

The Role of Consolidation in
Conceptual Memory

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Abstract

Concepts allow us to bring meaning to the world; they require the integration of information from across multiple episodes and events, and the abstraction of statistical patterns and regularities from both new and existing knowledge. Processes during consolidation have been shown to benefit the extraction of gist, the detection of hidden rules and the integration of memory elements into coherent representations. Consolidation may therefore play an important role in the development of conceptual memory.

To explore this, we used a range of consolidation delay manipulations and two paradigms that assessed the development of concept-based representations. In Chapter 2 and 3 we used an abstract cross-modal information-integration categorisation task, which allowed us to investigate the integration of information from across modalities (visual and auditory) and the extraction of an underlying category structure. In these experiments we did not find any immediate consolidation benefits on categorisation performance. However, post-consolidation improvements in category learning were observed, if participants had a sleep-filled delay; suggesting that processes during sleep may enhance the effectiveness of future concept-based learning. In Chapters 4 and 5, we used an associative memory task that allowed us to dissociate the impact of consolidation on generalised concept-based representations from trained item knowledge. In this task we found sleep-associated improvements in memory; however, these were specific to trained-item knowledge, with no sleep-associated benefits in measures of memory generalisation. An investigation into intrinsic brain connectivity in Chapter 5 suggests that general variations in functional connectivity can in part explain individual differences in long-term memory performance; with decoupling between heteromodal and sensory-motor brain regions supporting memory generalisation and the formation of concepts. Our results provide new insights into the role of consolidation in the development of conceptual memory and highlight important directions for future research.

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CHAPTER 1

General Introduction:

Concept Memory & Consolidation

1.1 Conceptual Memory

Concepts give the world stability (Smith & Medin, 1981). We would be overwhelmed by the diversity of our environment if we perceived each object and event as a unique entity that required a distinct name and memory representation. We would be unable to remember more than a fraction of our experiences and language would become incredibly complex making communication virtually impossible (Smith & Medin, 1981). Fortunately, we perceive, remember and talk about individual objects and events as instances of a class or concept, capturing the idea that our current experiences share properties with our existing knowledge. Furthermore, concepts allow us to go beyond the perceptual information in our environment to make inferences about non-perceptible attributes. For example, identifying an object as belonging to the class ‘hammer’ allows us to make inferences about its physical properties e.g. made of hard material, its action properties e.g. grasped in one hand and used to hit nails, and more abstract properties such as that it is a tool used by carpenters (Martin, 2015). Concepts therefore facilitate successful interaction with the world, they reduce demands placed on the cognitive

system and provide important building blocks for object recognition, action planning, language and thought (Goldstone & Kersten, 2003; Kiefer & Pulvermüller, 2012).

1.2 The Representation of Conceptual Knowledge

There is general agreement regarding the content of concepts; however, there is a large amount of debate surrounding how these concepts are structured and represented in the brain. Cognitive theories provide a range of models that focus upon the representation of category-based knowledge and the processes that facilitate successful categorisation, while more recent neuroimaging work has focused upon the brain basis of semantic memory – memory for facts, ideas meaning and concepts. The following sections will give a brief overview of these two areas of research.

1.2.1 Cognitive Models of Categorisation

Models of categorisation focus upon the cognitive representation of categories and the processes that facilitate the successful classification of stimuli. Due to the multifaceted nature of categorical memory, there is no formally accepted model of categorisation, instead, a number of different models have been proposed, generating a large amount of research in this area. Four models that highlight important elements of categorisation, which will be briefly discussed below, are: rule-based accounts, exemplar and prototype theories and decision boundary models.

Rule-based accounts of categorisation propose that categories can be defined by a necessary and sufficient set of features or properties (Smith & Medin, 1981). This has been termed the ‘classical view’ and suggests that concepts are formed by generating hypotheses or theories regarding different category features, typically these rules are easy to describe verbally and can be multidimensional (Ashby & Waldron, 1999). Generating categories and defining items based on a set of rules seems somewhat intuitive and can easily explain simple categorisations such as classifying geometric shapes i.e. if an object is two-dimensional with four equal straight sides and four right angles then it can be labelled as a square. However, these models suffer from a number of criticisms: i) not all categories can be easily described by a set of defining features i.e. it is very difficult to generate a set of rules to capture more abstract concepts such as ‘brilliance’ or ‘love’ ii) category membership is not always clear e.g. whether a starfish is a fish or a mammal iii)

not all members of a category are equal e.g. robins are judged as a more typical member of the category 'bird' and will be categorised as such faster than other birds such as chickens (Fujihara et al., 1998), and iv) individuals do not make consistent categorisations when asked to make the same category judgement at different times, suggesting category membership is changeable (McCloskey & Glucksberg, 1978). Despite these criticisms, rule-based accounts offer an intuitive description for how concepts may be represented and have been successful for describing simple forms of categorisation (Ashby et al., 1998; Smith & Medin, 1981).

In contrast to the classical view, prototype and exemplar theories emphasize the importance of similarity in categorisation. These two models are very similar and suggest categorisation is driven by a similarity comparison between a novel item and existing representations. The prototype theory suggests that this representation is an abstract summary – or prototype – of the most common or ideal features of a category (Minda & Smith, 2001). While, exemplar theories suggest the categories are represented by all previously encountered items – or exemplars – of the category (Medin & Schaffer, 1978; Nosofsky, 1986). Similarity judgements lead to a naturally graded representation of category membership, these models can therefore account for the typicality effects observed in categorisation and for complex categories that appear to have blurred or changeable boundaries. These models make successful predictions for categorisation and are not considered to be mutually exclusive, but may operate based on the demands of the task or category purpose (Pothos & Wills, 2011).

A further approach to understanding categorisation focuses upon category boundaries (Goldstone & Kersten, 2003). These models suggest that people use decision boundaries for dividing a multidimensional psychological space into category-response regions (Nosofsky & Stanton, 2005). By fitting a novel item within this response space, it is possible to then determine the classification and category. Within the literature, there is currently debate as to the mechanisms used to generate these decision boundaries, the COmpetition between Verbal and Implicit Systems (COVIS) model suggests that there are two category learning systems: an explicit system – that uses logical reasoning, working memory and executive attention and an implicit system – which draws on procedural learning mechanisms (Ashby et al., 1998; Ashby & Maddox, 2005; Ashby & O'Brien, 2005). In the COVIS model, the explicit system draws parallels with the rule-

based approach, using hypothesis testing and rule generation for successful categorisation. In contrast the implicit system is described as linking precepts (i.e. category exemplars) with actions (i.e. categorisation responses). The COVIS model has generated a large amount of behavioural, neuropsychological and neuroimaging support in recent decades, yet debate still remains as to their proposed two-system model of categorization (Cincotta & Seger, 2007; Filoteo et al., 2005; Maddox et al., 2004; 2008; Nomura et al., 2006; Carpenter et al., 2016; Edmunds, Milton & Wills, 2015; Gureckis, James & Nosofsky, 2011; Newell, Dunn & Kalish, 2010, 2011; Newell et al., 2013; Stanton & Nosofsky, 2013).

To summarise, a range of approaches to categorisation have gained experimental support, however there is no formally agreed model. One possible reason for this is the complexity of these representations, with theory-driven research developing paradigms and tasks that address a single aspect of the category representation. For instance, rule-based models have gained support from tasks that experimentally manipulate category structure using rules (Goldstone & Kersten, 2003). It remains to be determined whether a single framework will successfully account for the range and complexity of real-world categorical knowledge.

1.2.2 Semantic Memory in the Brain

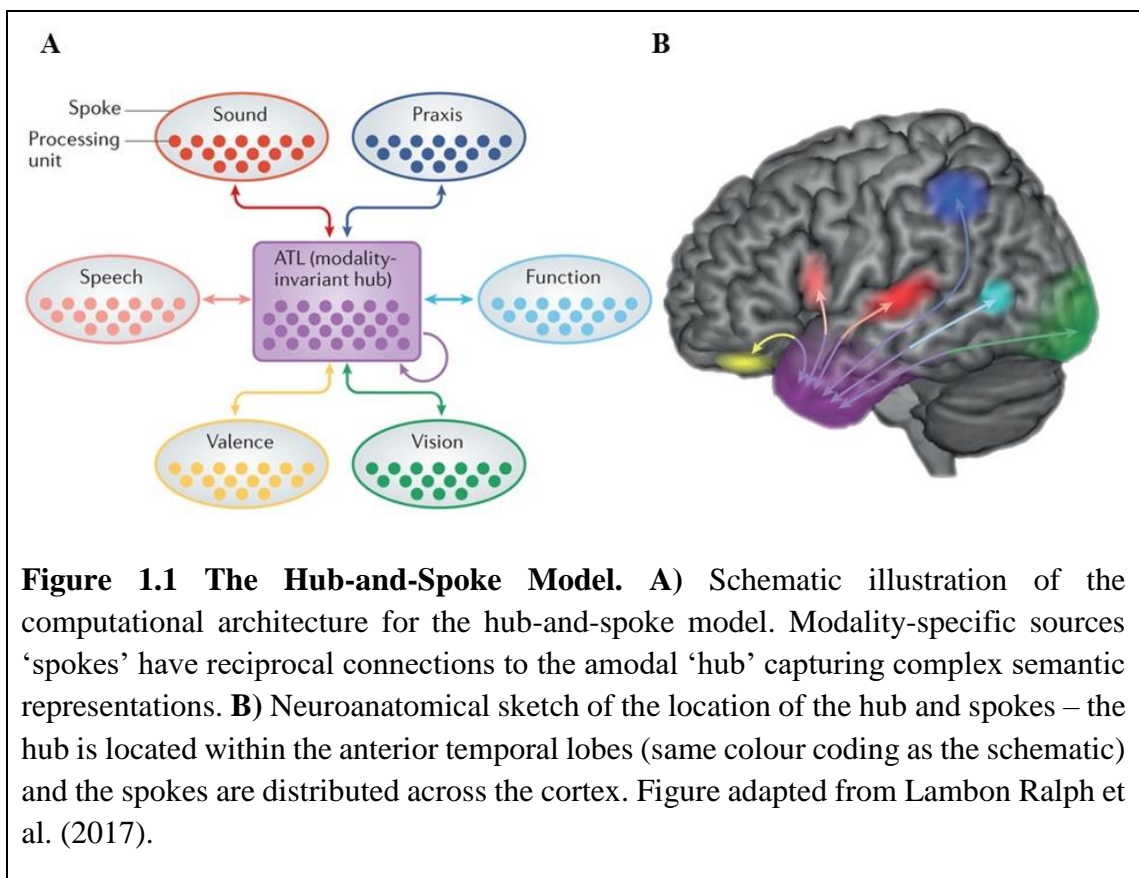
The study of semantic memory processing has been relatively limited in cognitive neuroscience due to a general emphasis upon object knowledge and stimulus-driven brain activity (Binder & Desai, 2011). However, together with insights from patients suffering from semantic memory loss, functional imaging data has begun to develop an anatomical model of semantic memory in the brain. Initial investigations were oriented around the idea that semantic memory is multimodal; we are able to determine the meaning of objects and events via all our senses, with each sense contributing different elements to our understanding (Patterson, Nestor & Rogers, 2007). There is strong neuroimaging evidence for the coupling between memory and the senses, with data showing differential brain activation in sensory and motor cortices during semantic comprehension tasks (Pulvermüller, Shtyrov & Ilmoniemi, 2005; Tettamanti et al., 2005). Furthermore, this sensory activation is observed in the absence of sensory input or output, for example, Kiefer et al. (2008) report activation in brain areas involved in sound perception (i.e.

posterior and middle temporal gyri) following recognition of words with acoustic features (e.g. telephone), and similar results have been reported in the visual and olfactory domain (Chao et al., 1999; Sim & Kiefer, 2005; González et al., 2006). These findings led to the suggestion that semantic knowledge is ‘embodied’ within modality-specific areas of the brain (Binder & Desai, 2011; Martin, 2007).

Neuropsychological evidence supports the role of sensory and motor processing in semantics by demonstrating conceptual impairments following localised brain damage. Lesions to cortical regions that are involved in object recognition (e.g. the sylvian fissure) have been shown to result in difficulties processing category specific concepts (e.g. tool knowledge), while damage to the motor cortex can lead to difficulties in processing ‘action’ related verbs (Cotelli et al., 2006; Warrington & McCarthy, 1987). Neuropsychological data is very revealing; however it is difficult to draw conclusive inferences given often widespread damage and large variations in damage across patients. Stronger causal evidence for the role of sensory processing in semantics is provided by neurostimulation techniques such as transcranial magnetic stimulation (TMS). TMS is a technique that involves delivering a painless magnetic pulse to the surface of the scalp, which in turn can temporally influence the functional state of small cortical brain areas in healthy participants (Hallett, 2000). By applying TMS to the hand or foot area of the motor cortex, Pulvermüller et al. (2005) demonstrated improved recognition of arm and leg related words – suggesting TMS to the motor cortex had influenced semantic processing. There is therefore converging evidence to suggest that conceptual representations are ‘embodied’ or grounded within sensory and motor regions of the brain.

However, not all semantic knowledge can be described on the basis of sensory or motor features and neuropsychological evidence from patients with Semantic Dementia suggests that semantics can also be represented in regions that are functionally and anatomically distinct from the sensory and motor cortices (Hodges et al., 1992; Jefferies, 2013a; Lambon Ralph et al., 2010; Lambon Ralph, Lowe & Rogers, 2007; Patterson et al., 2007). Semantic Dementia is a degenerative brain disease characterised by progressive degradation of the bilateral anterior temporal lobes (Patterson et al., 2007). These patients present deficits in semantic knowledge that generalise across modalities and conceptual domains, suggesting an amodal and central representation of knowledge

in the temporal lobes (Patterson et al., 2007; Lambon Ralph et al., 2017; Rogers et al., 2004). TMS applied to the anterior temporal lobes in healthy adults results in deteriorated performance in semantic association tasks – providing further evidence for an amodal ‘hub’ in semantic processing (Jefferies, 2013; Pobric, Jefferies & Lambon Ralph, 2010). Given the support for both modality-specific and amodal accounts for semantic processing in the brain, most recent theories have integrated these representations into a single model (Patterson et al., 2007; Lambon Ralph et al., 2017).



The ‘hub-and-spoke’ theory suggests multi-modal experiences are encoded within modality-specific cortices that are distributed across the brain (the ‘spokes’), while cross-modal interactions between these representations are mediated by an amodal ‘hub’ located in the anterior temporal lobes (see Figure 1.1; Binder, 2016; Patterson et al., 2007; Lambon Ralph et al., 2016; Rogers et al., 2004). This theory has generated a large amount of support, with bilateral amodal anterior temporal lobe activation, along with modality-specific activation across sensory cortices observed when participants perform semantic

memory tasks (Binney et al., 2010; Visser et al., 2012). Computationally, the ‘hub-and-spoke’ theory is able to explain how a given concept can be accessed via different sensory modalities at different points in time and is able to account for complex concepts that do not have strong sensory or motor representations (Lambon Ralph et al., 2017; Rogers & McClelland, 2004). The ‘hub-and-spoke’ theory therefore provides a neuroanatomical model that explains the representation of concept memory via the integration of multimodal experiences.

This section gave a brief overview of the literature concerned with the representation of conceptual memory. Cognitive models have provided intuitive theories for the representation of categories and processes related to categorisation, emphasising the wide range of categorical structures in the environment. Advances in understanding the brain basis of conceptual knowledge have been driven by neuropsychology, neuroimaging and neurostimulation research assessing semantic memory. The ‘hub-and-spoke’ model has been particularly successful for describing how multimodal experiences can be integrated to generate higher-order conceptual representations (Patterson et al., 2007; Ralph et al., 2017; Rogers & McClelland, 2004). One important aspect of conceptual knowledge that has not received attention within the literature however is the role of time. Conceptual memory is not fixed, but develops gradually and is updated with each new experience across the lifespan. The vast majority of category learning experiments focus solely on the initial acquisition and online training of category representations. In Chapter 2 and 3 we address this issue and explore the impact of offline consolidation on cross-modal category learning. The current literature related to offline consolidation, and the relationship with conceptual memory is discussed in the following sections.

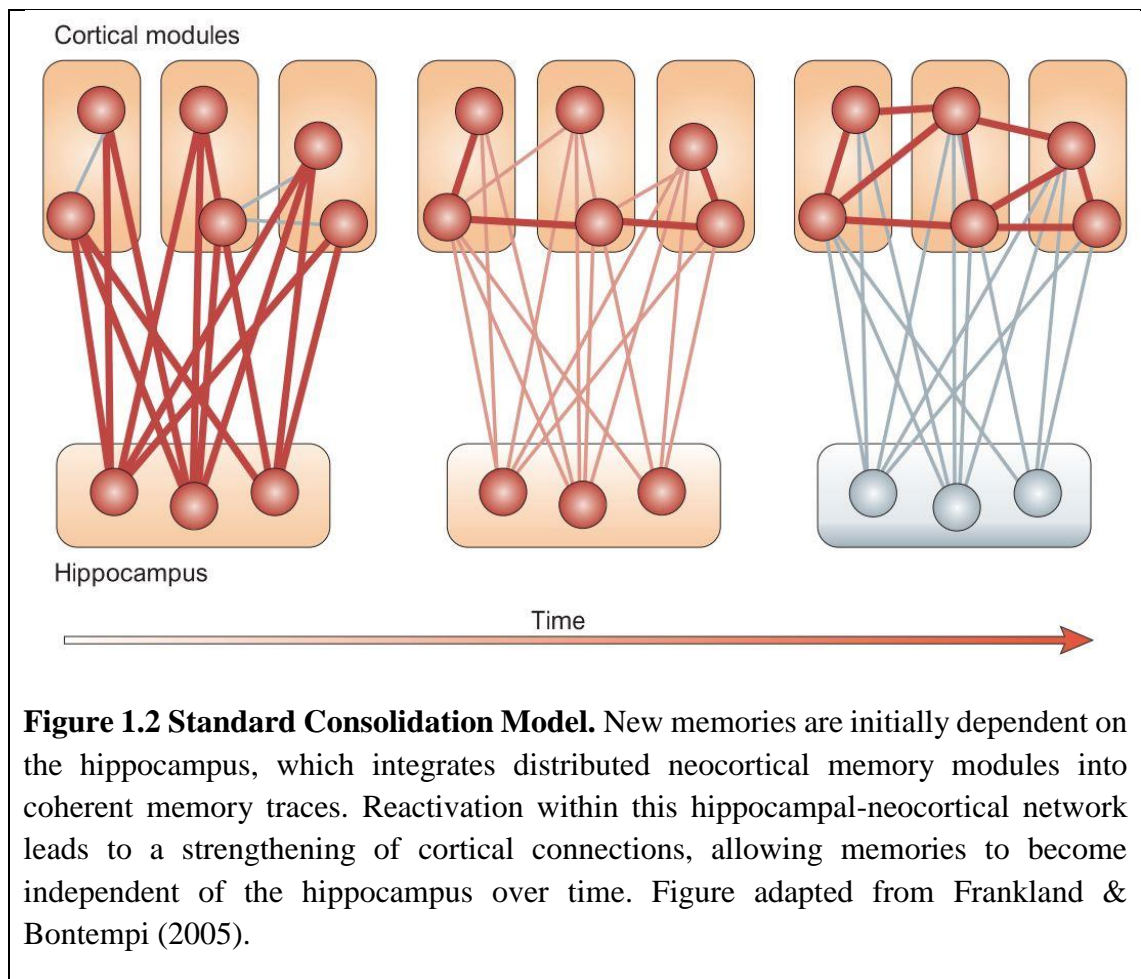
1.3 Memory Consolidation

There is no consensus as to the processes that should be covered by the term ‘memory consolidation’ (Stickgold, 2005). The term originally referred to a process of memory stabilisation, by which memories become resistant to interference (Müller & Pilzecker, 1900). However there is now a large amount of literature suggesting a role for consolidation mechanisms in memory enhancement and reorganisation, with newly formed weak and liable memories being transformed into strong and enduring

representations over time (Rasch & Born, 2013). After the initial acquisition of a memory, a series of cellular, molecular and systems level modifications take place. At the synaptic level, consolidation is accomplished within minutes to hours of learning and results in stabilisation at the neuronal level (Born, Rasch & Gais, 2006; Dudai, 2004; Dudai, Karni & Born, 2015; McClelland, McNaughton & O'Reilly, 1995). Systems level consolidation builds on synaptic consolidation and refers to processes that account for the redistribution and reorganisation of the memory representations for long-term storage (Rasch & Born, 2013). The exact processes and mechanisms responsible for systems level consolidation remains a matter of debate; the following sections will discuss the 'Standard Model of Consolidation' and the 'Multiple Trace Theory' to provide an overview of current accounts of consolidation.

1.3.1 The Standard Model of Systems-Level Consolidation

The standard model of consolidation proposes that memory consolidation processes are dependent upon two distinct memory stores; a hippocampal-dependent short-term memory store and a long-term store distributed across the neocortex (see Figure 2, Frankland & Bontempi, 2005). During learning, it is thought that information is encoded within both the short-term hippocampal circuitry and within long-term neocortical networks. Due to the distributed nature of the neocortical representations, which encompass the various multimodal components of an experience, retrieval of a new memory is proposed to require the hippocampus which acts to integrate and 'bind' the patterns of cortical activation into a coherent memory representation. Over time, and following covert reactivation of the hippocampal-neocortical connections, there is a progressive strengthening of connectivity between the cortical modules and a concurrent reduction in dependence on the hippocampus. As a result, memories become fully integrated within long-term memory stores and independent of the hippocampus. This has two complementary benefits for memory; the hippocampus maintains its encoding capacity ready for future learning, while the gradual integration of knowledge into long-term stores reduces the risk of catastrophic interference and memory 'overwriting' (see Figure 1.2; Frankland & Bontempi, 2005; McClelland et al., 1995).



Neuropsychological evidence in support of the standard model of consolidation is provided by patients who display temporally graded retrograde amnesia following lesions in the medial temporal lobe (MTL) and hippocampus (Ribot, 1882). One of the most prominent cases is of patient HM who had surgery to remove large parts of the MTL including the bilateral hippocampus. As a result of the surgery HM suffered from severe anterograde amnesia and was unable to create new long-term memory representations. HM also demonstrated temporally graded retrograde amnesia, whereby he was unable to retrieve the recent past i.e. memories that had been encoded shortly before the surgery, while older, more distant memories remained intact (Scoville & Milner, 2000). In contrast to the temporally graded nature of retrograde amnesia following MTL damage, which has been reported consistently in the literature (Bayley, Hopkins & Squire, 2006; Morris, 2009; Squire, Chace & Slater, 1976; Squire & Alvarez, 1995; Squire, 2004; Squire & Zola-morgan, 1991; Zola-Morgan, 1996), flat non-graded retrograde amnesia is also associated with neocortical trauma, suggesting that the role of the hippocampus is

temporally limited, while the long-term storage of memories is ultimately dependent upon the neocortex (Dudai, 2004; Squire, Clark & Knowlton, 2001).

A hippocampal-neocortical shift in memory retrieval has also been demonstrated in neuroimaging studies. Takashima et al. (2009; 2006) report that over time there is a differential change in connectivity strength during declarative memory retrieval. Across a 24-hour delay they report increased cortical activity and a reduction in overall connectivity with the hippocampus. At longer timescales, Sterpenich et al. (2009; 2007) has shown that hippocampal responses associated with image recollection after 3 days are absent when tested 6 months later – supporting the suggestion that systems level consolidation processes operate over timescales that can extend to days, weeks, months and even years after initial encoding (Stickgold, 2005). Although this neuroimaging evidence is compelling, comparing the neural correlates of a memory representation across long timescales (i.e. days, weeks and months) should be interpreted with caution. It is possible that the reduced hippocampal response is the consequence of a weaker memory trace rather than an active process of memory transfer and reorganisation.

The standard model of consolidation provides the basis of a core theory that is addressed throughout this thesis – the Complementary Learning Systems (CLS) account of consolidation. The CLS model provides a computational basis of consolidation and suggests that the hippocampus and neocortex may play distinct roles in representing memories (McClelland et al., 1995). These separate roles solve a trade-off between remembering specific experiences (e.g. where you left your keys), which benefit from separate representations for each event, and the extraction of regularities across experiences (e.g. where you would typically expect to find your keys), which benefit from overlapping memory representations. The CLS proposes that the hippocampus quickly stores memory traces for individual experiences by using a high learning rate and sparse, non-overlapping (pattern separated) representations. The neocortex, in contrast, has a slow learning rate and supports the development of overlapping representations gradually over time. These neocortical overlapping representations may therefore support the storage of regularities across events, allowing the neocortex to capture similarity structures that are not present within individual memory representations, and facilitate the development of conceptual memory representations (McClelland et al., 1995; O'Reilly et

al., 2014). The CLS model and its relationship with conceptual memory development is discussed throughout the Chapters in this thesis.

1.3.2 The Multiple Trace Theory of Consolidation

The standard model of consolidation suggests a time-limited role for the hippocampus in memory; however this has been disputed within the consolidation literature. Nadel & Moscovitch (1997) provide an account which suggests that the neocortex stores a ‘semantic’ version of a memory which is decontextualized and can be retrieved independently of the hippocampus (Nadel & Moscovitch, 1997). However, if the recall of rich contextual or spatial details is required, then the hippocampus becomes crucial for successful retrieval. This has been named the Multiple Trace Theory (MTT) and suggests that complete hippocampal damage will lead to loss of episodic (contextual) memory while semantic memory representations will remain intact (Frankland & Bontempi, 2005). Support for the MTT is provided by neuropsychological cases showing extensive and ungraded amnesia following hippocampal damage, while semantic knowledge remains largely intact (Cipolotti et al., 2001; Rosenbaum et al., 2009; Spiers, Maguire & Burgess, 2001).

Neuroimaging studies provide added support for the MTT when tasks require the formation of strong spatial or contextual memory elements. Janzen, Jansen & Turennout (2008) used an object recognition and spatial location task to demonstrate greater hippocampal activity for consolidated (encoded 12-hour prior to tests) compared to non-consolidated (encoded immediately before testing) objects, suggesting hippocampal activity increases as a function of consolidation for these representations. From the alternative perspective, reduced hippocampal activity has been reported following the decontextualization of event memories (Talamini & Gorree, 2012; Winocur et al., 2009) – these studies therefore highlight the specificity of hippocampal involvement in memory.

Although the MTT can account for instances of non-graded retrograde amnesia following MTL damage, and the specificity of hippocampal involvement following consolidation it is not without its drawbacks. As with the standard model of consolidation, caution should be taken when interpreting hippocampal activation levels across testing sessions. Increases in hippocampal activity could reflect new hippocampal memory encoding (related to the experience of retrieval) rather than a consolidation related change

in activity. Furthermore, the MTT is unable to account for all patterns of deficits reported in the neuropsychological literature; for example Teng & Squire (1999) report a patient who has retained spatial episodic information from their youth, despite extensive bilateral lesions to the MTL, including the hippocampus. This may suggest that the hippocampus is not required for the recall of very remote spatial memories, which contrasts with the predictions from the MTT.

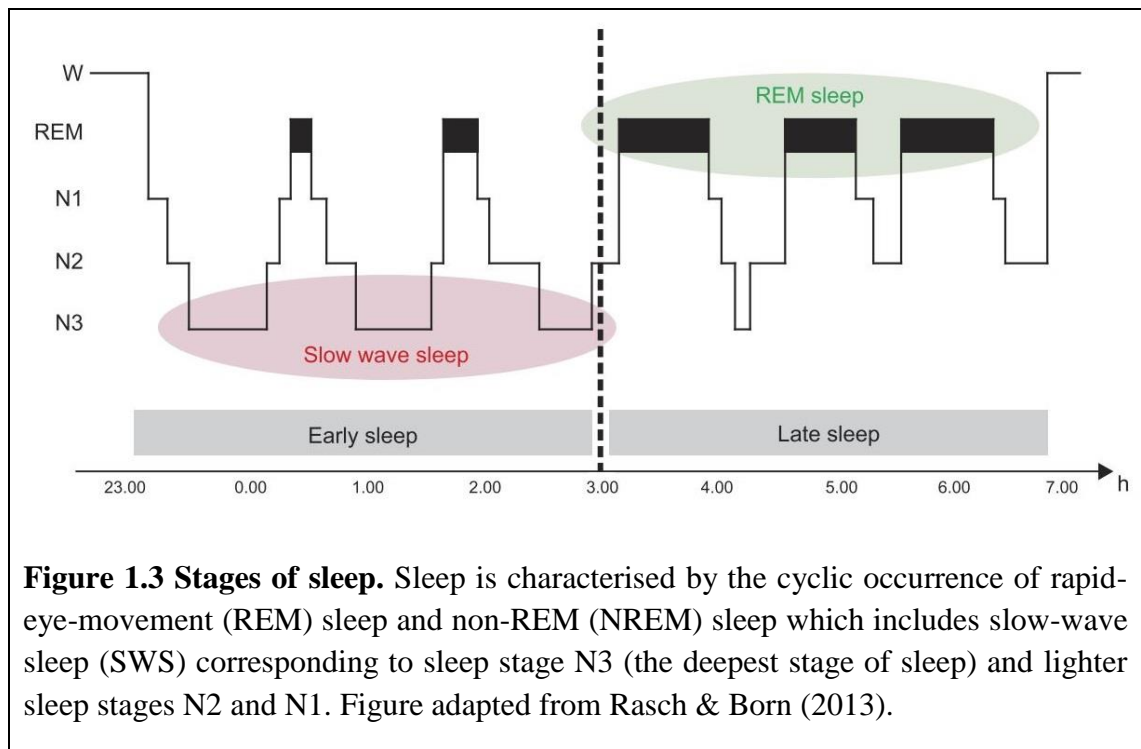
Despite differences in the time-dependent role of the hippocampus, both the standard model of consolidation and the MTT agree that there is a qualitative difference between hippocampal-dependent and hippocampal-independent memory representations. Hippocampal memories are context-rich and ‘episodic’ in nature, while long-term neocortical representations integrate information from across multiple experiences to generate more ‘semantic’ type representations. From this perspective, there is strong support for the role of consolidation in the development of semantic or conceptual memory, with neocortical representations requiring time and consolidation for long-term stabilisation. Consolidation may however happen in a number of different cognitive states and via a wide range of mechanisms and processes. This review will now go on to discuss the role of sleep and quiet wakefulness in memory consolidation – providing evidence for consolidation specific mechanisms and discussing how they may benefit the development of concept memory.

