounts; comparisons of semantic interference and proactive interference from recently-encoded events are relevant to the second account; studies of semantically-mediated episodic false memories, and episodically-mediated semantic interference effects help to test the predictions of the final account.

This chapter summarizes the main findings from previous chapters in order to establish which of these accounts of LIFG function is best able to capture the findings. Theoretical implications are considered. Finally, this chapter describes limitations of the research and outlines future directions.

2. Patients with Semantic Aphasia show parallel deficits in both semantic and episodic memory

In Chapter 2 we assessed episodic memory in patients with SA to test whether deficits were parallel across semantic and episodic tasks. SA patients have difficulty retrieving links between concepts (e.g. CAMEL – CACTUS) in the presence of alternative associations that are not relevant for the task at hand (e.g. SUNFLOWER, TREE, ROSE). In such circumstances, control demands are high because the required link between concepts is not dominant in the representational system and irrelevant associations can cause interference. In this chapter, we extended this work to verbal paired associate tasks tapping episodic memory. After learning lists of item-pairs (e.g. SUN – PHOTO), participants were asked to retrieve the second member of the pair when probed with the first (e.g. 'What was SUN paired with?'). This task requires a novel link between items to be recovered in the face of potential interference from both existing knowledge (i.e. SUN – CLOUD, eliciting false memories), and irrelevant episodic associations trained shortly before the critical judgments (giving rise to proactive interference). Previous work in the semantic domain has shown that when control demands are high, cues can increase performance in SA patients to near-normal levels, presumably because these cues reduce the need for internal constraint over retrieval (Jefferies and Lambon Ralph, 2006; Jefferies *et al.*, 2008b; Soni *et al.*, 2009; Noonan *et al.*, 2010). Here we tested if cues (probing the initial phonemes of the target, e.g. S…) were also helpful in episodic memory. In addition, we examined whether interference was promoted not only by semantic links in episodic tasks, but also by episodic memories (i.e. newly learnt associations) in semantic tasks. If LIFG is responsible for resolving competition between memories both within and between these representational systems, difficulties should be found in both instances. Finally, since SA patients' semantic difficulties are multimodal (i.e. extend across both verbal and pictorial stimuli; Corbett, Jefferies and Lambon Ralph, 2009), we expected to find episodic impairment using both words and pictures.

We first tested sensitivity to cues using the verbal paired associate recall task from the Wechsler Memory Scale. Accuracy was impaired relative to controls' and patients' erroneous responses were often words semantically related to the probe (e.g. they responded HEAVEN -instead of LADDER, when probed with STAR), but when phonological cues were provided patients' performance reached controls', showing initial evidence of episodic deficits when control demands are high. Despite this impairment, face recognition from the Wechsler Memory Scale was intact, showing that the SA cases were not amnesic. Since not all the patients could attempt cued recall, due to poor language production, we further assessed interference using a recognition version of the verbal paired-associates task, in which both semantic and episodic associations were available. In Experiments 1 and 3, patients were trained on unrelated and related (e.g. SUN – PHOTO or HOTEL – GUEST) word and picture pairs respectively. The patients' tendency to select semantic distractors (e.g. CLOUD or BEDROOM) during retrieval was measured. In the verbal version (Experiment 1), patients found it more difficult to learn new associations unsupported by existing knowledge (i.e. they had significantly lower performance for unrelated pairs), showed intrusion of semantic knowledge (i.e. they chose semantic distractors – e.g. CLOUD – significantly more often than controls) and when their response was related to the probe they had little insight about their accuracy. In verbal paired associates when existing knowledge was not supportive at encoding (i.e., all word pairs were unrelated; Experiment 2), performance was still impaired, suggesting that individuals with SA have difficulty forming and retrieving novel links between semantically-unrelated items, even when interference from long-term semantic knowledge was minimised (i.e. semantic distractors were not available). Together these results show that episodic memory benefits from coherence with existing knowledge in SA but retrieval is also prone to false memories when irrelevant yet dominant semantic distractors are presented alongside the target.

The design of Experiments 1, 2 and 3 also tested interference from episodic memories. These experiments followed an AB/AC structure (e.g. 1st list: SUN – PHOTO, 2nd list: SUN – STEEPLE), designed to elicit proactive interference. Patients showed an abnormal rate of interference from previously learnt episodic associations (in Experiment 1 and 2 but not in Experiment 3). Finally, to examine interference from episodic memories during semantic decisions, a novel task was designed (Experiment 4). Participants were trained on associations between unrelated words (such as TEA-MONEY) and, after showing evidence of consolidated learning, performed a semantic association task where they had to retrieve links between concepts (such as TEA - LEAVES). Critically, in half of the trials, one of the options was the episodic trained distractor (i.e. MONEY) – and patients but not controls showed impaired performance when episodic associations where available. The number of semantic errors made in Experiment 1 (i.e. in an episodic task) and episodic errors in Experiment 4 (i.e. in a semantic task) positively strongly correlated, as did accuracy for semantic and episodic control tasks. Finally, patients' accuracy was equally impaired using words and pictures (Experiment 1 and 3), suggesting that control processes may interact with heteromodal memory representations also in the episodic domain.

To summarize, SA patients presented a) deficits beyond semantic cognition when retrieval demands were high (e.g. without cues), b) difficulty suppressing irrelevant semantic knowledge but also interference from recently learnt material during both semantic and episodic tasks and c) multimodal episodic and semantic retrieval deficits. Collectively, these results show evidence of parallel deficits across memory domains. The evidence is in line with an equivalent role of LIFG in resolving competition between memory representations that are not only verbal in nature. However, one potential difference between modalities was observed: in the non-verbal task, there was no evidence of an increased rate of semantic false memories or proactive interference, although overall accuracy was still lower for patients than for controls. Picture stimuli are less abstract and more distinctive and rich than words; in addition, the hippocampus – which is intact in the patients – has strong coupling with visual-spatial regions. This might have helped patients discard novel semantically-related stimuli (i.e. semantic false memories) and items presented in previous trials (i.e. proactive interference). In Chapter 3, we further examined episodic memory using mostly non-verbal tasks. We used source memory tasks requiring decisions between two alternative options that remained constant across trials (preventing participants to take advantage from perceptual novelty to discard the competing option). This also allowed to identify circumstances when patients failed to resolve competition using non-verbal material.

3. Episodic deficits in patients with SA reflect difficulty resolving competition

In Chapter 2 we provided evidence that SA patients have difficulty resolving competition both within and between semantic and episodic domains. In Chapter 3 we used another memory paradigm (item familiarity vs. source memory) tapping control to assess circumstances when these deficits arose using mostly non-verbal material. Judging whether an item has been encountered before (i.e. item familiarity) does not require substantial control, because the specific features of the item itself act as a cue for recognition. In contrast, remembering which of two similar sources an item was paired with has higher control demands. This is because in order to retrieve the source, one has to resolve competition between two (or more) potential options. The contrast of source with item memory activates LIFG in fMRI studies (Dobbins *et al.*, 2002; Dobbins and Wagner, 2005; Han *et al.*, 2012; Barredo *et al.*, 2015) and we therefore expected SA patients with deficits of controlled retrieval to show impaired source but not item memory.

In addition, we hypothesised that control demands – and therefore the magnitude of the episodic memory deficit in SA – would be increased when competing sources are similar and lack distinguishing features. For example, it can be hard to remember the exact birthday on which a particular present was received, because birthdays share common features. However, if the present in question was given for a birthday with unique characteristics, e.g. 18th birthday, discarding other options becomes easier. In Chapter 3, spatial location, existing knowledge and self-referential processing were used to manipulate distinctiveness and competition between sources.

In Experiment 1, sources were either a blue or a red box positioned in front of the participant at encoding. Source memory was tested in two conditions. In the harder condition (i.e. no spatial cue) participants could only rely on the colour to distinguish sources, since the position of the boxes at encoding and retrieval did not match (i.e. boxes' position at retrieval was alternated across trials). The blue and the red boxes constituted two sources with strongly overlapping features and therefore high-levels of competition (i.e. the sources were only distinguishable by colour). In the easier condition (i.e. spatial cue), box position was maintained between encoding and retrieval, so participants could rely on spatial information to separate similar memories (e.g. the LEMON was not only in the "blue" box, but it was also on the participants' right hand-side). We found that patients showed spared item memory but greater source memory impairment when there were no spatial cues (i.e. when there were fewer features to distinguish the sources). We therefore found evidence of source memory impairment when competition between sources was likely to be high.

In contrast to Experiment 1, in which sources were different-coloured boxes, in Experiment 2, sources were rich and meaningful: they were shops such as BAKERY. In half of the trials, items were allocated to sources congruent with semantic knowledge (LEMON in GREENGROCER); in the other half they were paired with sources that were incongruent with semantic knowledge (CARROT in the BAKERY). In the incongruent trials, prior knowledge was in competition with the encoded memory (i.e. CARROTS are usually found at the GREENGROCER), whereas in the congruent condition, episodic memory was supported by existing knowledge. We again found that patients had spared item memory and impaired source memory: this impairment was driven by the "incongruent" trials in which items were placed within a shop that conflicted with long-term semantic knowledge. This condition was expected to produce interference between memory systems – i.e. between episodic representations relevant to the task and semantic knowledge. Therefore, the results of Experiments 1 and 2 may be explained in a similar way: there was a greater source memory impairment when the sources within episodic memory directly competed with each other, or competed with background knowledge irrelevant to the episodic memory task. These findings, taken together, complement the results of Chapter 2, by showing an episodic memory control deficit in SA even when a non-verbal paradigm was used.

Within Chapter 3, we also explored the possibility that self-reference could ameliorate the source memory deficit in SA. Self-relevant items show perceptual, memory and attentional-advantages and the self as a 'source' is likely to be highly meaningful and distinctive. Better memory for self-relevant items is seen in the healthy population (i.e. self-reference effect, SRE, Symons and Johnson, 1997) and is thought to rely on medial PFC (Kelley *et al.*, 2002; Philippi *et al.*, 2011), a region typically intact in patients with SA. Therefore, in Experiments 3 & 4 within Chapter 3, we tested whether self-referential processing could alleviate SA patients' problems in resolving competition between sources. In Experiment 3 participants were instructed to try to remember whether an item was allocated in their or the examiners' shopping basket. In Experiment 4, participants were instructed to encode personality-trait adjectives with reference to either the self or the Queen, or to judge whether words were presented in lower vs. uppercase. These tasks have been previously shown to elicit a self-reference effect and mPFC recruitment (Cunningham *et al.*, 2008; Turk *et al.*, 2011; De Caso *et al.*, 2017). In Experiments 3 and 4, we found patients' source memory did not differ from controls' and self-reference was equally beneficial in both groups. These experiments are consistent with the view that self-reference can reduce competition between sources, reducing episodic memory impairment in SA. Self-referential processing is likely to support source separation for several reasons: the "self" constitutes a very distinctive and unique concept, self-referenced material is salient and can promote motivation for memory (Sui *et al.*, 2015).

To summarize, the results of Experiments 1, 2, 3 and 4 within Chapter 3 provide further evidence that the episodic memory impairment found in SA patients reflects difficulty resolving competition between memory representations. This chapter also confirmed that these difficulties are seen in a highly non-verbal paradigm, building on the findings of Chapter 2, which was restricted to paired-associate learning.

4. Exploring training generalization across memory domains

Having established that the nature of SA patients' deficits is consistent with a failure to control competition within and between episodic and semantic memories, we investigated whether training focussed on promoting a more flexible and controlled pattern of conceptual retrieval would generalize to untrained semantic trials and episodic retrieval. In Chapter 4, we trained SA patients using a semantic associative task, administered for six sessions over two weeks, with feedback illustrating the associative link between concepts. For example, for the association between TAXI and PHONE, an image of a taxi phone was provided, and the association was explained to the patients if unclear. Distractor words were related to the target to increase control demands (e.g. E-MAIL, FAX) and trials were either repeated across all sessions (trained) or they were novel (untrained). Given that patients with SA showed parallel deficits in both semantic and episodic memory tasks, training effects were evaluated by assessing performance at baseline and after training in both domains. We explored generalization effects by testing i) semantic performance over the training sessions for both trained and untrained trials; ii) training effects on an equivalent version of the semantic associative task without feedback; iii) training effects on tasks tapping semantic control (i.e. Ambiguity, Object-use and Camel and Cactus tasks); iv) training effects on two episodic tasks tapping control, one of which presented trained semantic associations as distractors. This allowed us to test two alternative accounts of the training effects. If patients chose trained semantic associations in the episodic memory task, the effect of training could be attributed to learning of specific associations, as opposed to an improvement in controlled retrieval (i.e. the capacity to shape activation according to task and context). In contrast, if performance on episodic memory tasks was improved after training, with little or no interference from trained associations, we would conclude that controlled retrieval processes were strengthened, with advantages for both semantic and episodic performance.

We found that performance improved over the course of training for trained trials and that there was generalization to a non-verbal semantic control task (i.e. performance was significantly higher after training for the picture version of the Camel and Cactus task, CCT). Performance on the episodic tasks did not improve across the group. However, at the individual level, we found that two patients did show this pattern: they showed higher accuracy and made fewer semantic errors on a paired-associate learning task after training. One of these two also showed better performance for untrained semantic judgements in the training task (i.e. generalization to untrained items). In addition, one patient who improved on the trained semantic associations, yet failed to generalise this improvement to untrained items, showed poorer episodic memory performance when these trained semantic associations were presented as distractors. This patient was at the more impaired end of the case series, and did not appear to evidence of improved memory control following training.

While only two of the case-series showed good evidence for generalisation, these results are encouraging as they suggest that at least some individuals with SA may still be able to achieve better semantic cognition when controlled retrieval is practised with feedback. In addition, individual analysis provided evidence consistent with the idea that controlled processes are shared across domains. In fact, patients who showed stronger generalization to semantic memory, had better episodic memory after training, whereas in instances where there was lack of generalization to other semantic measures, training had the detrimental effect of promoting false memories by enhancing rigid retrieval of the newly-trained semantic associations. This is in line with the previous findings that the over-application of dominant semantic links can interfere with episodic judgment by promoting false memories based on dominant associations.

Future studies should seek to address why this type of training was more beneficial for some patients than others. We suggest that the current training task fails to directly promote competition resolution because patients are not directly trained to retrieve relevant associations according to different contextual requirements and this could affect some patients more than others. For example, training the same concepts during different contextual requirements on subsequent trials (e.g. TAXI - PHONE + TAXI – AIRPORT + TAXI - MONEY) could promote patterns of flexibility.

5. Summary of evidence in support for parallel semantic and episodic deficits

This section summarizes the evidence supporting parallel semantic and episodic deficits in patients with SA. Table 1 indicates experiments from the thesis and from previous literature in support of each deficit.

Multimodal deficits. SA patients have parallel semantic deficits across verbal and non-verbal stimuli. This is the case both for semantic judgements and for episodic memory tasks. Chapter 2 directly contrasted verbal and pictorial paired associate tasks, while Chapter 3 documented deficits using mostly non-verbal source memory tasks.

Sensitivity to cues. SA patients' semantic deficits are alleviated when cues are provided. This is found using both verbal (phonological) and non-verbal (spatial) cues. A similar pattern was observed here, since progressive phonological cueing aided episodic paired-associate recall, and spatial cues improved source memory judgements.

Difficulty resolving competition from irrelevant semantic associations. An extensive literature has shown that patients with SA have difficulty controlling semantic information during conceptual judgements, leading to incorrect semantic decisions. Here we found parallel deficits in episodic memory. SA patients found it difficult to discard irrelevant semantic associations in episodic tasks, leading to false memories.

Difficulty resolving competition from irrelevant episodic associations. We showed for the first time that patients with SA are vulnerable to proactive interference from recently encoded associations to the same probe words, during episodic memory tasks. Moreover, they experienced interference during semantic tasks from recently-acquired but irrelevant episodic associations. These findings taken together demonstrate that patients with SA not only have difficulty controlling semantic retrieval to suit the circumstances – they have a broader deficit in selecting relevant representations within and between the episodic and semantic systems.

Alleviating circumstances. Self-referential processing alleviated episodic memory impairment in patients with SA. The fact that the neural network underpinning this type of processing (i.e. DMN) is largely intact in these patients suggests that beneficial effects of self-reference could potentially be found in the semantic domain; further research is needed to test this possibility.

Training effects. We found that a training which encouraged patients with SA to retrieve non-dominant aspects of knowledge led to improved semantic control, at least in some cases. As would be predicted from shared controlled retrieval processes, this effect generalised to improved episodic retrieval in a subset of cases. However, this constitutes relatively weak evidence for shared control mechanisms since the effect of training was subtle and highly variable across the sample. Interestingly, when training was *not* effective in strengthening flexible semantic processing, there was some evidence that the trained semantic associations increased episodic memory impairment in a task in which these trained semantic associations were presented as distractors.

Table 1. Summary of evidence in support of parallel deficits

Phenomena	Semantic	Episodic
Multimodal deficits	*Corbett, Jefferies and Lambon Ralph, 2009; Corbett, Jefferies, Ehsan, et al., 2009; Corbett et al., 2011; Gardner et al., 2012; Thompson et al., 2015*	Verbal tasks (A, B, C) Non-verbal tasks (D, E, F, G, H)
Sensitivity to cues	*Jefferies et al., 2008; Corbett, Jefferies, Ehsan, et al., 2009; Noonan et al., 2010*	Benefit from phonological cues (A) Benefit from spatial cues (F)
Difficulty resolving semantic competition	*Noonan et al., 2010; Almaghyuli et al., 2012*	Semantic errors (A, B, M) Impaired when incongruent with semantic knowledge (B, G)
Difficulty resolving episodic competition	Episodic interference (E)	Episodic interference (B, F)
Alleviating circumstances	NT	Self-reference (H, I)
Training effects	Improvement (J or K)	Improvement (L, M)
	No improvement (J or K)	No improvement (L, M)

Table 1 Legend: Chapter 2. **A**: Paired associates recall test (WMS); **B**: Experiment 1 (Verbal paired associates recognition task); **C**: Experiment 2 (Verbal paired associated recognition task -unrelated and no semantic distractors); **D**: Experiment 3 (Non-verbal paired associates recognition task); **E**: Experiment 4 (Semantic judgment with episodic distractors). Chapter 3. **F**: Experiment 1a/b (Source memory task – no spatial cues/spatial cues, non-verbal); **G**: Experiment 2 (Source memory task – congruent/ incongruent trials, non-verbal); **H**: Experiment 3 (Source memory task -self-referential processing, non-verbal); **I**: Experiment 4 (Source memory task -self-referential processing, verbal). Chapter 4. **J**: Training tasks (semantic association with and without feedback, untrained trials); **K**: Semantic control tasks (Ambiguity task, Camel and Cactus, Object use); L: Episodic Experiment 1 (Verbal paired associates recognition task); M: Episodic Experiment 2 (Verbal paired associates recognition task with trained semantic associations). NT: not tested.