1.4 The Role of Sleep in Memory Consolidation

Sleep is defined as the natural and reversible state of reduced responsiveness to external stimuli, accompanied by inactivity and loss of consciousness (Rasch & Born, 2013). The cognitive and physical consequences of sleep deprivation, the evolutionary conservation of sleep in mammals and the rebound of sleep following sleep loss suggest that sleep serves an important purpose (Durmer & Dinges, 2005), however, a unified theory of sleep function remains elusive (Fuller et al., 2006). As well as energy conservation, brain thermoregulation, brain detoxification and tissue restoration, sleep provides optimal conditions for offline memory consolidation (Maquet, 2001). The review will first discuss the physiology of sleep and then provide evidence for an active role of sleep in memory consolidation.

1.4.1 Sleep Physiology

Sleep, as a state, is not unitary but is broadly divided into two phases based on distinct EEG oscillatory patterns; rapid-eye movement sleep (REM) and non-REM sleep (NREM, see Figure 1.3). NREM sleep is further divided into three distinct stages; stage I, stage II and stage III (also referred to as slow-wave sleep, SWS), with each stage representing a progressively deeper level of sleep (Iber et al., 2007). The three stages of NREM alternate throughout the night with REM sleep in ~ 90 minutes cycles. SWS dominates the first half of the night, while REM sleep prevails during the latter half (see Figure 1.3); this temporal shift in sleep stage across the night, is driven by homeostatic and circadian pressures (Borbely & Achermann, 1999; Borbely & Tobler, 1989).

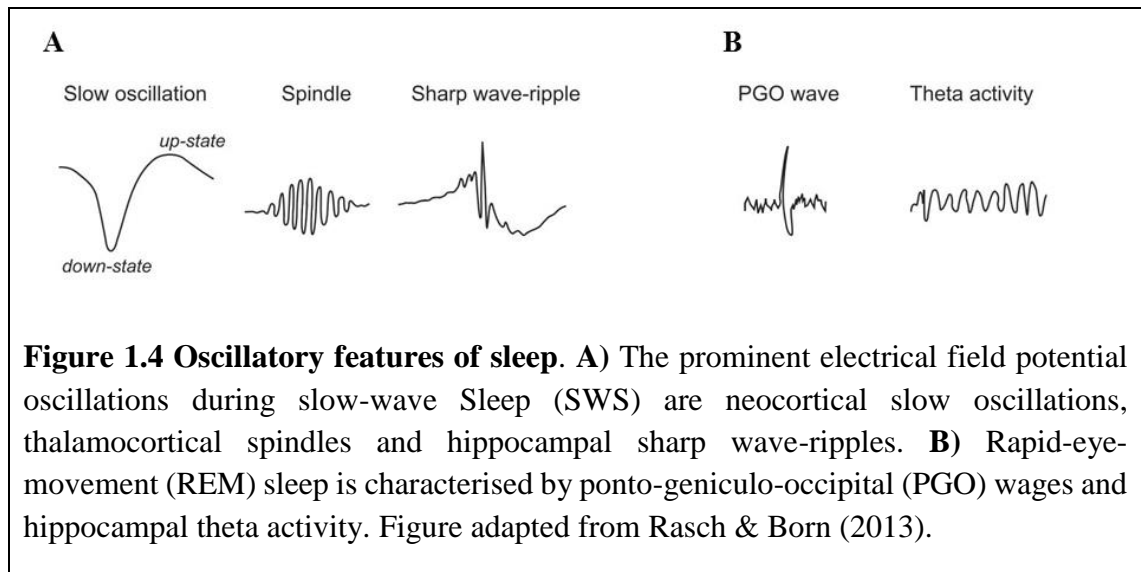


Sleep onset is characterised by Stage I of NREM sleep, a transitional phase between wakefulness and sleep, marked by the presence of vertex sharp waves characterised by EEG brain oscillations predominating in the 8 – 12 Hz alpha range and the 4 – 7 Hz theta range (Fuller et al., 2006). Stage I typically lasts for only a few minutes (~5% of total sleep time) before being followed by Stage II sleep which is characterised by EEG activity

in the 5 – 8 Hz theta range along with two unique oscillatory events; k-complexes and sleep spindles (Alger et al., 2015). K-complexes are brief high amplitude negative voltage peaks followed by a slower positive complex generated in the cortex (Alger et al., 2015). They are evoked by sensory stimuli and provide isolated down-states which are thought to suppress cortical activity and arousal (Cash et al., 2009). Sleep spindles are short bursts of alpha range activity; slow spindles (12 – 14 Hz range) are concentrated over frontal locations while fast spindles (14 – 16 Hz range) originate in central and parietal regions (see Figure 4, Zeitlhofer et al., 1997).

Stage III of NREM sleep (or SWS) is the deepest level of sleep and is characterised by high-amplitude, low-frequency oscillations in the 0.5 – 4 Hz delta range. During SWS, slow oscillations (0.5 – 1 Hz range) occur in phase across the whole brain along with sharp-wave ripples (SWR) that originate from the hippocampus (see Figure 4, Genzel et al., 2014). The SWRs occur during the up-states of slow oscillations and are temporally correlated with sleep spindle activity (Alger et al., 2015; Molle, 2006; Siapas & Wilson, 1998; Steriade, McCormick & Sejnowski, 1993).

REM sleep is defined by low-amplitude, hippocampal theta activity (4 – 8 Hz) along with sharp rapid-eye movements and a global reduction in muscle tone. REM sleep is punctuated and preceded by ponto-geniculo-occipital (PGO) waves originating in the brain stem (see Figure 1.4). These PGO waves are highest in amplitude in the visual cortex and may be responsible for the vivid experience of dreaming during REM sleep (Steriade & McCarley, 1990).



1.4.2 Models of Sleep-dependent Memory Consolidation

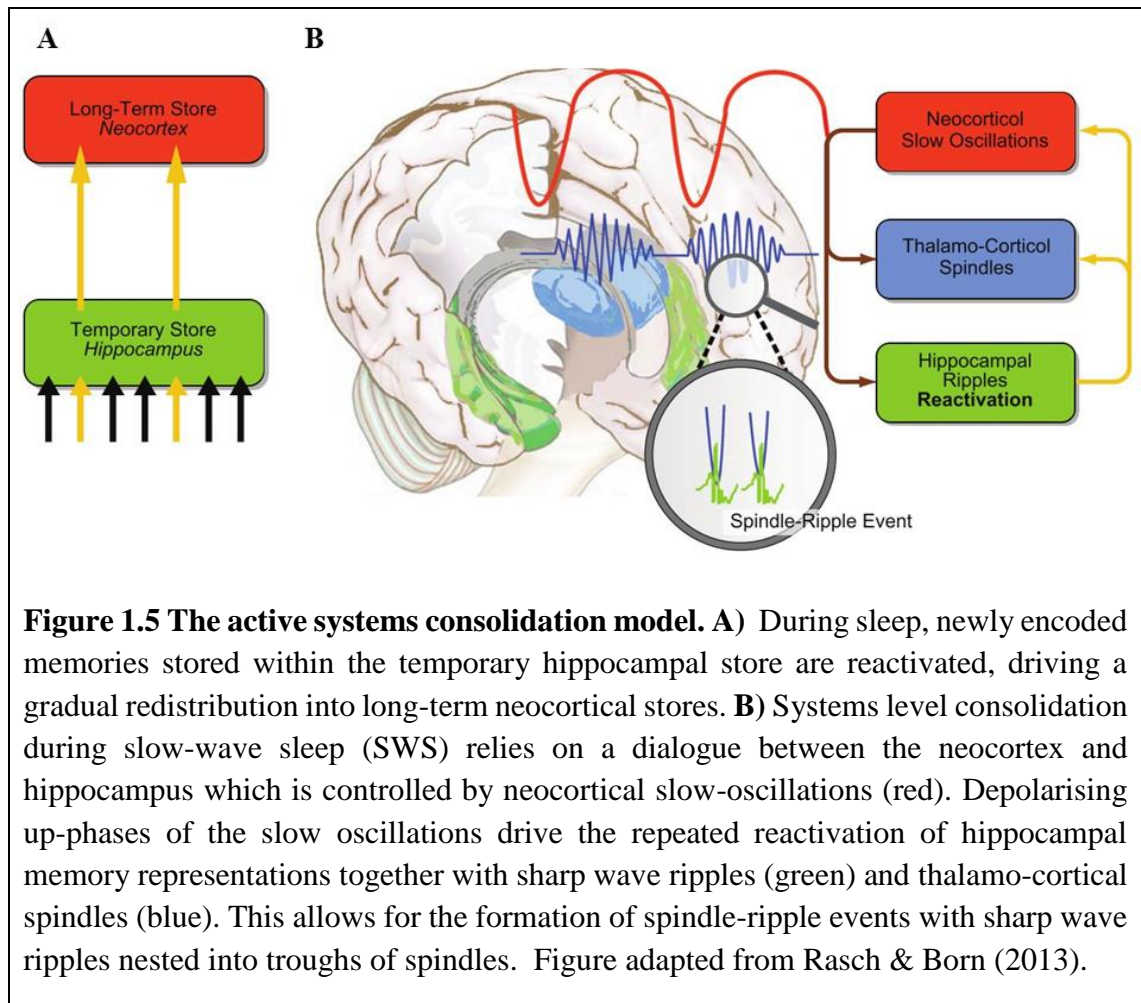
A growing body of research has focused upon the role of sleep in memory consolidation. The benefit of sleep on memory retention can be dated back to Ebbinghaus (1885) who noted that declarative memories appear to be sustained more by sleep than an equivalent period of wakefulness. Initial experimental work concluded that sleep provides passive protection against interference and this theory remained prominent for many decades (Jenkins & Dallenbach, 1924). However, more recent empirical work suggests that sleep plays a more active role in memory consolidation. Behavioural observations include memory strengthening, memory reorganisation and the transformation of memories following sleep (Batterink et al., 2014; Born et al., 2006; Diekelmann & Born, 2010; Dudai et al., 2015a; Ellenbogen et al., 2006; Fischer et al., 2006; Plihal & Born, 1997; Rasch & Born, 2013b; Wagner et al., 2004). Two prominent theories of consolidation have emerged from the sleep literature; the active systems consolidation model (ASC) (Born et al., 2006; Born & Wilhelm, 2012; Diekelmann & Born, 2010) and the synaptic homeostasis model (Tononi & Cirelli, 2003; 2006). Both of these models highlight the importance of SWS in memory processing, however they offer very different perspectives as to the consolidation mechanisms involved. An account of these two models, along with their supporting literature, is provided.

1.4.2.1 The Active Systems Consolidation Model

The Active Systems Consolidation Model (ASC) extends the standard model of consolidation to propose that the redistribution of memories in systems level consolidation is driven by slow oscillations, SWRs and sleep spindles occurring during SWS (Frankland & Bontempi, 2005; Walker, 2009). It is hypothesised that SWRs reflect cross-talk between the hippocampus and neocortex, while synchronisation between slow oscillations and sleep spindles induces long-term plastic changes within cortical networks (Rasch & Born, 2013). Sleep is therefore thought to facilitate a shift in memory dependency from the hippocampus to the neocortex, via a process of memory reactivation, in line with the standard model of memory consolidation (see Figure 1.5).

1.4.2.2 The Role of SWS: Slow Oscillations, SWRs and Sleep Spindles

Slow oscillations reflect widespread synchronised down-states of neural hyperpolarisation, followed by depolarising up-states of excitation across the neocortex (Fuller et al., 2006; Steriade et al., 1993). This slow oscillatory activity also synchronises activity from the thalamus and hippocampus, where sleep spindles and SWRs are generated respectively (Gennaro & Ferrara, 2003; Purcell et al., 2016; Alger et al., 2015). This coordination of activity leads to spindle-ripple events (see Figure 1.5) which are believed to mediate the transfer of hippocampal memory information to the neocortex (Born & Wilhelm, 2012). The depolarizing up-phase of the slow oscillation enables SWRs and accompanying memory information to become nested within the oscillatory troughs of spindles (Mölle et al., 2009; Siapas & Wilson, 1998). Spindles reaching the neocortex are thought to prime the respective neural networks, making them receptive for synaptic adjustments to facilitate long-term storage (Born & Wilhelm, 2012). Thus synchronous input to the neocortex, from the thalamus and hippocampus, is thought to be critical for the redistribution of declarative memory representations.



There is a large amount of evidence supporting the ASC model and the role of slow oscillations and spindle-ripple events. Notably, positive correlations between memory performance and the amount of SWS and spindle activity (both spindle quantity and density) have been observed following a range of different memory tasks (Clemens, Fabo & Halasz, 2005; Durrant, Cairney & Lewis, 2013; Durrant et al., 2011; Gais et al., 2002; Gruber et al., 2015; Lau, Alger & Fishbein, 2011; Lustenberger, Murbach & Tüshaus, 2015; Mölle et al., 2002; Schabus, Dang-Vu & Albouy, 2007; Schabus et al., 2004; Wilhelm et al., 2011). More direct evidence is provided by investigations of local brain regulation during sleep, whereby increased coherence of slow oscillations can be observed in brain regions involved in pre-sleep learning (Huber et al., 2004). Critically, the local change in activity was able to predict post-sleep task performance, suggesting an active role of slow oscillations in processes of memory consolidation.

Support is also provided by electrical stimulation techniques such as transcranial direct current stimulation (tDCS), which can induce slow-oscillation field potentials in healthy participants during sleep (Marshall et al., 2004). Following tDCS applied during SWS-rich sleep, increases in slow oscillations, sleep spindles and behavioural measures of memory retention have been reported (Barham et al., 2016; Marshall et al., 2006, 2011). Similar manipulations to the natural oscillations observed during sleep can be obtained using ‘Auditory Closed-Loop Stimulation’. This is a stimulation technique whereby auditory pulses, in phase with the rhythmic occurrence of slow oscillation up-states are presented to participants as they sleep (Ngo et al., 2013). This stimulation enhances the slow oscillation rhythms and subsequent memory retrieval (Ngo et al., 2013; 2015). Taken together, these studies provide strong support for the role of slow-oscillations in declarative memory consolidation.

1.4.2.2.1 Spontaneous Memory Reactivation

The ASC model suggests that memory reactivations drive memory consolidation. Evidence of spontaneous memory reactivation during sleep was provided originally by studies using rodents and single-cell recordings from hippocampal cells (Wilson & McNaughton, 1994). These studies show that hippocampal-dependent wake activity, observed during a spatial navigation task, can also be observed in post-navigation SWS (Kudrimoti, Barnes & McNaughton, 1999; Louie & Wilson, 2001; Sutherland & McNaughton, 2000; Wilson & McNaughton, 1994). The order of neuronal firing during wakefulness appears to be preserved during sleep, but is replayed in a temporally compressed manner (Lee & Wilson, 2002). Furthermore, neuronal firings observed during sleep are able to successfully predict later memory performance, suggesting a close coupling between these replay patterns and memory performance (Dupret et al., 2010).

In humans, spontaneous memory reactivation during sleep has been observed via positron emission tomography (PET) and sophisticated functional magnetic resonance imaging (fMRI) techniques. Peigneux et al. (2004) used PET to show that the same pattern of hippocampal activity observed during a spatial navigation task could also be observed in SWS in human participants. Interestingly, the amount of hippocampal activity observed during SWS was positively correlated with improvements in the navigation task the following day, highlighting a link between sleep-based reactivation and behavioural improvements in memory (Peigneux et al., 2004). Similar findings have

also been observed in a paired-associate memory task following multivariate pattern analysis (MVPA) on fMRI data (Deuker et al., 2013). The results showed the same patterns of stimulus-specific activation in both learning and post-learning sleep, where the frequency of reactivations predicted subsequent memory at the individual item level (Deuker et al., 2013). There is therefore convincing evidence for spontaneous memory reactivation during sleep, providing strong support for reactivation as a potential mechanism of consolidation.

1.4.2.2 Targeted Memory Reactivation

A causal role for memory reactivation during sleep has been investigated using targeted memory reactivation (TMR), a technique that takes advantage of the brain's ability to process external stimuli during sleep (Oudiette et al., 2013). The seminal study on TMR used odours as a contextual cue during a picture-location association task. Exposure to the same odour during SWS led to enhanced memory performance in a post-sleep test of recall (Rasch et al., 2007). To demonstrate the specificity of the technique Rudoy et al. (2009) used auditory cues in a similar task, where each trained association was paired with a unique sound cue. During a post-training nap containing SWS, half of the sounds from learning were replayed to participants as they slept. In a subsequent test of memory, participants showed enhanced memory recall, but only for the individual items for which the associated sound had been replayed. The benefit of TMR has been shown to be sleep specific, as the same cues presented during wakefulness do not lead to behavioural improvements in memory (Oudiette & Paller, 2013; Rudoy et al., 2009).

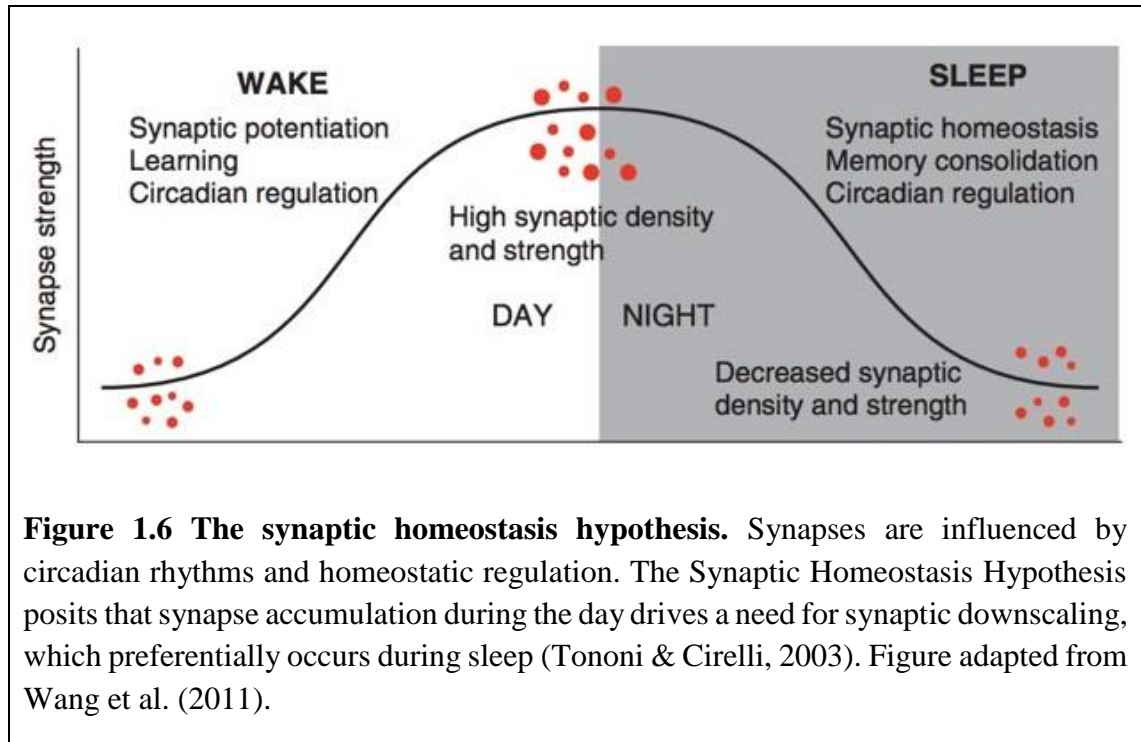
There is now a growing body of literature supporting these initial TMR findings, suggesting that memory reactivation can be induced externally to benefit the strength of memory (Batterink & Paller, 2017; Cairney et al., 2014; 2016; Cousins et al., 2014; Creery et al., 2015; Fuentemilla et al., 2013; Lehmann et al., 2016; Oyarzún et al., 2017; Schouten et al., 2017; Schreiner & Rasch, 2017, 2015; Tamminen, Lambon Ralph & Lewis, 2017; van Dongen et al., 2012). The major evidence implicating sleep in memory consolidation comes from comparisons between sleep and wake retention intervals, and therefore suffers from confounding factors such as circadian rhythms and alertness levels. Data from the TMR paradigm, which avoids these confounds, provides very strong evidence for a specific role for sleep-associated mechanisms of memory consolidation.

1.4.2.3 Synaptic Homeostasis Hypothesis

An alternative theory to the role of sleep in consolidation has also been proposed, the Synaptic Homeostasis Hypothesis, which focuses upon synaptic weights (Tononi & Cirelli, 2003). During wakefulness cortical circuits undergo long-lasting changes in synaptic strength as a result of experience and learning. Global restoration of synaptic strength is therefore required in order to renormalize cortical networks (Tononi & Cirelli, 2014). According to the synaptic homeostasis hypothesis (see Figure 1.6), SWS and slow oscillations actively promote a generalized depression and downscaling of synaptic strength, allowing synaptic weights to progressively return to baseline level and therefore creating synaptic homeostasis across sleep (Tononi & Cirelli, 2003, 2006). Importantly, synaptic strength is hypothesised to reduce proportionally, preserving the relative differences within cortical networks (Tononi & Cirelli, 2012). As a result the signal-to-noise ratio is increased, with strongly potentiated synapses (signal) being preserved (Rasch & Born, 2013; Tononi & Cirelli, 2012). This synaptic weakening could lead to enhanced memory and consolidation, if synaptic depression is greatest for weak, compared to strongly encoded representations.

There is strong evidence for synaptic potentiation during wake along with synaptic downscaling during sleep from the animal literature. Increased synaptic density and markers of synaptic plasticity have been observed in rodents following exploration of enriched environments (Cirelli, Gutierrez & Tononi, 2004; Cirelli & Tononi, 2000). Furthermore, Eyre et al. (2003) show that these plasticity levels returned to baseline following a 12-hour delay, yet task-based memory remained high. In humans, evidence for the model is provided from investigations of homeostatic pressure, with the assumption that following learning (and potentiation) there should be localised increases in slow-wave activity in the brain as a result of homeostatic pressure (Tononi & Cirelli, 2003). Support is provided by Huber et al. (2004) who observed increases in slow-wave activity in parietal brain regions following a motor adaptation task. Furthermore, the amount of slow-wave activity correlated with behavioural task improvements. This interpretation of the data fits with the synaptic homeostasis hypothesis, however increases in localised slow-wave activity could also reflect neural replay as hypothesised by the ACS model. With correlation evidence, it is difficult to determine the underlying

processes generating the behavioural response, and therefore caution should be taken when making firm interpretations of the data.



Both the ASC model and the synaptic homeostasis model implicate processes during SWS as driving memory consolidation. Although the models have gained support, they both struggle to explain critical aspects of sleep-dependent consolidation. The ASC model does not provide a strong neurophysiological explanation at the synaptic level to explain consolidation (Diekelmann & Born, 2010), while the synaptic homeostasis model does not account for the causal evidence showing a role for memory reactivation and hippocampal-neocortical cross-talk in the transfer of information over time. Indeed, it is not the case that these two theories are mutually exclusive; the two may in fact prove to be complementary if combined in a model that includes a role for both systems-level reorganisation and the maintenance of synaptic weights through homeostatic regulation (Feld & Born, 2017; Rasch & Born, 2013). This review will now go on to consider quiet wakefulness as an opportunity for memory consolidation and will then discuss the role of offline consolidation mechanisms in the development on conceptual memory representations.

1.5 Quiet Wakefulness and Memory Consolidation

Despite the growing body of literature highlighting a specific role for sleep in memory consolidation, it is also clear that a full night of sleep is not required to boost memory. Partial nights of sleep and short daytime naps (even naps as short as 6-minutes) also lead to memory benefits, with comparable effect sizes to overnight sleep (Brokaw et al., 2016; Mednick, Nakayama & Stickgold, 2003; Plihal & Born, 1997; Tucker et al., 2006; Tucker & Fishbein, 2009; Lahl et al., 2008). It has therefore been suggested that fast-acting consolidation mechanisms may not be dependent on the state of sleep, but may occur during any state (including both sleep and wakefulness) when the encoding of new information is sufficiently reduced; this has been referred to as the ‘Opportunistic Consolidation Hypothesis’ (Mednick et al., 2011).

Studies investigating the effects of sleep on memory typically use a wake control comparison focused upon ‘active wake’ – where participants are encoding new sensory information and engaging in tasks such as watching videos, listening to music or going about their usual daily activities (Ellenbogen, Payne & Stickgold, 2006; Lau, Tucker & Fishbein, 2010; Tucker et al., 2006). The effect of ‘quiet wake’ – wakefulness in the absence of cognitive tasks, activities of sensory encoding, has not been sufficiently characterised in the consolidation literature. However, recently evidence has emerged to suggest that quiet wake may facilitate processes of memory consolidation (Craig et al., 2015; Dewar et al., 2012; Dewar et al., 2014; Mercer, 2015; Schlichting & Bäuml, 2016). Dewar et al. (2012) showed that the degree of memory retention seven days after encoding was significantly altered by the cognitive activity that followed learning, with wakeful rest leading to a boost in memory retention in comparison to an active task. Furthermore, Dewar et al. (2014) report a wakeful rest benefit for the recognition and recall of unpronounceable nonwords, suggesting that the benefit of wakeful rest is not related to intentional rehearsal.

In addition, post-learning rest has also been shown to protect new memories from retroactive interference (Mercer, 2015), eliminate effects of directed forgetting (Schlichting & Bäuml, 2016) and promote memory integration (Craig et al., 2015; Craig et al., 2016). In a spatial learning virtual reality task, Craig et al. (2015) found 10-minutes of wakeful rest to boost retention for spatial memory and temporal order for up to seven

days after encoding. Moreover, in a similar virtual environment task, a benefit for wakeful rest was observed for spatial relations that were never directly experienced by the participants i.e. the task required participants to make inferences based on their training (Craig et al., 2016). This suggests that the mechanisms in wakeful rest may go beyond stabilising memories to actively integrate information to form coherent representations.

1.5.1 Quiet Rest and Slow-Wave Sleep: Two Similar States

There has been a large amount of research into the neurophysiological correlates of memory changes across sleep (Holz et al., 2012; Nishida & Walker, 2007; van Dongen et al., 2012), however similar investigations into quiet wakefulness are limited (Brokaw et al., 2016). Quiet wake does however share a number of properties with SWS and these properties may provide a ‘brain state’ that can be readily capitalised on by consolidation mechanisms. The review will now discuss four features shared by SWS and quiet wake which may act to promote mechanisms of consolidation, these include; 1) the reduction in sensory processing, 2) evidence of neural replay, 3) similar neurochemistry and analogous oscillatory activity.

1.5.1.1 Reduction in Sensory Processing

Both SWS and quiet wake are characterised by a dramatic reduction in sensory processing. During quiet rest, without the demands of stimulus processing, mental experience is focused inwards, and participants typically engage in ‘mind-wandering’ – a shift to self-generated thought such as thinking about the past or imagining the future (Smallwood & Schooler, 2015). Recent accounts suggest mind-wandering can be understood as a combination of different processes, including the decoupling of attention, which allows cognition to become independent of the external environment (Baird et al., 2014; Sneve et al., 2017), and the retrieval of semantic knowledge (Poerio et al., 2017). Indeed, increased hippocampal activity (related to episodic memory processing) is observed during states of mind-wandering (Ellamil et al., 2016) and evidence suggests that mental time-travel is linked to interactions between the hippocampus and cortical brain regions (Karapanagiotidis et al., 2017).

Mind-wandering is associated with a large scale neural network – the Default Mode Network (DMN) – which consists of a range of cortical regions (Raichle et al., 2001).

Notably these regions do not include any sensory or motor cortices, supporting the idea of stimulus-independent driven thought. In line with the idea that quiet rest may facilitate memory consolidation, the DMN has been shown to contain subsystems that relate to two different amodal memory stores, the first includes the anterior temporal cortex – implicated in the representation of concept knowledge (Lambon Ralph et al., 2017) and the second includes medial temporal lobe structures including the hippocampus – related to episodic memory processing (Moscovitch et al., 2016). Given that these regions are strongly implicated in memory and theories of consolidation, along with the reduction of external interference, quiet rest appears to provide optimal conditions for consolidation mechanisms to progress.

1.5.1.2 Neural Replay

Neural replay has been well documented during SWS and it has been suggested that consolidation may progress via the reactivation of recently encoded memory traces (Rasch & Born, 2013). Animal studies however, also reported neural replay during quiet wake (Carr, Jadhav & Frank, 2011; Dupret et al., 2010; Karlsson & Frank, 2009). Foster & Wilson (2006) report sequential replay in the rat hippocampus during wake periods that immediately follow spatial experiences. This observed replay is in a temporally reversed order, which may be particularly useful for the consolidation of functionally useful or important events. Recent evidence of neural replay in humans is provided by Deuker et al. (2013), who show spontaneous patterns of task-related replay during both sleep and quiet wake. Furthermore, the frequency of reactivations predicted subsequent memory performance, suggesting a functional benefit from this reactivation. Further evidence for neural replay during rest in humans is beginning to emerge, however direct causal evidence has yet to be established (Deuker et al., 2013; Tambini & Davachi, 2013; Tambini, Ketz & Davachi, 2010).

1.5.1.3 Neurochemistry: Acetylcholine

An important mechanism supporting the switch between encoding and consolidation may involve the neuromodulator Acetylcholine (ACh). Physiological research has demonstrated a number of effects of ACh within the hippocampus, neocortex and thalamus (Hasselmo, 1995). Importantly, high ACh levels, as seen in active wake and REM sleep, have been shown to promote attention and encoding, with the hippocampal

dynamics set for the inflow of information. In contrast, low ACh levels have been shown to facilitate the outflow of information by reducing hippocampal plasticity and promoting communication from the hippocampus to the neocortex (Hasselmo & McGaughy, 2004). Low ACh levels are therefore considered to shift the hippocampus into a ‘consolidation’ state (Mednick et al., 2011). Critically, low ACh levels are observed in both quiet wake and in SWS, suggesting that both states may provide the optimal conditions for processes of memory consolidation to occur (Mednick et al., 2011).

1.5.1.4 Brain Oscillatory Activity

Both sleep and quiet rest are associated with an overall slowing of electroencephalogram (EEG) oscillatory activity. Alpha is the signature of eyes-closed waking rest and is the main EEG correlate of the DMN. In line with the previous discussion of the DMN, alpha is associated with decreased focus on the external environment and increased attention to internal states (Foulkes & Fleisher, 1975). Alpha rhythms have been shown to be correlated with memory performance, suggesting they sub-serve memory processes and therefore strong alpha activity in waking rest may facilitate memory related processes of consolidation (Williams, Ramaswamy & Oulhaj, 2006). Slower EEG frequencies (~1Hz) most commonly described as signatures of SWS and described as being major contributors to systems-level consolidation, can also be observed during quiet rest (Demanuele & Sonuga-Barke, 2010). Brokaw et al. (2016) show enhanced memory recall following quiet rest along with an increase in slow oscillatory activity (<1Hz), suggesting that given the right conditions, non-sleep resting states may facilitate memory consolidation and this may be driven by similar oscillatory activity as in sleep.

This section has provided a discussion of the current literature related to the role of quiet wakefulness in memory consolidation. This area of research is very underdeveloped, however there is evidence to suggest that mechanisms of memory consolidation may not be sleep specific, but may operate in wakefulness given the right conditions. Quiet wake and SWS share a number of properties, however the role they play in the mechanism of consolidation has yet to be determined. Chapter 5 of this thesis investigates the neural correlates of quiet wake; determining whether brain connectivity during rest can predict behavioural measures of memory across consolidation. This

review will now go onto to discuss the current evidence for a role of consolidation beyond memory strengthening.

1.6 Consolidation: Beyond Stabilisation and Enhancement

Within the consolidation literature there has been a large focus upon item memory and the role of offline processing in the stabilisation and enhancement of individual memory representations. However, this is just one possible form of offline memory processing. Beyond memory strengthening, consolidation processes have also been found to lead to qualitative changes in the way a memory is represented, resulting in the generation of new knowledge that was not present during individual item encoding (Stickgold & Walker, 2013). This section of the review will discuss four areas of research that provide evidence for offline consolidation processes as driving these qualitative changes in memory, focusing upon; the extraction of gist, insight into hidden rules, memory integration and detecting regularities via statistical learning. The way in which these areas of research inform our understanding of concept memory will be highlighted throughout.

1.6.1 Extraction of Gist

Gist refers to the essence of an experience or memory, representing an abstraction of essential features that excludes idiosyncratic details (Lewis & Durrant, 2011). Gist extraction may therefore be particularly beneficial for the development of concept memory, where the general ‘meaning’ from a set of similar events or objects is more important than individual elements themselves. One, sometimes problematic consequence of gist extraction (e.g. eye witness testimony) is the generation of false memories – the recollection of events or stimuli that never took place, or which are remembered in a distorted way (Roediger & McDermott, 1995). The generation of false memories has been documented for some time in the literature (Bartlett, 1932; Loftus & Bernstein, 2005; Loftus & Palmer, 1974; Brewer, 1977) however it is only more recently that the relationship between false memories and processes during offline consolidation has been studied (Darsaud et al., 2011; Diekelmann, Born & Wagner, 2010; McKeon, Pace-Schott & Spencer, 2012a; Payne et al., 2009; Fenn et al., 2009; Lo, Sim & Chee, 2014; Cox, Carter & Willner, 2016; Lutz et al., 2017).

These studies typically used a simple word-list memorisation task, known as the Deese-Roediger-McDermott (DRM) paradigm (Deese, 1959; Roediger & McDermott, 1995). In these tasks, participants are presented with a list of semantically related words to memorize (e.g. bed, rest, awake, tired, dream, etc.). When asked to recall the list, participants often falsely remember an unrepresented, but semantically related critical 'lure' word (e.g. sleep) with the same level of confidence as the correctly remembered studied words (Roediger & McDermott, 1995). Although a range of studies have investigated the role of offline consolidation in the DRM task, the results are very mixed. Studies have reported increases in false memories following sleep (Darsaud et al., 2011; Diekelmann et al., 2010; McKeon et al., 2012a; Payne et al., 2009) and following sleep deprivation (Diekelmann et al., 2010; 2008; Frenda et al., 2014; Lo et al., 2016), while others report reduced rates of false memories after sleep (Fenn et al., 2009; Lo, Sim & Chee, 2014) or no overall effects of sleep (Cox, Carter & Willner, 2016; Lutz et al., 2017).

Although there is a large amount of inconsistency in the literature, themes do emerge from the data. Notably, enhanced recall of false memories appears to be greatest for participants who perform poorly on the DRM task (Diekelmann et al., 2010; McKeon, Pace-Schott & Spencer, 2012; Pardilla-Delgado & Payne, 2017). More generally within the consolidation literature, evidence suggests that offline memory consolidation may be greater for weak compared to strongly encoded representations (Diekelmann, Wilhelm & Born, 2009). This has been interpreted as the result of a preferential consolidation mechanism, which prioritises the consolidation of weaker memory traces in an attempt to protect them from forgetting (Diekelmann, Wilhelm & Born, 2009; Drosopoulos, Schulze & Fischer, 2007; Kuriyama, Stickgold & Walker, 2004). A gist extraction consolidation mechanism may therefore operate preferentially on the weakly encoded memories, explaining the increased rates of false memories for these lists. However, these weakly encoded lists may also be more susceptible to generating false memories as they lack strong individuating memory features. Teasing apart the impact of encoding strength from offline memory processing will be important for determining whether gist extraction is the result of offline consolidation.

A second theme to emerge from the data is that impact of sleep on false memory generation differs depending upon the type of memory being tested. Test of recall typically produces sleep-associated increases in false memory, while recognition tasks

have not shown wake- or sleep-associated differences (Diekelmann et al., 2008; Fenn et al., 2009; Darsaud et al., 2011). One possible explanation for these findings relates to the fact that the processes of retrieval fundamentally differ between free recall and recognition tasks (Tulving & Madigan, 1970). The direct presentation of items in recognition tasks can act to reinstate the context of encoding and associated contextual/sensory details of the studied word lists (Cabeza et al., 2001). Sleep has been shown to be particularly beneficial for strengthening contextual elements of a representation and this may therefore increase participants' ability to discriminate between studied and non-studied words, leading to reduced rates of false recognition (Curran et al., 1997). In contrast, free recall does not benefit from the presentation of sensory or contextual memory cues. Access to these memories may rely more heavily upon consolidated and 'gist' memory representations, which may lead to increased rates of recall for both true and false memories. These results are in line with the broader consolidation literature, where sleep benefits are stronger and more reliable in recall compared to recognition tasks (Diekelmann et al., 2009).

The literature from the DRM paradigm produces a very complex picture that lacks clarity, making it difficult to characterise the specific mechanisms and processes involved in gist extraction. Further research is required to determine the driving processes in gist extraction, along with further replication of the current results. Although the role of consolidation in the extraction of gist and generation of false memories remains to be established, the data does suggest a possible role for offline consolidation mechanisms during sleep.

1.6.2 Insight into Hidden Rules

One of the first studies to show a role for consolidation, and specifically sleep-based consolidation, beyond the stabilisation or enhancement of declarative memory was carried out by Wagner et al. (2004) using a number reduction task (NRT). In this task, participants are presented with a string of eight digits and are required to transform them into a new string through a stepwise digit-by-digit application of two simple rules. With increased practise, participants become faster at performing the transformation, however participants can show abrupt increases in speed by gaining insight into a hidden rule that provides a short-cut to the final digit. By measuring the speed at which participants

complete the task across a number of trials, it is possible to determine if, and when, the participant gained insight to the hidden rule. Wagner et al. (2004) found that more than twice as many participants gained insight into the hidden rule following an 8-hour delay containing sleep compared to wakefulness. Furthermore, Yordanova et al. (2008) showed that explicit knowledge of the hidden rule was significantly more likely following SWS-rich early-night sleep compared to REM-rich late-night sleep, suggesting a role for SWS in the development of insight in this task.

Tasks that assess motor skill performance also provide evidence for a role of consolidation in developing insight into hidden rules. The serial reaction time task (SRTT) is a choice reaction time task in which participants are required to respond as quickly and as accurately as possible (using a key press) following the appearance of target stimuli at one of several locations on a screen (Fischer et al., 2006). Unknown to the participant, the sequence of target locations follows a set of rules that can be acquired with repeated exposures during the task. Knowledge of this underlying sequence can be assessed implicitly, by measuring the difference in reaction time between trials that follow the trained sequence and probe trials that violate the sequence (Fischer et al., 2006). With practice, participants demonstrate evidence of implicit sequence knowledge (Fischer et al., 2006; Fischer, Wilhelm & Born, 2007), however performance on this measure does not change with a consolidation delay (Drosopoulos, Harrer & Born, 2011; Fischer et al., 2006; Fischer, Wilhelm & Born, 2007; Song, Howard & Howard, 2007; Spencer, Sunm & Ivry, 2006).

In contrast, when explicit sequence knowledge is tested, by asking participants to try to generate the underlying sequence, sleep-associated benefits in performance are observed (Drosopoulos, Harrer & Born, 2011; Fischer et al., 2006). A role for sleep is also supported by more recent attempts to manipulate performance in SRTTs using TMR. Following external reactivation during sleep, improved procedural skill and importantly increases in explicit sequence knowledge has been observed (Cousins et al., 2014; 2016; Diekelmann, Born & Rasch, 2016). This provides strong evidence for a role of sleep, and the mechanism of reactivation, in supporting the emergence of explicit knowledge of hidden rules.

The SRTT provides an interesting series of results, whereby knowledge of hidden rules is observed immediately following training when tested implicitly, but a period of

offline consolidation is required for this knowledge to be expressed explicitly. This may have an important impact when considering the development of concept memory, which may draw upon similar mechanisms to extract the shared and systematic features from experiences. As a result, throughout this thesis, an attempt has been made to test concept-based memory representations using tasks that target both implicit and explicit memory representations.

1.6.3 Detecting Regularities

Detecting statistical regularities is typically an implicit memory process, that involves discovering and extracting recurrent patterns and interrelationships from stimuli in the environment (Gilboa & Marlatte, 2017). Most statistical learning studies focus on repetition within a limited perceptual dimension and require passive observation or a simple motor response. However, enriching the learning context by varying stimulus characteristics and their associated motor responses can result in the extraction of dynamic knowledge structures. Statistical learning mechanisms may therefore prove to be particularly valuable when considering the development of conceptual memory.

Two experimental paradigms have proven useful for gaining insights into processes of statistical learning and offline consolidation: artificial grammar learning tasks and probability learning tasks. Though there are differences between these paradigms, they both require the acquisition of knowledge using stimuli that do not relate to existing long-term memory representations and therefore participants are unable to learn using conscious mnemonic strategies (Reber, 1989). As a result, these tasks provide an authentic example of real-world learning in which complex knowledge structures need to be acquired. In artificial grammar learning tasks, a complex set of rules are derived that defines the order of letters in a sequence. Participants typically complete a short exposure phase to the novel letter strings, and are then asked to make grammatical/non-grammatical classification judgements for novel strings that follow the trained grammar (grammatical) or random sequences (non-grammatical). In these classification tasks, participants typically perform above chance level, suggesting that they had gained knowledge about the underlying grammar. Typically however, participants are unable to provide sufficient reasons to explain their classification decisions – suggesting the acquired knowledge is implicit (Knowlton & Squire, 1996; Shanks, Johnstone & Le Staggs, 1997).

Nieuwenhuis et al. (2013) compared classification performance in an artificial grammar task following a 15-minute, 12-hour (containing sleep or wakefulness) or 24-hour delay. They found a specific improvement in classification accuracy following delays containing sleep and this benefit was specific to rule extraction. The results could not be explained by an increased ability to recognise sequences based on frequency of appearance in the training stream. These findings suggest that offline processes during sleep play a critical role in the extraction of statistical regularities.

Similar findings are reported by Batterink et al. (2014) who showed increased sensitivity to grammatical rules following an afternoon nap. Furthermore, they show this sensitivity to be correlated with both the amount of SWS and REM sleep obtained during the nap. They suggest that reactivation of the learning material during sleep facilitated the stabilisation of memory and the abstraction of complex patterns. They later provide supporting evidence for this interpretation using TMR to manipulate consolidation mechanisms during sleep (Batterink & Paller, 2017). By re-presenting phrases from an artificial language to participants during an afternoon nap, they were able to increase the number of grammatical generalisations – suggesting a causal role for sleep in grammar learning.

Detecting grammatical regularities has also been demonstrated outside statistical learning paradigms. Mirkovic & Gaskell (2016) created an artificial language learning task designed to incorporate both arbitrary and systematic stimuli mappings and which participants were trained in using a word-picture matching task. In this task, the pictures represented individual characters (e.g. ‘queen’, ‘pirate’) with each picture having an arbitrary matching novel word. However, each novel word also had determiner and suffix referents which reflected the natural gender of the picture (e.g. *tibscoiffesh* + ballerina, *kedjorool* + cowboy), creating a systematic grammar that could be extracted across items. Mirkovic & Gaskell (2016) report a sleep associated benefit in memory recall for the arbitrary aspects of the new language (word-picture mappings) but found no wake or sleep differences in tests targeting the systematic aspects of the new language (knowledge of grammatical regularities).

This result is surprising given that previous data suggests a causal role for sleep in the development of grammatical knowledge. However, there are large differences between this task and statistical learning paradigms. This was an associative memory task

that required participants to make explicit associations between novel words and known pictures. This provides participants with a large amount of semantic information regarding each novel word, allowing participants to integrate this new knowledge within existing networks. Generalisation in this test required participants to extract the regularities from across the novel words and apply these to new novel forms that they had no existing representations for.

In contrast, statistical learning paradigms present participants with only the novel phrases, with no attached semantic information. Participants are not required to make any explicit associations and instead either carry out a simple short-term memory task (e.g. recalling word order) or a phase of passive observation – regularities are therefore acquired in a much more implicit way. Grammatical generalisations in these tasks typically refer to the serial order of word chunks which requires participants to extract statistical regularities. However, in tests of generalisation the novel phrases often contain the same trained words (but presented in a novel order). These two tasks therefore draw upon different learning mechanisms and take different measures of generalisation. Consistent with previously discussed data, implicit learning appears to be most sensitive to sleep-associated consolidation mechanisms.

The role of consolidation in the detection of statistical regularities has also been demonstrated in probability sequence learning tasks. Durrant et al. (2011) used a paradigm that involved auditory tone sequences that had an underlying probability structure. They showed a strong sleep-associated consolidation effect, with participants better able to recognise sequences that conformed to the learned statistical pattern following sleep (both overnight sleep and following a daytime nap) compared to wakefulness. Using the same paradigm, Durrant et al. (2013) showed a consolidation benefit over a 24-hour delay, with the change in performance (from immediate to delayed tests) positively correlated with the percentage of time spent in SWS during the night between sessions.

In the study by Durrant et al. (2013) participants completed the tests at the same time as brain activity was being measured using fMRI. This allowed changes in brain activation across the 24-hour delay to be measured, and was compared with changes following a shorter 30-minute delay in a separate group. With consolidation, they report a shift from hippocampal to striatal memory systems – in line with the suggestion that

consolidation leads to the reorganisation of memory representations (Born et al., 2006). Like the behavioural response, they also found that differences in this functional response were predicted by the amount of SWS obtained between the testing sessions, suggesting that SWS may mediate memory reorganisation. This study therefore not only provides evidence for a role of sleep in the learning of probabilistic statistical structures, but also suggests that sleep may be actively involved in the neural reorganisation of statistical sequences. Given that conceptual memories represent statistical patterns in the environment; these studies provide strong evidence for a role of sleep in the development of conceptual memory representations.

As with grammar learning, the detection of regularities has also been demonstrated using associative memory tasks. Sweegers et al. (2014) developed an associative memory paradigm that required the learning of face-location associations and later retrieval of locations based on face cues. However, their task also allowed them to study the development of concept-based representations by manipulating the type of face that belonged to each location. Half of the material responded to complex associative regularities regarding the combination of facial features and locations. The other half of the faces were randomly assigned to one of the remaining locations. This created a set of ‘rule-locations’: locations that have a specific type of face associated with it, and a set of ‘no-rule locations’: locations that can be paired with any type of face.

In a series of studies, Sweegers et al. demonstrated that participants are able to extract the complex associative regularities and show enhanced learning and retention of the rule compared to no-rule associations. Importantly, they also demonstrated that participants are able to apply the extracted rules to novel stimuli at above chance levels, providing evidence of generalisation and suggesting that the extraction of regularities across multiple associative memories can lead to shared concept based memory representations (Sweegers et al., 2015; 2014; Sweegers & Talamini, 2014). When they assessed the impact of sleep and wake on memory for the individual face-location associations in this task they found no evidence for sleep-associated benefits. This is somewhat intriguing given that associative memory tasks are typically sensitive to sleep based consolidation, however they do report near ceiling level accuracy rates following learning which may minimize the impact of offline consolidation mechanisms in their task (Diekelmann, Wilhelm & Born, 2009).

By testing memory for novel items that have not been trained, but which follow the same regularities, Sweegers et al., (2014) are able to obtain a very clear test of category-based knowledge. This is particularly useful as it dissociates the effect of sleep on episodic based representations (which typically show strong benefits of sleep) from purer category-based representations that are independent from the individual category exemplars. The experiments presented in this thesis also aim to make a clear dissociation between category- and exemplar-based knowledge. Chapter 4 of the thesis uses an adapted version of the same face-location associated memory paradigm as Sweegers et al. to contrast memory for item versus category-based knowledge.

1.6.4 Memory Integration

Further evidence for a role of consolidation beyond memory stabilisation is data suggesting that consolidation can lead to the integration of distinct memories into coherent representations (Ellenbogen et al., 2007; Werchan & Gómez, 2013; 2014). Ellenbogen et al. (2007) used a transitive inference paradigm in which participants were required to learn the relationship between five pairs of arbitrary elements (e.g. $A > B$, $B > C$, $C > D$, $D > E$, $E > F$) which had an embedded hierarchical structure (e.g. $A > B > C > D > E > F$). Knowledge of both the trained pairs and the underlying structure was tested following an offline delay of either 20-minutes, 12-hours (either over a night of sleep, or across the day without sleep) or 24-hours. All groups showed very good retention of the arbitrary pairings following the delay, however only participants in the 12- and 24-hour delay conditions were able to make successful relational judgements, suggesting that relational memory develops during offline consolidation delays. A sleep-associated boost in relational memory was also observed, but only for the most distant judgements (e.g. $B > E$) suggesting that sleep may facilitate the binding of more distantly related information into coherent structures (Ellenbogen et al., 2007).

Lau, Tucker & Fishbein, (2010) also show an active role for sleep in the binding of memory representations using a relational memory paradigm. In this task participants learned two lists of direct associations between faces and objects, the objects however were common to both lists such that following learning each object was associated with two different faces. Following a 90-minute delay period, which either contained wake or sleep, the participant's memory was tested for both the trained associations and the

untrained relationship between the two faces that shared the same object. Sleep-associated benefits were observed for both trained and non-trained memories; furthermore the duration of SWS obtained during the nap was able to predict relational memory performance, suggesting a specific role for SWS in the development of these relational representations (Lau et al., 2010).

A second example of sleep-associated memory integration is the incorporation of novel words into the mental lexicon. When a newly learned word (e.g. cathedruke) is added to the mental lexicon, it competes during recognition with similar sounding existing words (e.g. cathedral), resulting in lexical competition. Importantly, the integration of novel words into the mental lexicon is an extended process that occurs over time and sleep has been shown to facilitate this process (Gaskell & Dumay, 2003; Dumay & Gaskell, 2007). Furthermore, the level of lexical competition has been shown to correlate with the number of sleep spindles observed in the post-training night of sleep (Tamminen, Lambon Ralph & Lewis, 2013) – suggesting that spindle activity during SWS plays an important role in the integration of new memories with existing knowledge. This type of memory integration goes beyond the transitive inference tasks described above (e.g. Ellenbogen et al., 2007) as it requires the integration of newly learned material with existing knowledge stores. This may be more representative of the mechanisms operating in the development of conceptual memory, as concepts need to be maintained and updated across multiple events spread across time.

These studies provide strong evidence for the role of offline consolidation, and specifically sleep, in the integration of memory representations. However, it should be noted that lexical competition can emerge without sleep given the right circumstances during learning (Lindsay & Gaskell, 2013; Szmalec, Page & Duyck, 2012). Lindsay and Gaskell (2013) suggest that online processes of integration across wake may happen when participants are aware of the relationship between novel and existing knowledge, and when these two types of representation are interleaved during learning (for instance in their study, presentation of both novel words e.g. *biscal* and known existing base words e.g. *biscuit*). This suggests that processes of memory integration may be strongly influenced by the conditions surrounding learning and similar factors may therefore play a role in the development of concept memory.

This section provides support for the role of offline consolidation processes in developing memory beyond the individual representations. These processes do not however appear to be universal or uniform across memories. The data reviewed highlights important factors that play a role in whether consolidation benefits across sleep and/or wake are observed, these include; the type of memory being assessed (e.g. implicit or explicit), the type of test (e.g. recognition or recall), explicit awareness of hidden rules/structures and the nature of the learning environment. The underlying neurophysiological mechanisms governing these processes are only beginning to be uncovered; however, the limited evidence to date supports a role for SWS and mechanisms such as neural reactivation. Despite inconsistencies within the current literature, it is clear that memory consolidation processes do go beyond memory stabilisation and enhancement and therefore consolidation processes may play a key role in the development of conceptual representations. The final section of this review will focus upon the narrow range of studies that have considered the role of consolidation in concept memory.

1.7 Consolidation and Multidimensional Concept Learning

Category learning paradigms have been used to bridge the literature between concept memory and mechanisms of consolidation. Category learning requires participants to learn the attributes that distinguish items as belonging to a category, on the understanding that each category has a set of common and relevant features. Importantly for learning, participants need to identify multidimensional features and derive a rule that best describes their combination. For example, the concept “birds” requires the learning of multiple features, such as having: wings, beaks, feathers and two legs. For something to qualify as a bird, these features need to co-occur, generating a defining rule (Rogers & McClelland, 2004). This type of approach to concept learning is somewhat simplified, however it captures the basic nature of concepts and provides the basis for a range of paradigms and studies that have studied the initial formation of categorical representations (Ashby et al., 1998; Ashby & Maddox, 2005; Ashby & Valentin, 2005; Kumaran et al., 2009; Maddox & Ashby, 2004; Smith et al., 2012). Only a handful of studies, however, have assessed the development of these categorical representations over time (Djonlagic et al., 2009; Graveline & Wamsley, 2017; Hennies, Lewis et al., 2014; Maddox et al., 2009). These studies use three types of classification task: the Weather

Prediction Task (WPT), the Dot Pattern Classification Task (DPC) and the Information-Integration category learning task. These tasks all assess the acquisition of multidimensional concepts and train participants to classify objects by presenting a set of examples along with their category labels, either via feedback-driven or observational learning. The impact of consolidation in these will be discussed in turn.

1.7.1 The Weather Prediction Task

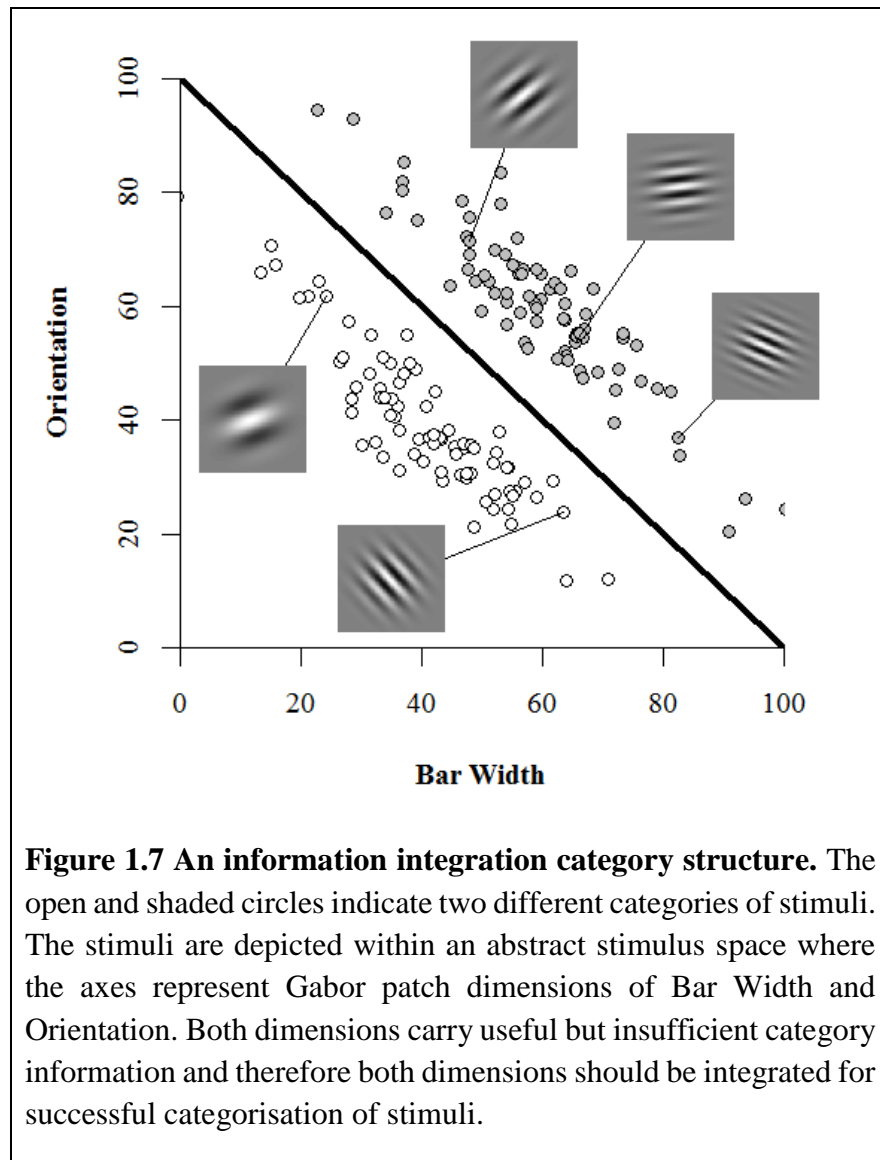
The WPT is a probability learning task which requires participants to make a weather prediction (sunshine or rain) based on the presence and/or absence of a set of four unique cards. Each card has a geometric pattern that partially predicts the weather, therefore the overall weather outcome is determined by evaluating the presented cards as a set (Gluck, 2002). Djonlagic et al. (2009) compared performance in the WPT across a 12-hour consolidation delay that contained either wakefulness or sleep. They report an overall role for time, as accuracy in this task increased over the 12-hour delay and these improvements were greatest for participants who had the opportunity to sleep between training and testing. However, this was only observed when participants completed the WPT under observational learning procedures (i.e. passive viewing of the cards and their associated outcomes); the same sleep benefit was not observed following feedback-driven training.

The authors suggest that this interaction between training method and benefit of offline consolidation in sleep may be a consequence of the underlying neural mechanisms during learning with observational learning recruiting MTL structures, which are implicated in sleep-based consolidation mechanisms, while feedback-driven training may recruit more striatal regions involved in reward learning (Djonlagic et al., 2009; Marshall & Born, 2007). Although this explanation may account for the differences in results, there is more recent evidence of sleep-associated consolidation benefits in other tasks that utilise striatal memory systems. For instance, Durrant et al. (2013) show sleep-based consolidation benefits in statistical learning of probabilistic sequences, with a shift between hippocampal and striatal memory stores across consolidation. To date, this is the only study to investigate the impact of consolidation on the WPT, replication of these effects is vital in order to truly appreciate and understand the interaction between learning strategy and sleep-associated consolidation. Despite these differences related to the role

of sleep, this study does provide evidence for a role of offline consolidation more generally in improving performance in this task, suggesting that time (both awake and asleep) may be beneficial for the development of category knowledge.

1.7.2 Information-Integration Category Learning

A similar improvement in performance as a result of time and offline consolidation has also been seen in information-integration category learning tasks (Hennies et al., 2014; Maddox et al., 2009). These are perceptual categorisation tasks in which participants are presented with simple two-dimensional stimuli that can be categorised into two categories. Importantly, a simple one-dimensional rule cannot describe the boundary between two categories; instead participants are required to integrate information from across the dimensions to make their category responses. An example of an information-integration category structure is presented in Figure 1.7 where the stimuli dimensions represented are the Orientation and Bar Width of Gabor patch stimuli. The bold line shows the category boundary, demonstrating the need to integrate both dimensions in order to make optimal category decisions. Following feedback-driven training, participants show good evidence of category learning suggesting they are able to learn these information-integration category structures (Ashby & Ell, 2001; Ashby, Ell & Waldron, 2003; Ashby & Gott, 1988; Ashby & Valentin, 2005; Maddox, Bohil & Ing, 2004).



Maddox et al. (2009) investigated the impact of sleep deprivation on information-integration category knowledge by measuring category accuracy after a 24-hour delay containing total sleep deprivation. They reported an overall performance deficit in accuracy following sleep deprivation, however when they controlled for the type of strategy used to complete the task, they found that participants using the optimal information-integration boundary did not show a decline in performance – instead accuracy remained stable. Performance in their control group, where participants were able to sleep during the 24-hour delay, showed a significant performance increase across the 24-hours. Although this study lacks a control group with short delay, which would provide a comparison in which there was a limited opportunity for offline consolidation,

this data does suggest that consolidation mechanisms may play a role in the development of category representations in this task.