6. Shared neurocognitive mechanisms of memory control

LIFG lies mostly outside the multiple-demand network (MDN), functionally defined as brain regions that show increased activation for harder tasks across multiple domains (e.g., perceptual, phonological and semantic; e.g., Duncan, 2010). In this way, it does not form part of the standard "executive control" network. Nevertheless, it is a key region within the semantic control network, implicated in the control of semantic cognition (Noonan *et al.*, 2013) and it is functionally activated during tasks tapping control of both semantic and episodic memories (e.g. Badre and Wagner, 2007). These observations suggest that LIFG might support memory control across these two domains (although this is still debated). Areas implicated in semantic control, including LIFG, show a degree of overlap with the default-mode regions (DMN, Yeo *et al.*, 2011). Semantic cognition (and potentially episodic retrieval) may require memory representations (supported by brain regions with strong connectivity to the DMN, such as anterior temporal cortex and hippocampus) to interact with goal-representations (supported by the MDN), to shape memory retrieval to suit the task demands (i.e. memory control). LIFG lies at the anatomical nexus between the DMN and MDN and a recent proposal from Davey et al. (2016) suggests that this region (along with others) may integrate memory and control processes that draw on these two typically anti-correlated neural systems. This section discusses how the neuropsychological evidence provided in this thesis informs the current debate on the neural basis of memory control, with a special focus on the role of LIFG. We discuss the contribution of the present neuropsychological data with respect to (i) theories of the role of LIFG in memory and (ii) hemispheric contributions to memory control.

6.1. Evidence for a parallel role of LIFG in semantic and episodic control

Although LIFG is activated during fMRI tasks tapping controlled episodic retrieval (Dobbins *et al.*, 2002; Badre and Wagner, 2005; Dobbins and Wagner, 2005; Han *et al.*, 2012; Barredo *et al.*, 2015), the role of LIFG during episodic memory decisions is still debated. The view that LIFG exclusively supports language is outdated; however, there is still controversy about whether this area is indirectly activated during episodic memory tasks as consequence of conceptual processing elicited by the meaningful material often used in these tasks (Dobbins *et al.*, 2002; Han *et al.*, 2012), or alternatively whether this region plays a parallel role in semantic and episodic memory by supporting retrieval in the face of competing irrelevant mnemonic representations, irrespective of whether these are semantic or episodic (Dobbins and Wagner, 2005; Badre and Wagner, 2007; Barredo *et al.*, 2015).

In this thesis we provided evidence in support of the second view. We found that patients with LIFG lesions and semantic control deficits have difficulties resolving competition *within* episodic and semantic memory and *between* these two memory systems. Competition in the semantic domain can be elicited in at least two ways: (i) by activation of dominant aspects of knowledge or related concepts which are not relevant for the task (e.g. thinking of BANK as financial institution, when it is used to refer to the edge of a lake); (ii) by recently encoded events (e.g. a recent visit to your bank can imperil your capacity to efficiently retrieve the non-dominant link between BANK and LAKE). Similarly, competition in the episodic domain is mainly promoted by (i) events that share features with the target event, resulting in proactive interference (e.g. remembering where you parked your car in the morning as opposed to other days); (ii) semantic knowledge that can lead to false memories (e.g. knowing that Christmas puddings are usually served at Christmas dinners can promote the false memory of having had one at a recent Christmas party). Our sample of SA patients with LIFG lesions showed deficits arising from competition *within* semantic knowledge during semantic decisions (i.e. difficulty discarding semantic distractors during semantic judgments), but also – critically - from recent episodic memories (i.e. interference from recently learnt event during semantic decisions). As noted above, a parallel pattern was found for episodic retrieval: performance was impaired as a consequence of interference from both semantic knowledge (i.e. false memories during episodic memory decisions) and episodic memories (i.e. proactive interference from recently learnt events). This suggests LIFG is not only necessary to resolve semantic competition, yet it may be necessary – more broadly – when memory representations or memory systems are in conflict.

In addition, we found episodic memory impairments using both words and pictures, in line with evidence that LIFG supports cognitive control of heteromodal representations (e.g. see Krieger-Redwood *et al.*, 2015). In both modalities patients had difficulties resolving competition, even when semantic processing was minimized. In verbal tasks, patients showed proactive interference from previously encoded items even when these were not semantically linked (Experiment 2, Chapter 2); in non-verbal tasks source memory was impaired when competing sources were not rich in meaning and therefore required minimal semantic processing (i.e. coloured boxes).

Finally, patients' deficits were alleviated by the provision of cues that helped to constrain retrieval to relevant aspects of memory. This builds on converging evidence from neuropsychology and rTMS stimulation, showing that LIFG is necessary for memory control only when context does not support relevant memory retrieval or cues are not available (Hoffman *et al.*, 2010). In our patient sample, deficits were ameliorated when (i) distinctiveness of memories was augmented by means of self-referential processing, (ii) the spatial representation at encoding matched that of retrieval, (iii) existing knowledge was congruent with episodic memory. Medial PFC has been shown to promote self-referential processing (Macrae *et al.*, 2004; Philippi *et al.*, 2011), the hippocampus is thought to be critical for the organisation of memories in space (Eichenbaum, 2017) and the ATL and mPFC have been implicated in processing of semantic knowledge (Binder *et al.*, 2009). All of these areas constitute pivotal nodes of the DMN and are mostly intact in our sample. One possible interpretation is that when retrieval is supported by the presentation of cues that activate these intact representations, controlled retrieval demands are alleviated and therefore the contribution of LIFG to task performance is reduced.

To conclude, the fact that memory-control deficits in patients with LIFG lesions were a) multimodal, i.e. affecting both words and pictures; b) present when the degree of semantic processing required by the stimuli was minimal; c) elicited, in both domains, by competing episodic and semantic representations; d) alleviated when cues and intact representations provided a strong link to memory – i.e. reducing the internal constrain for retrieval – suggest that this area may be necessary to resolve competition between heteromodal memory representations, irrespective of domain.

6.2. Differences in hemispheric contributions to memory control

The right PFC – and RIFG specifically – has been implicated in inhibition during memory control (e.g. see Aron *et al.*, 2004). In the think-no think paradigm, Anderson and colleagues trained word pairs and then asked participants to think of the associate for some words in the set (think condition), and actively supress the associate for other items (no-think condition). Memory inhibition (i.e. no-think trials), as opposed to active retrieval (i.e. think trials) reduces both the later retrieval of episodic associations and the availability of the suppressed item from an independent semantic cue (Anderson and Green, 2001). Suppression of unwanted memories has been associated with bilateral but predominantly right prefrontal (including DLPFC and IFG) activation and top down modulation of hippocampal activity (Anderson *et al.*, 2004, 2016; Benoit *et al.*, 2015). The right lateralized cortical activity in the no-think condition resembles activity associated with response inhibition in motor tasks (Garavan *et al.*, 1999) and RIFG damage has been shown to be critical for response inhibition during go/no-go tasks (Aron *et al.*, 2003). In line with this evidence, it has been suggested that right-lateralised regions recruited for general inhibition could support the control of memory retrieval (Levy and Anderson, 2002; see Aron *et al.*, 2004 for a review on RIFG role in response inibition).

Here we argue that controlling activation of interfering memories during retrieval can be distinguished from the deliberate suppression of unwanted memories. Anderson’s paradigm requires memory suppression that is elicited by an external cue – from the no-think instruction, participants can avoid retrieving the associate by, for example, focussing on the visual characteristics of the probe word. In contrast, the paradigms used in this thesis require selection amongst memories that are in competition because they are linked with the target in either semantic or episodic memory, i.e. the need for control is triggered *internally*. These memories need to be suppressed in order to shape retrieval to suit the task at hand; however, there is no external cue to specify which memories are targets and which are competitors. It would not be appropriate to adopt a strategy such as focussing on perceptual features instead of associations, since the goal is memory retrieval. These observations are compatible with the hypothesis that the left hemisphere plays a special role in circumstances in which memory itself specifies what needs to be selected, while the right hemisphere makes a greater contribution to domain-general inhibition, when the task instructions specify when a non-dominant response should be selected.

However, it is also likely that RIFG and LIFG, in view of their anatomical interconnection, play differential but complementary roles in memory control. For example, patients with unilateral left or right IFG damage show some overlap in the patterns of impairment during tasks tapping semantic control, i.e. sensitivity to cues/miscues and related distractors during summation tasks and effect of cyclical repetitions on word-picture matching (Thompson *et al.*, 2016). These tasks load working memory and monitoring processes that have been associated with RIFG (Aron *et al.*, 2014), as well as inhibition. In addition, Thompson et al. (2016) reports normal performance in patients with RIFG lesions on other semantic control tasks requiring the retrieval of distant associations between concepts (e.g Camel and Cactus Test, Thompson *et al.*, 2016). RIFG forms part of the semantic control network, although this is predominantly left lateralized (Noonan *et al.*, 2013) and an fMRI study adapting a go/no-go task so that it was based on semantic decisions found mostly right-lateralized prefrontal activation (Gonzalez Alam *et al.*, 2018). Together, this evidence suggests that right prefrontal cortex could play a complementary role in memory control, reflecting ancillary processes such as monitoring and/or inhibition that may be more necessary in some paradigms than others. This thesis cannot provide a definitive statement about the roles of the two hemispheres (as only patients with left-hemisphere infarcts were studied), although hemispheric differences could be assessed in patients with right hemisphere stroke and RIFG lesions, using the semantic and episodic paradigms adopted in this thesis.

7. Limitations and future directions

Although our data strongly support the hypothesis that LIFG plays a crucial role in the control of both episodic and semantic memory, there are of course limitations to this research. In common with other neuropsychological studies of SA, our patient sample had relatively large left hemisphere lesions. Although all of the patient volunteers had damage in a common part of LIFG, the patients' lesions extended outside this region. This limits the spatial resolution of our findings – for example, different patterns of damage to other regions relevant to memory control in LIFG might contribute to individual differences between patients in the severity of the semantic control deficit, and/or the effect of training. In particular, neuropsychological studies of patients with large lesions are not ideal for separating semantic control deficits from domain-general executive deficits, since these networks occupy adjacent regions on the cortical surface (Margulies et al., 2017), and consequently they tend to be damaged together. Recent studies have suggested there is a functional subdivision within LIFG, with mid-to-posterior LIFG playing a role in selection and anterior portions implicated in controlled memory access (Badre and Wagner, 2007; Barredo *et al.*, 2015). In line with this account, mid-to posterior LIFG was damaged in all patients; however this functional distinction cannot be addressed using the current sample. Furthermore, given that our patients had unilateral left hemisphere lesions, the contribution of the right hemisphere to memory control cannot be investigated.

In order to address these limitations, future studies should seek to test the contribution of bilateral IFG, pMTG and dAG/IPS to episodic memory control, complementing the current findings with methods with greater spatial resolution. TMS studies have elucidated the role of LIFG and pMTG in semantic control (Whitney, Kirk, *et al.*, 2011; Whitney *et al.*, 2012; Davey, Cornelissen, *et al.*, 2015) and this methodology could provide important advances in our understanding of the neural basis of episodic control and its overlap with semantic control. Similarly, fMRI studies could elucidate the contribution of LIFG and other brain areas to semantic judgements in the face of competition from episodic memory, and to episodic judgements in the face of competition from semantic memory, using paradigms developed in this thesis.

It is worth emphasising that the current sample was selected on the basis of their neuropsychological deficits and then lesions to LIFG were observed. It remains to be fully elucidated if the same deficits would have occurred in a sample of patients selected on the basis of lesions to LIFG and/or episodic control deficits. It would also be interesting to compare the episodic memory deficits in SA and amnesia following medial temporal lobe damage, and to establish a dissociation between episodic memory representations and control processes, equivalent to the dissociation between degraded semantic knowledge (in semantic dementia) and deregulated semantic retrieval (in semantic aphasia), described by Jefferies and Lambon Ralph (2006).

Finally, we have shown that self-referential processing alleviates patients' episodic control deficits and it would be worth exploring if the same beneficial effect could be found for semantic retrieval. Harnessing intrinsic motivation, for example via self-reference paradigms, could ameliorate the deficits observed in SA, and potentially increase the effects of training designed to increase flexibility in semantic retrieval. Similarly, the training paradigm described in Chapter 4 did not produce equivalent effects across patients. Reasons behind this variance are still to be elucidated.

8. Conclusions

The evidence presented in this thesis suggests that, as in the semantic domain, a distinction between representational systems and control processes can be drawn within episodic memory. Overlapping neurocognitive processes are argued to support semantic and episodic control, since the SA patients showed parallel deficits of controlled retrieval across the semantic and episodic domains. LIFG is likely to have a crucial role in resolving competition between active memory representations, both within semantic and episodic memory, and when there is conflict between these systems.

Accompanying materials

Appendix: Chapter 2

Appendix Table 1: List of stimuli for Experiment 1

List	Probe	Target	Distractors			Relatedness	Episodic strength
			SEM+EP	SEM	EP		
A	party	**children**	*cake*	balloon	basket	related	strong
	fruit	**cake**	*basket*	loaf	bus	related	strong
	school	**bus**	*children*	teacher	cake	related	strong
	bicycle	**basket**	*bus*	car	children	related	strong
	violin	**orchestra**	*conductor*	trumpet	bus	related	weak
	baton	**conductor**	*orchestra*	relay	basket	related	weak
	war	**army**	*navy*	soldier	cake	related	weak
	officers	**navy**	*army*	police	children	related	weak
B	party	**basket**	*children*	balloon	bus	unrelated	strong
	fruit	**bus**	*cake*	loaf	children	unrelated	strong
	school	**cake**	*bus*	teacher	basket	unrelated	strong
	bicycle	**children**	*basket*	car	cake	unrelated	strong
	violin	**army**	*orchestra*	trumpet	bus	unrelated	weak
	baton	**navy**	*conductor*	relay	children	unrelated	weak
	war	**conductor**	*army*	soldier	basket	unrelated	weak
	officers	**orchestra**	*navy*	police	cake	unrelated	weak
C	christmas	**bottle**	*turkey*	present	cow	unrelated	weak
	chicken	**glass**	*wing*	hen	donkey	unrelated	weak
	fairy	**donkey**	*angel*	wand	sea	unrelated	strong
	beach	**cow**	*sea*	sand	angel	unrelated	strong
	water	**turkey**	*glass*	tap	cow	unrelated	weak
	wine	**wing**	*bottle*	beer	donkey	unrelated	weak
	milk	**angel**	*cow*	cream	sea	unrelated	strong
	farm	**sea**	*donkey*	yard	angel	unrelated	strong
D	christmas	**turkey**	*angel*	present	sea	related	weak
	chicken	**wing**	*turkey*	hen	angel	related	weak
	fairy	**angel**	*wing*	wand	donkey	related	strong
	beach	**sea**	*donkey*	sand	cow	related	strong
	water	**glass**	*sea*	tap	donkey	related	weak
	wine	**bottle**	*glass*	beer	cow	related	weak
	milk	**cow**	*bottle*	cream	angel	related	strong
	farm	**donkey**	*cow*	yard	sea	related	strong
E	lunch	**soup**	*juice*	sandwich	rain	related	strong
	vegetable	**juice**	*soup*	broth	rain	related	strong
	stone	**picnic**	*cliff*	rock	juice	unrelated	strong
	bullet	**rain**	*gun*	pistol	picnic	unrelated	strong
	apple	**seed**	*tree*	orange	soup	related	weak

	pear	**tree**	*seed*	cider	soup	related	weak
	puddle	**cliff**	*rain*	drizzle	picnic	unrelated	weak
	bench	**gun**	*picnic*	chair	juice	unrelated	weak
F	lunch	**picnic**	*soup*	sandwich	tree	related	weak
	vegetable	**soup**	*juice*	broth	cliff	related	weak
	stone	**rain**	*cliff*	rock	gun	unrelated	weak
	bullet	**juice**	*gun*	pistol	seed	unrelated	weak
	apple	**tree**	*seed*	orange	cliff	related	strong
	pear	**seed**	*tree*	cider	gun	related	strong
	puddle	**gun**	*rain*	drizzle	tree	unrelated	strong
	bench	**cliff**	*picnic*	chair	seed	unrelated	strong
G	wedding	**dress**	*guest*	bride	biscuit	related	strong
	hotel	**guest**	*holiday*	bedroom	dress	related	strong
	church	**holiday**	*steeple*	vicar	dress	unrelated	strong
	camera	**biscuit**	*photo*	picture	guest	unrelated	strong
	garden	**grass**	*swing*	pond	guest	related	weak
	playground	**swing**	*grass*	slide	holiday	related	weak
	sun	**photo**	*dress*	cloud	biscuit	unrelated	weak
	coffee	**steeple**	*biscuit*	cappuccino	holiday	unrelated	weak
H	wedding	**guest**	*dress*	bride	grass	related	weak
	hotel	**holiday**	*guest*	bedroom	steeple	related	weak
	church	**biscuit**	*steeple*	vicar	swing	unrelated	weak
	camera	**dress**	*photo*	picture	grass	unrelated	weak
	garden	**swing**	*grass*	pond	steeple	related	strong
	playground	**grass**	*swing*	slide	photo	related	strong
	sun	**steeple**	*holiday*	cloud	photo	unrelated	strong
	coffee	**photo**	*biscuit*	cappuccino	swing	unrelated	strong

Appendix Table 1 Legend. Related and Unrelated = probe paired with a semantically related/unrelated target at encoding; Strong = repeated 5 times at encoding; Weak = presented only once at encoding; SEM: novel and semantically related to the probe; SEM+EP: semantically related to the probe and target word for another probe; EP: target on a different trial but not semantically related to the probe.