Further support for a role of offline consolidation in the information-integration task is provided by Hennies et al. (2014) who used a modified version of the category learning task. In this modified paradigm, the information-integration category structure was secondary to a simple one-dimensional rule. Critically, the information-integration stimuli preceded each trial and as a result, participants could increase the speed of their responses. Hennies et al. (2014) measured performance on the task across two sessions; to assess the role of time, experiment one compared a delay period of 15-minutes with 24-hours, while experiment two went on to investigate the separate contributions of wake and sleep across 12-hours. Participants did not show any evidence of utilising the information-integration category following initial training on this task. However, following the 24-hour delay in experiment one, and with further training on the task, participants showed evidence of using the information-integration stimuli with significantly faster response times than the control condition (in which no predictive information was presented). Planned comparisons show that this difference was only significant in the 24-hour condition, suggesting a benefit of offline consolidation, in line with the previous data from Maddox et al. (2009).

A similar result is also observed in experiment two, with increased reaction times compared to baseline following the delay; however, this was observed in the delay containing 12-hours of wakefulness, and not in the delay containing sleep (Hennies et al., 2014). The authors suggest that an important element of learning the shared properties of a category is the ‘forgetting’ of non-shared irrelevant features, a process that may happen preferentially during wakefulness, or be inhibited during sleep as a result of consolidation that strengthens whole representations, including both the shared and non-shared elements (Hennies et al., 2014). This is supported by similar results in a study investigating generalisation of memory in young children, where time awake (and not sleep) was beneficial for generalisation (Werchan & Gómez, 2014). This highlights a very important point when considering concept-based memory as consolidation may require successful forgetting as well as remembering. Processes in both wake and sleep may therefore have important roles to play.

1.7.3 The Dot Pattern Classification Task

The final classification paradigm used is the DPC task, in which participants are required to classify abstract dot patterns into novel categories. The patterns in each category are statistically derived by distorting a single prototype pattern (Posner, Goldsmith & Welton, 1967). As a result, you can measure category knowledge for trained stimuli, as well as concept knowledge more generally by presenting novel items that are derived from the same prototype, but have not been previously trained. Performance on these novel items is particularly interesting as participants cannot draw upon individual associations between episodic memory for the exemplar and the category label. To assess the impact of sleep- and wake-based consolidation in this task, Graveline & Wamsley (2017) trained participants before a 12-hour delay that contained either wakefulness or sleep. They found sleep to lead to superior classification of the trained items, novel items and the original exemplars; suggesting sleep plays a role in the development of these category-based representations.

The categorisation tasks discussed in this section provide valuable paradigms for assessing the acquisition and development of concept knowledge. The majority of the evidence shows that conceptual representations remain relatively stable, or improve across time, suggesting concept memory is less vulnerable to decay. However, the evidence for a specific role of wake- or sleep-based consolidation is inconsistent; there is a very limited amount of research and with numerous paradigms and tasks that take different measurements of category knowledge. It is therefore difficult to integrate and interpret the current literature to generate informative conclusions as to the role of sleep- or wake-associated consolidation mechanisms on the development of concept-based representations.

1.8 Summary

Concepts allow us to bring meaning to the world based on shared properties between our current experiences and existing knowledge. The formation of coherent conceptual representations requires the integration of information across multiple episodes and events that are spaced across time and requires the abstraction of statistical patterns and regularities from both new and existing knowledge. Systems consolidation

is thought to drive the gradual redistribution of memories into long-term memory stores, leading not only to memory stabilisation and enhancement but to a qualitative change in the representation. This qualitative change has been shown to lead to the extraction of gist, the detection of hidden rules and regularities and the integration of memory elements into coherent representations. Offline consolidation mechanisms, during both wake and sleep, have been shown to facilitate this qualitative change in memory and therefore offline consolidation is identified as potentially playing an important role in the development of concept memory. The relationship between the development of concept-based representations and offline consolidation has however received very little attention in the current literature and there are many questions that have yet to be addressed.

1.9 Research Objectives

The overarching aim of this thesis was to investigate the role of offline consolidation on the development of concept-based representations. Several processes that may contribute to the development of concept-based representations have been shown to benefit from offline consolidation during sleep, but other important aspects of concept development have yet to be investigated. The integration of information from multiple modalities is a key aspect of real-world concept knowledge and this has received very little attention in the consolidation literature. In Chapter 2 and Chapter 3 of this thesis we therefore aimed to examine the formation of abstract cross-modal conceptual representations using the information-integration categorisation paradigm. This task required the integration of information from across modalities (visual and auditory) and the extraction of an underlying category structure. In Chapter 2 we examined the overall benefit of time on the development of these cross-modal integrative representations and in Chapter 3 we explored the separate contribution of wake and sleep. In both of these chapters, we compared the impact of offline consolidation on concept knowledge with a declarative paired-associate memory task. This task has consistently been shown to benefit from offline consolidation during sleep, allowing us to assess the impact of consolidation on these two types of memory representation.

Building upon these results, in Chapter 4 we integrated the development of conceptual and declarative associative memories into a single paradigm, allowing us to investigate how these memories may differentially develop over time and the relationship

between them. In this study we investigated the impact of both sleep and wakefulness on memory performance, and extended the study to investigate how post-consolidation learning may impact the integration of new information into these consolidated knowledge structures. In Chapter 5 we examined how these memories may be represented in the brain by investigating whether intrinsic functional connectivity measured at rest could predict behavioural measures of item and concept-based memory.

CHAPTER 2

Cross-Modal Categorisation: A Role for Time?

Jennifer E. Ashton, Elizabeth Jefferies, M. Gareth Gaskell

2.1 Abstract

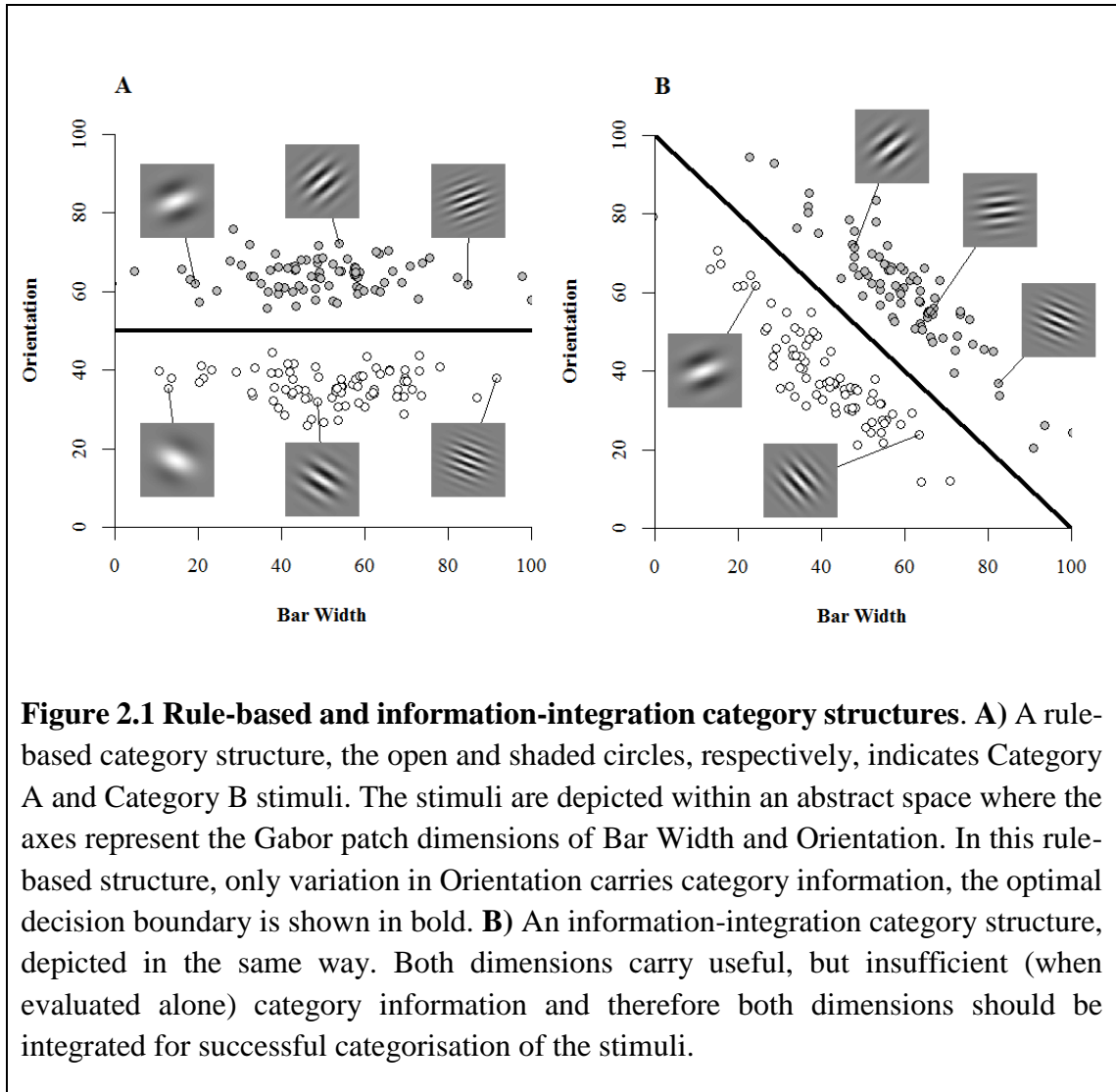
The ability to categorise objects and events depends upon the representation of multimodal conceptual representations. This study investigated the impact of an offline consolidation delay on the development of cross-modal (visual-auditory) category knowledge. Participants performed an information-integration categorisation task twice, with each session separated by either a 15-minute or a 24-hour delay, followed by a set of follow-up tasks to assess category knowledge. Participants showed evidence of cross-modal integration, with high categorisation accuracy rates and use of optimal integration strategies as demonstrated by modelling individual response patterns. There were no differences in performance between the two delay groups when accuracy was measured during category training, however when performance was measured in a speeded version of the task there was significantly higher accuracy in the 24-hour delay condition – suggesting a possible role for offline consolidation in the development of categorical memory representations. These results complement previous research investigating cross-

modal category learning and extend this research by examining the role of offline consolidation in the development of cross-modal category knowledge.

2.2 Introduction

Memory consolidation describes a post-encoding process of stabilisation where new information is integrated into long-term memory stores (Born et al., 2006). There is now a large amount of research that suggests that offline consolidation mechanisms during periods of waking rest and sleep, act to stabilise and strengthen individual memory representations (Mednick et al., 2011; Rasch & Born, 2013; Stickgold & Walker, 2007). Furthermore, this benefit is now believed to extend beyond enhanced memory retention, by actively promoting a process of memory reorganisation, which facilitates the extraction of patterns and regularities from the environment (Wagner et al., 2004; Djonlagic et al., 2009; Durrant et al., 2011; Graveline & Wamsley, 2017; Lewis & Durrant, 2011). Offline consolidation mechanisms may therefore play an important role in the formation of ‘concepts’, which require the extraction of regularities from a set of related stimuli to generate generalized concept or category knowledge (Smith & Medin, 1981).

Concepts allow us to adaptively respond to novel situations, objects and events and require the integration of information from across multiple modalities and episodes to form complex similarity structures of the environment (Lambon Ralph et al., 2017). Demonstrations of perceptual integration have been shown in categorisation paradigms. These require participants to form categorical representations by integrating information from multiple stimuli dimensions (Ashby & Ell, 2001; Ashby, Ell, & Waldron, 2003; Ashby & Gott, 1988). Typically, these categorisation tasks have used very simple stimuli such as sine-wave gratings with the two dimensions e.g. bar width and orientation (see Figure 2.1 for an example of the stimuli). To visualise the category structures, each stimulus can be represented graphically in a two-dimensional space, where each axis represents one stimulus dimension as is shown in Figure 2.1. Stimuli can then be grouped together and categorised based on their position within this space. The overall category structure can be manipulated by changing the boundary between different categories (bold lines in Figure 2.1) and this in turn changes the level of dimension integration required for optimal categorisation.



Two different category structures are presented in Figure 2.1; the first is referred to as ‘rule-based’, with only variation along one stimulus dimension (i.e. ‘orientation’) carrying useful category information (Figure 2.1A). Category knowledge is easily acquired from these structures and following training participants are able to generate simple one-dimensional rules to describe their categorisation strategies e.g. “respond A if the bars are oriented to the left and respond B if they are oriented to the right” (Ashby & Gott, 1988). The second category structure (Figure 2.1B) is referred to as ‘information-integration’ and in this case both stimulus dimensions provide useful category information. Optimal categorisation therefore requires this information to be integrated before a category decision can be made. The Competition between Verbal and Implicit Systems (COVIS) model suggests that the acquisition of information-integration category

structures draws upon implicit procedural-learning mechanisms, rather than explicit rule-based processes (Ashby & Gott, 1988). Like the rule-based structures, participants can reach high levels of categorisation accuracy following training on these information-integration structures and in line with the multi-modal nature of conceptual memory, previous research provides evidence for cross-modal (i.e. visual-auditory) integration (Maddox, Ing & Lauritzen, 2006; Smith et al., 2014). In line with these findings, this study used the information-integration categorisation structure with cross-modal (visual-auditory) dimensions to study the development of multi-modal categorical representations across time.

A large amount of research has been generated investigating the initial acquisition of these category representations (Ashby & Ell, 2001; Ashby, Ell & Waldron, 2003; Ashby & Gott, 1988; Ashby & Valentin, 2005; Maddox, Bohil & Ing, 2004). However, only two previous studies have investigated the impact of offline consolidation on the development of these representations (Hennies et al., 2014; Maddox et al., 2009). The first of these was carried out by Maddox et al. (2009) who investigated the impact of a 24-hour delay on category learning. Between two category learning sessions, they manipulated whether participants maintained their usual sleep-wake cycle or completed 24-hours of total sleep-deprivation. For those who maintained their usual cycle, significant gains in performance were observed across the delay, suggesting a possible role for offline consolidation in the enhancement of category knowledge. Unfortunately, Maddox et al. (2009) did not include a shorter delay period (e.g. 15-minutes) and therefore it is not possible to determine whether the gain in performance was the result of offline consolidation mechanisms, or a more general improvement as a consequence of re-exposure to the task in session two of their study. Improvements in performance were not observed following total sleep-deprivation, although again it is difficult to dissociate the impact of sleep loss from general fatigue as a result of deprivation in their paradigm. Although much more support is required, Maddox et al. (2009) provided the first evidence to suggest a possible role for offline consolidation in the maintenance and enhancement of category knowledge.

The second study to investigate the role of offline consolidation in category learning was presented by Hennies et al. (2014) who carried out two experiments using a modified version of the categorisation paradigm. In their study, participants made distinctions

between two abstract categories using a one-dimensional visual rule. However, successful and faster categorisation could be achieved by using cross-modal information, which followed an information-integration category structure (an aurally presented tone and visual spatial location), that was presented before the onset of each visual stimulus. In their first experiment, Hennies et al. (2014) compared performance in this task across two sessions that were separated by a delay of either 24-hours or 15-minutes. After initial training, they found no evidence to suggest participants were sensitive to the predictive nature of the cross-modal cues. However, following a delay of 24-hours and with further training, participants showed significant speed increases in categorisation, indicating they were able to utilise the cross-modal information to make their responses. This increase in speed was not observed following the shorter 15-minute delay, suggesting a specific benefit from time for offline consolidation.

In their second experiment, Hennies et al. (2014) investigated the specific role of sleep and wake on categorisation. Unlike much of the previous consolidation literature, which report selective benefits of sleep, they found only wakefulness to provide an offline consolidation benefit. This result is similar to that of Werchan & Gómez (2014) who also showed a wake-associated consolidation benefit in young children, in a task that required the abstraction of shared features from across a set of related items. They argue that forgetting idiosyncratic memory features during wakefulness may promote the generalisation and abstraction of information by emphasising the elements across memories which are shared (Werchan & Gómez, 2014). It may therefore be the case that offline consolidation during wake provides optimal conditions for the development of conceptual memories, which rely upon shared features from the environment.

However, Hennies et al. (2014) made a number of important modifications to the original categorisation paradigm and these may have impacted upon their findings. Notably, they changed the focus of the task, with the information-integration structure predictive of category membership, but secondary to categorisation – which was based on a one-dimensional visual rule. This is likely to have had a large impact on learning given that the participants were not required to use the category structure to achieve accurate categorisation. A second modification, which makes it difficult to integrate their results with the existing categorisation literature, is their measurement of integration. They focus upon differences in reaction time by comparing the speed of categorisation

across trials with and without the predictive cues. This contrasts with measurements of accuracy which are typically reported in categorisation tasks. In the current literature therefore, there has been no direct investigation into the role of offline consolidation using the traditional information-integration categorisation paradigm using cross-modal stimuli. The current study aimed to address this by investigating the impact of a 24-hour offline consolidation delay using an unmodified information-integration categorisation paradigm with cross-modal (visual-auditory) stimuli (Ashby & Gott, 1988). A 15-minute delay condition was also included to dissociate the impact of offline consolidation from potential benefits related to re-exposure to the task following the offline delay.

This study also aimed to compare the impact of offline consolidation on category knowledge, with the typical consolidation benefits observed within the declarative memory domain. Declarative memory has received a great deal of attention from the consolidation literature, with an increasing amount of studies highlighting a role for offline consolidation, and specifically sleep, in the stabilisation and enhancement of memory (Born et al., 2006; Diekelmann et al., 2009; Steffen Gais & Born, 2004; Björn Rasch & Born, 2013; Stickgold, 2009; Stickgold & Walker, 2007). If categorical representations draw upon these same consolidation mechanisms, then similar consolidation related changes in performance are hypothesised to be observed. To test this, a paired-associate memory task, which shows robust consolidation benefits, was included in this study – allowing direct comparisons between tasks to be made (Diekelmann et al., 2009; Jenkins & Dallenbach, 1924; Plihal & Born, 1997; Tucker et al., 2006).

To summarise, the current study aimed to investigate the role of offline consolidation on the development of cross-modal categorical representations and used a traditional information-integration category structure and paradigm (Ashby & Gott, 1988). Basic two-dimensional cross-modal (auditory-visual) stimuli were created and participants were expected to demonstrate sensory integration in order to form category representations. By comparing performance following a 15-minute and 24-hour delay, this study was able to assess the contribution of offline consolidation on category knowledge. As previous research shows robust consolidation benefits within the declarative memory domain, a paired-associate task was included to compare the impact of offline consolidation on declarative and categorical memory.

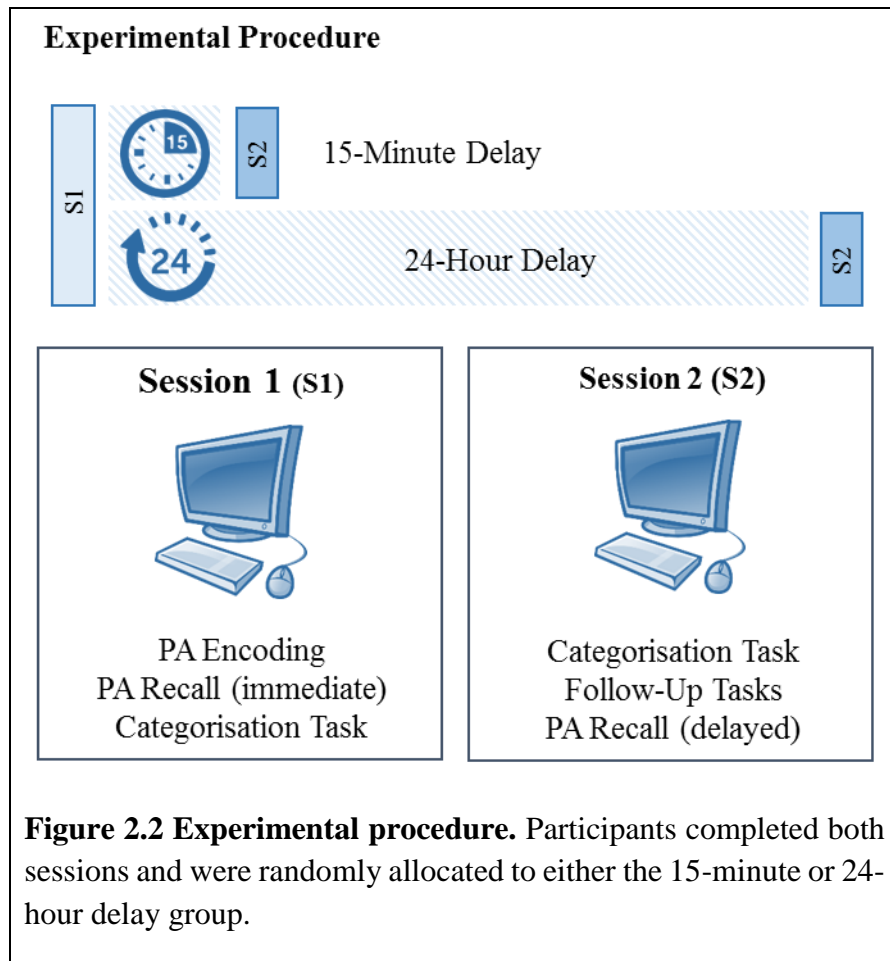
2.3 Methods

2.3.1 Participants

Participants were 44 undergraduate students recruited from the University of York in fulfilment of course credit or payment. Participants reported normal/corrected vision and hearing and were randomly allocated to one of two groups; a 15-minute delay group (N = 22, mean age: 19.86, S.D. \pm 1.28, 19 female) or a 24-hour delay group (N = 22, mean age: 21.41, S.D. \pm 5.58, 19 female).

2.3.2 Procedure

The study comprised of two sessions, separated by a delay; 15-minutes or 24-hours (see Figure 2.2). At the beginning of each session participants completed the Stanford Sleepiness Scale (SSS, Hoddes et al., 1973) to measure general ratings of sleepiness. In Session 1, participants then completed the paired-associate encoding and immediate cued-recall task, followed by categorisation training (~45 min). In Session 2, participants completed the category training for a second time, along with three categorisation follow-up tasks; i) a speeded categorisation task – this task allowed a measure of category knowledge to be taken in the absence of further training and included stimuli from both the trained category distribution, along with items that were from outside this distribution, but which could still be categorised using the same category decision boundary. It was therefore possible to determine if participants could apply the extracted category structure to non-trained stimulus space. ii) A two-alternative forced choice task – to assess whether category knowledge acquired in the training could be utilized in a new task with a different response structure. And iii) a category recall task – to test whether participants could explicitly generate category exemplars. Participants finished the session by completing the paired-associate delayed recall task (~60 min).



2.3.3 Tasks

2.3.3.1 Categorisation Task

2.3.3.1.1 Stimuli

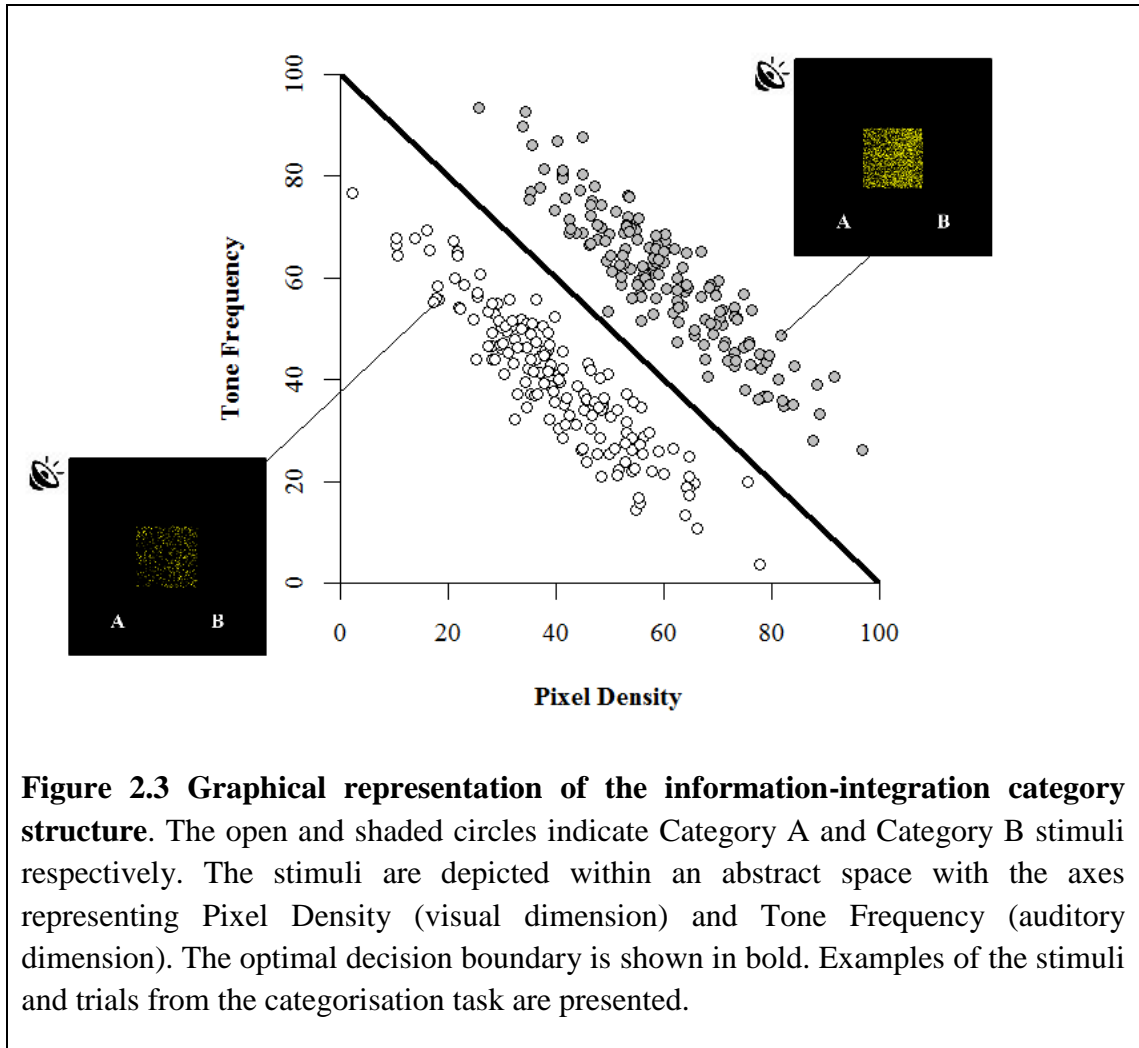
Category exemplars were conjoint visual-auditory stimuli that replicated the stimuli described in Smith et al., (2014). The visual dimension was a 142 x 142 pixel unframed box containing randomly placed yellow pixels, presented on a black background. There were one hundred-and-one levels of pixel density with the number of yellow pixels at each level defined by $\text{pixels} = \text{round}(850 \times 1.0181^{\text{level}})$. Pixel density therefore varied from 850 lit pixels (level 0), to 5,061 lit pixels (level 100) out of a total of 20,164. The auditory dimension was a pure tone that varied in frequency (Hz), defined by $\text{frequency} = 220 \times 2^{(\text{level}/120)}$. For levels 0 and 100 the pitches were 220 Hz and 392 Hz respectively. All stimuli were generated using the open-source package PsychoPy (Pierce, 2007) with sounds presented through headphones.

2.3.3.1.2 Category Structure

Table 2.1 provides the population distribution that governed the selection of Category A and Category B stimuli. Throughout the course of the experiment each participant received his or her own sample of 320 category exemplars and therefore individuals experienced their own unique statistical samples of a category's probability distribution. Category exemplars were created using Ashby and Gott's (1988) randomisation technique. Categories were defined by a bivariate distribution along the two stimulus dimensions (normalised to a 0-100 scale) and each conjoint stimulus was created by drawing a random sample (x, y) from each category distribution (see Figure 2.3). As the structures are created using an arbitrary 0-100 scale, each (x, y) coordinate pair were then transformed into concrete conjoint visual and auditory stimuli using the formulae described above.

Table 2.1 Category distribution parameters (mean (μ), variance (σ^2) and covariance (Cov(x, y)) for the pixel density (x) and tone frequency (y) dimensions in the information integration category structure.

Category Distribution Parameters					
Category	μ_x	μ_y	σ_x^2	σ_y^2	Cov (x,y)
A	40.00	40.00	185.94	185.94	-169.61
B	60.00	60.00	185.94	185.94	-169.61



2.3.3.1.3 Categorisation Trials

Each trial consisted of the presentation of one conjoint visual-auditory category exemplar, taken from either category A or B. The response icons ‘A’ and ‘B’ were presented on the lower left and right hand of the screen respectively, and participants were asked to categorise each stimulus by pressing the ‘A’ or ‘B’ keyboard keys, spatially positioned to correspond to the A and B on the screen (see Figure 2.3). The stimuli were presented until the participant made a response, or for a maximum of 10 seconds. If the participant failed to make a response in this time the trial was scored as incorrect. If participants correctly categorised the stimulus they were presented with the word “Correct!” on the screen and received a ‘point’ (presented as a running point total in the centre of the screen). When participants made an incorrect response, they were presented with the word “Incorrect!” and a point was deducted from their current total. This

feedback immediately followed their response and remained on the screen for 1000ms. Participants completed a total of 160 trials in each session of the category training (80 trials in one block of learning, 320 trials across the entire experiment).

2.3.3.1.4 Instructions

Participants were told that each trial of the categorisation task contained a pixel box and an auditory tone and their task was to learn to accurately categorise each stimulus as belonging to Category A or B. They were instructed to guess to begin with, but to use the corrective feedback throughout the training to help them learn to accurately categorise the trials. They were told that they would receive points for correct answers and lose points for incorrect responses. A monetary prize for the highest overall points total was offered to encourage high performance, with the focus on accuracy rather than reaction times.

2.3.3.2 Categorisation Follow-Up Tasks

Follow-up tasks aimed to assess participants' knowledge of the category structure, and to apply their knowledge in more flexible ways. The stimuli used in these tasks were generated as described above.

2.3.3.2.1 Speeded Categorisation

The speeded categorisation task followed the same procedure as category training, however participants did not receive feedback on their performance and were asked to make their category decisions as accurate and as fast as possible. Participants completed two variations of the task; a version in which the stimuli were sampled from the same distribution as learning (Trained) and one in which the stimuli were sampled from beyond the trained distribution (Non-Trained). In both versions, perfect accuracy could be achieved by using the category knowledge gained during training. By testing category accuracy for non-trained category exemplars, this test assessed whether participants could apply their category knowledge to new and untrained stimuli. Participants completed 80 trials in each speeded task.