Appendix Table 2: List of stimuli Experiment 2

List	Probe	Target	Distractors			Episodic strength
			EP 1	Novel	EP 2	
A	party	**mineral**	storm	cat	sponge	strong
	fruit	**storm**	sponge	tap	duck	strong
	school	**duck**	mineral	sand	storm	strong
	bicycle	**sponge**	duck	present	mineral	strong
	violin	**rose**	shirt	beer	duck	weak
	baton	**shirt**	rose	tiger	sponge	weak
	war	**fur**	bottle	cream	storm	weak
	officers	**bottle**	fur	hammer	mineral	weak
B	party	**sponge**	mineral	cat	duck	strong
	fruit	**duck**	storm	tap	mineral	strong
	school	**storm**	duck	sand	sponge	strong
	bicycle	**mineral**	sponge	present	storm	strong
	violin	**fur**	rose	beer	duck	weak
	baton	**bottle**	shirt	tiger	mineral	weak
	war	**shirt**	fur	cream	sponge	weak
	officers	**rose**	bottle	hammer	storm	weak
C	christmas	**rabbit**	volcano	car	pencil	weak
	chicken	**poster**	mail	teacher	number	weak
	fairy	**number**	wheel	trumpet	college	strong
	beach	**pencil**	college	graph	wheel	strong
	water	**volcano**	poster	police	pencil	weak
	wine	**mail**	rabbit	balloon	number	weak
	milk	**wheel**	pencil	relay	college	strong
	farm	**college**	number	kiss	wheel	strong
D	christmas	**volcano**	wheel	car	college	weak
	chicken	**mail**	volcano	teacher	wheel	weak
	fairy	**wheel**	mail	trumpet	number	strong
	beach	**college**	number	graph	pencil	strong
	water	**poster**	college	police	number	weak
	wine	**rabbit**	poster	balloon	pencil	weak
	milk	**pencil**	rabbit	relay	wheel	strong
	farm	**number**	pencil	kiss	college	strong
E	lunch	**court**	star	slide	queen	strong
	vegetable	**star**	court	cloud	queen	strong
	stone	**birth**	minister	cappuccino	star	strong
	bullet	**queen**	kite	pond	birth	strong
	apple	**poet**	rectangle	vicar	court	weak
	pear	**rectangle**	poet	bride	court	weak
	puddle	**minister**	queen	picture	birth	weak
	bench	**kite**	birth	rock	star	weak

F	lunch	**birth**	court	slide	rectangle	weak
	vegetable	**court**	star	cloud	minister	weak
	stone	**queen**	minister	cappuccino	kite	weak
	bullet	**star**	kite	pond	poet	weak
	apple	**rectangle**	poet	vicar	minister	strong
	pear	**poet**	rectangle	bride	kite	strong
	puddle	**kite**	queen	picture	rectangle	strong
	bench	**minister**	birth	rock	poet	strong
G	wedding	**turtle**	rubber	lion	river	strong
	hotel	**rubber**	skull	pliers	turtle	strong
	church	**skull**	ear	orange	turtle	strong
	camera	**river**	horse	cider	rubber	strong
	garden	**island**	screw	hair	rubber	weak
	playground	**screw**	island	pistol	skull	weak
	sun	**horse**	turtle	chain	river	weak
	coffee	**ear**	river	nurse	skull	weak
H	wedding	**rubber**	turtle	lion	island	weak
	hotel	**skull**	rubber	pliers	ear	weak
	church	**river**	ear	orange	screw	weak
	camera	**turtle**	horse	cider	island	weak
	garden	**screw**	island	hair	ear	strong
	playground	**island**	screw	pistol	horse	strong
	sun	**ear**	skull	chain	horse	strong
	coffee	**horse**	river	nurse	screw	strong

Appendix Table 2 Legend: Strong = repeated 5 times at encoding; Weak = presented only once at encoding; EP 1 and 2 = target on a different trial but not semantically related to the probe.

Appendix Table 3: List of stimuli Experiment 3

List	Probe	Target	Distractors			Relatedness	Episodic strength
			SEM+EP	SEM	EP		
A	pen	notebook	scissors	pencil	button	related	strong
	needle	scissors	button	spool	school uniform	related	strong
	teacher	school uniform	notebook	textbooks	scissors	related	strong
	shirt	button	school uniform	trousers	notebook	related	strong
	violin	piano	conductor	trumpet	school uniform	related	weak
	saxophone	conductor	piano	musical score	button	related	weak
	bomb	war helmet	machine gun	soldier	scissors	related	weak
	panzer	machine gun	war helmet	cannon	notebook	related	weak
B	pen	button	notebook	pencil	school uniform	unrelated	strong
	needle	school uniform	scissors	spool	notebook	unrelated	strong
	teacher	scissors	school uniform	textbooks	button	unrelated	strong
	shirt	notebook	button	trousers	scissors	unrelated	strong
	violin	war helmet	piano	trumpet	school uniform	unrelated	weak
	saxophone	machine gun	conductor	musical score	notebook	unrelated	weak
	bomb	conductor	war helmet	soldier	button	unrelated	weak
	panzer	piano	machine gun	cannon	scissors	unrelated	weak
C	plant	glass	watering can	flower pot	cow	unrelated	weak
	lawn mower	wine glass	grass	shears	well	unrelated	weak
	tree	well	roots	leaf	bottle	unrelated	strong
	water	cow	bottle	tap	roots	unrelated	strong
	wine	watering can	wine glass	corkscrew	cow	unrelated	weak
	bowl	grass	glass	cup	well	unrelated	weak
	milk	roots	cow	yoghurt	bottle	unrelated	strong
	barn	bottle	well	tractor	roots	unrelated	strong
D	plant	watering can	roots	flower pot	bottle	related	weak

	lawn mower	grass	watering can	shears	roots	related	weak
	tree	roots	grass	leaf	well	related	strong
	water	bottle	well	tap	cow	related	strong
	wine	wine glass	bottle	corkscrew	well	related	weak
	bowl	glass	wine glass	cup	cow	related	weak
	milk	cow	glass	yoghurt	roots	related	strong
	barn	well	cow	tractor	bottle	related	strong
E	arm	hand	eye	foot	drum	related	strong
	ear	eye	hand	nose	drum	related	strong
	chick	finger	chicken	eggs	eye	unrelated	strong
	bullet	drum	gun	shotgun	finger	unrelated	strong
	apple	banana	cherry	grapes	hand	related	weak
	strawberry	cherry	banana	pineapple	hand	related	weak
	harp	chicken	drum	accordion	finger	unrelated	weak
	ring	gun	finger	necklace	eye	unrelated	weak
F	arm	finger	hand	foot	cherry	related	weak
	ear	hand	eye	nose	chicken	related	weak
	chick	drum	chicken	eggs	gun	unrelated	weak
	bullet	eye	gun	shotgun	banana	unrelated	weak
	apple	cherry	banana	grapes	chicken	related	strong
	strawberry	banana	cherry	pineapple	gun	related	strong
	harp	gun	drum	accordion	cherry	unrelated	strong
	ring	chicken	finger	necklace	banana	unrelated	strong
G	rocking chair	chair	lamp	sofa	dress	related	strong
	light bulb	lamp	ceiling lamp	light switch	chair	related	strong
	zebra	ceiling lamp	lion	monkey	chair	unrelated	strong
	car	dress	truck	motorbike	lamp	unrelated	strong
	corn	asparagus	artichoke	celery	lamp	related	weak

	pumpkin	artichoke	asparagus	carrot	ceiling lamp	related	weak
	table	truck	chair	desk	dress	unrelated	weak
	waistcoat	lion	dress	coat	ceiling lamp	unrelated	weak
H	rocking chair	lamp	chair	sofa	asparagus	related	weak
	light bulb	ceiling lamp	lamp	light switch	lion	related	weak
	zebra	dress	lion	monkey	artichoke	unrelated	weak
	car	chair	truck	motorbike	asparagus	unrelated	weak
	corn	artichoke	asparagus	celery	lion	related	strong
	pumpkin	asparagus	artichoke	carrot	truck	related	strong
	table	lion	ceiling lamp	desk	truck	unrelated	strong
	waistcoat	truck	dress	coat	artichoke	unrelated	strong

Appendix Table 3 Legend. Related and Unrelated = probe paired with a semantically related/unrelated target at encoding; Strong = repeated 5 times at encoding; Weak = presented only once at encoding; SEM: novel and semantically related to the probe; SEM+EP: semantically related to the probe and target word for another probe; EP: target on a different trial but not semantically related to the probe.

Appendix Table 4: List of stimuli Experiment 4

List				Distractors				Episodic training	
		Probe	Target	EPI/UNR1	FAM	UNR2	Relatedness	List 1	List 2
D	A	bicycle	**oil**	petrol	*pill*	duck	related	trained	untrained
		bicycle	**pump**	petrol	*pill*	bacon	related	trained	untrained
		bicycle	**spokes**	petrol	*pill*	plant	unrelated	trained	untrained
		bicycle	**shed**	petrol	*pill*	mushroom	unrelated	trained	untrained
		plate	**fish**	sea	*petrol*	cactus	related	trained	untrained
		plate	**cod**	sea	*petrol*	torch	related	trained	untrained
		plate	**lid**	sea	*petrol*	badge	unrelated	trained	untrained
		plate	**tin**	sea	*petrol*	porch	unrelated	trained	untrained
		soap	**tablet**	pill	*yellow*	tree	related	trained	untrained
		soap	**water**	pill	*yellow*	missile	related	trained	untrained
		soap	**brush**	pill	*yellow*	cliff	unrelated	trained	untrained
		soap	**face**	pill	*yellow*	moose	unrelated	trained	untrained
		lipstick	**purple**	yellow	*sea*	fennel	related	trained	untrained
		lipstick	**pink**	yellow	*sea*	cork	related	trained	untrained
		lipstick	**collar**	yellow	*sea*	sofa	unrelated	trained	untrained
		lipstick	**powder**	yellow	*sea*	duvet	unrelated	trained	untrained
B		jug	**orange**	tree	*sun*	bridge	related	untrained	trained
		jug	**flowers**	tree	*sun*	oyster	related	untrained	trained
		jug	**glass**	tree	*sun*	radiator	unrelated	untrained	trained
		jug	**pint**	tree	*sun*	parachute	unrelated	untrained	trained
		scarf	**rain**	sun	*tree*	teeth	related	untrained	trained
		scarf	**wind**	sun	*tree*	jeep	related	untrained	trained
		scarf	**knot**	sun	*tree*	keyboard	unrelated	untrained	trained

	scarf	**knit**	sun	*tree*	zoo	unrelated	untrained	trained
	doll	**dress**	coat	*money*	boat	related	untrained	trained
	doll	**rag**	coat	*money*	seal	related	untrained	trained
	doll	**plastic**	coat	*money*	worm	unrelated	untrained	trained
	doll	**sister**	coat	*money*	sunset	unrelated	untrained	trained
	tea	**bag**	money	*coat*	pen	related	untrained	trained
	tea	**shop**	money	*coat*	blouse	related	untrained	trained
	tea	**leaves**	money	*coat*	submarine	unrelated	untrained	trained
	tea	**spoon**	money	*coat*	train	unrelated	untrained	trained
C	cage	**prison**	court	*cake*	notebook	related	trained	untrained
	cage	**imprisonment**	court	*cake*	foam	related	trained	untrained
	cage	**monkey**	court	*cake*	cushion	unrelated	trained	untrained
	cage	**box**	court	*cake*	pretzel	unrelated	trained	untrained
	robe	**king**	castle	*medicine*	car	related	trained	untrained
	robe	**queen**	castle	*medicine*	tobacco	related	trained	untrained
	robe	**priest**	castle	*medicine*	fist	unrelated	trained	untrained
	robe	**overcoat**	castle	*medicine*	cello	unrelated	trained	untrained
	tweezers	**doctor**	medicine	*castle*	bin	related	trained	untrained
	tweezers	**hospital**	medicine	*castle*	road	related	trained	untrained
	tweezers	**skin**	medicine	*castle*	dwarf	unrelated	trained	untrained
	tweezers	**lash**	medicine	*castle*	shell	unrelated	trained	untrained
	penguin	**chocolate**	cake	*court*	gym	related	trained	untrained
	penguin	**eggs**	cake	*court*	shop	related	trained	untrained
	penguin	**suit**	cake	*court*	coin	unrelated	trained	untrained
	penguin	**wing**	cake	*court*	pipe	unrelated	trained	untrained
D	candle	**chapel**	pope	*aeroplane*	stapler	related	untrained	trained
	candle	**church**	pope	*aeroplane*	calf	related	untrained	trained

candle	**bottle**	pope	*aeroplane*	park	unrelated	untrained	trained
candle	**match**	pope	*aeroplane*	parcel	unrelated	untrained	trained
bag	**baggage**	aeroplane	*pope*	chimp	related	untrained	trained
bag	**luggage**	aeroplane	*pope*	worm	related	untrained	trained
bag	**leather**	aeroplane	*pope*	lawn	unrelated	untrained	trained
bag	**golf**	aeroplane	*pope*	river	unrelated	untrained	trained
sword	**pistol**	policeman	*parrot*	hay	related	untrained	trained
sword	**gun**	policeman	*parrot*	honey	related	untrained	trained
sword	**silver**	policeman	*parrot*	tooth	unrelated	untrained	trained
sword	**edge**	policeman	*parrot*	tinsel	unrelated	untrained	trained
pillow	**feather**	parrot	*policeman*	chalk	related	untrained	trained
pillow	**down**	parrot	*policeman*	nest	related	untrained	trained
pillow	**fight**	parrot	*policeman*	hippie	unrelated	untrained	trained
pillow	**sheets**	parrot	*policeman*	broom	unrelated	untrained	trained

Appendix Table 4 Legend: Untrained trials on one list became trained trials in another, ensuring that differences between conditions could only be explained in terms of the effects of training. Related and Unrelated = EPI/UNR1 distractors semantically related or unrelated with target; Trained = probe episodically-associated with episodic distractor during episodic training; Untrained = probe not presented during episodic training; EPI = episodic distractor associated with the probe during episodic training; FAM = associated with a different probe during episodic training; UNR1, 2, 3 = novel unrelated distractors

Appendix: Chapter 3

Appendix Table 1a: List of stimuli Experiments 1a, 1b, 2 and 3

List 1		List 2		List 3		List 4	
Cat.	Item	Cat.	Item	Cat.	Item	Cat.	Item
Fruits & Vegetables	apples	General households	air freshener	Tinned and canned items	anchovy fillets	Toys	action figures
	asparagus		aluminium foil		artichokes		ball
	aubergines		baking paper		asparagus		barbie
	baby corn		bin bags		beans		bike
	bananas		bleach		beef spread		board game
	broccoli		broom		chestnuts		boat
	brussels sprouts		candles		chopped tomato		building blocks
	butternut squash		canister		cockles		car
	carrots		cleaning cloths		corned beef		cards
	cauliflower		cleaning wipes		custard		colouring book
	celery		cling film		evaporated milk		crayons
	chillies		dishwasher salt		green peas		dolls house
	courgettes		dishwasher tablets		hotdog		fire truck
	garlic		floor cleaner		jelly		games console
	grapes		food containers		lentil soup		jigsaw
	green beans		food bags		mackerel		kite
	leeks		kitchen roll		mashed potatoes		lego
	lemons		laundry liquid		olives		nurf gun
	melon		laundry tablets		passata		plane
	mushroom		light bulb		peaches		play dough
	onions		matches		pesto		sand pit
	oranges		mop		pineapple		scooter

	parsnips		mop pail		red cabbage		seesaw
	peppers		scourer		rice pudding		skateboard
	pineapple		sponges		salmon		slide
	potatoes		surface cleaner		spaghetti		teddy
	pumpkin		tissue		spam		till
	spinach		toilet cleaner		sweetcorn		train
	strawberries		toilet rolls		tomato soup		video game
	swede		washing-up liquid		tuna		walkie-talkie
Bakery products	bagel	Toiletries and Health	aftershave lotion	Drinks	7up	Clothes	blouse
	baguette		antiseptic		apple juice		bow tie
	biscuits		body cream		baileys		cardigan
	bread loaf		body wash		beer		dress
	bread roll		brush		blackcurrant juice		gloves
	brownie		comb		champagne		hat
	cheesecake		conditioner		cider		hoodie
	ciabatta bread		dental floss		cognac		jeans
	croissant		deodorant		cola		joggers
	crumpet		electrical toothbrush		dr pepper		jumper
	cupcake		facial wipes		earl grey tea		leather jacket
	flapjacks		hair colourant		flavoured water		leggings
	focaccia bread		hair spray		gin		mini skirt
	fruit loaf		hand wash		ground coffee		pencil skirt
	garlic bread		interdental brush		hot chocolate		play suit
	hot cross buns		lemsip		instant coffee		robe
	hot-dog rolls		make-up remover		lemonade		scarf
	italian bread		mouthwash		orange juice		shirt
	madeleine		nail polish remover		ovaltine		shorts

muffin	paracetamol	pimms	socks
pain au chocolate	plasters	red wine	suit jacket
pancakes	razors	red bull	suit trousers
pitta	sanitary napkin	rum	sweatshirt
pizza	shampoo	sparkling water	swim shorts
scones	shaving foam	tequila	swimsuit
shortbread	shower puff	tomato juice	trench coat
sliced bread	styling gel	tonic water	t-shirt
sponge cake	toothbrush	vodka	underpants
tart	toothpaste	whisky	vest
tortillas	vitamins	yorkshire tea	waistcoat

Appendix Table 1a Legend. Cat. = category

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Appendix Table 1b. List of stimuli and sources for each experiment

Experiment	List 1	List 2	List 3	List 4	Sources	
1a	✓			✓	Red box	Blue box
1b	✓	✓	✓			
2	✓			✓	Fruits and vegetables shop[a] Toy shop[b]	Bakery shop[a] Clothes shop[b]
3	✓	✓	✓		Self	Other

Appendix Table 1b Legend. a = for list 1; b = for list 4

Appendix Table 2. List of stimuli experiment 4

Target Adjectives	List 1	List 2	List 3	Distractors Adjectives
indifferent	other	self	case	unhappy
silly	other	self	case	compulsive
indecisive	other	self	case	worrying
crafty	other	self	case	withdrawn
critical	other	self	case	impractical
self-conscious	other	self	case	fearful
inexperienced	other	self	case	preoccupied
theatrical	other	self	case	unpopular
naive	other	self	case	passive
shy	other	self	case	unskilled
impulsive	other	self	case	tough
quiet	other	self	case	silent
suave	other	self	case	frivolous
painstaking	other	self	case	meek
moderate	other	self	case	dissatisfied
convincing	other	self	case	resigned
definite	other	self	case	undecided
comical	other	self	case	lonely
direct	other	self	case	stern
artistic	other	self	case	rebellious
sad	self	case	other	conventional
tense	self	case	other	daredevil
timid	self	case	other	cunning
withdrawing	self	case	other	extravagant

old-fashioned	self	case	other	strict
dependent	self	case	other	lonesome
eccentric	self	case	other	authoritative
ordinary	self	case	other	emotional
restless	self	case	other	average
unpredictable	self	case	other	blunt
changeable	self	case	other	hesitant
excitable	self	case	other	aggressive
bold	self	case	other	outspoken
meticulous	self	case	other	forward
proud	self	case	other	methodical
daring	self	case	other	shrewd
dignified	self	case	other	cautious
candid	self	case	other	unconventional
careful	self	case	other	persistent
orderly	self	case	other	prudent
demanding	case	other	self	reserved
sarcastic	case	other	self	excited
gullible	case	other	self	sensitive
troubled	case	other	self	normal
radical	case	other	self	subtle
anxious	case	other	self	fearless
opinionated	case	other	self	systematic
forceful	case	other	self	mathematical
unlucky	case	other	self	righteous
solemn	case	other	self	sentimental
conservative	case	other	self	sophisticated
innocent	case	other	self	obedient
deliberate	case	other	self	quick
satirical	case	other	self	persuasive
lucky	case	other	self	disciplined
objective	case	other	self	idealistic
serious	case	other	self	religious
confident	case	other	self	social
philosophical	case	other	self	precise
fashionable	case	other	self	scientific

Appendix Table 2 Notes: List 1, 2 and 3 denotes the different allocation of adjective to encoding condition (e.g. self vs. other vs. case). Participants were randomly assigned to one of the three list.