2.3.3.2.2 *Two-Alternative Forced Choice (2AFC)*

Participants completed a two-alternative forced choice (2AFC) task to assess their ability combine the stimulus dimensions to make a category exemplar. On each trial participants were presented with a target category in the centre of the screen (Category A or Category B). On 24 of the trials, they were also presented with a single auditory tone, along with two pixel boxes. Each pixel box when combined with the auditory tone made a legitimate Category A or Category B stimulus. The participant's task was to select the pixel box (using a mouse click) that combined with the tone to match the target category. On a further remaining 24 trials, participants were presented with a target category along with a single pixel box. Two different auditory tones could be heard by hovering (with the mouse) over two different red boxes presented on the screen. After listening to the tones, participants were instructed to select the tone that combined with the pixel box to create a category exemplar matching the target category. Participants completed 6 practise trials to familiarise themselves with the task procedure (3 trials of each type) and completed a total of 48 test trials. Participants were given 10 seconds to make their response and were instructed to respond as accurately as possible.

2.3.3.2.3 *Category Recall*

Participants completed a recall task to assess their ability to generate category exemplars. Like in the 2AFC task, participants were presented with a target category (either Category A or B) in the centre of the screen and a fixed visual or auditory stimulus. They were also presented with a non-fixed stimulus from the opposite dimension, along with a 150-point scale. Participants were instructed to alter the non-fixed stimulus (using plus and minus buttons placed at either end of the scale, and controlled using mouse clicks) to combine with the fixed stimulus in order to match the target category. Participants completed a total of 40 trials; on 20 trials the fixed stimulus was a pixel box and they had to manipulate the frequency of the auditory tone, and in 20 trials the fixed stimulus was the auditory tone and they were required to manipulate the density of the pixel box presented. Participants were instructed to respond as accurately as possible and were given an unlimited amount of time to make their responses.

2.3.3.3 Paired-Associate Task

2.3.3.3.1 *Stimuli*

100 words were selected from an adapted version of The University of South Florida (USF) word association, rhyme, and word fragment norms (Nelson et al., 2004) to create 50 semantically unrelated cue and target word pairs (e.g. owl – frame). Both the cue and target words were singular, had high USF concreteness ratings (mean \pm standard deviation; cues = 5.81 ± 0.73 ; targets = 5.81 ± 0.43 , $t(98) = 0.01$, $p = .996$) and were matched for frequency (cues = 38.74 ± 58.93 ; targets = 36.62 ± 50.36 , $t(98) = 1.93$, $p = .847$), word length (cues = 5.12 ± 1.35 ; targets = 5.02 ± 1.02 , $t(98) = .418$, $p = .677$) and number of syllables (cues = 1.42 ± 0.64 ; targets = 1.50 ± 0.58 , $t(98) = -0.65$, $p = .515$). There were no pre-existing forward- or backward-association relationships between any of the words, reducing the likelihood of erroneous associations between words in separate pairs.

2.3.3.3.2 *Encoding*

Participants were presented with each word pair for 5000 ms and were instructed to memorize the two words as a pair for a future memory test. To help memorize the word pairs participants were instructed to use visual imagery.

2.3.3.3.3 *Immediate Recall*

To test their memory immediately after encoding, participants were presented with the cue from each pair (i.e. the first word of the pair) and given 10 s to recall the target word (i.e. the second word of the pair). Participants made their responses by typing the target word into the computer, they were instructed to use the backspace if they made a mistake and pressed the enter key to submit their response. Participants received immediate feedback following each response (3500 ms), and on incorrect trials the correct cue and target were re-presented and participants were instructed to try to re-learn that word-pair. This immediate recall procedure was repeated until participants correctly recalled a minimum of 60% of the word pairs, or until they had completed the recall procedure a maximum of three times. This criterion was set to try to maintain a similar level of performance across participants, without large differences in the number exposures to the stimuli.

2.3.3.3.4 Delayed Recall

Delayed recall followed the same procedure as immediate recall; however participants did not receive feedback on their performance and completed the task just once.

2.4 Results

2.4.1 Sleepiness

Measures of sleepiness were taken using the SSS at the beginning of each session (four participants did not complete the SSS, 2 participants from each group). Scores (see Table 2.2) were analysed using an analysis of variance (ANOVA) with the factors Group (15-minute delay, 24-hour delay) and Session (Session 1, Session 2). This analysis revealed no main effects (Group; $F(1, 38) = 1.84, p = .183$, Session; $F(1, 38) = 1.00, p = .324$) or interactions ($F(1, 38) = 1.00, p = .324$), suggesting that ratings of sleepiness were comparable across groups and sessions in this study.

Table 2.2 Stanford Sleepiness Scale (SSS) scores for each group in Session 1 and Session 2. SSS ratings are marked on a 7-point scale with a score of 1 representing most alert; mean scores are presented with standard error of the mean in brackets.

	Stanford Sleepiness Scale	
	Session 1	Session 2
15-minute Delay	2.30 (± 0.16)	2.05 (± 0.18)
24-hour Delay	2.45 (± 0.15)	2.45 (± 0.18)

2.4.2 Categorisation Task

2.4.2.1 Accuracy-based Analysis

Each session of the categorisation task was analysed separately. The average proportion of correctly categorised items in each condition was calculated for each block of training in Session 1 (see Table 2.3). The data was analysed using an ANOVA with the between-subjects factor Group (15-minute, 24-hour) and the within subjects factor

Block (Block 1, Block 2). There was no main effect of Group in the analysis ($F(1, 42) = 1.54, p = .221$). As expected, there was a main effect of Block ($F(1, 42) = 47.70, p < .001, \eta^2 = 0.53$) providing evidence to suggest that participants became more proficient in their categorisation as a result of the feedback provided during training. The interaction between these factors was non-significant ($F(1, 42) = 3.55, p = .067$).

Participants completed a further two blocks of category training in Session 2 of the study (see Table 2.3). To assess whether Session 2 performance was influenced by the type of delay provided between sessions, performance was analysed using an analysis of covariance (ANCOVA) with the factors Group (15-minutes, 24-hours) and Block (Block 1, Block 2) with average Session 1 accuracy included as a covariate to account for individual learning levels. This analysis did not reveal a main effect of Group, suggesting that participants' performance on the task did not differ as a consequence of the delay type ($F(1, 41) = 0.33, p = .571$). There was no main effect of Block ($F(1, 41) = 0.96, p = .333$) and no interaction between these factors ($F(1, 41) = 0.10, p = .757$).

Table 2.3 The proportion of correctly categorised trials in the categorisation task. Mean scores are presented with Session 2 scores showing covariate adjusted means, as evaluated with average Session 1 performance as the covariate. The retention score is defined as the % change in accuracy from the second block in Session 1 to the first block of Session 2 (Session 2 block 1 – Session 1 block 2). Standard error of the mean is presented in brackets.

	Categorisation Task Performance			
	Session 1		Session 2	
	Block 1	Block 2	Block 1	Block 2
15-minute Delay	.63 ($\pm .02$)	.70 ($\pm .03$)	.77 ($\pm .02$)	.78 ($\pm .02$)
24-hour Delay	.65 ($\pm .02$)	.75 ($\pm .02$)	.79 ($\pm .02$)	.80 ($\pm .02$)

2.4.2.2 Model-Based Analysis

General Recognition Theory (GRT) based analysis determines which of a predefined set of decision-boundary models best describes the classification strategy

adopted by each participant (Ashby & Gott, 1988). This analysis assesses whether participants were truly adopting an information-integration decision boundary to separate Category A from Category B exemplars. Four models were considered in this analysis: one-dimensional, conjunction, general linear classifier and random.

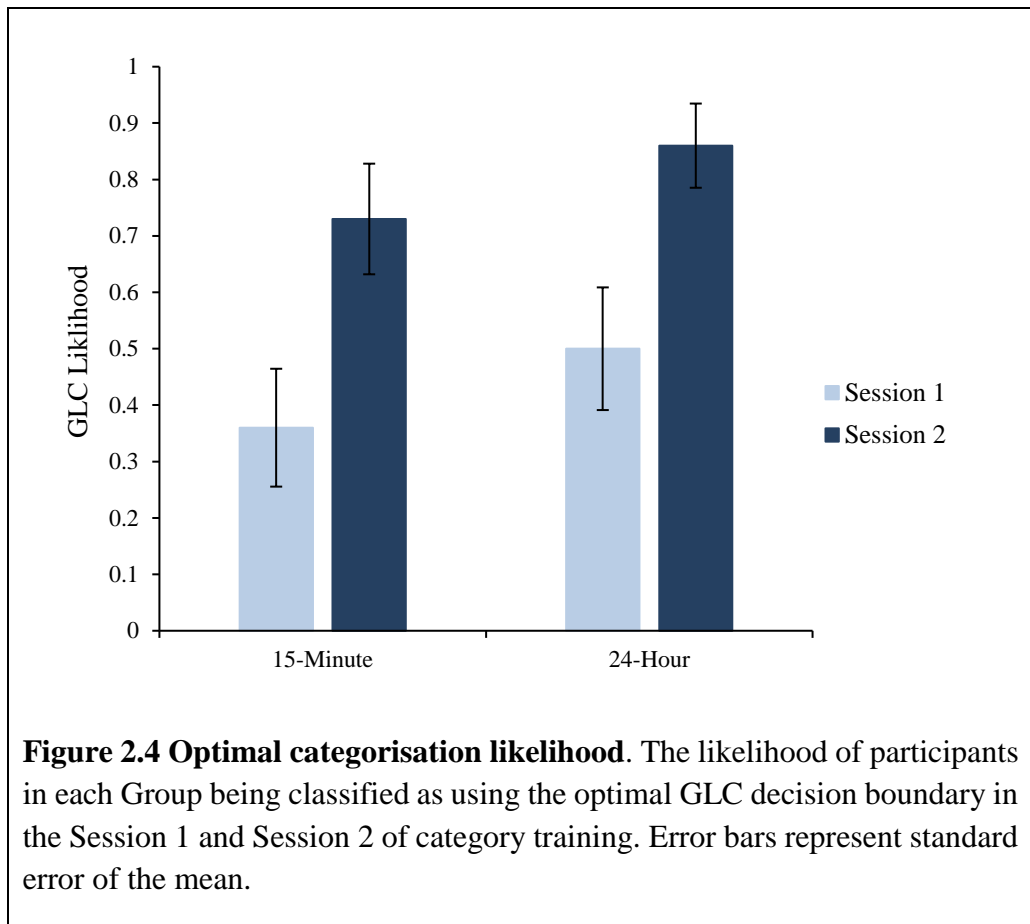
The one-dimensional models assume that participants use a single dimension in order to classify stimuli by comparing each stimulus with a determined criterion value. An example using the tone frequency dimension in the current study would be “Respond Category A for high tones and Category B for low tones”. These models have two parameters: the criterion value and the variance of internal noise. The conjunction model suggests that participants hold a criterion value along both dimensions and combine the judgements to determine category membership. An example of a conjunction model would be “If the tone frequency is high and the pixel density is low assign Category A otherwise, assign Category B”. This model has three parameters: the two criterion values and internal noise. The general linear classifier (GLC) model assumes a straight-line decision boundary can describe classification. The model can vary in gradient and intercept but suggests that participants are integrating across both dimensions to determine category membership. The GLC model has three parameters: the intercept, gradient and noise. The random model assumes that participants are responding randomly and this model has no parameters.

For each participant, and in each session of category training, the best fit of each of these models was calculated and the best fitting model was selected using Akaike’s information criterion (Akaike, 1974). These analyses were performed using the `grt` package in R environment (Matsuki, 2017) and are reported in Table 2.4. A mixed-effects model was fitted with the likelihood of GLC classification as the dependent measure. The model included Group (15-minute and 24-hour), Session (Session 1, Session 2) and their interaction as fixed effects. Both fixed effects were coded with Helmert contrasts, with the 15-minute delay and Session 1 conditions acting as the reference levels. This meant that there was one Group contrast, with the 15-minute delay group compared with the 24-hour delay group, and there was one Session contrast, comparing Session 1 with Session 2. Random effects included by-subject intercepts only, which was the maximal random effect structure justified by the data (Baayen, Davidson & Bates, 2008). The `lme4` package in R, with the logit link function (Bates et al., 2015; Jaeger, 2008) was used to

conduct the analysis. There was a significant effect for the Session contrast, with both groups showing an increase in GLC classification in Session 2 compared to Session 1 ($\beta = 2.53$, standard error (SE) = 0.90, $z = 2.81$, $p = .005$, see Figure 2.4). The Group contrast was non-significant ($\beta = -0.43$, SE = 0.48, $z = -0.91$, $p = .364$) as was the interaction ($\beta = -0.18$, SE = 0.61, $z = -0.29$, $p = 0.77$).

Table 2.4 Proportion of participants best described by each model according to the model-based analyses for each Session of the Categorisation Task. (1D = one-dimensional, GLC = general linear classifier, CJ = conjunction, RDN = random).

		Categorisation Strategies			
		1D	GLC	CJ	RND
15-minute Delay	Session 1	.36	.36	.23	.05
	Session 2	.18	.73	.09	.00
24-hour Delay	Session 1	.18	.50	.32	.00
	Session 2	.00	.86	.14	.00



2.4.3 Categorisation Follow-Up Tasks

2.4.3.1 Speeded Categorisation

Participants completed two speeded categorisation tasks, one with stimuli from the trained distribution (Trained) and a second with stimuli taken from outside the trained stimulus space which therefore had not been trained but could be categorised using the same category structure (Non-Trained). Accuracy is presented in Table 2.5. One-sampled t-tests confirmed that both groups were able to categorise both the Trained and the Non-Trained stimuli at above chance (0.5) level (all p 's < .001). To assess differences between the groups, performance was analysed using an ANOVA with the between-subject variable Group (15-minute, 24-hour) and within-subject variable Training (Trained, Non-Trained). This analysis revealed a main effect of Group, with greater accuracy in the 24-hour compared to the 15-minute delay group ($F(1, 42) = 4.92, p = .032, \eta^2 = 0.12$), suggesting an offline consolidation benefit in this speeded version of the categorisation

task. There was no main effect of Training ($F(1, 42) = 0.00, p = .983$) and no interaction between the variables Training and Group ($F(1, 42) = 0.07, p = .788$).

2.4.3.2 Two-Alternative Forced Choice (2AFC)

The 2AFC task aimed to assess knowledge of category membership by asking participants to combine the two stimulus dimensions in order to create a specific category exemplar. Due to missing data, two participants were not included in this analysis (one participant from each delay condition). Accuracy is calculated as the proportion of correct responses and is presented in Table 2.5. One sampled t-tests confirmed participants were performing above the level of chance (0.5) in both groups (p 's < .001). The groups did not show any differences in performance in this task ($t(40) = -1.32, p = .196$).

2.4.3.3 Category Recall

Participants in the recall task were given a 150-point scale to select the optimal category dimension to create an authentic category exemplar. An error score was calculated by measuring the difference between the level chosen by the participant and the mean level described by the line of best fit for each category distribution. Due to the nature of the stimuli, a varied number of responses would create valid category representations; participants were therefore scored correct if their error score fell within 10% of the calculated level. Accuracy data is presented in Table 2.5, an independent samples t-test showed no significant differences in accuracy between the groups ($t(42) = -1.00, p = .322$).

Table 2.5 Performance in the three Categorisation follow-up tasks. Speeded Categorisation shows the mean accuracy for trials from the trained distribution and trials from outside the trained distribution (non-trained). Mean accuracy in each group is presented for the two-alternative forced choice (2AFC) and Recall Task. Standard error of the mean is presented in brackets.

	Categorisation Follow-Up Tasks			
	Speeded Categorisation		2AFC	Recall
	Trained	Non-Trained		
15-minute	.72 (\pm .02)	.72 (\pm .03)	.60 (\pm .03)	.35 (\pm .03)
24-hour Delay	.79 (\pm .02)	.79 (\pm .03)	.64 (\pm .02)	.38 (\pm .03)

2.4.4 Paired-Associate Task

Performance in the paired-associate task was calculated as the number of correctly recalled word pairs, measured after learning in Session 1 (immediate) and at the end of testing in Session 2 (delayed). Accuracy in the immediate and delayed tests is presented in Table 2.6. To assess the impact of the consolidation delay, the delayed recall accuracy was analysed using an ANCOVA with the factor Group (15-minute, 24-hour) and with the covariate of immediate recall to control for individual differences in memory performance. This analysis revealed a significant main effect of Group ($F(1, 41) = 21.23$, $p < .001$, $\eta^2 = 0.34$), with the 15-minute group showing higher accuracy compared to the 24-hour group, suggesting a general effect of memory decay in the 24-hour group.

Table 2.6 Proportion of correctly recalled items in the paired associate recall task. Delayed recall shows covariate adjusted means (as evaluated with the covariate immediate recall). Standard error of the mean is presented in brackets.

	Paired-Associate Task Performance	
	Immediate Recall	Delayed Recall
15-minute Delay	.75 (\pm .02)	.89 (\pm .02)
24-hour Delay	.74 (\pm .02)	.77 (\pm .02)

2.4.5 Categorisation and Paired-Associate Learning

It is not known whether the paired-associate and category learning task assessed in this study show similar changes in performance as a result of offline consolidation. To assess whether consolidation impacted performance in similar ways, a difference score was calculated for each measure to capture the change in performance across the delay (paired-associated task; delayed recall – immediate recall and categorisation task; Session 2 Block 1 accuracy – Session 1 Block 2 accuracy). For each group, a correlation between these two difference scores was calculated (15-minute; $r = -0.34$, $p = .123$, 24-hour; $r = 0.23$, $p = .300$). These correlations were non-significant suggesting that offline consolidation did not have a similar behavioural impact on performance in these two tasks.

2.5 Discussion

This study investigated the role of offline consolidation on the development of cross-modal category representations using a traditional information-integration categorisation task (Ashby & Gott, 1988). This task required participants to integrate visual and auditory information from abstract stimuli in order to make successful category judgements. Participants showed clear evidence of cross-modal integration with high levels of categorisation accuracy. This was further supported by modelling individual response strategies – with participants showing a significant shift to two-dimensional linear integration strategies from the first to the second session of training. In the category training task, there were no differences in performance between groups that had a 24-hour or 15-minute delay between the testing sessions, suggesting that offline consolidation did not impact upon the development of these categorical representations during training. However, when category knowledge was tested with an emphasis on speed, a benefit in the 24-hour delay group was observed, suggesting a possible role of consolidation in facilitating speeded category decisions. There was no correlation between the offline consolidation benefit in this categorisation task and the declarative memory measure of paired-associate recall, suggesting that offline consolidation may have a differential impact upon these two types of memory representation.

This study was able to capture the multi-modal nature of real-world concepts by utilising a categorisation paradigm that required participants to integrate information from visual and auditory dimensions to generate categorical representations. Only two previous studies have examined cross-modal category learning and the results of this study complement this previous research by showing high levels of categorisation following training with visual-auditory stimuli (Maddox et al., 2006; Smith et al., 2014). Similarly, there has been little research investigating the role of time in the development of categorical representations, however in line with Maddox et al. (2009) this study found improvements in category knowledge following a delay of 24-hours. To assess whether these improvements were due to mechanisms of offline consolidation, a shorter 15-minute delay group was included in the current study – this group showed similar improvements in performance suggesting that improvement in performance may be due to re-exposure to the task rather than the result of offline consolidation.

However, differences between the 24-hour and 15-minute delay groups were observed when performance was assessed in a speeded version of the categorisation task, with greater accuracy for participants who had a 24-hour delay between the two training sessions. This is interesting given that the only change to the task was the shift in focus to speed and the removal of feedback following each response. The COVIS model of categorisation emphasises the role of procedural and implicit learning mechanisms in successful categorisation using information-integration category structures. By changing the focus of the task to speed, it may be the case that participants allowed their responses to be driven by more automatic or procedural response systems (Ashby & Valentin, 2005; Maddox & Ashby, 2004). Within the consolidation literature, robust consolidation related enhancements in procedural memory have been observed following both time awake (Diekelmann et al., 2009; Fischer, Hallschmid, Elsner & Born, 2002; Robertson, Pascual-Leone & Miall, 2004) and time asleep (Fischer et al., 2002; Gais et al., 2000; Plihal & Born, 1997; Stickgold et al., 2000; Walker et al., 2003). Speeded tasks may therefore provide a more sensitive measure for assessing the impact of consolidation on category knowledge. It should however be noted that the size of the observed effect in the speeded task is relatively small and numerical benefits in the other follow up tasks (i.e. the 2AFC and recall task) are also observed for the 24-hour delay group.

Nevertheless, these results are in line with the those from Hennies et al. (2014), who also report a performance benefit following a 24-hour delay when using an information-integration category structure to increase the speed of categorisation judgements. Like in the current experiment, this benefit was not observed following a shorter 15-minute delay, suggesting a possible role for offline consolidation. Hennies et al. (2014) modified the traditional categorisation paradigm by making the information-integration category structure secondary to a one-dimensional visual rule that could be used for categorisation; as a result, they describe their information-integration category structure as implicit. Interestingly, when they tested explicit knowledge of the underlying category structure, they found no differences between their 15-minute and 24-hour delay groups. This pattern of results supports the current data by showing differential impacts of offline consolidation on explicit and implicit measurements of category knowledge, where more explicit measurements appear to be less sensitive to the effects of offline consolidation.

A further interesting finding from this study is that the 24-hour benefit for speeded categorisation was observed for both items that were sampled within the trained distribution and from beyond the trained stimulus space. This suggests that the benefit of time may extend to the overall category structure, allowing the categorisation of novel stimuli to benefit from the consolidation delay. The flexible use of a category structure is critical when considering broader conceptual memory which facilitates memory generalisations based on shared properties between novel objects/events and existing knowledge. Although the stimuli are very simplistic in the current study, the data suggests that the flexible use of broader knowledge structures (and not just trained knowledge) may benefit from mechanisms operating during offline consolidation. Chapter 4 of this thesis aims to address this idea using an associative memory paradigm which allows a clear dissociation to be made between the categorisation of trained items and the categorisation of novel items which requires the use of a developed category structure.

Due to the nature of the traditional categorisation paradigm, in which participants are continually presented with feedback following each response, it is difficult to dissociate the impact of consolidation from the effects of feedback (and as a result post-consolidation learning) in this and previous studies (Hennies et al., 2014; Maddox et al., 2009). It is not clear whether the 24-hour benefit in speeded categorisation reflects

memory enhancement (and would therefore be present prior to any further category training), or whether it is due to a combination of consolidation and further exposure to category training. Data from the consolidation literature does provide evidence of memory enhancements following offline consolidation delays (Fischer et al., 2002; Gais et al., 2000; Steffen Gais & Born, 2004; Plihal & Born, 1997; Tucker et al., 2006). However, the Complementary Learning Systems (CLS) model of consolidation suggests that offline consolidation may also lead to the improved learning of new information when it is consistent with existing knowledge (McClelland, 2013; McClelland et al., 1995). By this account, processes of offline consolidation during the 24-hour delay may have stabilised the previously trained categorical representations, which then acts to support swifter and more effective learning in the second session of training. Determining the exact contribution of offline consolidation on these representations is addressed in Chapter 3 of this thesis, where measurements of category knowledge (without feedback) were taken both at the end of the initial training period and prior to any further training following a number of consolidation delays. This allowed memory enhancement to be dissociated from improved category knowledge as a result of increased post-consolidation learning.

‘Offline consolidation’ encompasses a wide range of processes that may operate to benefit memory. The consolidation literature to date has placed a large focus upon sleep, with a growing amount of research highlighting an active role for sleep in the stabilisation, enhancement and reorganisation of long-term memory representations (Born et al., 2006; Ellenbogen et al., 2006; Rasch & Born, 2013). However, there is also emerging evidence to suggest that quiet wakefulness may also provide benefits for memory (Craig et al., 2015; Craig et al., 2016; Dewar et al., 2012; Mednick et al., 2011) and Hennies et al. (2014) provide the first evidence to suggest that wakefulness may play a role in the offline consolidation of categorical representations. The specific role of wake- and sleep-associated consolidation on the development of category knowledge, using this traditional information-integration categorisation task, is assessed in Chapter 3 of this thesis.

Participants were able to integrate cross-modal (visual-auditory) information to generate categorical representations. The role of offline consolidation was assessed in this study by comparing performance following a 24-hour delay with a shorter 15-minute delay. In category training, there were no changes in accuracy across the delay groups,

however in a speeded follow-up task a significant increase in accuracy following a delay of 24-hours was observed, suggesting offline consolidation may benefit the development of categorical memory representations. Our results are consistent with, and extend the two previous studies that have aimed to assess the development of categorical representations across time. We however used an unmodified version of the categorisation paradigm and included a shorter 15-minute delay to control for changes in performance as a result of post-consolidation exposure to the task. Although the results of this study offer evidence to suggest a role for offline consolidation in the development of category knowledge, they also highlight two important factors that have yet to be addressed; i) whether category learning benefits from consolidation alone, or if the benefit emerges only in combination with post-consolidation exposure to the task, and ii) if there is a specific contribution from sleep and/or wake related mechanisms in the development of categorical representation across time.

CHAPTER 3

A Role for Consolidation in Cross-Modal Category Learning

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¹ JA designed and wrote the paper under the supervision of GG and EJ. JA completed all data collection and analysis.

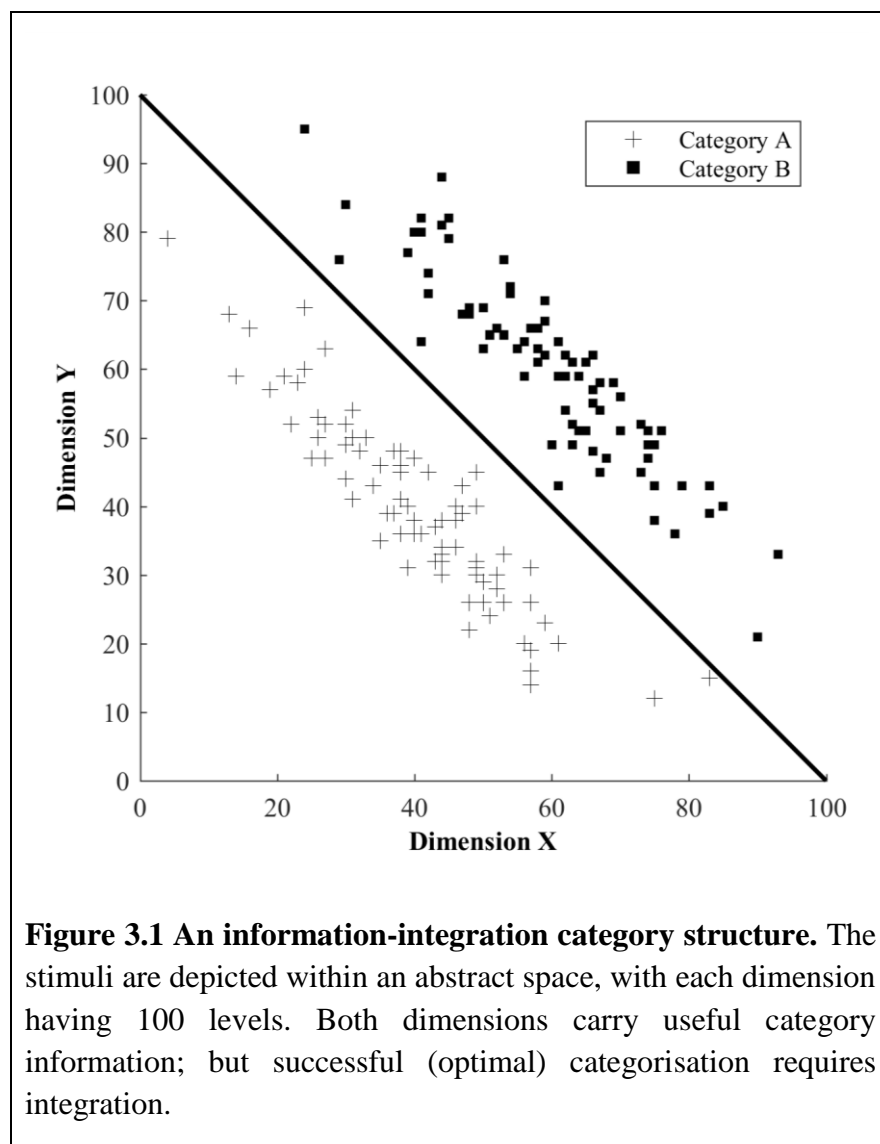
3.1 Abstract

The ability to categorise objects and events is a fundamental human skill that depends upon the representation of multimodal conceptual knowledge. This study investigated the acquisition and consolidation of categorical information that required participants to integrate information across visual and auditory dimensions. The impact of wake- and sleep-dependent consolidation was investigated using a paradigm in which training and testing were separated by a delay spanning either an evening of sleep or daytime wakefulness, with a paired-associate episodic memory task used as a measure of classic sleep-dependent consolidation. Participants displayed good evidence of category learning, but did not show any wake- or sleep-dependent changes in memory for category information immediately following the delay. This is in contrast to paired-associate learning, where a sleep-dependent benefit was observed in memory recall. To replicate real-world concept learning, in which knowledge is acquired across multiple distinct episodes, participants were given a second opportunity for category learning following the consolidation delay. Here we found an interaction between consolidation and learning; with greater improvements in category knowledge as a result of the second learning session for those participants who had a sleep filled delay. These results suggest a role for sleep in the consolidation of recently acquired categorical knowledge; however this benefit does not emerge as an immediate benefit in memory recall, but by enhancing the effectiveness of future learning. This study therefore provides insights into the processes responsible for the formation and development of conceptual representations.

3.2 Introduction

Conceptual knowledge refers to the information we possess that enables us to bring meaning to the words, objects and events we encounter daily (Lambon Ralph et al., 2010; 2016). This information is essential for communication and cognition and draws on abstract representations that describe the categorical and functional relationships between items (Kintsch & Walter, 1988). The development of conceptual knowledge is thought to require the integration of information across different sensory modalities (e.g. vision and sound) and multiple learning episodes, giving rise to higher-order similarity structures that take into account all available sources of information (Lambon Ralph et al., 2016; Patterson et al., 2007). For any given concept, cross-modality integration is important, as

similarity in one modality may not be sufficient to extract appropriate conceptual relationships. For example; pears and light bulbs are similar in shape but are not related in meaning. Studies investigating perceptual category learning provide successful demonstrations of feature integration in order to develop conceptual representations (Ashby & Ell, 2001; Ashby et al., 2003; Ashby & Valentin, 2005; Ashby & Casale, 2003). However, little research has focused upon the acquisition of cross-modal representations and in particular their development across time (Maddox et al., 2006; 2009; Hennes et al., 2014).



To study the acquisition of cross-modal category representations, it is necessary to create arbitrary ‘artificial’ categories. The categorisation literature provides a useful paradigm for creating such stimuli and allows the underlying structure of the categories to be experimentally manipulated in order to promote integration across multiple features or dimensions. Categories that require the integration of two (or more) stimulus dimensions are referred to as information-integration category structures (an example is presented in Figure 3.1). When presented with stimuli from this type of structure, information about category identity is available in both dimensions; however, neither dimension alone is sufficient to make precise categorisations. For optimal categorisation, information from both dimensions needs to be integrated in order to determine the category boundary (the bold line in Figure 3.1 shows the optimal category boundary). Through feedback-driven exposure to category exemplars, participants are able to acquire knowledge of information-integration category structures and show high levels of categorisation accuracy (Ashby & Maddox 2005; 2011).

Most studies within the categorisation literature have focused on two-dimensional category structures within a single (visual) domain (e.g. Gabor patches – sinusoidal gratings that vary on the dimensions of orientation and frequency) overlooking the cross-modal nature of much conceptual knowledge. However, information-integration category structures can be created using cross-modal stimuli; Maddox et al. (2006) used visual-auditory stimuli dimensions, and subsequent work has shown high levels of categorisation when the category structure is manipulated such that the categories overlap (Smith et al., 2014). In accordance with these findings and to capture the cross-modal nature of conceptual knowledge, the current study utilised a cross-modal (visual-auditory) information-integration categorisation paradigm to study the development of category knowledge across time.

Research investigating the development of memory across time has typically focused upon episodic declarative memory, which requires rapid learning at a specific point in time. However, conceptual information is extracted from features present across multiple spatially and temporally distinct episodes (Rogers & McClelland, 2004). Given the gradual emergence of conceptual knowledge, it is therefore important to consider (i) the influence of consolidation processes that may occur in between learning episodes and

(ii) the effects of prior learning on the information that can be extracted from new experiences.

There has been a large amount of research into memory consolidation; the processes that serve to maintain, strengthen and modify memories. These processes may occur across both wake and sleep; however tasks that assess episodic declarative memory suggest a specific role for sleep in memory consolidation (Diekelmann et al., 2009). One task that reliably demonstrates sleep-dependent consolidation benefits is paired-associate learning, in which participants are required to learn lists of associated word-pairs. Memory for the learned pairs is usually assessed using cued-recall procedures, which follows a post-learning delay that is manipulated to contain either sleep or wakefulness. Consistently, studies report better memory retention after a delay containing sleep (compared to wake) suggesting a role for sleep-dependent consolidation in long-term memory retention (Jenkins & Dallenback, 1924; Plihal & Born, 1997; Tucker et al., 2006; Diekelmann et al., 2009).

It was originally hypothesised that sleep benefits memory by offering passive protection from interference and forgetting (Ellenbogen et al., 2006). However, there is now strong evidence to suggest that sleep plays an active role in consolidation by promoting systems-level memory transfer (Diekelmann & Born, 2010). The active systems consolidation hypothesis suggests that during sleep, newly encoded information is integrated within long-term memory networks and is reorganised to enable the extraction of invariant features (Born & Wilhelm, 2012). Strong support for the specific role of sleep has been provided by numerous studies which show a correlation between the change across a sleep delay and sleep physiology, specifically slow-wave sleep (SWS) (for a review see Rasch & Born, 2013). Causal evidence is provided by studies which have re-exposed participants to encoding associated cues (e.g. odours or auditory cues) during SWS – which leads to enhanced memory performance, highlighting a role for memory reactivation as a possible mechanism of sleep-associated consolidation (Rasch et al., 2007; Rudoy et al., 2009; Rasch & Born, 2013). Consolidation during sleep is therefore thought to not only strengthen individual representations, but also to facilitate the extraction of shared and systematic features from the environment – a potentially critical mechanism for the development of concept or categorical memory representations.

Sleep-dependent consolidation beyond isolated episodic memories has received much less attention; however there is evidence to suggest that sleep plays a role in the extraction of regularities (Lau et al., 2011). Ellenbogen et al. (2007) used a transitive inference paradigm to examine the role of wake- and sleep-dependent consolidation on the extraction of an implicit hierarchical structure. Participants learned arbitrary “premise pairs” (e.g. $A > B$, $B > C$, $C > D$ etc.) followed by a wake- or sleep-filled post-learning delay. Participants were then tested on their memory for the trained pairs (e.g. $A > B$) and their knowledge of the untrained hierarchy (e.g. $B > D$). The two groups showed comparable memory for trained items; however the sleep group outperformed the wake participants when knowledge of the more distant untrained hierarchy was assessed, suggesting sleep had facilitated extraction of the underlying hierarchical information (Ellenbogen et al., 2007).

A sleep-dependent benefit for the extraction of regularities is not however consistently reported. In a declarative language learning task, Mirkovic & Gaskell (2016) report sleep-dependent benefits for arbitrary vocabulary knowledge, but fail to find differences between wake and sleep groups when assessing knowledge for systematic aspects of the trained language (i.e. grammatical regularities). It is these systematic aspects of learning that are thought to contribute to conceptual memory; however few studies take into account the real-world nature of conceptual learning which develops across distinct episodes. Evidence from animals (Tse et al., 2007), humans (van Kesteren et al., 2013) and computational models (McClelland et al., 2013) suggests that new learning is facilitated by prior schematic knowledge, with accelerated integration when new and existing information are consistent (McClelland et al., 2013). The acquisition of conceptual information across time may therefore rely heavily on an interaction between consolidation processes and subsequent learning episodes. A single post-delay test, the typical procedure used in consolidation research, may therefore fail to capture the true impact of consolidation on the development of conceptual knowledge across time. In an attempt to replicate realistic category learning, and to capture potential interactions between consolidation and learning mechanisms, this study included a second learning opportunity following the consolidation delay.

To our knowledge, two studies have used the information-integration categorisation task described above to study the development of category knowledge

across time. Maddox et al. (2009) examined the influence of sleep deprivation on information-integration category learning. They provided category training in two sessions separated by 24-hours during which participants were kept awake or were able to maintain their usual wake-sleep cycle. Maddox et al. reported poorer performance for participants who remained awake between sessions, however, due to the sleep deprivation paradigm, this study cannot separate the effects of sleep-based consolidation from those of fatigue.

A second study reports an offline consolidation benefit in category learning when comparing a delay of 24-hours with 15-minutes (Hennies et al., 2014). Unlike immediate post-delay consolidation effects which are reported in studies assessing episodic declarative memory, the benefit in this study emerged only after further training following the delay; suggesting a subtle benefit of consolidation which increased the effectiveness of post-delay learning. Hennies et al. (2014) went on to compare the effects of sleep and wake separately by using a 12-hour delay that spanned either a night of sleep or a day of wakefulness; they found a specific consolidation benefit for the wake, but not the sleep, delay condition. This result contrasts with those typically observed within the consolidation literature and suggests that categorisation may not benefit from sleep-based consolidation in the same way as declarative memory. However, Hennies et al. (2014) made a number of modifications to the categorisation paradigm. These changes made the information-integration structure predictive of category membership, but secondary to categorisation – which was based on a one-dimensional visual rule that was provided to participants. This is likely to have had a large impact on learning in the task, given that participants were not required to use the category structure to achieve accurate categorisation. Furthermore, in contrast to the typical measurement of accuracy that is used in categorisation studies, their measurement of integration was based upon changes in reaction time, making it difficult to compare their results with the existing categorisation literature. In the current study, we wanted to assess the role of wake and sleep based consolidation using the traditional, and unmodified, information-integration category learning structure.

Thus, while the role of sleep-dependent consolidation in the development of episodic declarative memory is relatively well-established, the contribution of consolidation in the development of conceptual memory has not been widely investigated.

It is unknown whether the behavioural consequence of sleep-dependent consolidation is consistent across memory types, or indeed whether sleep- or wake-dependent mechanisms have a specific role to play in the consolidation of conceptual memory. The potential influence of such a mechanism on the stabilisation of previously encoded information and the impact on subsequent learning has yet to be established.

Accordingly, the current study investigated the role of consolidation on both traditional paired-associate declarative memory and conceptual categorisation in a cross-modal information-integration paradigm (Ashby & Gott, 1988). Basic two-dimensional cross-modal (auditory-visual) stimuli were created and participants were expected to demonstrate sensory integration in order to form cross-modal categorical representations. By employing a 15-minute and 12-hour sleep or wake delay between two sessions of learning, we assessed independent contributions of time and of wake- and sleep-dependent consolidation on (i) the retention of previously-encoded episodic and categorical representations, and (ii) the capacity to further develop category knowledge after consolidation. The effects of sleep were then replicated in a second sample with concurrent polysomnography recordings although for ease of exposition all groups are presented in the same analysis.

3.3 Methods

3.3.1 Participants

Participants were 95 undergraduate students recruited from the University of York in fulfilment of course credit or for payment. Participants reported normal or corrected-to-normal vision and hearing and were randomly assigned to one of four experimental conditions: a 12-hour wake group ($n = 23$, mean age: 20.52, S.D. ± 3.54 , 17 female), a 12-hour sleep group ($n = 22$, mean age: 20.05, S.D. ± 1.32 , 19 female), a PSG-monitored overnight sleep group ($n = 23$, mean age: 20.87, S.D. ± 2.49 , 16 female) or a 15-minute delay group ($n = 27$, mean age: 20.67, S.D. ± 3.54 , 21 female). Participants in the overnight PSG-monitored sleep group were required to be free from psychoactive drugs, including alcohol and caffeine, and to refrain from daytime napping for 24 hours preceding and throughout the study period.

3.3.2 Study overview

All participants were tested on a measure of declarative episodic memory (paired-associate learning) and a conceptual category learning task. Participants completed two sessions of the study; to assess paired-associate memory a typical consolidation paradigm was utilised where participants completed encoding and immediate cued-recall in session 1, followed by a delayed cued-recall test in session 2. Category training followed a similar procedure, however following the delayed test in session 2, participants completed a second round of training and a final test before completing a number of categorisation follow-up tasks. The two sessions were separated by a delay of varying lengths (15-minutes vs. 12-hours) that were manipulated to separately assess the contribution of wake- and sleep-dependent consolidation.

3.3.3 Experimental Tasks

3.3.3.1 Paired-Associate Learning

3.3.3.1.1 *Paired-Associate Stimuli*

80 words were selected from an adapted version of The University of South Florida (USF) word association, rhyme, and word fragment norms (Nelson et al., 2004) to create 40 semantically unrelated cue and target word pairs (e.g. owl – frame). Both the cue and target words were singular, had high USF concreteness ratings (cues = 5.90 ± 0.61 ; targets = 5.85 ± 0.41 , $t(39) = 0.39$; $p = .696$) and were matched for frequency (cues = 35.10 ± 41.09 ; targets = 40.73 ± 55.26 , $t(39) = -4.71$; $p = .640$), word length (cues = 5.18 ± 1.34 ; targets = 5.15 ± 1.05 , $t(39) = 0.09$; $p = .933$) and number of syllables (cues = 1.45 ± 0.68 ; targets = 1.55 ± 0.60 , $t(39) = -0.73$; $p = .472$). There were no pre-existing forward- or backward-association relationships between any of the words, reducing the likelihood of erroneous associations between words in separate pairs.

3.3.3.1.2 *Paired-Associate Encoding*

Participants were presented with each word pair for 5000 ms and were instructed to memorize the two words as a pair for a future memory test. To help memorize the word pairs participants were instructed to use visual imagery.

3.3.3.1.3 Paired-Associate Immediate Recall

To test their memory immediately after encoding, participants were presented with the cue from each pair (i.e. the first word of the pair) and given 10 s to recall the target word (i.e. the second word of the pair). Participants made their responses by typing the target word into the computer; they were instructed to use the backspace if they made a mistake and pressed the enter key to submit their response. Participants received immediate feedback following each response (3500 ms), and on incorrect trials the correct cue and target was re-presented and participants were instructed to try to re-learn that word-pair. Cued-recall with feedback offers the opportunity for extra learning for incorrectly recalled pairs. As a result, it is expected that memory accuracy will increase between this and future memory tests. This immediate recall procedure was repeated until participants correctly recalled a minimum of 60% of the word pairs, or until they had completed the recall procedure a maximum of three times. This criterion was set to try and maintain a similar level of performance across participants, without large differences in the number exposures to the stimuli.

3.3.3.1.4 Paired-Associate Delayed Recall

Delayed recall followed the same procedure as immediate recall; however participants did not receive feedback on their performance and completed the task just once.

3.3.3.2 Categorisation Task

3.3.3.2.1 Category Stimuli

All stimuli were generated using MATLAB (PsychToolBox). Category exemplars were two-dimensional conjoint visual-auditory stimuli based on Smith et al. (2014). The visual dimension was a 150 x 150 pixel unframed box containing randomly placed yellow pixels, presented on a black background. There were one hundred-and-one levels of pixel density with the number of yellow pixels at each level defined by $pixels = round(850 \times 1.0181^{level})$. Pixel density therefore varied from 850 lit pixels (level 0), to 5,061 lit pixels (level 100) out of a total of 22,500. The auditory dimension was a pure tone that varied in frequency (Hz), defined by $frequency = 220 \times 2^{(level/120)}$. For levels 0 and 100 the pitches were 220 Hz and 392 Hz respectively. Stimuli were presented on the right- or left-hand

side of the screen. The placement of each stimulus was determined by its position within the stimulus space (see Figure 3.2); a boundary line orthogonal to the category boundary separated the stimuli, with trials on one side of the boundary presented on the left hand side of the screen during training (the shaded area in Figure 3.2) and trials on the other side presented on the right hand side of the screen (the non-shaded area in Figure 3.2). Although systematic, screen location did not provide any information about category identity and was therefore considered task-irrelevant.

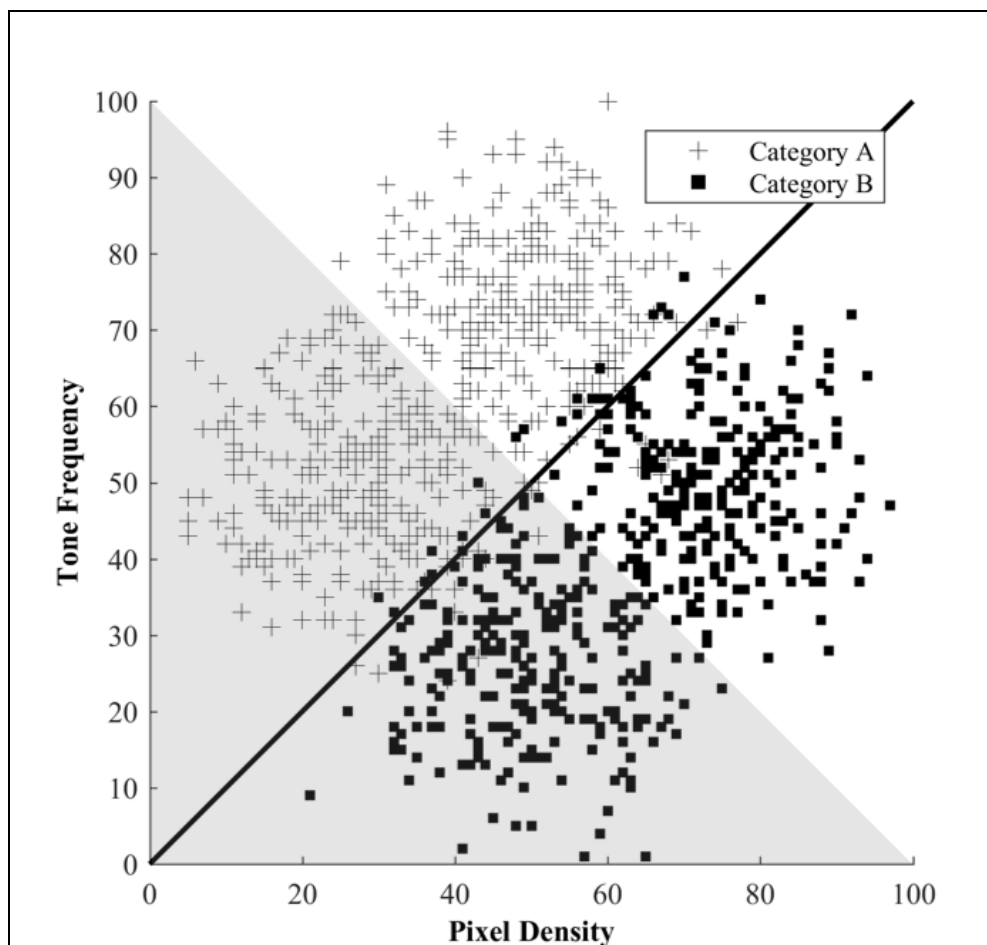


Figure 3.2 The information-integration category structure. The points are normalised to a 100-point scale. The solid line denotes the optimal linear decision boundary; the corsairs and squares represent Category A and Category B respectively. Items that fall within the shaded region were presented on the left-hand side of the screen and those in the non-shaded region presented on the right-hand side of the screen.

3.3.3.2.1 Category Structure

Category exemplars were created using Ashby and Gott's (1988) randomisation technique. Categories were defined by bivariate distributions along the two stimulus dimensions following the information-integration condition of Filoteo et al. (2010) (see Table 3.1). Each stimulus was created by drawing a random sample (x , y) from the stimulus space. Stimuli sets were created for each individual, with each set normalised to match the overall category distribution before being transformed into concrete visual and auditory stimuli using the formulae above. This normalisation ensured that each participant had the same statistical information, despite receiving their own unique set of individual exemplars. Maximum accuracy using the optimal linear boundary as shown in Figure 3.2 would be 95% as there is a 5% category overlap.

Table 3.1 Category distribution parameters (mean (μ) and standard deviation (σ)) for the pixel density (x) and tone frequency (y) dimensions in the information integration category structure.

Category Distribution Parameters				
Category	μ_x	μ_y	σ_x	σ_y
A	26.67	50.00	10	10
A	50.00	73.33	10	10
B	50.00	26.67	10	10
B	73.33	50.00	10	10

3.3.3.2.2 Category learning trials

Participants completed two blocks of sixty trials in each learning session, (with 60 Category A and 60 Category B trials presented in a randomised order). On each trial, one conjoint visual-auditory category exemplar was presented. The response icons ‘A’ and ‘B’ were presented in the lower left- and right- hand side of the screen, and participants were asked to categorise each stimulus by pressing the ‘A’ or ‘B’ keyboard keys. The stimuli were presented for a maximum of 8 s and terminated immediately following a response, if no response was given with the 8 s the trial ended and this was scored as incorrect. Participants received immediate feedback following each response, with the word “Correct!” or “Incorrect!” presented in the centre of the screen. To encourage good performance and to engage participants throughout the task a points system was used such that points were added or deducted from a running total following each response. A monetary reward was offered for the highest performing participant. A detailed example of two trials from the category learning task is presented in Figure 3.3.

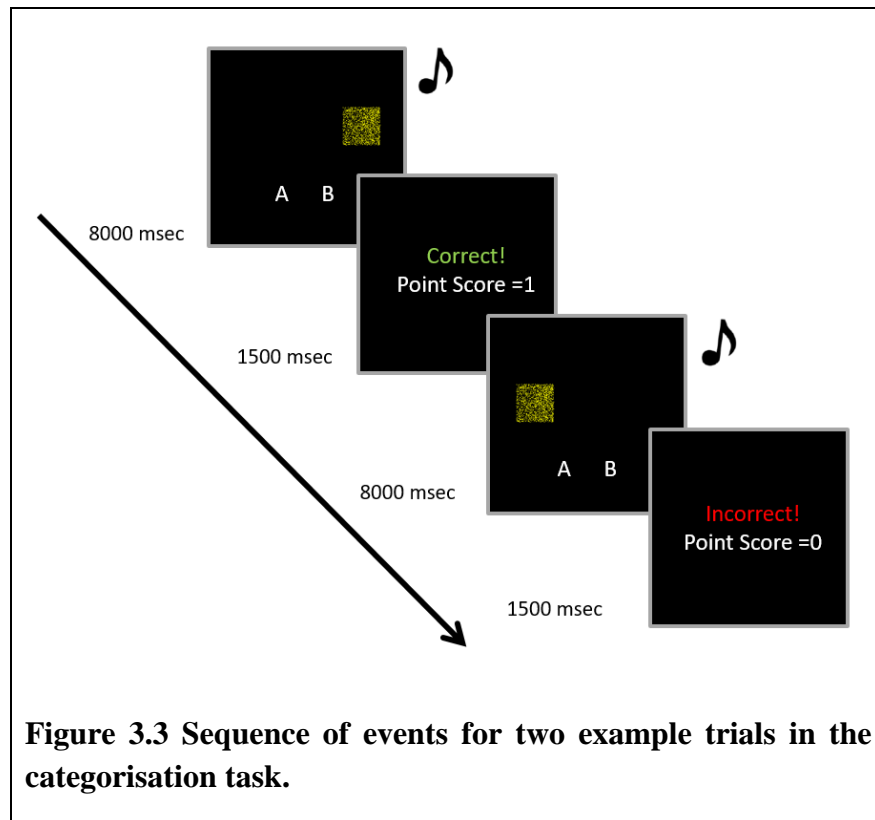


Figure 3.3 Sequence of events for two example trials in the categorisation task.

3.3.3.3 Instructions

Participants were told that each trial of the categorisation task contained a pixel box and an auditory tone, with the chance of each trial belonging to category A or B being equal. They were instructed to categorise each trial by pressing the “A” or “B” keyboard key and that they would need to guess at first, but with practise they would be able to categorise the stimuli accurately. Participants were instructed to focus on the density of the pixels and the pitch of the tone to make their decisions; they were informed that the pixel box would be located on the left or right-hand side of the screen, but that this was not important for making their categorisation decisions. Participants were encouraged to focus on being as accurate as possible during learning.

3.3.3.4 Categorisation Follow-Up Tasks

Follow-up tasks aimed to assess participants’ knowledge of the category structure, as learned in the categorisation task. The stimuli used in these tasks were the same as described above.

3.3.3.4.1 Categorisation Test

The categorisation test included 60 trials which followed a similar procedure to categorisation learning; however, participants did not receive feedback on their performance. A fixation-cross of 1500 ms was presented before the onset of each trial and participants were instructed to respond both as accurately and as quickly as possible, using the knowledge they had gained during learning to guide their decisions. Participants performed the categorisation test three times; immediately following learning in session one, straight after the delay in session two and finally after the second round of category training in session two (see Figure 3.4).

3.3.3.4.2 Two-Alternative Forced Choice (2AFC) Task

Participants completed a 2AFC task to assess their ability to identify category exemplars. On each trial participants were presented with a ‘target Category’ (either A or B) in the centre of the screen. The task was divided such that in half of the trials they were presented with a single auditory tone, and two pixel boxes (pixel trials) while in the other half of trials they were presented with one pixel box and two auditory tones (tone trials).

In both trial types, stimuli could be combined to make legitimate category A or B items. The participants' task was to select the stimuli they thought combined to create an exemplar of the target category. For example, on 'pixel trials' participants had to select (from the two pixel boxes) the one they thought combined with the auditory tone to match the target category. Participants completed 80 trials in total (40 pixel trials, 40 tone trials) and were instructed to respond as accurately as possible; a fixation cross (1000 ms) preceded the onset of each trial.

3.3.3.4.3 Recall Task

Participants completed a recall task to assess their ability to generate category exemplars. On each trial participants were presented with a scale which represented the normalised level of either the density of a pixel box or the frequency of a tone (ranging from level -25 to 125). They were also presented with a 'target category' (either A or B) in the centre of the screen, along with a fixed stimulus from one dimension (e.g. a pixel box). Their task was to change the scale representing the non-presented dimension (e.g. the frequency of the tone) to match the target category. Participants used the mouse to click their chosen position on the scale and were able to change position an unlimited amount of times. In half of the trials the fixed dimension was the pixel box, while in the other half of trials the tone was fixed. Participants were instructed to be as accurate as possible. Each trial was preceded by a fixation cross presented for 2000 ms and participants completed 60 trials in total (30 of each type).

3.3.3.4.4 Location Task

The location task was used to assess participants' knowledge of the task-irrelevant location dimension. This was considered to be task irrelevant as screen location did not provide any cues to category membership. We included this manipulation to assess whether participants were sensitive to information that was not relevant for successful categorisation and if knowledge of this information developed differently across delays containing sleep or wake. On each trial they were provided with a conjoint visual-auditory stimulus and its category in the centre of the screen. They had to indicate whether they believed the stimulus belonged on the left or right-hand side of the screen. Each trial was preceded by a fixation cross for 1000 ms and participants were instructed to respond as accurately and as quickly as possible. They completed 60 trials in total.

3.3.3.5 Psychomotor Vigilance Task (PVT)

The PVT is a sustained-attention, reaction-timed task that measures the speed with which participants respond to visual stimuli. The PVT task was obtained from <http://bhsai.org/downloads/pc-pvt/> (Khitrov et al., 2014). During the task, participants were presented with a blank black screen, at random intervals, a millisecond counter began to scroll, and participants had to left click the mouse to stop the counter as quickly as possible. After clicking, the counter displayed the achieved reaction time for 1000 ms, providing the subject with feedback on performance. Inter-stimulus intervals were distributed randomly from 2 to 10 seconds, and the task lasted for a total of 3 minutes.

3.3.4 Sleep Recording with Polysomnography (PSG)

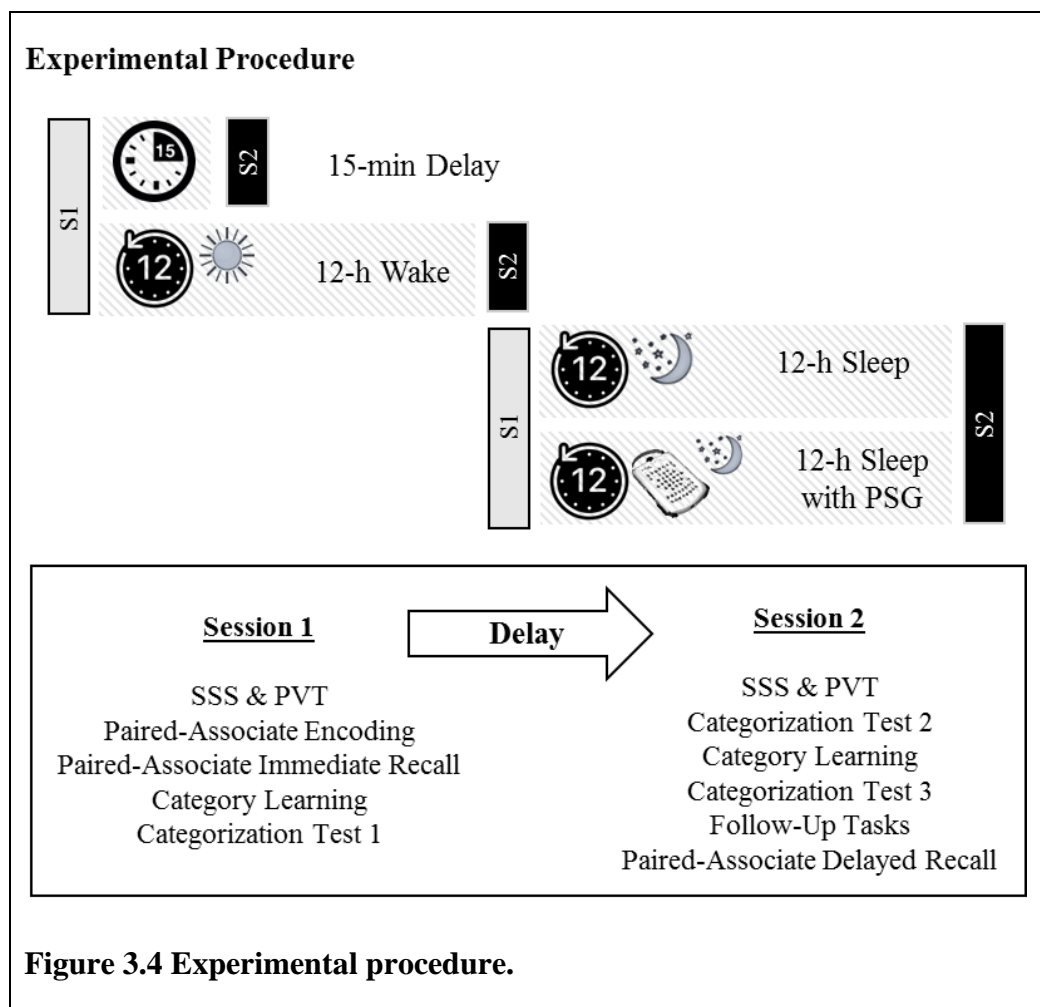
For participants in the overnight PSG group, an Embla N7000 PSG system with RemLogic version 3.4 software was used to monitor sleep. After the scalp was cleaned with NuPrep exfoliating agent (Weave and Company), gold plated electrodes were attached using EC2 electrode cream (Grass Technologies). EEG scalp electrodes were attached according to the international 10-20 system at six standardised locations: central (C3 and C4), occipital (O1 and O2) and frontal (F3 and F4), and each was referenced to an electrode on the contralateral mastoid (A1 or A2). Left and right electrooculography electrodes were attached, as were electromyography electrodes at the mentalis and submentalis bilaterally, with a ground electrode attached to the forehead. Each electrode had a connection impedance of $< 5 \text{ k}\Omega$ and all signals were digitally sampled at 200 Hz.