Appendix: Chapter 4

Appendix Table 1: List of stimuli training task

Set	Probe	Target	Distractor 1	Distractor 2	Association Coefficient (EAT)	Semantic strength	Condition
1	bee	**honey**	sugar	syrup	6.71	high	novel
1	goggles	**swimming pool**	golf course	gym	6.71	high	novel
1	wet suit	**dive**	paddle	sunbathe	6.29	high	novel
1	tap shoes	**dance studio**	film studio	music studio	6.25	high	novel
1	stingray	**ocean**	pool	pond	6.25	high	novel
1	heels	**dress**	jacket	blouse	5.82	high	novel
1	sunflower	**garden**	shed	garage	5.82	high	novel
1	train	**toy track**	lego	toy house	5.82	high	novel
1	peacock	**tail**	leg	arm	5.71	high	novel
1	pumpkin	**pie**	crumble	tart	5.46	medium	novel
1	pistol	**finger-print**	id card	signature	5.46	medium	novel
1	harmonica	**jazz cafe**	restaurant	tea room	4.04	medium	novel
1	bowler hat	**banker**	lawyer	doctor	4	medium	novel
1	peanut	**butter**	milk	cream	4.29	medium	novel
1	bulldog	**thug**	assassin	terrorist	4.25	medium	novel
1	yacht	**sunbathe**	ice cream	beach ball	5.25	medium	novel
1	dog	**hunt**	fish	shoot	5.25	medium	novel
1	chameleon	**tank**	box	cage	4.61	medium	novel
1	caterpillar	**cabbage**	coleslaw	soup	4.75	medium	novel
1	courgette	**compost**	shed	skip	3.93	low	novel

1	apricot	**tin**	bag	basket	3.93	low	novel
1	ant	**eggs**	larva	spawn	2.86	low	novel
1	butterfly	**eggs**	larva	spawn	2.86	low	novel
1	sofa	**cafe**	restaurant	takeaway	NA	low	novel
1	tennis ball	**dog**	rabbit	cat	2.25	low	novel
2	double decker	**London**	oxford	cambridge	6.61	high	novel
2	snail	**shell**	skin	fur	6.57	high	novel
2	strawberry	**jam**	marmalade	curd	6.57	high	novel
2	wet suit	**surf**	skate	ski	6.11	high	novel
2	yacht	**dock**	garage	hangar	6.11	high	novel
2	cleaver	**kitchen**	garage	shed	6.07	high	novel
2	bus	**ticket**	leaflet	receipt	5.86	high	novel
2	chillies	**curry**	paella	pasta	5.86	high	novel
2	parrot	**cage**	tank	hutch	5.86	high	novel
2	mini cooper	**street**	alleyway	path	5.61	high	novel
2	hummingbird	**trees**	vegetables	grass	5.43	medium	novel
2	mango	**fruit bowl**	punch bowl	salad bowl	5.43	medium	novel
2	porridge oats	**apple crumble**	apple tart	apple pie	4.18	medium	novel
2	slingshot	**lead balls**	bullets	arrows	4.18	medium	novel
2	labrador	**police**	paramedics	coastguards	4.29	medium	novel
2	dog	**frisbee**	basketball	balloon	4.64	medium	novel
2	limo	**premiere**	concert	cinema	5.04	medium	novel
2	almond	**snack box**	hamper	can	5	medium	novel
2	pigeon	**bread**	pasta	rice	4.93	medium	novel
2	melon	**drink**	milk	liquor	3.93	low	novel
2	potato	**vodka**	brandy	whisky	3.61	low	novel
2	broccoli	**cheese**	milk	cream	2.89	low	novel
2	train	**box**	cage	wrapper	2.89	low	novel

2	sofa	**lorry**	train	car	NA	low	novel
2	seahorse	**spines**	fins	quills	2.29	low	novel
3	cornflakes	**breakfast**	dinner	lunch	6.79	high	novel
3	grapefruit	**breakfast**	dinner	lunch	6.79	high	novel
3	baguette	**flour**	cocoa	sugar	5.93	high	novel
3	canary	**nest**	burrow	den	5.93	high	novel
3	sparrow	**tree**	moss	roots	5.93	high	novel
3	flamingo	**zoo**	pet shop	park	5.89	high	novel
3	trumpet	**band**	choir	quartet	6.04	high	novel
3	eel	**sea**	pond	stream	6	high	novel
3	hammerhead shark	**sea**	river	lake	6	high	novel
3	moth	**light bulb**	candle	torch	5.43	medium	novel
3	lifeboat	**first aid**	surgery	plaster	5.43	medium	novel
3	trout	**oven**	toaster	microwave	4.18	medium	novel
3	daffodil	**bulb**	fruit	seed	4.14	medium	novel
3	hawk	**fish**	lobster	crab	4.29	medium	novel
3	weetabix	**cupboard**	fridge	dishwasher	4.75	medium	novel
3	clogs	**holland**	germany	denmark	4.71	medium	novel
3	orange	**cocktail**	wine	cider	4.71	medium	novel
3	comb	**mirror**	window	door	4.68	medium	novel
3	pepper	**cupboard**	sink	desk	4.75	medium	novel
3	submarine	**toy store**	sports store	department store	3.89	low	novel
3	apricots	**packet**	wrapper	carton	3.86	low	novel
3	carrot	**mould**	bacteria	stale	2.93	low	novel
3	soap	**box**	jar	desk	2.89	low	novel
3	rug	**car**	bus	bike	NA	low	novel
3	trumpet	**church**	library	museum	2.46	low	novel
4	orange	**juice**	water	milk	6.79	high	novel

4	porridge	**breakfast**	lunch	dinner	6.79	high	novel
4	sole	**aquarium**	box	cage	6.21	high	novel
4	vw bus	**hippie**	yuppie	student	6.21	high	novel
4	smart car	**petrol**	propane gas	paraffin	6.18	high	novel
4	herring	**sea**	pool	pond	6	high	novel
4	swordfish	**sea**	stream	pond	6	high	novel
4	stingray	**aquarium**	cage	hutch	5.71	high	novel
4	sunflower	**oil**	butter	lard	5.71	high	novel
4	naan bread	**pizza**	roll	baguette	5.39	medium	novel
4	eagle	**america**	europe	africa	5.36	medium	novel
4	pineapple	**knife**	scissors	mallet	4.14	medium	novel
4	magpie	**luck**	charm	witchcraft	4.14	medium	novel
4	jump suit	**painter**	nurse	businessman	4.32	medium	novel
4	peach	**market stall**	butchers	bakery	5.25	medium	novel
4	trench coat	**fashion show**	museum	exhibition	5.25	medium	novel
4	ant	**hill**	burrow	nest	5.21	medium	novel
4	hot air balloon	**wicker basket**	cabin	seat	5.21	medium	novel
4	strawberry	**cheesecake**	coffee cake	angel cake	4.75	medium	novel
4	courgette	**saucepan**	poacher	kettle	3.86	low	novel
4	runner bean	**saucepan**	toaster	tray	3.86	low	novel
4	machete	**tool box**	suitcase	cutlery drawer	2.96	low	novel
4	melon	**parma ham**	gammon	bacon	2.96	low	novel
4	rug	**mosque**	church	synagogue	NA	low	novel
4	space suit	**newspaper**	book	leaflet	2.46	low	novel
5	goldfish	**fish tank**	cage	box	6.75	high	novel
5	baguette	**bakery**	butcher	greengrocer	6.71	high	novel
5	snooker ball	**cue**	stick	pole	6.21	high	novel
5	swan	**lake**	stream	pool	6.21	high	novel

5	bee	**wax**	glue	oil	6	high	novel
5	cockatoo	**seeds**	carrot	hay	5.79	high	novel
5	corgi	**the queen**	prime minister	the pope	5.79	high	novel
5	blackbird	**garden**	conservatory	shed	5.68	high	novel
5	bread roll	**sandwich**	salad	wrap	5.57	high	novel
5	necklace	**evening dress**	skirt	blouse	5.36	medium	novel
5	lizard	**rock**	shell	pebble	5.36	medium	novel
5	rich tea	**chocolate**	toffee	sweets	4.14	medium	novel
5	shortbread	**chocolate**	honey	mints	4.14	medium	novel
5	runner bean	**seeds**	nuts	bulb	4.39	medium	novel
5	seagull	**rubbish**	recycling	junk	4.39	medium	novel
5	goose	**flock**	herd	pack	5.21	medium	novel
5	rugby ball	**mouth guard**	retainer	braces	5.21	medium	novel
5	spider	**attic**	toilet	sofa	5.21	medium	novel
5	track suit	**marathon**	skating	swimming	4.75	medium	novel
5	tortilla	**chicken**	egg	milk	3.86	low	novel
5	beetle	**museum**	library	town hall	3.82	low	novel
5	jump suit	**bin man**	secretary	chemist	3.07	low	novel
5	caterpillar	**rose**	candle	chocolates	3.04	low	novel
5	key	**metal detector**	shopping trolley	walking stick	NA	low	novel
5	barge	**coal**	gas	oil	2.57	low	novel
6	ring	**wedding**	funeral	christening	6.64	high	novel
6	wasp	**sting**	bite	rash	6.61	high	novel
6	wool hat	**winter**	spring	summer	6.29	high	novel
6	clarinet	**orchestra**	jazz band	rock band	6.29	high	novel
6	concorde	**airport**	station	garage	5.68	high	novel
6	aubergine	**supermarket**	butchers	department store	5.64	high	novel
6	blackberry	**pie**	pasty	loaf	5.64	high	novel

6	cherry	**pie**	soufflé	pasty	5.64	high	novel
6	crossbow	**target**	clay pigeon	glass bottle	5.64	high	novel
6	tap shoes	**broadway**	wall street	times square	5.36	medium	novel
6	wellies	**festival**	musical	opera	5.36	medium	novel
6	swordfish	**net**	basket	cage	4.14	medium	novel
6	pepper	**cafe**	fishmongers	newsagents	4.11	medium	novel
6	bowling ball	**party**	meeting	conference	4.43	medium	novel
6	cymbal	**marching band**	floats	carnival	4.39	medium	novel
6	hawk	**nest**	shelter	burrow	5.21	medium	novel
6	baseball cap	**sports**	art	music	5.18	medium	novel
6	xylophone	**river**	exhibition	film	5.18	medium	novel
6	cat	**string**	rope	blue tac	NA	medium	novel
6	raspberry	**stain**	residue	grease	3.75	low	novel
6	dates	**stone**	pip	seed	3.71	low	novel
6	speedboat	**trailer**	cart	carriage	3.11	low	novel
6	cashew nut	**curry**	casserole	stew	3.07	low	novel
6	key	**mat**	towel	cloth	NA	low	novel
6	bazooka	**aeroplane**	bike	train	2.21	low	novel
7	dog	**pet**	zoo animal	livestock	6.79	high	novel
7	trainers	**gym**	office	school	6.39	high	novel
7	spear	**greek god**	christian God	druid	6.32	high	novel
7	ostrich	**zoo**	pet	farm	5.89	high	novel
7	penguin	**zoo**	pet shop	park	5.89	high	novel
7	blue tit	**seeds**	spices	herbs	5.79	high	novel
7	butterfly	**flower**	grass	bush	5.79	high	novel
7	garlic	**supermarket**	restaurant	café	5.64	high	novel
7	ginger	**supermarket**	shopping centre	museum	5.64	high	novel
7	gooseberry	**pie**	mousse	pudding	5.64	high	novel

7	bagel	**cream cheese**	yoghurt	milk	5.32	medium	novel
7	grasshopper	**field**	car park	lake	5.32	medium	novel
7	polo	**shop**	library	gym	4.11	medium	novel
7	moth	**display cabinet**	shoes rack	bookcase	4.11	medium	novel
7	raisins	**baking**	boiling	frying pan	4.46	medium	novel
7	mini cooper	**rally**	riding	formula 1	4.46	medium	novel
7	accordion	**folk music**	rap music	rock music	5.14	medium	novel
7	track suit	**exercise**	sleep	work	5.14	medium	novel
7	carrot	**dinner**	breakfast	treat	5.14	medium	novel
7	banjo	**radio**	telephone	walkie-talkie	3.71	low	novel
7	bulldog	**postman**	officer	salesman	3.68	low	novel
7	paddle boat	**oar**	rope	anchor	3.14	low	novel
7	bagel	**marmalade**	coffee	ketchup	2.75	low	novel
7	cat	**farm**	zoo	forest	NA	low	novel
7	prunes	**toilet**	bathtub	sink	2.61	low	novel
8	submarine	**navy**	army	air force	6.61	high	novel
8	soap	**bath tub**	toilet	cupboard	6.43	high	novel
8	snowdrop	**bouquet**	wreath	button hole	6.39	high	novel
8	recorder	**orchestra**	pop group	choir	6.29	high	novel
8	trench coat	**rain**	wind	sun	5.89	high	novel
8	blue tit	**birdhouse**	cage	kennel	5.89	high	novel
8	bazooka	**army**	police	navy	5.71	high	novel
8	melon	**greengrocer**	butchers	department store	5.71	high	novel
8	jellyfish	**aquarium**	hutch	cage	5.64	high	novel
8	lizard	**desert**	beach	park	5.64	high	novel
8	grenade	**soldier**	policeman	sailor	5.32	medium	novel
8	lifeboat	**coast**	mountain	city	5.32	medium	novel
8	dates	**wine**	germany	japan	4.11	medium	novel

8	cauliflower	**allotment**	gold course	library	4.07	medium	novel
8	swan	**marina**	jetty	dock	4.5	medium	novel
8	radish	**salad**	curry	pasta sauce	4.46	medium	novel
8	toucan	**zoo**	park	pet shop	5.14	medium	novel
8	lolly pop	**dentist**	optician	doctor	5.07	medium	novel
8	toothbrush	**dentist**	physiotherapist	surgeon	5.07	medium	novel
8	blackbird	**car park**	garage	show room	2.61	low	novel
8	fruit pastilles	**summer fayre**	nativity	sports day	3.64	low	novel
8	rice krispies	**marshmallow**	candy	toffee	3.21	low	novel
8	bowtie	**professor**	technician	doctor	3.18	low	novel
8	bottle	**allotment**	tree	bush	NA	low	novel
8	tuba	**football pitch**	squash court	hockey pitch	2.61	low	novel
9	tennis ball	**racket**	bat	paddle	6.57	high	novel
9	dog	**bone**	muscle	tendon	6.57	high	novel
9	penguin	**iceberg**	mountain	cliff	5.89	high	novel
9	willow	**shade**	sun	wind	5.89	high	novel
9	dandelion	**spring**	winter	autumn	5.82	high	novel
9	golf ball	**club**	bat	racket	5.82	high	novel
9	smart car	**electric**	telephone	water	5.79	high	novel
9	seahorse	**aquarium**	stream	pond	5.64	high	novel
9	bracelet	**present**	balloon	card	5.64	high	novel
9	caravan	**holiday**	business trip	school trip	5.61	high	novel
9	naan bread	**oven**	microwave	hob	5.32	medium	novel
9	poppy	**field**	hill	mountain	5.32	medium	novel
9	flamingo	**fish**	squid	seeds	4.07	medium	novel
9	gooseberry	**allotment**	flower bed	verge	4.07	medium	novel
9	cauliflower	**fridge**	sink	oven	4.5	medium	novel
9	mango	**chutney**	marmalade	pickle	4.5	medium	novel

9	pheasant	**shotgun**	pistol	sword	5.04	medium	novel
9	plane	**lifejacket**	rubber ring	arm bands	5.04	medium	novel
9	salt	**sea**	lake	river	5.04	medium	novel
9	prunes	**dessert**	main course	starter	3.61	low	novel
9	turkey	**barn**	stable	kennel	3.61	low	novel
9	shortbread	**caramel**	syrup	honey	3.25	low	novel
9	accordion	**classical music**	jazz	pop music	3.25	low	novel
9	bottle	**message**	leaflet	newsletter	NA	low	novel
9	snowdrop	**christmas**	birthday	halloween	3.68	low	novel
10	tractor	**farm**	park	factory	6.57	high	novel
10	swimsuit	**pool**	pond	stream	6.57	high	novel
10	vw bus	**beach**	park	town centre	6.5	high	novel
10	parrot	**pirate**	soldier	sailor	6.46	high	novel
10	school bus	**bus pass**	credit card	loyalty card	5.86	high	novel
10	battleship	**war**	peace	rally	5.86	high	novel
10	finch	**seeds**	pips	bulbs	5.79	high	novel
10	locket	**gift**	donation	legacy	5.61	high	novel
10	euro star	**holiday**	meeting	interview	5.61	high	novel
10	fly	**repellent**	paste	powder	5.61	high	novel
10	rich tea	**coffee**	juice	wine	5.32	medium	novel
10	robin	**christmas card**	birthday card	anniversary card	5.32	medium	novel
10	harp	**wedding**	disco	conference	4.07	medium	novel
10	peacock	**quill**	feather	ink	4.07	medium	novel
10	mosquito	**camping**	hiking	cycling	4.61	medium	novel
10	raisins	**lunchbox**	tin	can	4.61	medium	novel
10	top hat	**wedding**	baptism	party	4.93	medium	novel
10	bell	**church**	post office	factory	4.89	medium	novel
10	hair brush	**dresser**	cabinet	drawer	4.89	medium	novel

10	battleship	**game**	program	book	3.61	low	novel
10	bowler hat	**umbrella**	parasol	handbag	3.61	low	novel
10	helicopter	**photography**	directing	acting	3.39	low	novel
10	goose	**grass**	hedge	allotment	3.36	low	novel
10	goggles	**cyclist**	gymnastics	horse rider	1.43	low	novel
10	aubergine	**barbeque**	microwave	toaster	2.61	low	novel
11	pumpkin	**halloween**	easter	new years eve	6.82	high	novel
11	space suit	**moon**	earth	asteroid	6.79	high	novel
11	spider	**web**	nest	den	6.5	high	novel
11	swimsuit	**beach**	forest	city	6.5	high	novel
11	budgie	**cage**	stable	box	5.86	high	novel
11	turkey	**christmas**	birthday	halloween	5.86	high	novel
11	kayak	**paddle**	pole	oar	5.82	high	novel
11	herring	**smoked**	steamed	glazed	5.79	high	novel
11	school bus	**driver**	sailor	pilot	5.79	high	novel
11	hovercraft	**holiday**	business trip	commute	5.61	high	novel
11	bicycle	**journey**	drive	flight	5.29	medium	novel
11	broccoli	**steamer**	oven	kettle	5.29	medium	novel
11	ostrich	**sand**	mud	snow	4.04	medium	novel
11	rowboat	**shipwreck**	accident	car crash	4.04	medium	novel
11	slingshot	**pebble**	sand	shell	4.57	medium	novel
11	dagger	**sheath**	box	case	4.57	medium	novel
11	mosquito	**net**	cage	box	4.89	medium	novel
11	pheasant	**roadside**	high street	alleyway	4.89	medium	novel
11	pigeon	**rooftop**	car roof	mountain top	4.89	medium	novel
11	snail	**race**	show	festival	3.61	low	novel
11	tractor	**race**	public transport	delivery service	3.61	low	novel
11	racing car	**champagne**	beer	vodka	3.43	low	novel

11	dog	**fighting**	wrestling	punching	3.39	low	novel
11	bullet	**moose**	fox	mouse	2	low	novel
11	snooker ball	**cloth**	metal	paper	2.68	low	novel
12	poppy	**remembrance day**	st david's day	valentine's day	6.82	high	novel
12	tuba	**orchestra**	choir	dj	6.54	high	novel
12	seagull	**beach**	city	town	6.5	high	novel
12	spitfire	**war**	hit man	terrorist	5.86	high	novel
12	willow	**park**	town square	backyard	5.86	high	novel
12	toothbrush	**mouthwash**	eye drops	cream	5.79	high	novel
12	euro star	**driver**	captain	pilot	5.79	high	novel
12	jaffa cake	**biscuit tin**	bag	tupperware	5.71	high	novel
12	sweets	**multipack**	can	jar	5.71	high	novel
12	melon	**summer**	autumn	winter	5.61	high	novel
12	conifer	**forest**	jungle	plantation	5.29	medium	novel
12	rain coat	**coat rack**	shoe rack	tie rack	5.29	medium	novel
12	stork	**fish**	frog	lobster	4.07	medium	novel
12	trainers	**physiotherapist**	counsellor	psychiatrist	4.07	medium	novel
12	iguana	**tree branch**	bush	grass	4.57	medium	novel
12	radish	**fridge**	freezer	microwave	4.57	medium	novel
12	sparrow	**berries**	apples	oranges	4.82	medium	novel
12	cashew nut	**snack**	lunch	breakfast	4.79	medium	novel
12	fur coat	**aristocracy**	working class	middle class	4.79	medium	novel
12	tortilla	**dip**	chutney	vinegar	3.54	low	novel
12	peach	**cider**	port	wine	3.5	low	novel
12	ring	**cushion**	blanket	pillow	3.46	low	novel
12	magpie	**rubbish bags**	cardboard box	recycle bin	3.43	low	novel
12	canary	**mine**	cloisters	sewer	2.18	low	novel

12	rifle	**strap**	belt	braces	2.68	low	novel
1 to 12	ivy	**flower pot**	allotment	vegetable patch	3.89	low	repeated
	taxi	**phone**	email	fax	3.07	low	repeated
	boots	**snow**	rain	wind	3.54	low	repeated
	sandals	**socks**	tights	leggings	2.57	low	repeated
	sail boat	**sport**	jogging	gymnastics	2.54	low	repeated
	blueberry	**punnet**	jar	bag	3.86	low	repeated
	dog	**customs**	ticket inspector	fireman	2.71	low	repeated
	bmw	**ferry**	train	plane	2.5	low	repeated
	rose	**confectionery**	pastries	popcorn	2.79	low	repeated
	motorbike	**delivery**	reserve	collect	3.14	low	repeated
	ski boots	**shop**	furniture store	café	4.5	medium	repeated
	ladybird	**leaf**	tree	vegetable	5.32	medium	repeated
	woolly hat	**knitting needles**	sewing machine	pin cushion	4.32	medium	repeated
	jet ski	**race**	commute	track	4.29	medium	repeated
	pitta	**lunch**	fry up	carvery	4.86	medium	repeated
	digestive	**chocolate**	popcorn	marshmallow	5.39	medium	repeated
	knife	**drawer**	cupboard	shelf	5.11	medium	repeated
	piano	**tuner**	engineer	mechanic	5.43	medium	repeated
	puffin	**cliff**	valley	beach	4.75	medium	repeated
	grapes	**lunch**	roast	afternoon tea	4.86	medium	repeated
	woodpecker	**forest**	mountain	field	4.61	medium	repeated
	pistachio	**ice cream**	milk	sorbet	4.14	medium	repeated
	smarties	**cookie**	pastry	bread	4.68	medium	repeated
	jelly bean	**newsagents**	butchers	florist	4.64	medium	repeated
	raft	**life jacket**	bomber jacket	dinner jacket	4.36	medium	repeated
	crow	**nest**	den	burrow	5.93	high	repeated

hen	**eggs**	cheesecake	milk	6.79	high	repeated
jet ski	**expensive**	cheap	saving	5.71	high	repeated
cabbage	**coleslaw**	chips	pickle	5.75	high	repeated
daisy	**grass**	bush	tree	5.75	high	repeated
cargo	**port**	beach	pier	6	high	repeated
coach	**trip**	show	event	5.96	high	repeated
kiwi	**fruit salad**	potato salad	rice salad	5.96	high	repeated
mercedes	**motorway**	alleyway	runway	5.79	high	repeated
onion	**frying pan**	glass dish	steamer	5.79	high	repeated
fighter plane	**aircraft carrier**	freight ship	battleship	5.75	high	repeated
hard hat	**power station**	train station	airport	5.75	high	repeated
cobra	**venom**	puss	saliva	6.57	high	repeated
bluebell	**garden**	yard	pond	5.79	high	repeated
basketball	**trainers**	sandals	boots	5.71	high	repeated

Appendix Table 1 Legend: Novel: non-repeated across all 6 training sessions. Repeated: presented during all 6 training sessions. EAT: Edinburgh Association Thesaurus; association coefficient between probe and target.

Notes: Each training protocol entailed 6 sets, each administered on separate sessions. Each participant was trained with stimuli from either sets 1-to-6 or 7-to-12.

Appendix Table 2: List of stimuli for semantic associative task without feedback

Set	Probe	Target	Distractor 1	Distractor 2	Association Coefficient (EAT)	Semantic strength	Condition Training task
1	bagpipes	**tartan**	rag	cloth	6.54	high	untrained
1	banjo	**strings**	keys	reed	6.07	high	untrained
1	beetle	**garden**	road	driveway	4.64	medium	untrained
1	bicycle	**stunt**	pit	hurdle	5.46	medium	untrained
1	collie	**farmer**	fisherman	bee keeper	6.07	high	untrained
1	conifer	**hedge**	pond	fence	4.61	medium	untrained
1	corgi	**show**	gig	concert	3.93	low	untrained
1	cricket ball	**commentator**	spokesperson	manager	5.32	medium	untrained
1	dingy	**storm**	explosion	fire	4	medium	untrained
1	fighter plane	**computer game**	pacman	solitaire	3.96	low	untrained
1	fly	**flower**	hedge	tree	3.54	low	untrained
1	football	**boots**	shoes	pumps	5.54	high	untrained
1	helicopter	**rescue service**	public transport	hiking	6.11	high	untrained
1	hen	**shed**	greenhouse	garage	4	medium	untrained
1	jammie dodger	**lunchbox**	clingfilm	salad bowl	4.61	medium	untrained
1	lolly pop	**sweet shop**	bakery	butchers	6.39	high	untrained
1	owl	**prey**	victim	herd	6	high	untrained
1	paddle boat	**garage**	conservatory	shed	1.89	low	untrained
1	palm tree	**coconut**	banana	pineapple	3.57	low	untrained
1	potato	**chips**	rice	pasta	6.39	high	untrained
1	sweets	**lorry**	bike	tanker	1.68	low	untrained
1	sweets	**newsagents**	takeaway	butchers	5.5	high	untrained
1	top hat	**magician**	musician	comedian	5.25	medium	untrained

1	xylophone	**orchestra**	choir	brass band	5.46	medium	untrained
2	beach ball	**pump**	tube	fan	4.64	medium	untrained
2	bell	**school**	post office	bank	5.57	high	untrained
2	bullet	**gun**	cannon	knife	6.43	high	untrained
2	caravan	**motorway**	runway	track	4.54	medium	untrained
2	cargo	**rivet**	screw	nail	4	medium	untrained
2	centipede	**garage**	bedroom	living room	1.89	low	untrained
2	centipede	**soil**	sand	cement	5.46	medium	untrained
2	chives	**soil**	clay	sand	5.46	medium	untrained
2	cruise ship	**casino**	betting shop	pawn shop	4	medium	untrained
2	dalmation	**film**	video game	tv show	5.11	medium	untrained
2	double decker	**garage**	warehouse	hangar	1.89	low	untrained
2	dove	**olive branch**	oak branch	holly branch	4.57	medium	untrained
2	dove	**sky**	stars	moon	6.39	high	untrained
2	dragonfly	**wings**	arms	legs	6.07	high	untrained
2	ford	**assembly line**	kiln	conveyor belt	3.39	low	untrained
2	fruit pastilles	**sweet shop**	bakery	grocery store	6.39	high	untrained
2	hamburger	**takeaway**	grocery store	bakery	6.43	high	untrained
2	holly	**park**	allotment	golf course	3.43	low	untrained
2	hound	**show**	exhibition	production	3.93	low	untrained
2	locket	**photograph**	drawing	painting	3.93	low	untrained
2	pistachio	**nutcracker**	scissors	mallet	5.54	high	untrained
2	pistol	**hit man**	thief	spy	6.11	high	untrained
2	smarties	**tube**	box	can	5.57	high	untrained
2	stork	**lake**	net	protest	5.21	medium	untrained
3	barge	**canal**	lake	river	6.43	high	untrained
3	basket ball	**cheerleader**	gymnast	acrobat	4.5	medium	untrained
3	comb	**nits**	worms	spiders	5.54	high	untrained
3	crow	**road**	traffic lights	sign	3.89	low	untrained
3	daffodil	**shop**	factory	museum	4.5	medium	untrained

3	drums	**army march**	union march	parade	5.07	medium	untrained
3	ice skates	**rink**	ring	pitch	6.29	high	untrained
3	ivy	**flower arrangement**	hedge	lawn	4.11	medium	untrained
3	kayak	**olympic**	ashes	five nations	4.71	medium	untrained
3	kingfisher	**tree**	shed	trellis	5.46	medium	untrained
3	kiwi	**sorbet**	cream	custard	3.36	low	untrained
3	knife	**tin lid**	bottle	jam jar	1.93	low	untrained
3	lab coat	**scientist**	librarian	postman	6.29	high	untrained
3	onion	**gravy**	sauce	ketchup	3.93	low	untrained
3	pineapple	**cake**	biscuit	bread	3.39	low	untrained
3	plum	**supermarket**	bakery	butchers	5.64	high	untrained
3	rice krispies	**milk**	juice	water	6.18	high	untrained
3	rifle	**target**	goal	net	6.18	high	untrained
3	robin	**garden**	patio	driveway	5.43	medium	untrained
3	salt	**pepper**	cumin	paprika	5.68	high	untrained
3	speedboat	**river**	brook	stream	5.04	medium	untrained
3	wasp	**litter bin**	store	warehouse	4	medium	untrained
3	owl	**pest control**	bug spray	mouse trap	2.79	low	untrained
3	palm tree	**beach**	river	field	6.5	high	untrained
4	bluebell	**bouquet**	chocolates	perfume	5.43	medium	untrained
4	bmw	**showroom**	warehouse	supermarket	6.11	high	untrained
4	boxer	**ring**	pitch	court	6.46	high	untrained
4	cleaver	**butcher**	farm	grocery store	6.46	high	untrained
4	dalmation	**kennel**	cage	stable	6.04	high	untrained
4	dandelion	**tea**	coffee	juice	3.29	low	untrained
4	ferry	**dock**	wharf	marina	6.11	high	untrained
4	ginger	**wine**	brandy	port	4.11	medium	untrained
4	golf ball	**dog**	rabbit	wolf	2.25	low	untrained
4	grapefruit	**tree**	bush	plantation	3.82	low	untrained

4	hair brush	**shop**	takeaway	office	4.5	medium	untrained
4	harp	**angels**	fairies	ghosts	5.43	medium	untrained
4	helmet	**horse**	sheep	cow	4.11	medium	untrained
4	jaffa cake	**tea**	juice	milk	3.29	low	untrained
4	jellyfish	**fishing rod**	anchor	sails	2.71	low	untrained
4	kingfisher	**pond**	ocean	pool	4.5	medium	untrained
4	land rover	**military**	fire service	government	3.89	low	untrained
4	limo	**funeral**	cemetery	morgue	5.57	high	untrained
4	peanut	**allergy**	disease	illness	6.04	high	untrained
4	raspberry	**jam**	marmalade	honey	6.21	high	untrained
4	rowboat	**lake**	stream	pond	6.21	high	untrained
4	trident	**weapon**	tank	base	5	medium	untrained
4	trout	**river**	waterfall	sea	5.04	medium	untrained
1 to 4	bagpipes	**air**	water	steam	4.25	medium	untrained
	baseball cap	**rapper**	singer	actor	4.86	medium	untrained
	bowling ball	**alley**	pitch	court	6.46	high	untrained
	brazil nut	**nutcracker**	knife	scissors	5.54	high	untrained
	bread roll	**toaster**	kettle	blender	4.61	medium	untrained
	budgie	**flock**	pack	herd	4.14	medium	untrained
	bus	**lane**	path	track	4.71	medium	untrained
	cockatoo	**eggs**	larva	spawn	2.86	low	untrained
	cockroach	**pest**	toy	pet	6.18	high	untrained
	dagger	**museum**	restaurant	library	4.5	medium	untrained
	digestive	**cheesecake**	coffee cake	fruit cake	4.75	medium	untrained
	eagle	**mountain**	field	waterfall	5.14	medium	untrained
	flip-flops	**market stall**	convenience store	grocery store	3.46	low	untrained
	garlic	**puree**	sauce	jam	3.86	low	untrained
	goldfish	**pellets**	nuggets	biscuits	4.57	medium	untrained

	guitar	**band**	orchestra	choir	6.04	high	untrained
	holly	**christmas**	easter	halloween	6.57	high	untrained
	hovercraft	**millionaire**	hippie	fisherman	3.25	low	untrained
	ice skates	**lake**	stream	ocean	4	medium	untrained
	land rover	**safari**	sea life centre	zoo	6.04	high	untrained
	mercedes	**caravan park**	hanger	marina	1.64	low	untrained
	motorbike	**leathers**	jumpsuit	uniform	6.32	high	untrained
	necklace	**handbag**	rucksack	briefcase	2.32	low	untrained
	plane	**airport**	motorway	quay	5.68	high	untrained
	racing car	**helmet**	cap	hat	5.5	high	untrained
	rugby ball	**pitch**	court	ring	6.07	high	untrained
1 & 2	barge	**coal**	gas	oil	2.57	low	trained (novel)*
	cockatoo	**seeds**	carrot	hay	5.79	high	trained (novel)*
	hawk	**fish**	lobster	crab	4.29	medium	trained (novel)*
	slingshot	**lead balls**	bullets	arrows	4.18	medium	trained (novel)*
	sofa	**cafe**	restaurant	takeaway		low	trained (novel)*
	swordfish	**net**	basket	cage	4.14	medium	trained (novel)*
	swordfish	**sea**	stream	pond	6	high	trained (novel)*
	wet suit	**dive**	paddle	sunbathe	6.29	high	trained (novel)*
3 & 4	battleship	**war**	peace	rally	5.86	high	trained (novel)*
	canary	**mine**	cloisters	sewer	2.18	low	trained (novel)*
	cauliflower	**fridge**	sink	oven	4.5	medium	trained (novel)*
	goggles	**cyclist**	gymnastics	horse rider	1.43	low	trained (novel)*
	lizard	**desert**	beach	park	5.64	high	trained (novel)*
	moth	**display cabinet**	shoe rack	bookcase	4.11	medium	trained (novel)*
	pigeon	**rooftop**	car roof	mountain top	4.89	medium	trained (novel)*
	toothbrush	**mouthwash**	eye drops	cream	5.79	high	trained (novel)*

1 to 4	bmw	**ferry**	train	plane	2.5	low	trained (repeated)
	coach	**trip**	trip	event	5.96	high	trained (repeated)
	dog	**customs officer**	ticket inspector	fireman	2.71	low	trained (repeated)
	fighter plane	**aircraft carrier**	freight ship	battleship	5.75	high	trained (repeated)
	hard hat	**power station**	train station	airport	5.75	high	trained (repeated)
	jelly bean	**newsagents**	butchers	florist	4.64	medium	trained (repeated)
	jet ski	**race**	race	track	4.29	medium	trained (repeated)
	kiwi	**fruit salad**	potato salad	rice salad	5.96	high	trained (repeated)
	mercedes	**motorway**	alleyway	runway	5.79	high	trained (repeated)
	onion	**frying pan**	glass dish	steamer	5.79	high	trained (repeated)
	pistachio	**ice cream**	milk	sorbet	4.14	medium	trained (repeated)
	pitta	**lunch**	fry up	carvery	4.86	medium	trained (repeated)
	raft	**life jacket**	bomber jacket	dinner jacket	4.36	medium	trained (repeated)
	rose	**confectionery**	pastries	popcorn	2.79	low	trained (repeated)
	sail boat	**sport**	jogging	gymnastics	2.54	low	trained (repeated)
	smarties	**cookie**	pastry	bread	4.68	medium	trained (repeated)

Appendix Table 2 Legend: Untrained: not presented during training task. Trained (novel): presented once during training task. Trained (repeated): repeatedly presented across all sessions during training task. EAT: Edinburgh Association Thesaurus.

Notes: The stimulus list provided here entails 4 sets of trials. Each participant was randomly allocated to only 2, administered prior and after training. There were 82 trials per set. In each set 58 trials were untrained and 24 were trained. To avoid repetitions, trials are presented as follows in the current table: a) Untrained trials entail: 24 unique trials for each set; 26 trials that were common across all sets; 8 additional trials*; b) Trained trials entail: 16 repeatedly presented during training (trained, repeated); 8* that were trained only once (trained, novel). Trials with * denotes association that were either trained or untrained, depending on which training sessions (either 1 to 6 or 7 to 12) the participant was allocated during training.