3.3.5 Procedure

The experiment consisted of two experimental sessions separated by a delay of varying lengths across the four conditions. The two 12-hour delay groups spanned either daytime wakefulness, in which participants continued with their usual daytime activities, or an evening of sleep, where participants returned home to sleep. For these two groups Session 1 began at 8.30am and 8.30pm respectively with Session 2 being completed exactly 12-hours later. Participants in the overnight PSG group were required to arrive at the lab at 8.30 pm and completed the experimental tasks after PSG set-up (9.45 pm \pm 30 minutes). These participants remained in the lab to sleep and were awoken from sleep at approximately 7.30 am; they completed Session 2 tasks at 8.30 am. Participants in the 15-

minute delay group completed Session 1 between 9.00 am and 12.00 pm. These participants were instructed to take a 15-minute break and were encouraged to leave the testing lab in order to avoid fatigue before completing Session 2.

A schematic illustration of the experimental procedure is shown in Figure 3.4. Both sessions began with completion of the Stanford Sleepiness Scale (SSS) (Hoddes et al., 1973) followed by the PVT to obtain measures of sleepiness, alertness and vigilance. In Session 1, participants completed paired-associate encoding and immediate cued-recall, followed by category learning and the first categorisation test (Session 1 ~45 minutes). Session 2 tasks involved a second categorisation test, a further session of category learning and a final categorisation test. Participants then completed the categorisation follow-up tasks and finally paired-associate delayed recall (Session 2 ~1 hour).



3.4 Results

Data were analysed in SPSS 23. All effects that reached a significance level of $p < .1$ are reported, with effects where $p < .05$ considered significant. Bonferroni-corrected t-tests were used to evaluate main effects for factors with more than two levels.

3.4.1 Stanford Sleepiness Scale and Psychomotor Vigilance Task

Alertness measures were taken using the SSS (ratings of sleepiness) and performance on the PVT, focusing upon measures of reaction time (RT) and attentional lapses (RT > 500ms, data is presented in Table 3.2). Each measure was analysed using an analysis of variance (ANOVA) with the between-subjects variable Group (15-minute, PSG, 12-hour wake, 12-hour sleep) and repeated-measures variable Session (Session 1, Session 2). There were no differences in the levels of rated sleepiness across groups ($F(3, 90) = 2.36, p = .077$), however there was a main effect of session, with participants rating themselves as sleepier in session one when compared to session two ($F(1, 90) = 9.25, p = .003$); there was no interaction between these factors ($p > .69$). No differences were observed when measuring alertness by mean RT (Group; $F(1, 89) = 0.90, p = .443$, Session; $F(1, 89) = 0.001, p = .980$) or the number of lapses in the PVT (Group; $F(1, 89) = 0.39, p = .758$, Session; $F(1, 89) = 0.25, p = .620$). This suggests that general levels of alertness cannot account for any effects of Group in the experimental tasks.

Table 3.2 Stanford Sleepiness Scale (SSS) and Psychomotor Vigilance Task (PVT) scores for each group in Session 1 and Session 2. SSS ratings are marked on a 7-point scale with a score of 1 representing most alert; mean scores are presented. PVT scores represent mean reaction time (RT) in ms and the mean number of lapses in attention (RT > 500ms). Standard error of the mean is presented in brackets.

	Sleepiness & Vigilance					
	Session 1			Session 2		
	SSS	PVT <i>RT (ms)</i>	PVT <i>Lapse</i>	SSS	PVT <i>RT (ms)</i>	PVT <i>Lapse</i>
15-minute	2.73 (.16)	254 (4.91)	.08 (.05)	2.23 (.14)	272 (9.05)	.65 (.36)
PSG	3.17 (.17)	279 (6.18)	.17 (.08)	2.52 (.15)	275 (6.71)	.52 (.23)
12h – Sleep	3.18 (.20)	278 (9.83)	.48 (.19)	2.81 (.23)	268 (6.16)	.24 (.10)
12h – Wake	2.70 (.23)	274 (7.42)	.74 (.27)	2.47 (.21)	270 (5.77)	.35 (.12)

3.4.2 Paired-Associate Learning

Analysis of paired-associate memory focused upon accuracy in the final recall attempt from the immediate test (if participants were required to repeat the test to meet the 60% recall criterion) and delayed cued-recall. Two participants were removed from the analysis due to computer failures during delayed recall (both from the 15-minute delay condition). To examine changes in performance across the delay, an analysis of covariance (ANCOVA) was performed on delayed recall with the variable Group (15-minute, PSG, 12-hour wake, 12-hour sleep) and covariate immediate cued recall (see Table 3.3). The ANCOVA revealed a significant effect of Group ($F(3, 93) = 10.02, p < .001, \eta^2 = 0.26$). Post-hoc Bonferroni-corrected pairwise comparisons showed that this effect was driven by a smaller proportion of correctly recalled items in the 12-hour wake group compared to all other conditions (15-minute delay $p = .001$, 12-hour sleep $p < .001$, PSG overnight group $p < .001$). Therefore, in this assessment of episodic declarative memory, we observe a sleep-associated benefit for delayed cued-recall.

Table 3.3 Accuracy in the immediate paired associated cued-recall test (data taken from the final recall attempt, mean proportion correct presented) and delayed cued-recall (covariate adjusted means are presented with the covariate immediate recall). Standard error of the mean is presented in brackets.

	Paired-Associate Recall	
	Immediate Test	Delayed Test
15-minute	.73 (.03)	.84 (.16)
PSG	.71 (.03)	.86 (.16)
12h – Sleep	.71 (.02)	.86 (.17)
12h – Wake	.78 (.03)	.75 (.16)

3.4.3 Category Learning

3.4.3.1 Categorisation - Session 1

The rate of category learning in Session 1 was assessed by comparing the number of correctly categorised trials in the two blocks of training. Performance is presented in Table 3.4 and was analysed using an ANOVA with the within-subjects variable Block (Block 1, Block 2) and between-subjects variable Group (15-minute, PSG, 12-hour wake, 12-hour sleep). A main effect of Block was observed ($F(1, 91) = 20.93, p < .001, \eta^2 = 0.19$), demonstrating improvements in categorisation across training. There were no Group differences ($F(3, 91), 0.44, p = .727$) and no interaction between the variables ($F(3, 91) = 0.96, p = .418$).

The first categorisation test provides a measure of Session 1 category learning. All groups performed above chance level, as determined by one-sample t-tests with chance level performance as 0.5 ($p < .001$ for all groups). Data is presented in Table 3.4 (Test1), a between-subjects ANOVA with the variable Group was non-significant ($F(3, 91) = 1.85, p = .143$). There was however some variation in condition means and so performance at this time-point was used as a covariate in subsequent analyses.

Table 3.4 Performance in the categorisation learning task and tests. Session 1 scores represent the mean proportion of correctly categorised trials. Session 2 scores show covariate adjusted means (as evaluated with the covariate Test 1). Standard error of the mean is presented in brackets.

Categorisation Task Performance							
	Session 1			Session 2			
	Learning		Test 1	Test 2	Learning		Test 3
	<i>Block 1</i>	<i>Block 2</i>			<i>Block 1</i>	<i>Block 2</i>	
15-minute	.66 (.02)	.70 (.02)	.71 (.02)	.73 (.01)	.73 (.02)	.77 (.02)	.74 (.02)
PSG	.64 (.02)	.69 (.02)	.68 (.03)	.74 (.02)	.76 (.02)	.77 (.02)	.77 (.02)
12h – Sleep	.65 (.02)	.72 (.02)	.76 (.02)	.71 (.02)	.74 (.02)	.80 (.02)	.77 (.02)
12h – Wake	.66 (.02)	.69 (.02)	.75 (.02)	.71 (.02)	.73 (.02)	.73 (.02)	.69 (.02)

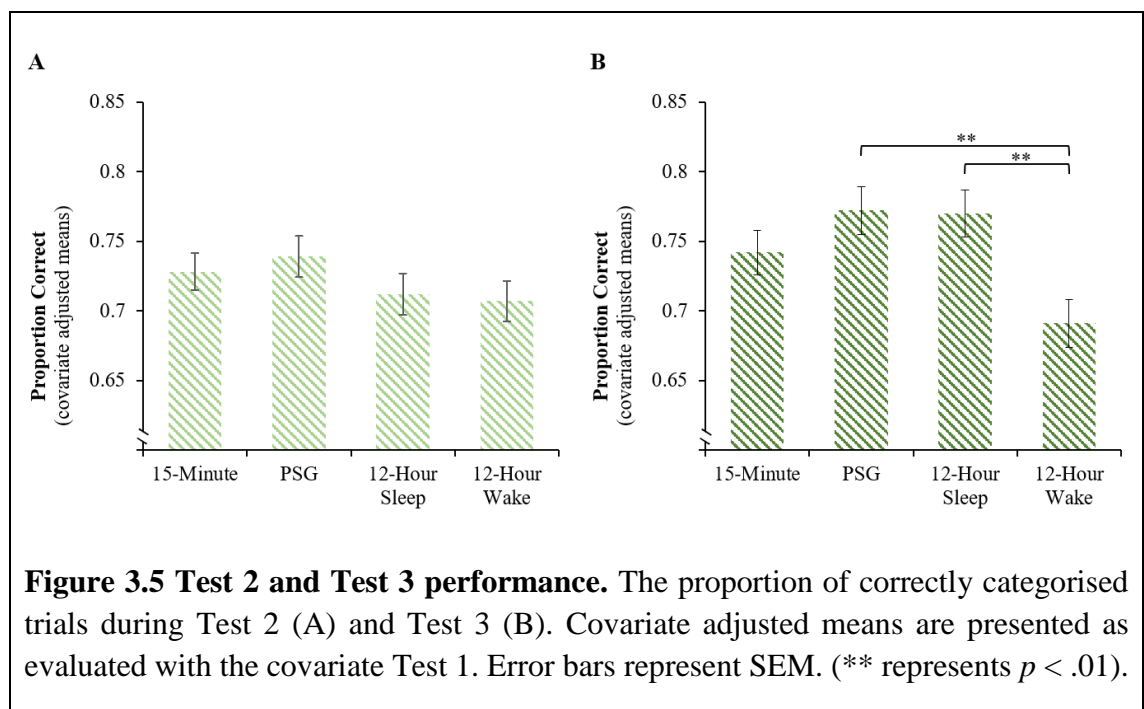
3.4.3.2 Categorisation – Session 2

Category knowledge was re-assessed with a test at the beginning of Session 2 to measure the retention of category knowledge across the delay. Again, all groups performed above chance level (0.5) when tested with one-sample t-tests ($p < .001$ for all groups). Performance in this test (see Figure 3.5A) was assessed using an ANCOVA with the variable Group (15-min, PSG, 12-hour wake, 12-hour sleep) and covariate Test 1. A non-significant effect of Group suggests that all groups were performing at a similar level ($F(3, 90) = 1.00, p = .397$). There was no evidence for immediate consolidation effects on the retention and retrieval of categorical knowledge acquired in Session 1; this is in contrast to the declarative paired associate task where we observed a sleep-associated benefit.

Participants then went on to complete two further blocks of category training; performance was assessed by comparing the number of correctly categorised trials across

each block (see Table 3.4). An ANCOVA with the within-subject variable Block (Block 1, Block 2), between-subjects variable Group (15-min, PSG, 12-hour wake, 12-hour sleep) and covariate Test 1 revealed a main effect of Block, suggesting that participants were able to use the extra learning in session 2 to boost their category knowledge ($F(1, 90) = 5.53, p = .021, \eta^2 = 0.06$). A main effect of Group was not observed ($F(3, 90) = 1.88, p = .138$) and there was no interaction with the factor Block ($F(3, 90) = 2.61, p = .056, \eta^2 = 0.08$).

The third and final categorisation test assessed category knowledge following both the consolidation delay and Session 2 training. Performance is shown in Figure 3.5B. An ANCOVA with the factors Group (15-min, PSG, 12-hour wake, 12-hour sleep) and covariate Test 1 revealed a main effect of Group; $F(3, 89) = 4.89, p = .003, \eta^2 = 0.14$. Bonferroni-corrected pairwise comparisons suggest that this main effect was driven by superior performance in the 12-hour sleep ($p = .009$) and PSG ($p = .008$) groups in comparison to the 12-hour wake condition. Participants who had sleep-filled consolidation delays, followed by further category training, showed higher rates of categorisation compared to participants who stayed awake during the delay.



3.4.3.3 Category Learning – Follow-up Tasks

ANCOVAs with the variable Group (15-min, PSG, 12-hour wake, 12-hour sleep) and covariate Test 1 were performed separately for each follow-up task. Accuracy in the 2AFC and location task was calculated as the proportion of correct responses. Accuracy in the recall task was calculated as an error score, i.e. the difference between the participants response and the target response (the point of best fit based on the category distribution); a small error score is indicative of accurate performance in this task. All task scores are presented in Table 3.5; in the 2AFC and Location Task all groups performed above chance level (chance = 0.5, p 's < .05). Group differences were not observed in the 2AFC task ($F(3, 89) = 1.75, p = .163$), the recall task ($F(3, 89) = 2.25, p = .089$) or the location task ($F(3, 89) = 0.35, p = .788$).

In Session 2 of this study participants completed multiple tests to assess the role of consolidation on memory. Across these tests we find a significant effect of group in paired associate recall ($p < .001$) and in the third categorisation task ($p = .003$). Given that we take multiple measures of performance across Session 2 (a total of 7 different measures) a more careful correction for multiple comparisons, including all post-consolidation tests, would be a Bonferroni corrected alpha level of $p = .007$ ($0.05/7$). The significant effects of Group observed in this study survive this more conservative correction for multiple comparisons.

Table 3.5 Accuracy scores in the category follow-up tasks. Covariate adjusted means are presented (as evaluated with the covariate Test 1 accuracy). Standard error of the mean is presented in brackets.

	Categorisation Follow-Up Tasks		
	2AFC (proportion correct)	Recall (error score)	Location Task (proportion correct)
15-minute	.62 (.02)	39.17 (2.66)	.57 (.03)
PSG	.61 (.02)	37.95 (2.86)	.57 (.03)
12h – Sleep	.62 (.02)	33.90 (2.92)	.56 (.03)
12h – Wake	.56 (.02)	43.70 (2.84)	.55 (.03)

3.4.4 Sleep Stage Analysis

One participant was excluded from sleep analyses due to PSG equipment failure ($N = 22$). PSG recordings were scored in accordance with the criteria of the American Academy of Sleep Medicine (Iber et al. 2007). Sleep data was partitioned according to the proportion of total sleep time spent in stage I, stage II, slow-wave sleep (SWS) and rapid-eye-movement (REM) sleep. Sleep stage data is presented in Table 3.6. To establish whether the sleep related behavioural effects were driven by specific architectures of sleep, improvement scores were calculated between (i) delayed and immediate paired-associate recall, (ii) categorisation accuracy in Test 2 and Test 1 and (iii) categorisation accuracy in Test 3 and Test 1. Bivariate correlations were then performed between these behavioural measures and the proportion of time spent in (i) non-rapid-eye-movement (NREM) sleep (combined time in stage I, stage II and SWS), (ii) stage II sleep and (iii) and SWS. Correlations for each behavioural measure were tested against a Bonferroni-corrected alpha level of $p \leq .006$.

A positive correlation was observed between the proportion of time spent in NREM sleep and paired-associate learning ($r = .514$, $p = .014$) however this did not survive the Bonferroni corrected alpha level. Correlations with the proportion of time in stage II sleep ($r = .317$, $p = .150$) and SWS ($r = .038$, $p = .868$) were non-significant. No correlations were observed between improvement scores in the categorisation task and each of the stages of sleep (all $p > .5$).

Table 3.6 Percentage of time spent in each sleep stage. (NREM – non-rapid eye movement sleep, SWS – slow-wave sleep, REM – rapid eye movement sleep, TST – total sleep time). Standard error of the mean is presented in brackets.

Sleep Stage Data					
NREM	Stage 1	Stage 2	SWS	REM	TST (min)
80.28	8.45	43.85	27.98	19.72	441.38
(0.74)	(0.66)	(1.32)	(1.43)	(0.74)	(11.10)

3.4.5 Model-based Analyses

General Recognition Theory (GRT)-based analysis determines which of a predefined set of decision–boundary models best describes the classification adopted by each participant (Ashby & Gott, 1988). This analysis allows us to assess whether participants were truly adopting an information-integration decision boundary to separate Category A from Category B exemplars. Four models were considered in this analysis: one-dimensional, conjunction, general linear classifier and random.

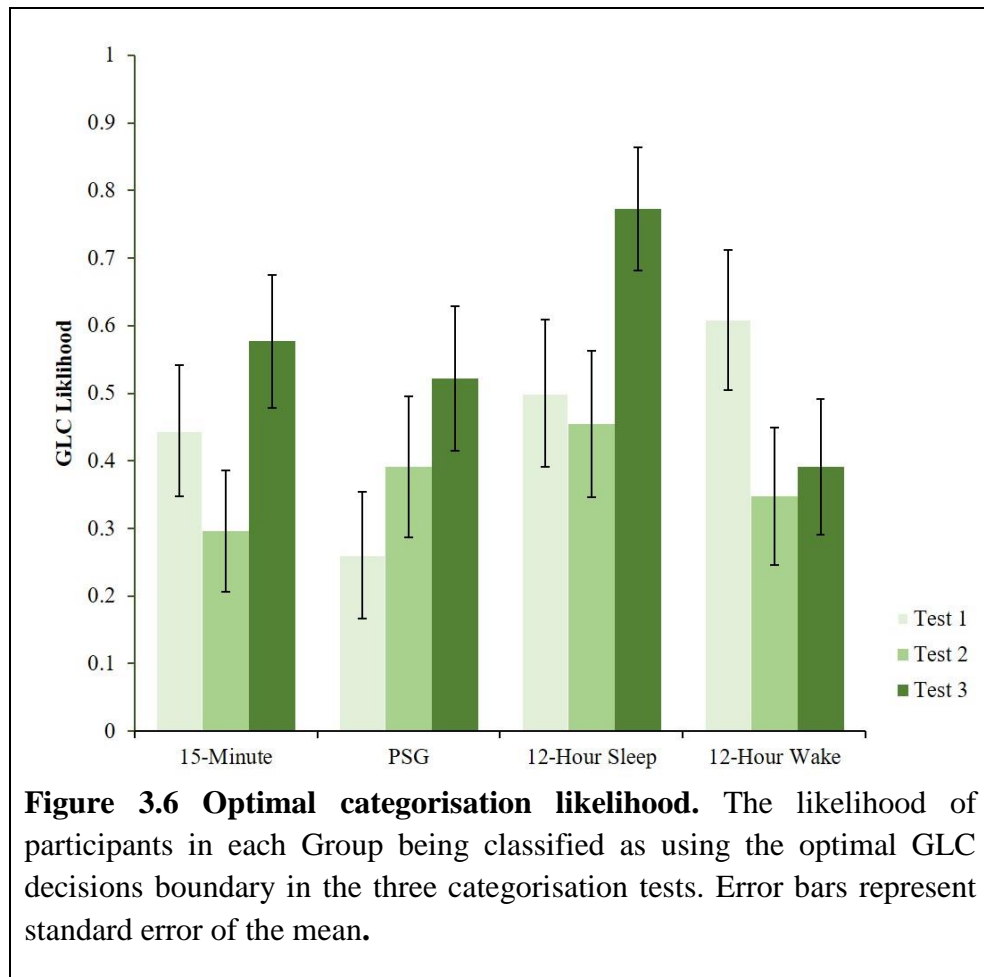
The *one-dimensional* models assume that participants use a single dimension in order to classify stimuli by comparing each stimulus with a determined criterion value. An example using the tone frequency dimension in the current study would be “Respond Category A for high tones and Category B for low tones”. These models have two parameters: the criterion value and the variance of internal noise. The *conjunction* model suggests that participants hold a criterion value along both dimensions and combine the judgements to determine category membership. An example of a conjunction model would be “If the tone frequency is high and the pixel density is low assign Category A, otherwise assign Category B”. This model has three parameters: the two criterion values and internal noise. The *general linear classifier* (GLC) model assumes that a straight diagonal decision boundary can describe classification. The model can vary in gradient and intercept but suggests that participants are integrating across both dimensions to determine category membership. The GLC model has three parameters: the intercept, gradient and noise. The *random* model assumes that participants are responding randomly and this model has no parameters.

For each participant, and in each of the three categorisation tests, the best fit of each of these models was calculated and the best fitting model was selected using Akaike’s information criterion (Akaike, 1974). These analyses were performed using the *grt* package in R environment (Matsuki, 2017) and are reported in Table 3.7. A mixed-effects model was fitted with the likelihood of a GLC classification as the dependent measure. The model included Group (15-minute, PSG, 12-hour sleep and 12-hour wake), Test (Test 1, Test 2 and Test 3) and their interactions as fixed effects. Both fixed effects were coded with Helmert contrasts, with Test 1 and 15-minute delay conditions acting as the reference levels. This meant that for Test a first contrast

compared Test 1 with Tests 2 and 3, and a second contrast compared Test 2 with Test 3. For Group, a first test compared the three long delay groups (12-hour wake, 12-hour sleep and PSG) with the 15-minute delay group, a second contrast compared the PSG and 12-hour Sleep groups to the 12-hour Wake group, and a third contrast compared the PSG and 12-hour Sleep conditions. Random effects included by-subject intercepts only, which was the maximal random effect structure justified by the data (Baayen, Davidson & Bates, 2008). We used the lme4 package in R with the logit link function (Bates et al., 2015; Jaeger, 2008) to conduct the analysis. There was a significant interaction between the second Group contrast (comparing the PSG and 12-hour Sleep groups to the 12-hour Wake group) and first Test contrast (comparing Test 1 with Tests 2 and 3), $\beta = -0.24$, standard error = 0.09, $z = -2.83$, $p = .005$. GLC classification in the PSG and 12-hour sleep groups tended to increase between Test 1 and the two subsequent Tests, while there was a decrease in GLC classification in the 12-hour Wake Group (see Figure 3.6). There was also a significant effect for the second Test contrast (comparing Test 2 with Test 3), with all groups showing an increase in GLC classification across these two testing points ($\beta = 0.53$, standard error = 0.18, $z = 2.95$, $p = .003$). All other contrasts and interactions were non-significant (p 's > .062). Although modelling categorisation data is typical in this area of research, the modelling results should be interpreted with caution given the restricted set of models tested and the small number of trials used for each test in the current study (Donkin et al., 2014).

Table 3.7 Proportion of participants best described by each model according to the model-based analyses for each categorisation test. (1D = one-dimensional, GLC = general linear classifier, CJ = conjunction, RND = random, T1 = Test 1, T2 = Test 2, T3 = Test 3).

	Categorisation Strategies											
	1D			GLC			CJ			RND		
	T1	T2	T3	T1	T2	T3	T1	T2	T3	T1	T2	T3
15-minute	48	52	31	44	30	58	04	18	08	04	00	04
PSG	48	39	22	26	39	52	22	22	22	04	00	04
12-hour Sleep	32	41	14	50	45	77	14	09	09	05	05	00
12-hour Wake	39	39	35	61	35	39	00	26	26	00	00	00



3.5 Discussion

This study investigated the role of consolidation in both a declarative paired-associate memory task, and on the emergence of cross-modal conceptual representations using an information-integration categorisation paradigm. In line with previous literature, we observed a clear sleep-associated consolidation benefit for paired-associate memory, with participants showing better retention following a consolidation delay that contained sleep compared to wakefulness. This result is consistent with the view that processes during sleep act to promote the consolidation of declarative memory (Diekelmann et al., 2009; Rasch & Born, 2013). Our assessments of category knowledge provide good evidence for sensory-integration, with participants successfully acquiring the cross-modal (auditory – visual) category structure. As real-world conceptual knowledge comprises information across multiple modality dimensions (Patterson et al., 2007) this task, albeit in a very simplistic form, resonates with natural concept learning. However, in contrast

to paired-associate memory, we did not observe any immediate post-delay wake- or sleep-associated changes in categorisation accuracy. Instead, we found a facilitative effect of sleep-associated consolidation on subsequent learning, with participants showing greater category knowledge and shifts towards more optimal decision strategies after training in session two, if they had a delay filled with sleep.

These results suggest that the behavioural benefits of sleep-associated consolidation are dependent upon the type of memory being assessed. Episodic memory, as assessed by the paired-associate task, produces immediate sleep benefits in memory recall, whereas the advantages for conceptual memory emerge only after an opportunity for further learning. This result draws attention to the relationship between sleep-associated consolidation and the effectiveness of post-consolidation learning; an important finding when considering the development of conceptual memory which develops across temporally distinct episodes interleaved with consolidation opportunities.

These results are in agreement with theories of consolidation which suggest that sleep facilitates systems-level memory reorganisation, allowing new and consistent information to be assimilated into long-term memory networks at a quicker rate (McClelland et al., 1995; McClelland, 2013; Kumaran et al., 2016; Tse et al., 2007; van Kesteren et al., 2013). Sleep-dependent training benefits in this study may therefore be the consequence of subtle sleep-dependent mechanisms which facilitated the storage of category knowledge acquired in session one; thus providing the architecture required for enhanced assimilation of new and consistent information the following day. This interpretation is also supported by modelling the decision strategies of participants; those who had the opportunity to sleep between sessions showed a shift to the optimal linear decision strategy following the delay and session two training. Memory reorganisation during sleep, which may promote the development of category structure, along with further task training, may have allowed participants to align their response strategies with the optimal linear decision boundary in this task. This same shift in response strategy was not observed following 12 hours of wakefulness, supporting the suggestion of a sleep-associated mechanism in the consolidation of category knowledge.

Significant differences were observed between the 12-hour wake group and both of the groups that contained sleep in the final test of category knowledge. However, it should be noted that the 15-minute delay group showed similar numerical performance

to the sleep group (and not the wake group) in the categorization task. Unfortunately, direct correlations between features of sleep (as studied using PSG) and behavioural measures of category knowledge were not observed in this study. It is therefore difficult to determine whether the ‘sleep-associated’ benefit is specific to sleep, or whether other factors (e.g. the level of interference between sessions) may also play a role in the behavioural effects observed.

These results do however highlight the importance of assessing consolidation across multiple learning episodes when studying the development of categorical memory representations. An interesting question that remains is whether the benefits of sleep on second session learning are specific to the trained categorisation structure, or whether these benefits extend to perceptually and/or structurally similar categorisation tasks. Understanding the flexibility of consolidated categorical representations will be important for determining the role of consolidation in broader conceptual memory.

We observed differences in the sleep-associated benefit observed across the two tasks in this study. One possible reason for this is due to the nature of encoding. Paired-associate learning requires participants to make associations between two previously unrelated items, creating very strong episodic memory representations which place high demands on the medial temporal lobe system in the brain, in particular the hippocampus (Cameron et al., 2001). The hippocampus plays a pivotal role in theories of memory consolidation, with the suggestion that it is responsible for both the rapid encoding of information during wake and then the redistribution of encoded material to the neocortex during sleep (McClelland et al., 1995; Diekelmann & Born, 2010). In contrast to paired-associate learning, the categorisation task considerably reduces the value of episodic encoding by using a continuous category structure without a definitive category boundary (i.e. there was a degree of category overlap). This results in each trial being perceptually very similar, without any discriminative or arbitrary features to allow trial-by-trial individuation.

The immediate sleep-dependent benefit for paired-associates may therefore reflect a component of the consolidation mechanism which is strongly linked to episodic memory. We were not able to compare episodic and conceptual memory within the same paradigm in the current study, however Graveline & Wamsley (2017) were able to do this using a classification task in which participants were trained to discriminate between dot

patterns that were derived from category prototypes. Importantly, participants were trained on individual category exemplars, that although they were perceptually very similar, were repeatedly presented during training, allowing participants to develop strong representations for individual items. In line with our paired-associate data, they show sleep-dependent benefits in memory for these trained items. However, they also show sleep benefits for the categorisation of novel and untrained category patterns, suggesting that sleep also benefitted the extraction of shared category knowledge. This highlights a complex interplay between episodic and conceptual memory, where sleep may benefit concept-based representations when strong individual episodic representations are held in memory.

The sleep-dependent benefit in post-consolidation learning in this study is in contrast to the wake-dependent consolidation benefit observed in the category learning study by Hennes et al. (2014). In a similar categorisation task, they found that wake, rather than sleep, facilitated the development of category knowledge. Two factors may account for these contradictory results; the first is the selectivity of sleep-dependent consolidation (Rasch & Born, 2013). Sleep-dependent consolidation effects are more robust under explicit learning conditions and are improved by motivational factors such as relevance for future goals (Robertson et al., 2004; Fischer et al., 2006; Walker et al., 2003; Cohen et al., 2005; Diekelmann et al., 2008; Wilhelm et al., 2011). In the current study, participants were explicitly aware of the relevant information needed for determining category membership (i.e. the visual and auditory dimensions) despite the nature of the category structure itself being initially unknown. In contrast, the underlying category structure was truly implicit in Hennes et al., (2014). They manipulated the traditional categorisation paradigm such that the information-integration category structure was hidden within a pre-stimulus event, which if utilised would increase reaction time, but was not necessary for accurate categorisation. Explicit appreciation for the relevant integrative dimensions may therefore make the stimulus in this experiment more susceptible to sleep-dependent consolidation mechanisms.

A second factor that may explain the differences observed between these studies relates to the level of initial learning. Stickgold (2009) proposed that sleep mainly benefits memories encoded at intermediate memory strengths, such that there is an inverted-U shaped curve to the sleep benefit. As a result, both very weak and very strong memories

would fail to benefit from sleep-based consolidation mechanisms. In the current study participants were able to categorise stimuli above chance level after training in session one, but did not reach ceiling levels. According to the theory proposed by Stickgold (2009), learning was therefore within the optimal range to benefit from sleep-dependent consolidation. In contrast, Hennessey et al. (2014) found no evidence of implicit category learning before the consolidation delay; participants may have been insensitive to sleep-dependent consolidation mechanisms in their study.