Appendix Table 3: List of stimuli for Episodic Experiment 1

List				Distractors			Episodic
	Probe	Target	SEM+EP	SEM	EP	Relatedness	strength
A	party	**basket**	*children*	balloon	bus	unrelated	strong
	fruit	**bus**	*cake*	loaf	children	unrelated	strong
	violin	**orchestra**	*conductor*	trumpet	bus	related	strong
	baton	**conductor**	*orchestra*	relay	basket	related	strong
	school	**cake**	*bus*	teacher	basket	unrelated	weak
	bicycle	**children**	*basket*	car	cake	unrelated	weak
	war	**army**	*navy*	soldier	cake	related	weak
	officers	**navy**	*army*	police	children	related	weak
B	party	**children**	*cake*	balloon	basket	related	weak
	fruit	**cake**	*basket*	loaf	bus	related	weak
	violin	**army**	*orchestra*	trumpet	bus	unrelated	weak
	baton	**navy**	*conductor*	relay	children	unrelated	weak
	school	**bus**	*children*	teacher	cake	related	strong
	bicycle	**basket**	*bus*	car	children	related	strong
	war	**conductor**	*army*	soldier	basket	unrelated	strong
	officers	**orchestra**	*navy*	police	cake	unrelated	strong
C	arm	**hand**	*eye*	foot	drum	related	strong
	ear	**eye**	*hand*	nose	drum	related	strong
	chick	**finger**	*hen*	eggs	eye	unrelated	strong
	bullet	**drum**	*gun*	shotgun	finger	unrelated	strong
	apple	**banana**	*cherry*	grapes	hand	related	weak
	strawberry	**cherry**	*banana*	pineapple	hand	related	weak
	harp	**hen**	*drum*	accordion	finger	unrelated	weak
	ring	**gun**	*finger*	necklace	eye	unrelated	weak
D	arm	**finger**	*hand*	foot	cherry	related	weak
	ear	**hand**	*eye*	nose	hen	related	weak
	chick	**drum**	*hen*	eggs	finger	unrelated	weak
	bullet	**eye**	*gun*	shotgun	drum	unrelated	weak
	apple	**cherry**	*banana*	grapes	hen	related	strong
	strawberry	**banana**	*cherry*	pineapple	gun	related	strong
	harp	**gun**	*drum*	accordion	hen	unrelated	strong
	ring	**hen**	*finger*	necklace	banana	unrelated	strong
E	lunch	**soup**	*juice*	sandwich	rain	related	strong
	vegetable	**juice**	*soup*	broth	rain	related	strong
	stone	**picnic**	*cliff*	rock	juice	unrelated	strong
	bullet	**rain**	*gun*	pistol	picnic	unrelated	strong
	apple	**seed**	*tree*	orange	soup	related	weak
	pear	**tree**	*seed*	cider	soup	related	weak
	puddle	**cliff**	*rain*	drizzle	picnic	unrelated	weak

	bench	**gun**	*picnic*	chair	juice	unrelated	weak
F	lunch	**picnic**	*soup*	sandwich	tree	related	weak
	vegetable	**soup**	*juice*	broth	cliff	related	weak
	stone	**rain**	*cliff*	rock	picnic	unrelated	weak
	bullet	**juice**	*gun*	pistol	rain	unrelated	weak
	apple	**tree**	*seed*	orange	cliff	related	strong
	pear	**seed**	*tree*	cider	gun	related	strong
	puddle	**gun**	*rain*	drizzle	cliff	unrelated	strong
	bench	**cliff**	*picnic*	chair	gun	unrelated	strong
G	wedding	**dress**	*guest*	bride	biscuit	related	strong
	hotel	**guest**	*holiday*	bedroom	dress	related	strong
	church	**holiday**	*steeple*	vicar	dress	unrelated	strong
	camera	**biscuit**	*photo*	picture	guest	unrelated	strong
	garden	**grass**	*swing*	pond	guest	related	weak
	playground	**swing**	*grass*	slide	holiday	related	weak
	sun	**photo**	*dress*	cloud	biscuit	unrelated	weak
	coffee	**steeple**	*biscuit*	cappucino	holiday	unrelated	weak
H	wedding	**guest**	*dress*	bride	grass	related	weak
	hotel	**holiday**	*guest*	bedroom	steeple	related	weak
	church	**biscuit**	*steeple*	vicar	holiday	unrelated	weak
	camera	**dress**	*photo*	picture	biscuit	unrelated	weak
	garden	**swing**	*grass*	pond	steeple	related	strong
	playground	**grass**	*swing*	slide	photo	related	strong
	sun	**steeple**	*holiday*	cloud	photo	unrelated	strong
	coffee	**photo**	*biscuit*	cappucino	steeple	unrelated	strong

Appendix Table 2 Legend. Related and Unrelated: probe paired with a semantically related/unrelated target at encoding; Strong: repeated 5 times at encoding; Weak: presented only once at encoding; SEM: novel and semantically related to the probe; SEM+EP: semantically related to the probe and target word for another probe; EP: target on a different trial but not semantically related to the probe.

Notes: The stimulus set provided here entail 8 sets of trials. Each participant was randomly allocated to only 2, administered prior and after training.

Appendix Table 4: List of stimuli for Episodic Experiment 2

List	Probe	Target	SEM Trained distractor	Unrelated distractor 1	Unrelated distractor 2	Episodic strength	Semantic strength SEM Trained
A	ivy	**burrow**	flower pot	den	pin cushion	strong	low
	taxi	**milk**	phone	cheesecake	lunch	strong	low
	boots	**nest**	snow	commute	chips	weak	low
	sandals	**pickle**	socks	marshmallow	cheap	weak	low
	sail boat	**bush**	sport	grass	roast	weak	low
	pistachio	**freight ship**	ice cream	newsagents	alleyway	strong	medium
	woodpecker	**trainers**	forest	pickle	popcorn	strong	medium
	raft	**saliva**	life jacket	milk	power station	weak	medium
B	blueberry	**port**	punnet	drawer	beach	weak	low
	dog	**trip**	customs	engineer	fruit salad	weak	low
	bmw	**potato salad**	ferry	show	cliff	strong	low
	rose	**runway**	confectionery	bread	glass dish	strong	low
	motorbike	**steamer**	delivery	mountain	puss	weak	low
	jelly bean	**garden**	newsagents	expensive	aircraft carrier	weak	medium
	ski boots	**train station**	shop	fry up	ice cream	strong	medium
	jet ski	**roast**	race	bush	yard	strong	medium

Appendix Table 4 Legend: SEM Trained distractor: item paired with probe during trials repeated across the 6 sessions of the training task. Strong: repeated 5 times at encoding; Weak: presented only once at encoding.

References

Abel TJ, Rhone AE, Nourski K V., Kawasaki H, Oya H, Griffiths TD, et al. Direct Physiologic Evidence of a Heteromodal Convergence Region for Proper Naming in Human Left Anterior Temporal Lobe. J. Neurosci. 2015; 35: 1513–1520.

Adlam A-LR, Patterson K, Bozeat S, Hodges JR. The Cambridge Semantic Memory Test Battery: Detection of semantic deficits in semantic dementia and Alzheimer's disease. Neurocase 2010; 16: 193–207.

Almaghyuli A, Thompson H, Lambon Ralph MA, Jefferies E. Deficits of semantic control produce absent or reverse frequency effects in comprehension: Evidence from neuropsychology and dual task methodology. Neuropsychologia 2012; 50: 1968–1979.

Anderson JR. Effects of prior knowledge on memory for new information. Mem. Cognit. 1981; 9: 237–246.

Anderson JR. A spreading activation theory of mind. Readings Cogn. Sci. a Perspect. from Psychol. Artif. Intell. 1988: 137–154.

Anderson MC, Bjork R a, Bjork EL. Remembering can cause forgetting: retrieval dynamics in long-term memory. J. Exp. Psychol. Learn. Mem. Cogn. 1994; 20: 1063–87.

Anderson MC, Bunce JG, Barbas H. Prefrontal–hippocampal pathways underlying inhibitory control over memory. Neurobiol. Learn. Mem. 2016; 134: 145–161.

Anderson MC, Green C. Suppressing unwanted memories by executive control. Nature 2001; 410: 366–369.

Anderson MC, Neely JH. Interference and inhibition in memory retrieval. 1996.

Anderson MC, Ochsner KN, Kuhl B, Cooper J, Robertson E, Gabrieli SW, et al. Neural Systems Underlying the Suppression of Unwanted Memories. Science (80-.). 2004; 303: 232–236.

Anderson NH. Likableness ratings of 555 personality-trait words. J. Pers. Soc. Psychol. 1968; 9: 272–279.

Aron AR, Fletcher PC, Bullmore ET, Sahakian BJ, Robbins TW. Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. Nat. Neurosci. 2003; 6: 115–116.

Aron AR, Robbins TW, Poldrack RA. Inhibition and the right inferior frontal cortex. Trends Cogn. Sci. 2004; 8: 170–177.

Aron AR, Robbins TW, Poldrack RA. Inhibition and the right inferior frontal cortex: One decade on. Trends Cogn. Sci. 2014; 18: 177–185.

Baddeley AD, Hitch GJ. Is the Levels of Processing effect language-limited?. J. Mem. Lang. 2017; 92: 1–13.

Badre D, Poldrack RA, Paré-Blagoev EJ, Insler RZ, Wagner AD. Dissociable Controlled Retrieval and Generalized Selection Mechanisms in Ventrolateral Prefrontal Cortex. Neuron 2005; 47: 907–918.

Badre D, Wagner AD. Frontal lobe mechanisms that resolve proactive interference. Cereb. Cortex 2005; 15: 2003–2012.

Badre D, Wagner AD. Left ventrolateral prefrontal cortex and the cognitive control of memory. Neuropsychologia 2007; 45: 2883–2901.

Baldo J V., Paulraj SR, Curran BC, Dronkers NF. Impaired reasoning and problem-solving in individuals with language impairment due to aphasia or language delay. Front. Psychol. 2015; 6: 1–14.

Barredo J, Öztekin I, Badre D. Ventral fronto-temporal pathway supporting cognitive control of episodic memory retrieval. Cereb. Cortex 2015; 25: 1004–1019.

Bartlett FC. Remembering: a study in experimental and social psychology. Cambridge University Press; 1932.

Benoit RG, Hulbert JC, Huddleston E, Anderson MC. Adaptive Top–Down Suppression of Hippocampal Activity and the Purging of Intrusive Memories from Consciousness. J. Cogn. Neurosci. 2015; 27: 96–111.

Berryhill ME, Phuong L, Picasso L, Cabeza R, Olson IR. Parietal lobe and episodic memory: bilateral damage causes impaired free recall of autobiographical memory. J. Neurosci. 2007; 27: 14415–14423.

Berthier ML. Unexpected brain-language relationships in aphasia: Evidence from transcortical sensory aphasia associated with frontal lobe lesions. Aphasiology 2001; 15: 99–130.

Binder JR, Desai RH, Graves WW, Conant LL. Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies. Cereb. Cortex 2009; 19: 2767–2796.

Binney RJ, Embleton K V., Jefferies E, Parker GJM, Lambon Ralph MA. 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. Cereb. Cortex 2010; 20: 2728–2738.

Binney RJ, Parker GJM, Lambon Ralph M a. Convergent Connectivity and Graded Specialization in the Rostral Human Temporal Lobe as Revealed by Diffusion-Weighted Imaging Probabilistic Tractography. J. Cogn. Neurosci. 2012; 24: 1998–2014.

Bird CM, Burgess N. The hippocampus and memory: Insights from spatial processing. Nat. Rev. Neurosci. 2008; 9: 182–194.

Blumenfeld RS, Ranganath C. Prefrontal cortex and long-term memory encoding: an integrative review of findings from neuropsychology and neuroimaging. Neuroscientist 2007; 13: 280–291.

Bonnici HM, Richter FR, Yazar Y, Simons JS. Multimodal Feature Integration in the Angular Gyrus during Episodic and Semantic Retrieval. J. Neurosci. 2016; 36: 5462–5471.

Borden NM. 3D Angiographic Atlas of Neurovascular Anatomy and Pathology. Cambridge University Press; 2006.

Bozeat S, Lambon Ralph M a., Patterson K, Garrard P, Hodges JR. Non-verbal semantic impairment in semantic dementia. Neuropsychologia 2000; 38: 1207–1215.

Brownsett SLE, Warren JE, Geranmayeh F, Woodhead Z, Leech R, Wise RJS. Cognitive control and its impact on recovery from aphasic stroke. Brain 2014; 137: 242–254.

Buchler NG, Light LL, Reder LM. Memory for Items and Associations: Distinct Representations and Processes in Associative Recognition. J. Mem. Lang. 2008; 59: 183–199.

Buckner RL, Andrews-Hanna JR, Schacter DL. The brain's default network: Anatomy, function, and relevance to disease. Ann. N. Y. Acad. Sci. 2008; 1124: 1–38.

Burgess P, Shallice T. The Hayling and Brixton Tests. Bury St Edmunds: Thames Valley Test Company; 1997.

Burianova H, Grady CL. Common and Unique Neural Activations in Autobiographical, Episodic, and Semantic Retrieval. J. Cogn. Neurosci. 2007; 19: 1520–1534.

Burianova H, McIntosh AR, Grady CL. A common functional brain network for autobiographical, episodic, and semantic memory retrieval. Neuroimage 2010; 49: 865–874.

Butler CR, Brambati SM, Miller BL, Gorno-Tempini ML. The neural correlates of verbal and non-verbal semantic processing deficits in neurodegenerative disease. Cogn Behav Neurol. 2009; 22: 73–80.

Cabeza R, Ciaramelli E, Olson IR, Moscovitch M. The parietal cortex and episodic memory: an attentional account. Nat. Rev. Neurosci. 2008; 9: 613–625.

Cabeza R, Ciaramelli E, Olson IR, Moscovitch M. Parietal Cortex and Episodic Memory: An Attentional Account. 2009; 9: 613–625.

Cabeza R, Locantore JK, Anderson ND. Lateralization of prefrontal activity during episodic memory retrieval: evidence for the production-monitoring hypothesis. J. Cogn. Neurosci. 2003; 15: 249–259.

Cabeza R, Mazuz YS, Stokes J, Kragel JE, Woldorff MG, Ciaramelli E, et al. Overlapping Parietal Activity in Memory and Perception: Evidence for the Attention to Memory Model. J. Cogn. Neurosci. 2011; 23: 3209–3217.

De Caso I, Karapanagiotidis T, Aggius-Vella E, Konishi M, Margulies DS, Jefferies E, et al. Knowing me, knowing you: Resting-state functional connectivity of ventromedial prefrontal cortex dissociates memory related to self from a familiar other. Brain Cogn. 2017; 113: 65–75.

Chalfonte BL, Johnson MK. Feature memory and binding in young and older adults. Mem. Cognit. 1996; 24: 403–416.

Chertkow H, Bub D, Deaudon C, Whitehead V. On the Status of Object Concepts in Aphasia and typical and fail to capture many neurolinguistic categories (Caplan , 1992), both the Western Aphasia Battery (WAB) and the Boston Diagnostic Apha- sia Exam (BDAE) test single-word auditory comprehensi. Brain Lang. 1997; 232: 203–232.

Conn MP. Neuroscience in medicine. Springer Science & Business Media; 2008.

Corbett F, Jefferies E, Ehsan S, Lambon Ralph MA. Different impairments of semantic cognition in semantic dementia and semantic aphasia: Evidence from the non-verbal domain. Brain 2009; 132: 2593–2608.

Corbett F, Jefferies E, Lambon Ralph MA. The use of cueing to alleviate recurrent verbal perseverations: Evidence from transcortical sensory aphasia. Aphasiology 2008; 22: 363–382.

Corbett F, Jefferies E, Lambon Ralph MA. Exploring multimodal semantic control impairments in semantic aphasia: Evidence from naturalistic object use. Neuropsychologia 2009; 47: 2721–2731.

Corbett F, Jefferies E, Lambon Ralph MA. Deregulated semantic cognition follows prefrontal and temporo-parietal damage: evidence from the impact of task constraint on nonverbal object use. J. Cogn. Neurosci. 2011; 23: 1125–1135.

Craik FIM, Lockhart RS. Levels of processing: A framework for memory research. J. Verbal Learning Verbal Behav. 1972; 11: 671–684.

Craik FIM, Tulving E. Depth of processing and the retention of words in episodic memory. J. Exp. Psychol. Gen. 1975; 104: 263–294.

Cunningham SJ, Brady-Van den Bos M, Turk DJ. Exploring the effects of ownership and choice on self-memory biases. Memory 2011; 19: 449–461.

Cunningham SJ, Turk DJ, Macdonald LM, Neil Macrae C. Yours or mine? Ownership and memory. Conscious. Cogn. 2008; 17: 312–318.

D'Esposito M, Postle BR, Jonides J, Smith EE. The neural substrate and temporal dynamics of interference effects in working memory as revealed by event-related functional MRI. Proc. Natl. Acad. Sci. U. S. A. 1999; 96: 7514–7519.

Damasio H, Damasio AR. Lesion analysis in neuropsychology. New York: Oxford University Press; 1989.

Damasio H, Grabowski TJ, Tranel D, Hichwa RD, Damasio AR. A neural basis for lexical retrieval. Nature 1996; 380: 499–505.

Daselaar SM, Fleck MS, Cabeza R. Triple dissociation in the medial temporal lobes: recollection, familiarity, and novelty. J. Neurophysiol. 2006; 96: 1902–1911.

Davey J, Cornelissen PL, Thompson HE, Sonkusare S, Hallam G, Smallwood J, et al. Automatic and Controlled Semantic Retrieval: TMS Reveals Distinct Contributions of Posterior Middle Temporal Gyrus and Angular Gyrus. J. Neurosci. 2015; 35: 15230–9.

Davey J, Rueschemeyer S, Costigan A, Murphy N, Krieger-redwood K, Hallam G, et al. Shared neural processes support semantic control and action understanding. Brain Lang. 2015; 142: 24–35.

Davey J, Thompson HE, Hallam G, Karapanagiotidis T, Murphy C, De Caso I, et al. Exploring the role of the posterior middle temporal gyrus in semantic cognition: Integration of anterior temporal lobe with goal-oriented cognition. Neuroimage 2016; 137: 165–177.

Davis A, Pring T. Therapy for word-finding deficits: more on the effects of semantic and phonological approaches to treatment with dysphasic patients. Neuropsychol. Rehabil. 1991; 1: 135–145.

Dede AJO, Wixted JT, Hopkins RO, Squire LR. Hippocampal damage impairs recognition memory broadly, affecting both parameters in two prominent models of memory. Proc. Natl. Acad. Sci. 2013; 110: 6577–6582.

Dennis NA, Bowman CR, Turney IC. Functional neuroimaging of false memories. In: Duarte A, Addis DR, Barense M, editor(s). The cognitive neuroscience of human memory. Wiley-Blackwell.; 2015.

Dennis NA, Johnson CE, Peterson KM. Neural correlates underlying true and false associative memories. Brain Cogn. 2014; 88: 65–72.

DeWitt MR, Knight JB, Hicks JL, Ball BH. The effects of prior knowledge on the encoding of episodic contextual details. Psychon. Bull. Rev. 2012; 19: 251–257.

Dobbins IG, Foley H, Schacter DL, Wagner AD. Executive control during episodic retrieval: multiple prefrontal processes subserve source memory. Neuron 2002; 35: 989–996.

Dobbins IG, Rice HJ, Wagner AD, Schacter DL. Memory orientation and success: Separable neurocognitive components underlying episodic recognition. Neuropsychologia 2003; 41: 318–333.

Dobbins IG, Wagner AD. Domain-general and domain-sensitive prefrontal mechanisms for recollecting events and detecting novelty. Cereb. Cortex 2005; 15: 1768–1778.

Dronkers NF, Wilkins DP, Van Valin RD, Redfern BB, Jaeger JJ. Lesion analysis of the brain areas involved in language comprehension. Cognition 2004; 92: 145–177.

Dulas MR, Newsome RN, Duarte A. The effects of aging on ERP correlates of source memory retrieval for self-referential information. Brain Res. 2011; 1377: 84–100.

Duncan J. The multiple-demand (MD) system of the primate brain: mental programs for intelligent behaviour. Trends Cogn. Sci. 2010; 14: 172–179.

Durbin KA, Mitchell KJ, Johnson MK. Source memory that encoding was self-referential: the influence of stimulus characteristics. Memory 2017; 25: 1191–1200.

Eichenbaum H. On the Integration of Space, Time, and Memory. Neuron 2017; 95: 1007–1018.

Fedorenko E, Duncan J, Kanwisher N. Broad domain generality in focal regions of frontal and parietal cortex. Proc. Natl. Acad. Sci. U. S. A. 2013; 110: 16616–21.

Fillingham JK, Sage K, Lambon Ralph MA. Further explorations and an overview errorless and errorful therapy for aphasic word-finding difficulties: The number of naming attempts during therapy affects outcome. Aphasiology 2005; 19: 597–614.

Fillingham JK, Sage K, Lambon Ralph MA. The treatment of anomia using errorless learning. Neuropsychol. Rehabil. 2006; 16: 129–154.

Fillingham JK, Sage K, Ralph MAL. Treatment of anomia using errorless versus errorful learning: Are frontal executive skills and feedback important? Int. J. Lang. Commun. Disord. 2005; 40: 505–523.

Garavan H, Ross TJ, Stein E a. Right hemispheric dominance of inhibitory control: an event-related functional MRI study. Proc. Natl. Acad. Sci. U. S. A. 1999; 96: 8301–8306.

Gardner HE, Lambon Ralph MA, Dodds N, Jones T, Ehsan S, Jefferies E. The Differential Contributions of pFC and Temporo-parietal Cortex to Multimodal Semantic Control: Exploring Refractory Effects in Semantic Aphasia. J. Cogn. Neurosci. 2012; 24: 778–793.

Garoff-Eaton RJ, Kensinger E a, Schacter DL. The neural correlates of conceptual and perceptual false recognition. Learn. Mem. 2007; 14: 684–92.

Geranmayeh F, Brownsett SLE, Wise RJS. Task-induced brain activity in aphasic stroke patients: What is driving recovery? Brain 2014; 137: 2632–2648.

Geranmayeh F, Chau TW, Wise RJS, Leech R, Hampshire A. Domain-general subregions of the medial prefrontal cortex contribute to recovery of language after stroke. Brain 2017; 140: 1947–1958.

Gershberg FB, Shimamura AP. Impaired use of organizational strategies in free recall following frontal lobe damage. Neuropsychologia 1995; 13: 1305–1333.

Gilboa A, Marlatte H. Neurobiology of Schemas and Schema-Mediated Memory. Trends Cogn. Sci. 2017; 21: 618–631.

Glosser G, Goodglass H. Disorders in executive control functions among aphasic and other brain-damaged patients. J. Clin. Exp. Neuropsychol. 1990; 12: 485–501.

Gold BT, Buckner RL. Common prefrontal regions coactivate with dissociable posterior regions during controlled semantic and phonological tasks. Neuron 2002; 35: 803–812.

Gold J, Smith C, Bayley P, Shrager Y, Brewer J, Stark C, et al. Item memory, source memory, and the medial temporal lobe: Concordant findings from fMRI and memory-impaired patients. Proc. Natl. Acad. Sci. U. S. A. 2006; 103: 9351–6.

Gonzalez Alam T, Murphy C, Smallwood J, Jefferies E. Meaningful inhibition: Exploring the role of meaning and modality in response inhibition [Internet]. Neuroimage 2018Available from: https://linkinghub.elsevier.com/retrieve/pii/S1053811918305810

Goodglass H, Kaplan E. The assessment of aphasia and related disorders (2nd Edition). Philadelphia: Lea & Febiger; 1983.

Gough PM, Nobre AC, Devlin JT. Dissociating linguistic processes in the left inferior frontal cortex with transcranial magnetic stimulation. J. Neurosci. 2005; 25: 8010–8016.

Graham KS, Barense MD, Lee ACH. Going beyond LTM in the MTL: A synthesis of neuropsychological and neuroimaging findings on the role of the medial temporal lobe in memory and perception. Neuropsychologia 2010; 48: 831–853.

Graham KS, Becker JT, Hodges JR. On the relationship between knowledge and memory for pictures : Evidence from the study of patients with semantic dementia and Alzheimer ' s disease. J. Int. Neuropsychol. Soc. 1997; 3: 534–544.

Graham KS, Hodges JR. Differentiating the role of the hippocampal complex and the neocortex in long-term memory storage : evidence from the study of Semantic Dementia and Alzheimer's Disease. Neuropsychology 1997; 11: 77–89.

Graham KS, Kropelnicki A, Goldman WP, Hodges JR. Two further investigations of autobiographical memory in semantic dementia. Cortex 2003; 39: 729–750.

Graham KS, Simons JS, Pratt KH, Patterson K, Hodges JR. Insights from semantic dementia on the relationship between episodic and semantic memory. Neuropsychologia 2000; 38: 313–324.

Hallam GP, Whitney C, Hymers M, Gouws AD, Jefferies E. Charting the effects of TMS with fMRI: Modulation of cortical recruitment within the distributed network supporting semantic control. Neuropsychologia 2016; 93: 40–52.

Hamami A, Serbun SJ, Gutchess AH. Self-Referencing Enhances Memory Specificity with Age. Psychol. Aging 2011; 26: 636–646.

Han K, Chapman SB, Krawczyk DC. Neuroplasticity of cognitive control networks following cognitive training for chronic traumatic brain injury. NeuroImage Clin. 2018; 18: 262–278.

Han S, O'Connor AR, Eslick AN, Dobbins IG. The Role of Left Ventrolateral Prefrontal Cortex during Episodic Decisions: Semantic Elaboration or Resolution of Episodic Interference? J. Cogn. Neurosci. 2012; 24: 223–234.

Hart J, Gordon B. Delineation of single-word semantic comprehension deficits in aphasia, with anatomical correlation. Ann. Neurol. 1990; 27: 226–31.

Hartley T, Lever C, Burgess N, Keefe JO, B PTRS. Space in the brain : how the hippocampal formation supports spatial cognition Space in the brain : how the hippocampal formation supports spatial cognition. 2014

Hasson U, Yang E, Vallines I, Heeger DJ, Rubin N. A Hierarchy of Temporal Receptive Windows in Human Cortex. J. Neurosci. 2008; 28: 2539–2550.

Hayes SM, Buchler N, Stokes J, Kragel J, Cabeza R. Neural correlates of confidence during item recognition and source memory retrieval: evidence for both dual-process and strength memory theories. J. Cogn. Neurosci. 2011; 23: 3959–3971.

Head H. Aphasia and kindred disorders of speech, Volume II. Cambridge University Press, New York; 1926.

Van Hees S, Angwin A, McMahon K, Copland D. A comparison of semantic feature analysis and phonological components analysis for the treatment of naming impairments in aphasia. Neuropsychol. Rehabil. 2013; 23: 102–132.

Henson RNA, Shallice T, Josephs O, Dolan RJ. Functional Magnetic Resonance Imaging of Proactive Interference during Spoken Cued Recall. Neuroimage 2002; 17: 543–558.

Heredia CG, Sage K, Lambon Ralph MA, Berthier ML. Relearning and retention of verbal labels in a case of semantic dementia. Aphasiology 2009; 23: 192–209.

Van Heuven WJB, Mandera P, Keuleers E, Brysbaert M. SUBTLEX-UK: A new and improved word frequency database for British English. Q. J. Exp. Psychol. 2014; 67: 1176–1190.

Hillis AE, Wityk RJ, Tuffiash E, Beauchamp NJ, Jacobs M a., Barker PB, et al. Hypoperfusion of Wernicke's area predicts severity of semantic deficit in acute stroke. Ann. Neurol. 2001; 50: 561–566.

Hirshorn EA, Thompson-Schill SL. Role of the left inferior frontal gyrus in covert word retrieval: Neural correlates of switching during verbal fluency. Neuropsychologia 2006; 44: 2547–2557.

Hoffman P, Binney RJ, Lambon Ralph M a. Differing contributions of inferior prefrontal and anterior temporal cortex to concrete and abstract conceptual knowledge. Cortex 2015; 63: 250–266.

Hoffman P, Jefferies E, Lambon Ralph MA. Ventrolateral prefrontal cortex plays an executive regulation role in comprehension of abstract words: convergent neuropsychological and repetitive TMS evidence. J. Neurosci. 2010; 30: 15450–15456.

Hoffman P, McClelland JL, Lambon Ralph MA. Concepts, control, and context: A connectionist account of normal and disordered semantic cognition. Psychol. Rev. 2018; 125: 293–328.

Hoffman P, Rogers TT, Ralph MAL. Semantic diversity accounts for the ‘missing’ word frequency effect in stroke aphasia: insights using a novel method to quantify contextual variability in meaning. J. Cogn. Neurosci. 2011; 23: 2432–2446.

Humphreys GF, Hoffman P, Visser M, Binney RJ, Lambon Ralph M a. Establishing task- and modality-dependent dissociations between the semantic and default mode networks. Proc. Natl. Acad. Sci. 2015; 112: 201422760.

Humphreys GF, Lambon Ralph MA. Fusion and Fission of Cognitive Functions in the Human Parietal Cortex. Cereb. cortex 2015; 25: 3547–60.

Humphreys GF, Ralph MAL. 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. Cereb. Cortex 2017; 27: 4199–4212.

Humphreys GW, Riddoch MJ. A case series analysis of ‘category-specific’ deficits of living things: The HIT account. Cogn. Neuropsychol. 2003; 20: 263–306.

Humphreys GW, Sui J. The salient self: Social saliency effects based on self-bias. Eur. J. Cogn. Psychol. 2015; 27: 129–140.

Hutchinson JB, Uncapher MR, Wagner AD. Posterior parietal cortex and episodic retrieval: convergent and divergent effects of attention and memory. Learn. Mem. 2009; 16: 343–56.

Incisa Della Rocchetta A, Milner B. Strategic search and retrieval inhibition: The role of the frontal lobes. Neuropsychologia 1993; 31: 503–524.

Jacoby LL. A process dissociation framework: Separating automatic from intentional uses of memory. J. Mem. Lang. 1991; 30: 513–541.

Janowsky JS, Shimamura AP, Squire LR. Source memory impairment in patients with frontal lobe lesions. Neuropsychologia 1989; 27: 1043–1056.

Jefferies E. The neural basis of semantic cognition: Converging evidence from neuropsychology, neuroimaging and TMS. Cortex 2013; 49: 611–625.

Jefferies E, Baker SS, Doran M, Ralph MAL. Refractory effects in stroke aphasia: A consequence of poor semantic control. Neuropsychologia 2007; 45: 1065–1079.

Jefferies E, Lambon Ralph MA. Semantic impairment in stroke aphasia versus semantic dementia: A case-series comparison. Brain 2006; 129: 2132–2147.

Jefferies E, Patterson K, Jones RW, Lambon Ralph MA. Comprehension of concrete and abstract words in semantic dementia. Neuropsychology 2009; 23: 492–499.

Jefferies E, Patterson K, Lambon Ralph MA. Deficits of knowledge versus executive control in semantic cognition: Insights from cued naming. Neuropsychologia 2008a; 46: 649–658.

Jefferies E, Patterson K, Lambon Ralph MA. Deficits of knowledge versus executive control in semantic cognition: Insights from cued naming. Neuropsychologia 2008b; 46: 649–658.

Jonides J, Smith EE, Marshuetz C, Koeppe RA, Reuter-Lorenz PA. Inhibition in verbal working memory revealed by brain activation. Proc Natl Acad Sci U S A 1998; 95: 8410–8413.

Kay J, Lesser R, Coltheart M. Psycholinguistic assessments of language processing in aphasia (PALPA). Hove (UK): Lawrence Erlbaum Associates; 1992.

Kelley WM, Macrae CN, Wyland CL, Caglar S, Inati S, Heatherton TF. Finding the self? An event-related fMRI study. J. Cogn. Neurosci. 2002; 14: 785–94.

van Kesteren MTR, Beul SF, Takashima A, Henson RN, Ruiter DJ, Fernández G. Differential roles for medial prefrontal and medial temporal cortices in schema-dependent encoding: From congruent to incongruent. Neuropsychologia 2013; 51: 2352–2359.

van Kesteren MTR, Rijpkema M, Ruiter DJ, Morris RGM, Fernández G. Building on Prior Knowledge: Schema-dependent Encoding Processes Relate to Academic Performance. J. Cogn. Neurosci. 2014; 26: 2250–2261.

Van Kesteren MTR, Ruiter DJ, Fernàndez G, Henson RN. How schema and novelty augment memory formation. Trends Neurosci. 2012; 35: 211–219.

Kim H, Cabeza R. Differential contributions of prefrontal, medial temporal, and sensory-perceptual regions to true and false memory formation. Cereb. Cortex 2007; 17: 2143–2150.

Kiran S, Bassetto G. Evaluating the Effectiveness of Semantic-Based Treatment for Naming Deficits in Aphasia: What Works? Semin. Speech Lang. 2008; 29: 71–82.

Kirchhoff BA, Wagner AD, Maril A, Stern CE. Prefrontal-Temporal Circuitry for Episodic Encoding and Subsequent Memory. J. Neurosci. 2000; 20: 6173–6180.

Kiss GR, Armstrong CA, Milroy R, Piper J. An associative thesaurus of English and its computer analysis. In: Aitken AJ, Bailey RW, Hamilton-Smith N, editor(s). The Computer and Literary Studies. Edinburgh: University Press; 1973.

Krieger-Redwood K, Jefferies E. TMS interferes with lexical-semantic retrieval in left inferior frontal gyrus and posterior middle temporal gyrus: Evidence from cyclical picture naming. Neuropsychologia 2014; 64: 24–32.

Krieger-Redwood K, Jefferies E, Karapanagiotidis T, Seymour R, Nunes A, Ang JWA, et al. Down but not out in posterior cingulate cortex: Deactivation yet functional coupling with prefrontal cortex during demanding semantic cognition. Neuroimage 2016; 141: 366–377.

Krieger-Redwood K, Teige C, Davey J, Hymers M, Jefferies E. Conceptual control across modalities: graded specialisation for pictures and words in inferior frontal and posterior temporal cortex. Neuropsychologia 2015; 76: 92–107.

Kuhl B a, Dudukovic NM, Kahn I, Wagner AD. Decreased demands on cognitive control reveal the neural processing benefits of forgetting. Nat. Neurosci. 2007; 10: 908–914.

Kumaran D, McClelland JL. Generalization through the recurrent interaction of episodic memories : a model of the hippocampal system. Psychol. Rev. 2012; 119: 573–616.

Laham D, Steinhart D. Latent Semantic Analysis. 1998[cited 2015 Mar 1] Available from: http://lsa.colorado.edu/.

Lambon Ralph MA, Jefferies E, Patterson K, Rogers TT. The neural and computational bases of semantic cognition. Nat. Rev. Neurosci. 2017; 18: 1–14.

Lerner Y, Honey CJ, Silbert LJ, Hasson U. Topographic mapping of a hierarchy of temporal receptive windows using a narrated story. J. Neurosci. 2011; 6: 247–253.

Levy BJ, Anderson MC. Inhibitory processes and the control of memory retrieval. Trends Cogn. Sci. 2002; 6: 299–305.

Luria AR. The working brain: an introduction to Neuropsychology. Penguin Books; 1973.

Macrae CN, Moran JM, Heatherton TF, Banfield JF, Kelley WM. Medial prefrontal activity predicts memory for self. Cereb. Cortex 2004; 14: 647–654.

Mahon BZ, Caramazza A. Concepts and Categories: A Cognitive Neuropsychological Perspective. Annu. Rev. Psychol. 2009; 60: 27–51.

Mahon BZ, Caramazza A. What drives the organization of object knowledge in the brain? The distributed domain-specific hypothesis. Trends Cogn. Sci. 2011; 15: 97–103.

Mandler G. Recognizing: The judgment of previous occurrence. Psychol. Rev. 1980; 87: 252–271.

Mangels JA, Gershberg FB, Shimamura AP, Knight RT. Impaired retrieval from remote memory in patients with frontal lobe damage. Neuropsychology 1996; 10: 32–41.

Manns JR, Hopkins RO, Squire LR. Semantic memory and the human hippocampus. Neuron 2003; 38: 127–133.

Marshall J, Pound C, White-thomson M, Pring T. The use of picture/word matching tasks to assist word retrieval in aphasic patients. Aphasiology 1990; 4: 167–184.

Martin A. The Representation of Object Concepts in the Brain. Annu. Rev. Psychol. 2007; 58: 25–45.

Mayberry EJ, Sage K, Ehsan S, Lambon Ralph MA. Relearning in semantic dementia reflects contributions from both medial temporal lobe episodic and degraded neocortical semantic systems: Evidence in support of the complementary learning systems theory. Neuropsychologia 2011; 49: 3591–3598.

Mayberry EJ, Sage K, Lambon Ralph MA. At the edge of semantic space: the breakdown of coherent concepts in semantic dementia is constrained by typicality and severity but not modality. J. Cogn. Neurosci. 2011; 23: 2240–2251.

McClelland JL, Mcnaughton BL, Reilly RCO, O’Reilly RC. Why there are complementary learning systems in the hippocampus and neortex: Insights from the successes and failures of connectionist models of learning and memory. Psychol. Rev. 1995; 102: 419–457.

McKinnon MC, Black SE, Miller B, Moscovitch M, Levine B. Autobiographical memory in semantic dementia: implication for theories of limbic-neocortical interaction in remote memory. Neuropsychologia 2006; 44: 2421–2429.

Melby-Lervåg M, Hulme C. Is working memory training effective? A meta-analytic review. Dev. Psychol. 2013; 49: 270–291.

Monsell S. Recency, Immediate Recognition and Reaction Time. Cogn. Psychol. 1978; 10: 465–501.

Moser EI, Kropff E, Moser M-B. Place Cells, Grid Cells, and the Brain's Spatial Representation System. Annu. Rev. Neurosci. 2008; 31: 69–89.

Mummery CJ, Patterson K, Price CJ, Ashburner J, Frackowiak RSJ, Hodges JR. A voxel-based morphometry study of semantic dementia : relationship between temporal lobe atrophy and semantic memory. Ann. Neurol. 2000; 47: 36–45.

Murphy C, Jefferies E, Rueschemeyer SA, Sormaz M, Wang H ting, Margulies DS, et al. Distant from input: Evidence of regions within the default mode network supporting perceptually-decoupled and conceptually-guided cognition. Neuroimage 2018; 171: 393–401.

Nadel L, Moscovitch M. Memory consolidation and the hippocampal complex. Curr. Opin. Neurobiol. 1997; 7: 217–227.

Naveh-Benjamin M. Adult age differences in memory performance: Tests of an associative deficit hypothesis. J. Exp. Psychol. Learn. Mem. Cogn. 2000; 26: 1170–1187.

Nelson JK, Reuter-Lorenz PA, Persson J, Sylvester CYC, Jonides J. Mapping interference resolution across task domains: A shared control process in left inferior frontal gyrus. Brain Res. 2009; 1256: 92–100.

Nestor PJ, Fryer TD, Hodges JR. Declarative memory impairments in Alzheimer's disease and semantic dementia. Neuroimage 2006; 30: 1010–1020.

Noonan KA, Jefferies E, Corbett F, Lambon Ralph MA. Elucidating the nature of deregulated semantic cognition in semantic aphasia: evidence for the roles of prefrontal and temporo-parietal cortices. J. Cogn. Neurosci. 2010; 22: 1597–1613.

Noonan KA, Jefferies E, Visser M, Lambon Ralph MA. Going beyond inferior prefrontal involvement in semantic control: evidence for the additional contribution of dorsal angular gyrus and posterior middle temporal cortex. J. Cogn. Neurosci. 2013; 25: 1824–50.

O'Reilly RC, Bhattacharyya R, Howard MD, Ketz N. Complementary learning systems. Cogn. Sci. 2014; 38: 1229–1248.

Patterson K, Nestor PJ, Rogers TT. Where do you know what you know? The representation of semantic knowledge in the human brain. Nat. Rev. Neurosci. 2007; 8: 976–987.

Phan TG, Donnan GA, Wright PM, Reutens DC. A digital map of middle cerebral artery infarcts associated with middle cerebral artery trunk and branch occlusion. Stroke 2005; 36: 986–991.

Philippi CL, Duff MC, Denburg NL, Tranel D, Rudrauf D. Medial PFC Damage Abolishes the Self-reference Effect. 2011: 475–481.

Poldrack RA, Wagner AD, Prull MW, Desmond JE, Glover GH, Gabrieli JD. Functional specialization for semantic and phonological processing in the left inferior prefrontal cortex. Neuroimage 1999; 10: 15–35.

Postle BR, Brush LN. The neural bases of the effects of item-nonspecific proactive interference in working memory. Cogn Affect Behav Neurosci 2004; 4: 379–392.

Pring T, Hamilton A, Harwood A, Macbride L. Generalization of naming after picture/word matching tasks: only items appearing in therapy benefit. Aphasiology 1993; 7: 383–394.

Purdy M. Executive function ability in persons with aphasia. Aphasiology 2002; 16: 549–557.

Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL. A default mode of brain function. Proc. Natl. Acad. Sci. U. S. A. 2001; 98: 676–82.

Rajah MN, McIntosh a R. Overlap in the functional neural systems involved in semantic and episodic memory retrieval. J. Cogn. Neurosci. 2005; 17: 470–482.

Ramanan S, Piguet O, Irish M. Rethinking the Role of the Angular Gyrus in Remembering the Past and Imagining the Future: The Contextual Integration Model. Neurosci. 2017: 107385841773551.

Raven J. Coloured Progressive Matrices sets A, AB, B. London: H.K. Lewis; 1962.

Reitan RM. Validity of the trail making test as an indicator of organic brain damage. Percept. Mot. Skills 1958; 8: 271–276.

Roberts DJ, Woollams AM, Kim E, Beeson PM, Rapcsak SZ, Lambon Ralph MA. Efficient visual object and word recognition relies on high spatial frequency coding in the left posterior fusiform gyrus: Evidence from a case-series of patients with ventral occipito-temporal cortex damage. Cereb. Cortex 2013; 23: 2568–2580.

Robertson I, Ward T, Ridgeway V, Nimmo-Smith I. The Test of Everyday Attention. London: Thames Valley Test Company; 1994.

Robin J, Moscovitch M. The effects of spatial contextual familiarity on remembered scenes, episodic memories, and imagined future events. J. Exp. Psychol. Learn. Mem. Cogn. 2014; 40: 459–475.

Robson H, Sage K, Lambon Ralph MA. Wernicke's aphasia reflects a combination of acoustic-phonological and semantic control deficits: A case-series comparison of Wernicke's aphasia, semantic dementia and semantic aphasia. Neuropsychologia 2012; 50: 266–275.

Roediger HL, Balota DA, Watson JM. Spreading activation and arousal of false memories. The nature. American Psychological Association; 2001.

Roediger HL, McDermott KB. Creating false memories: remembering words not presented in lists. J. Exp. Psychol. Learn. Mem. Cogn. 1995; 21: 803–814.

Rogers TB, Kuiper NA, Kirker WS. Self-reference and the encoding of personal information. J. Pers. Soc. Psychol. 1977; 35: 677–688.

Rogers TT, Lambon Ralph MA, Garrard P, Bozeat S, McClelland JL, Hodges JR, et al. Structure and Deterioration of Semantic Memory: A Neuropsychological and Computational Investigation. Psychol. Rev. 2004; 111: 205–235.

Rogers TT, Patterson K, Jefferies E, Lambon Ralph MA. Disorders of representation and control in semantic cognition: effects of familiarity, typicality and specificity. Neuropsychologia 2015; 76: 220–239.

Rosa NM, Gutchess AH. Source Memory for Action in Young and Older Adults: Self vs. Close or Unknown Others. Source Mem. Action Young Older Adults Self vs. Close or Unkn. Others 2011; 26: 625–630.

Ross RS, Slotnick SD. The hippocampus is preferentially associated with memory for spatial context. J. Cogn. Neurosci. 2008; 20: 432–446.

Samson D, Connolly C, Humphreys GW. When 'happy' means 'sad': neuropsychological evidence for the right prefrontal cortex contribution to executive semantic processing. Neuropsychologia 2007; 45: 896–904.

Savage SA, Ballard KJ, Piguet O, Hodges JR. Bringing words back to mind-Improving word production in semantic dementia. Cortex 2013; 49: 1823–1832.

Schacter DL. Memory , amnesia , and frontal lobe dysfunction. Psychobiology 1987; 15: 21–36.

Schwartz MF, Kimberg DY, Walker GM, Brecher A, Faseyitan OK, Dell GS, et al. Neuroanatomical dissociation for taxonomic and thematic knowledge in the human brain. Proc. Natl. Acad. Sci. U. S. A. 2011; 108: 8520–8524.

Scoville WB, Milner B. Loss of recent memory after bilateral hippocampal lesions. J. Neurol. Neurosurg. Psychiatry 1957; 20: 11–21.

Seghier ML, Ramlackhansingh A, Crinion J, Leff AP, Price CJ. Lesion identification using unified segmentation-normalisation models and fuzzy clustering. Neuroimage 2008; 41: 1253–1266.

Serbun SJ, Shih JY, Gutchess AH. Memory for details with self-referencing. Memory 2011; 19: 1004–1014.

Sestieri C, Corbetta M, Romani GL, Shulman GL. Episodic memory retrieval, parietal cortex, and the Default Mode Network: functional and topographic analyses. J. Neurosci. 2011; 31: 4407–4420.

Sestieri C, Shulman GL, Corbetta M. The contribution of the human posterior parietal cortex to episodic memory. Nat. Rev. Neurosci. 2017; 18: 183–192.

Shimamura AP. Episodic retrieval and the cortical binding of relational activity. Cogn. Affect. Behav. Neurosci. 2011; 11: 277–291.

Shimamura AP, Jurica PJ, Mangels J a., Gershberg FB, Knight RT. Susceptibility to Memory Interference Effects following Frontal Lobe Damage: Findings from Tests of Paired-Associate Learning. J. Cogn. Neurosci. 1995; 7: 144–152.

Simic T, Rochon E, Greco E, Martino R. Baseline executive control ability and its relationship to language therapy improvements in post-stroke aphasia: a systematic review. Neuropsychol. Rehabil. 2017; 0: 1–45.

Smith SM, Handy JD, Angello G, Manzano I. Effects of similarity on environmental context cueing. Memory 2014; 22: 493–508.

Snodgrass JG, Vanderwart M. A standardized set of 260 pictures: norms for name agreement, image agreement, familiarity, and visual complexity. J. Exp. Psychol. Hum. Learn. Mem. 1980; 6: 174–215.

Snowden J, Goulding P, Neary D. Semantic dementia: A form of circumscribed cerebral atrophy. Behav. Neurol. 1989; 2: 167–182.

Soni M, Lambon Ralph MA, Noonan K, Ehsan S, Hodgson C, Woollams AM. ‘L’ is for tiger: effects of phonological (mis)cueing on picture naming in semantic aphasia. J. Neurolinguistics 2009; 22: 538–547.

Squire LR, Wixted JT, Clark RE. Recognition memory and the medial temporal lobe: a new perspective. Nat. Rev. Neurosci. 2007; 8: 872–883.

Squire LR, Wixted JT, Clark RE. Recognition memory and the medial temporal lobe: a new perspective. Nat. Rev. Neurosci. 2007; 8: 872–83.

Stampacchia S, Thompson HE, Ball E, Nathaniel U, Hallam G, Smallwood J, et al. Shared processes resolve competition within and between episodic and semantic memory: Evidence from patients with LIFG lesions. Cortex 2018; 108: 127–143.

Sui J, He X, Humphreys GW. Perceptual effects of social salience: Evidence from self-prioritization effects on perceptual matching. J. Exp. Psychol. Hum. Percept. Perform. 2012; 38: 1105–1117.

Sui J, Humphreys GW. Self-referential processing is distinct from semantic elaboration: Evidence from long-term memory effects in a patient with amnesia and semantic impairments. Neuropsychologia 2013; 51: 2663–2673.

Sui J, Humphreys GW. The Integrative Self: How Self-Reference Integrates Perception and Memory. Trends Cogn. Sci. 2015; 19: 719–728.

Sui J, Liu M, Mevorach C, Humphreys GW. The salient self: The left intraparietal sulcus responds to social as well as perceptual-salience after self-association. Cereb. Cortex 2015; 25: 1060–1068.

Symons CS, Johnson BT. The Self-Reference Effect in Memory: A Meta- Analysis. Psychol. Bull. 1997; 121: 371–394.

Thompson-Schill SL. Neuroimaging studies of semantic memory: inferring ‘how’ from ‘where’. Neuropsychologia 2003; 41: 280–292.

Thompson-Schill SL, D’Esposito M, Aguirre GK, Farah MJ. Role of left inferior prefrontal cortex in retrieval of semantic knowledge: a reevaluation. Proc. Natl. Acad. Sci. U. S. A. 1997; 94: 14792–14797.

Thompson HE, Almaghyuli A, Noonan KA, barak O, Lambon Ralph MA, Jefferies E. The contribution of executive control to semantic cognition: Convergent evidence from semantic aphasia and executive dysfunction. J. Neuropsychol. 2018

Thompson HE, Henshall L, Jefferies E. The role of the right hemisphere in semantic control: A case-series comparison of right and left hemisphere stroke. Neuropsychologia 2016; 85: 44–61.

Thompson HE, Robson H, Lambon Ralph MA, Jefferies E. Varieties of semantic ‘access’ deficit in Wernicke’s aphasia and semantic aphasia. Brain 2015a; 138: 3776–3792.

Thompson HE, Robson H, Lambon Ralph MA, Jefferies E. Varieties of semantic ‘access’ deficit in Wernicke’s aphasia and semantic aphasia. Brain 2015b; 138: 3776–3792.

Tulving E. Episodic memory: from mind to brain. Annu. Rev. Psychol. 2002; 53: 1–25.

Tulving E, Thomson DM. Encoding specificity and retrieval processes in episodic memory. Psychol. Rev. 1973; 80: 352–373.

Turk DJ, van Bussel K, Waiter GD, Macrae CN. Mine and me: exploring the neural basis of object ownership. J. Cogn. Neurosci. 2011; 23: 3657–68.

Turriziani P, Smirni D, Oliveri M, Semenza C, Cipolotti L. The role of the prefrontal cortex in familiarity and recollection processes during verbal and non-verbal recognition memory: an rTMS study. Neuroimage 2010; 52: 348–357.

Tylén K, Christensen P, Roepstorff A, Lund T, Østergaard S, Donald M. Brains striving for coherence: Long-term cumulative plot formation in the default mode network. Neuroimage 2015; 121: 106–114.

Vargha-Khadem F, Gadian DG, Watkins KE, Connelly a, Van Paesschen W, Mishkin M. Differential effects of early hippocampal pathology on episodic and semantic memory. Science 1997; 277: 376–380.

Vas A, Chapman S, Aslan S, Spence J, Keebler M, Rodriguez-Larrain G, et al. Reasoning training in veteran and civilian traumatic brain injury with persistent mild impairment. Neuropsychol. Rehabil. 2016; 26: 502–531.

Vatansever D, Menon DK, Manktelow AE, Sahakian BJ, Stamatakis EA. Default mode network connectivity during task execution. Neuroimage 2015; 122: 96–104.

Verfaellie M, Koseff P, Alexander MP. Acquisition of novel semantic information in amnesia: Effects of lesion location. Neuropsychologia 2000; 38: 484–492.

Vilberg KL, Rugg MD. Memory retrieval and the parietal cortex: A review of evidence from a dual-process perspective. Neuropsychologia 2008; 46: 1787–1799.

Visser M, Jefferies E, Embleton K V., Lambon Ralph MA. Both the middle temporal gyrus and the ventral anterior temporal area are crucial for multimodal semantic processing: distortion-corrected fMRI evidence for a double gradient of information convergence in the temporal lobes. J. Cogn. Neurosci. 2012; 24: 1766–1778.

Visser M, Jefferies E, Ralph MAL. Semantic processing in the anterior temporal lobes: a meta-analysis of the functional neuroimaging literature. J. Cogn. Neurosci. 2009; 22: 1083–1094.

Visser M, Lambon Ralph MA. Differential contributions of bilateral ventral anterior temporal lobe and left anterior superior temporal gyrus to semantic processes. J. Cogn. Neurosci. 2011; 23: 3121–3131.

Wagner AD, Paré-Blagoev EJ, Clark J, Poldrack RA. Recovering Meaning. Neuron 2001; 31: 329–338.

Warrington EK, Cipolotti L. Word comprehension. The distinction between refractory and storage impairments. Brain 1996; 119: 611–625.

Warrington EK, McCarthy R. Category specific access dysphasia. Brain 1983: 859–878.

Wechsler D. Wechsler Memory Scale-Third Edition. 1997

Westmacott R, Black SE, Freedman M, Moscovitch M. The contribution of autobiographical significance to semantic memory: evidence from Alzheimer's disease, semantic dementia, and amnesia. Neuropsychologia 2004; 42: 25–48.

Westmacott R, Moscovitch M. The contribution of autobiographical significance to semantic memory. Mem. Cognit. 2003; 31: 761–774.

Wheeler ME, Buckner RL. Functional dissociation among components of remembering: control, perceived oldness, and content. J Neurosci 2003; 23: 3869–3880.

Whitney C, Jefferies E, Kircher T. Heterogeneity of the left temporal lobe in semantic representation and control: Priming multiple versus single meanings of ambiguous words. Cereb. Cortex 2011; 21: 831–844.

Whitney C, Kirk M, O'Sullivan J, Lambon Ralph MA, Jefferies E. The neural organization of semantic control: TMS evidence for a distributed network in left inferior frontal and posterior middle temporal gyrus. Cereb. Cortex 2011; 21: 1066–1075.

Whitney C, Kirk M, O'Sullivan J, Lambon Ralph MA, Jefferies E. Executive Semantic Processing Is Underpinned by a Large-scale Neural Network: Revealing the Contribution of Left Prefrontal, Posterior Temporal, and Parietal Cortex to Controlled Retrieval and Selection Using TMS. J. Cogn. Neurosci. 2012; 24: 1–10.

Wimber M, Alink A, Charest I, Kriegeskorte N, Anderson MC. Retrieval induces adaptive forgetting of competing memories via cortical pattern suppression. Nat. Neurosci. 2015; 18: 582–589.

Wimber M, Rutschmann RM, Greenlee MW, Bäuml K-H. Retrieval from episodic memory: neural mechanisms of interference resolution. J. Cogn. Neurosci. 2009; 21: 538–549.

Wong S, Irish M, Leshikar ED, Duarte A, Bertoux M, Savage G, et al. The self-reference effect in dementia: Differential involvement of cortical midline structures in Alzheimer's disease and behavioural-variant frontotemporal dementia. Cortex 2017; 91: 169–185.

Xia M, Wang J, He Y. BrainNet Viewer: A Network Visualization Tool for Human Brain Connectomics. PLoS One 2013

Yeo B, Krienen F, Sepulcre J, Sabuncu M, Lashkari D, Hollinshead M, et al. The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J. Neurophysiol. 2011; 106: 1125–1165.

Yonelinas a. The nature of recollection and familiarity: A review of 30 years of research. J. Mem. Lang. 2002; 46: 441–517.

Yonelinas AP, Otten LJ, Shaw KN, Rugg. Separating the Brain Regions Involved in Recollection and Familiarity in Recognition Memory. J. Neurosci. 2005; 25: 3002–3008.

Zahn R, Moll J, Krueger F, Huey ED, Garrido G, Grafman J. Social concepts are represented in the superior anterior temporal cortex. Proc. Natl. Acad. Sci. 2007; 104: 6430–6435.

Zeithamova D, Preston AR. Flexible Memories: Differential Roles for Medial Temporal Lobe and Prefrontal Cortex in Cross-Episode Binding. J. Neurosci. 2010; 30: 14676–14684.