Given that the results of the current study contrast with those from Hennessey et al. (2014) it is important to note that we did provide a direct replication of our sleep effect by using two sleep group comparisons. This study was initially run as a comparison between two groups with a 12-hour delay containing wake or sleep. Following data collection and preliminary analyses, the 15-minute and PSG monitored group were added to i) provide a short delay comparison and ii) to replicate the sleep effect observed in the initial 12-hour sleep group with concurrent PSG recordings. We successfully replicated the initial sleep-associated benefit but present all groups within a single comparison in the current paper to streamline the analysis. Replication of the sleep benefit observed in this study, as well as further investigation more generally within the domain of consolidation and categorisation is certainly required to fully understand the development of category knowledge across time. The design we used in this experiment, which compares nocturnal sleep with daytime wakefulness, like many others in the consolidation literature, does not control for circadian effects on memory that may influence performance (Rasch & Born, 2013). Although ratings of sleepiness and vigilance suggest that participants' general alertness levels were comparable in the current study, a replication of the sleep-based effects using a nap design would remove potential 'circadian' and 'time-of-day' confounds.

This study compared the role of consolidation in a declarative paired-associate task, and on the emergence of cross-modal categorical memory representations. We provide good evidence for a role of sleep-dependent consolidation in paired-associate learning, with participants showing post-sleep benefits in memory recall that correlate with signatures of sleep. This finding is in line with a growing body of research suggesting that processes during sleep play an active role in the consolidation of declarative memory (Rasch & Born, 2013). Using a perceptual categorisation task, we were able to

demonstrate cross-modal category learning, a key feature of real-world conceptual memory for which information is drawn from multiple sensory dimensions. We also observe a sleep-dependent consolidation benefit in category learning; however, unlike paired-associate memory, this benefit emerges only when sleep-based consolidation is paired with further category training. This result highlights an important interaction between those mechanisms responsible for consolidation and those responsible for learning. Establishing the exact nature of this relationship will be important for (i) understanding how we develop, update and maintain conceptual memory representations and (ii) understanding why we observe different behavioural consequences of sleep-dependent consolidation across episodic declarative and conceptual memory representations.

CHAPTER 4

A Role for Sleep in Associative Memory but Not Rule Extraction

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This Chapter is based on a manuscript that be being prepared for
submission for peer-review.

4.1 Abstract

There is strong evidence for a role of sleep in the consolidation of individual associative memory representations; however, sleep's role in the extraction of associative regularities occurring across memories remains to be determined. The current study assessed participants' ability to extract complex regularities and to generalise this knowledge following a 12-hour consolidation delay containing wakefulness or sleep. A task in which participants were required to learn face-location associations was used and to facilitate generalisation, the stimuli were manipulated such that combinations of crucial facial features predicted screen location. This provided a set of 'rules' that could be

extracted across multiple memory representations. A contextual background image was also presented with each associative pairing; this provided a further cue for learning and was predictive for some face-location associations. Sleep-associated consolidation benefits were observed; however, these were specific for trained associations and not seen in measurements of generalisation. The results highlight a possible dissociation between the benefits of sleep-associated consolidation on individual memory representations and memory generalisation that requires regularity extraction. The results also showed that the predictive context cue supported learning and appeared to protect memory against wake-based forgetting.

4.2 Introduction

Conceptual knowledge is fundamental for human cognition, it refers to a portion of long-term memory that stores general knowledge for facts, objects, people and relations that are acquired across the lifetime (Kiefer & Pulvermüller, 2012; Tulving, 1972). Though there may be multiple routes to generating conceptual representations, one may involve the extraction of regularities from across multiple associative memories through a process of systems level consolidation (Battaglia & Pennartz, 2011; McClelland, McNaughton & O'Reilly, 1995; Winocur & Moscovitch, 2011). Such processes may allow knowledge acquired across multiple episodes to be integrated into a single and coherent conceptual representation. These representations provide a crucial advantage for successful interaction in the world, allowing flexible access to stored information in order to make generalisations and predictions in novel situations. Understanding their development is therefore important to appreciate real-world memory processing.

Systems level consolidation involves the gradual reorganisation of memory representations in the brain, it is a prolonged and dynamic process that occurs over days, weeks, months and years (Frankland & Bontempi, 2005). The 'Standard Model' of consolidation proposes that information is initially stored within both neocortical and hippocampal memory networks (Squire & Alvarez, 1995; Squire et al., 1992; Alvarez & Squire, 1994). The neocortical representation is highly distributed, with different memory elements stored within modality-specific (e.g. vision, sound etc.) regions of cortex. This physical separation creates a 'binding' problem for memory retrieval, and therefore the

hippocampal system plays a critical role by binding the physically separated neocortical elements into a single memory representation. Through processes of offline consolidation, the neocortical elements of a memory develop greater coherence by strengthening existing, and creating new, cortical-cortical connections. Over time, this allows new memories to become independent of the hippocampus and fully integrated with pre-existing knowledge. This consolidation process is hypothesized to occur predominantly during sleep and is thought to be driven by coordinated memory reactivation or replay across the hippocampal and neocortical networks (Alvarez & Squire, 1994; Frankland & Bontempi, 2005; Squire & Alvarez, 1995; Squire et al., 1992).

The Complementary Learning Systems (CLS) theory extends the standard model by providing a computational basis of consolidation and suggests that the hippocampus and neocortex may play distinct roles in representing memories (McClelland et al., 1995). These separate roles solve a trade-off between remembering specific experiences (e.g. where you left your keys), which benefit from separate representations for each event, and the extraction of regularities across experiences (e.g. where you would typically expect to find your keys), which benefit from overlapping memory representations. The CLS proposes that the hippocampus quickly stores memory traces for individual experiences by using a high learning rate and sparse, non-overlapping (pattern separated) representations. The neocortex, in contrast, has a slow learning rate and supports the development of overlapping representations gradually over time. These neocortical overlapping representations may therefore support the storage of regularities across events, allowing the neocortex to capture similarity structures that are not present within individual memory representations (McClelland et al., 1995; O'Reilly et al., 2014).

The CLS does not make specific predictions related to sleep-associated consolidation; however it does suggest that consolidation is mediated initially by memory reinstatement within the hippocampal system (McClelland et al., 1995). This suggestion is now consistent with a growing body of literature that suggests consolidation during sleep is driven by hippocampally mediated memory reactivation (Kumaran, Hassabis & McClelland, 2016; O'Neil et al., 2010; Rudoy et al., 2009; Wilson & McNaughton, 1994). At the mechanistic level, this reactivation is considered to occur through a network of communication between the hippocampus and neocortex which facilitates long-term memory integration and storage (Rasch & Born, 2013). Given the memory system

distinction proposed by the CLS and the sleep-associated mechanism of hippocampal replay, Mirkovic & Gaskell (2016) proposed that representations that are strongly reliant on the hippocampal system, i.e. the specific details of events, may show greater benefits from offline consolidation during sleep. In contrast, consolidation processes during sleep may play little or no role in the development of shared memory features, which may to some extent be learned by the neocortical system without hippocampal involvement via the gradual extraction of regularities.

Mirkovic & Gaskell (2016) tested this hypothesis using an artificial language task that was designed to incorporate both arbitrary and systematic stimuli mappings with the same stimulus set. Participants were exposed to a new language using a word-picture matching task in which the pictures represented individual known characters (e.g. ‘queen’, ‘cowboy). In this task, arbitrary mappings refer to each word-picture association, while a systematic grammar could be extracted across the novel words as determiner and suffix referents reflected the natural gender of the pictured characters (e.g. *tibscoiffesh* + queen, *kedjorool* + cowboy). The arbitrary aspects were therefore expected to place greater demands on the hippocampal system, requiring pattern separation for storing the unique memory mappings, while the overlapping systematic mappings may be extracted and stored neocortically, and so be less reliant on the hippocampus. Following training, memory was assessed after a two-hour delay which contained sleep or wakefulness. Mirkovic & Gaskell (2016) reported a sleep-associated benefit in memory recall for the arbitrary aspects of the new language (word-picture mappings) but found no wake or sleep differences in tests targeting the systematic aspects of the stimuli (knowledge of grammatical regularities).

The pattern of data from Mirkovic & Gaskell (2016) is consistent with the predictions of the CLS and a sleep-associated benefit for memory representations that place high storage demands on the hippocampus (Kumaran, Hassabis & McClelland, 2016; McClelland et al., 1995; Mirkovic & Gaskell, 2016). Their results also suggest that systematic elements across memories, which may be processed using overlapping representations in the neocortex, may be less sensitive to mechanisms of sleep-associated consolidation. Importantly, Mirkovic & Gaskell (2016) do not argue that sleep cannot facilitate the storage of shared memory representations in the neocortex, but that there may be a prioritisation process during sleep. This prioritisation is hypothesised to be for

the most hippocampally reliant components of memory that are not supported by neocortical representations (Mirkovic & Gaskell, 2016; Stickgold & Walker, 2013).

Indeed, beyond the language domain, there is support for a role of offline consolidation during sleep in the development of knowledge regarding underlying regularities and structure (Durrant, Cairney & Lewis, 2013, 2016; Durrant et al., 2015; 2011; Ellenbogen et al., 2007; Lau, Tucker & Fishbein, 2010). For instance, Durrant et al. (2011) showed a sleep-associated consolidation benefit when participants were required to identify novel sequences that followed a previously trained probabilistic structure. These previous studies however typically used paradigms from which item-based memory could not be clearly dissociated from knowledge of regularity structure. Consequently, it is difficult to determine whether sleep-associated consolidation differentially influenced item- and concept-based knowledge in these tasks. In an attempt to address this, the current study used an associative spatial memory task that allowed regularity knowledge to be extracted from individual associative representations, allowing the impact of consolidation on these two types of memory to be separately assessed.

Associative memory requires the ability to learn and remember arbitrary relationships between initially unrelated items. It is widely accepted that these representations draw strongly upon hippocampal learning systems and they show strong benefits of sleep-associated consolidation (Diekelmann, Wilhelm & Born, 2009; Plihal & Born, 1997; Talamini et al., 2008; Tucker et al., 2006). The paradigm used in this study is adapted from a task developed by Sweegers et al. (2014) in which participants were required to learn face-location associations, then later retrieve the locations based on face cues. Importantly, this task could assess the development of concept-based representations by manipulating the type of face that belonged to each location. In Sweegers et al. (2014), half of the associations followed complex associative regularities regarding the combination of facial features and locations, while the other half of the faces were randomly assigned to the remaining locations. This created a set of ‘rule-locations’: locations that have a specific type of face associated with them, and a set of ‘no-rule locations’: locations that can be paired with any type of face. In a series of studies, Sweegers et al. showed that participants were able to extract the complex associative

regularities along with enhanced learning and retention of the rule compared to no-rule associations (Sweegers et al., 2015; 2014; Sweegers & Talamini, 2014).

Importantly, Sweegers et al. (2014) also demonstrate that participants are able to successfully apply the rules to novel faces that have not been trained but can be located based on the extracted regularities (Sweegers & Talamini, 2014). They therefore provide evidence of memory generalisation, which suggests that the extraction of regularities across multiple associative memories can lead to shared concept-based memory representations. When they assessed memory across delays containing sleep and wakefulness in this task they found no evidence for a sleep-associated benefit in generalisation performance (Sweegers et al., 2015; Sweegers & Talamini, 2014). However, they also failed to observe a sleep benefit for the trained associations, which is somewhat intriguing given that associative memory tasks are typically sensitive to sleep-associated consolidation (Diekelmann, Wilhelm & Born, 2009; Plihal & Born, 1997). A possible reason for this is their very high, near ceiling level, accuracy rates following encoding. There is currently debate in the literature as to whether sleep has differential impacts on memory as a function of memory strength and it is suggested that the benefit of sleep may be weak for memories trained to a high degree of accuracy (Cairney et al., 2016; Creery et al., 2015; Stickgold, 2009).

Given that the face-location associative memory paradigm allows item-based memory to be clearly dissociated from knowledge of underlying regularity structure, it provides a clear basis from which to determine whether sleep-associated consolidation has differential effects on these two types of memory. In the current study, the original face-location task was modified to include only ‘rule-locations’ in an attempt to maximise regularity extraction. Similarly, overall encoding levels were reduced to avoid ceiling effects which may mask sleep-associated benefits in performance. By testing performance across delays manipulated to contain sleep or wakefulness, the current study aimed to assess the impact of sleep- and wake-based consolidation on trained item knowledge and concept-based knowledge measured by generalisation. In line with the CLS and predictions from Mirkovic & Gaskell (2016) we hypothesised to find greater sleep-associated consolidation benefits for the individual item-level representations, when compared to memory generalisation.

A second element of real-world concept learning addressed in the current study was the idea that learning does not happen in isolation but occurs in complex environments. Furthermore, co-occurring environmental information may be predictive of concept-based knowledge, even if it is not directly tied to main content of the concept. For instance, a child may learn about different types of birds while playing in the garden. Contextual information relating to the garden does not contribute to the distinguishing features of birds (animals with feathers and two legs etc.) however it may become predictive of the 'bird' category and facilitate later identification. In this way, co-occurring information can be considered as part of the broader memory schema, and may help to organise knowledge by contributing to the framework accessed to determining meaning (Rumelhart, 1980). Schemas have been shown to be highly beneficial for memory processing and understanding, for example, memory for semantically unusual sentences can be substantially increased by providing a mental framework in which to integrate the sentences with (Bransford & Johnson, 1972; Tse et al., 2007).

Moreover, following offline consolidation during sleep, new information that is consistent with an existing schema shows enhanced assimilation into long-term memory networks (Durrant et al., 2015; Gilboa & Marlatte, 2017; McClelland, 2013; Tse et al., 2007). For example in rats, it has been shown that training various flavour-place associations requires multiple sessions and time, however after this initial acquisition phase, new associations can be learnt in just a single trial (Tse et al., 2007). Similarly, in humans, schema knowledge regarding the types of fabric generally used to make particular products was shown to aid memory for congruent product-fabric pairs (van Kesteren et al., 2010). In line with the idea of a schema-related benefit for memory processing, memory encoding that is accompanied by a wider predictive context in this study, may lead to the development of a broader memory network, or schema. Following sleep-associated consolidation, new learning of schema-congruent information may then show enhanced assimilation and integration into long-term memory. To test this prediction, the current study included a contextual image with each of the trained face-location pairings. These context images were manipulated to be predictive or non-predictive of screen location, i.e. some locations were strongly associated with one context type, while other locations were associated with different contexts. This manipulation allowed us to assess whether having predictive co-occurring information

during encoding, can lead to boosts in memory performance following offline consolidation.

To align the current study with the findings from Chapter 3 of this thesis, and to assess the impact of offline consolidation on schema integration, we incorporated a second round of post-consolidation training into the experimental paradigm. This allowed us to assess whether wake- and sleep-associated consolidation influenced the integration of new information into existing knowledge structures. Previous tasks that have assessed differences in associative and concept-based representations within a single experimental paradigm have not assessed memory representations further than an initial post-consolidation test (Mirkovic & Gaskell, 2016; Sweegers & Talamini, 2014). The current study therefore offers an important extension to the literature and contributes to our understanding of how sleep- and wake-based consolidation may impact upon these two types of memory representation across a longer time-scale.

To summarise, the current study investigated the impact of sleep and wake associated consolidation on trained item-based memory and the generalisation of concept-based regularities using an associative memory task. This allowed the influence of sleep-associated consolidation on these two memory types to be separately determined. This study also included a contextual image cue that was either predictive or non-predictive of screen location, allowing the impact of co-occurring predictive information on memory, and the interaction with sleep-associated consolidation, to be assessed. To our knowledge, these research questions have not been previously addressed within a single study.

4.3 Methods

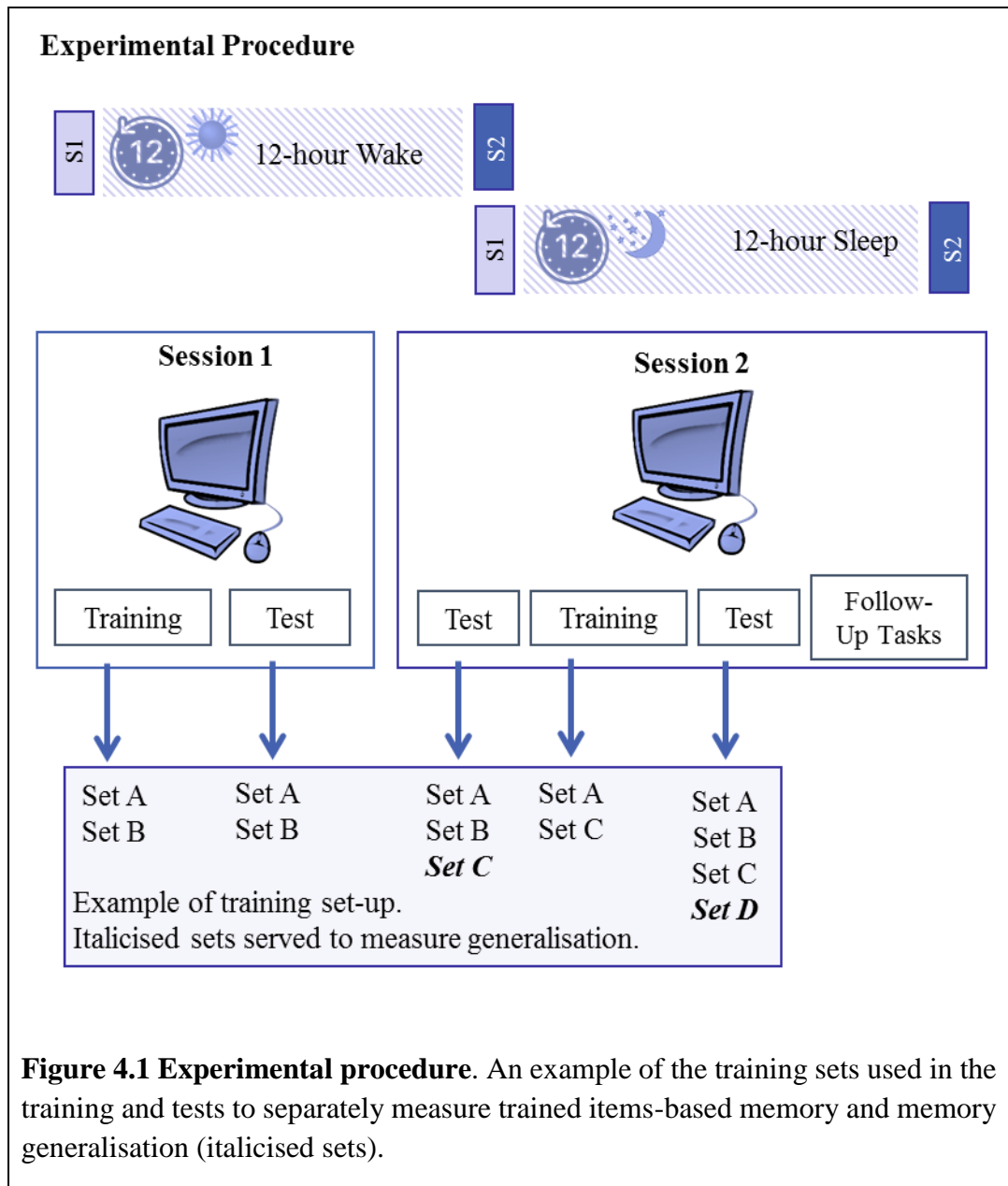
4.3.1 Participants

Participants were 87 undergraduate students recruited from the University of York in fulfilment of course credit or payment. 7 participants were excluded from the analysis either due to not completing both sessions of the study (3 participants) or showing very poor levels of initial learning (4 participants). This was determined by calculating an efficiency score (mean reaction time/mean accuracy) in Test 1 for each participant (mean score = 5.60, SD = 3.329); participants were excluded if their score was above 2.5 standard deviations from the mean (excluded participants; mean = 17.64, SD = 2.02).

Prior to completing the experiment, participants were randomly assigned to one of two conditions; a 12-hour wake group (N = 40, mean age: 20.83, S.D. \pm 3.47, 31 female) or a 12-hour sleep group (N = 40, mean age: 20.48, S.D. \pm 1.54, 27 female).

4.3.2 Procedure

The experiment consisted of two experimental sessions separated by a delay of 12-hours (see Figure 4.1) This delay contained either daytime wakefulness, in which participants continued with their usual daytime activities (but were told not to sleep or take naps) or an evening of sleep, in which participants returned home to sleep overnight between the two sessions. Participants were randomly allocated to the wake or sleep group and completed the sessions of the study at 8.30 am or 8.30pm. Both sessions of the study began with completion of the Stanford Sleepiness Scale (SSS, Hoddes et al., 1973) and a psychomotor vigilance task (PVT, Khitrov et al., 2014) in order to obtain a measure of sleepiness, alertness and vigilance. In Session 1, participants completed the face-location association training followed by a test of trained items (Session 1 ~ 50minutes). In Session 2, participants completed a second test for the trained association, a second round of training, and a final test. They then went on to complete two follow-up tasks to assess their memory for task stimuli (Session 2 ~ 90 minutes). Details of the tasks are described in the following sections.



4.3.3 Stimuli

4.3.3.1 Faces

Stimuli were taken from Sweegers & Talamini (2014) and consisted of one hundred and forty-four greyscale pictures of emotionally neutral faces (created using TM Software, IQ Biometrix, 2003). The faces contained a range of non-critical elements (e.g. gender, the presence of glasses, moles and dark/light hair colour) as well as three critical features that were used to generate face categories; these features were: age – young adult

or aged, face shape – slender or stout and headwear – with headwear (caps, hats or headbands) or without headwear (see Figure 4.2). To maintain perceptual distinctiveness in the stimuli the features were perceptually distinct across the faces (e.g. different headwear, wrinkle patterns, etc.). Six out of eight possible three-way combinations of critical features were selected for the experiment; creating six face categories that could be characterised by a unique combination of three features. However, for each face category just two (out of the three) critical features sufficed to distinguish that category; this 2-feature combination did not occur in any other category. Twenty-four faces were created for each of the six categories. Each face was allocated to one of four experimental sets (containing 6 faces from each category).

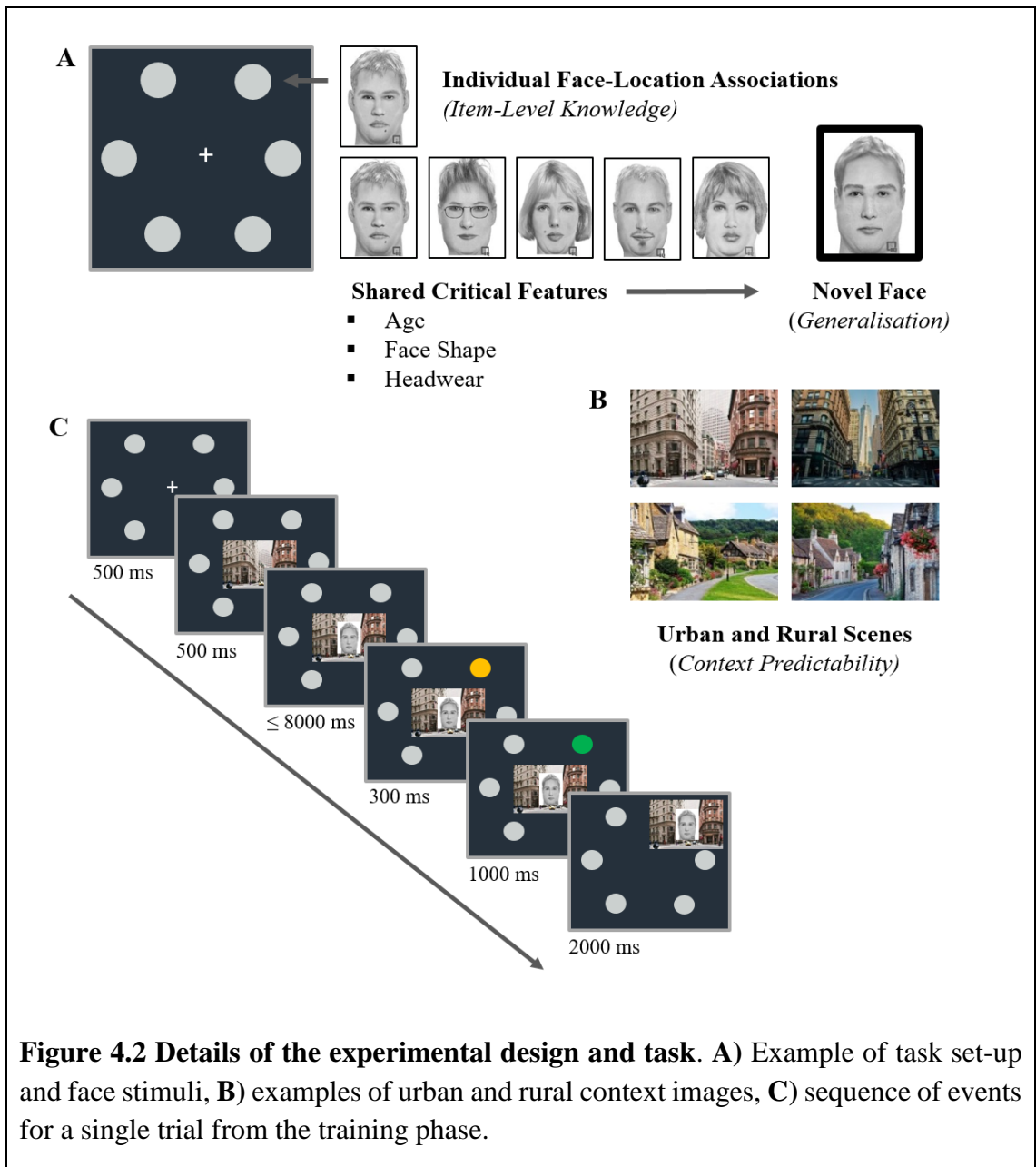
4.3.3.2 Context Images

Twenty images were selected from the internet to represent contextual scenes. These chosen images were of street scenes with buildings (see Figure 4.2). Half of the images were taken from a city location (10 images) to generate an ‘urban’ context set, and the other half were taken from a village location to generate a ‘rural’ context set. Twenty-seven participants (independent to the main study) classified each image as belonging to the intended context, confirming the urban/rural manipulation. Similarity ratings, between every image within each context type were collected using a 7-point scale (1- very different, 7 – very similar). All images were rated as being similar (urban images; (mean \pm standard deviation) 5.26 ± 0.12 , rural images; 5.22 ± 0.15) with equivalent levels of similarity between the two context types ($t(18) = 0.58, p = .568$).

4.3.3.3 Stimuli Set-Up

Each face was coupled to one of six screen locations in order to create face-location associations. The faces assigned to a single location all belonged to the same category (determined by the combination of critical facial features described above). Thus the associations to be learned adhered to regularities between location and facial features. Each face was also presented with a context image (either rural or urban). The type of image presented with each face was determined by whether the category that face belonged to was allocated to a predictive-high, predictive-low or non-predictive condition (2 locations were assigned to each type). The faces from each category were presented with one type of context (urban or rural) 83% of the time in the predictive-high condition,

67% of the time in the predictive-low condition and 50% of the time in the non-predictive condition. The type of context (urban or rural) was counterbalanced across the two locations assigned to each condition. Due to similar performance in the two predictive conditions, in the results we combine predictive-high and predictive-low into a single predictive condition.



4.3.4 Tasks

4.3.4.1 Face-Location Association Training

In Session 1, two sets of faces were selected to be trained (72 faces in total). In Session 2, one set of already trained items were selected, along with a non-trained set (72 faces in total). This resulted in participants learning a total of 108 face-location associations across the experiment (the selected sets were counterbalanced across participants and sessions). Participants were instructed to try to learn the individual face-location associations; to begin with they were told to guess, but to use the feedback provided with each trial to help make the correct associations. Participants were told that they could learn regularities to help them place the faces in the correct location, however they were not informed as to what elements of the stimuli contributed to this regularity information.

Each trial began with a fixation cross in the centre of the screen with the six screen locations depicted by grey circles, which were arranged hexagonally around the centre. For each trial, a context image (randomly selected from the assigned context set for that Trial) was presented in the centre of the screen for 500ms; a single face was then presented in front of this context image. The face covered only the central 20% of the context image ensuring that strong contextual information provided from buildings etc. remained clearly visible throughout the trial. Participants were instructed to use the mouse to select the screen location they believed that face to belong to. Participants were given up to 8000ms to make their responses with the selected location changing from grey to orange after being selected (300ms). If the participant made a correct response, this location changed to green (1000ms) and the face and context image moved to this location, remaining on the screen for a further 2000ms. If the participant made an incorrect response, the selected location changed to red (1000ms) and the correct location changed to green (1000ms), the face and context image then moved to the correct location and remained on the screen for 2000ms. A fixation cross presented in the centre of the screen separated each trial (1000ms) and short breaks were provided throughout. In each session, participants completed three blocks of training, with each face presented once in each block.

4.3.4.2 Face-Location Association Test

Participants completed a test phase to assess their memory for the trained associations; this was completed three times, immediately following learning in Session 1, following the consolidation delay in Session 2, and after the second session of training. In all three tests, all items that had been trained to that point in the experiment were tested. In the second and third test, a set of untrained items, that followed the same regularity structure were included to assess regularity generalisation (see Figure 4.1 for an example of the testing set-up).

The test followed the same procedures as learning; on each trial a context image (500ms) followed by a face was presented in the centre of the screen along with the six hexagonally arranged screen locations. Participants were instructed to use the mouse to select the location they believed that face to belong to (presented for up to 8000ms), and the selected location changed from grey to orange after being selected (300ms). Participants did not receive feedback during the test, and were instead asked to provide a confidence judgement for each response. They were presented with a 5-point scale (1 – low confidence, 5 – high confidence) and were asked to click using the mouse on the scale to rate each response, an unlimited amount of time was given to make this confidence judgement. A fixation cross in the centre of the screen separated each trial (1000ms) and short breaks were provided throughout.

4.3.4.3 Follow-up Tasks

After the final test in Session 2, participants were asked to complete two follow-up tasks that aimed to assess their memory for different aspects of the stimuli. In these tasks all faces from the experiment were presented (144 stimuli) and they were presented without a context image.

4.3.4.3.1 Features Task

This task aimed to assess memory for individual face and context pairings, as well as for individual facial features that were either critical to the category membership (presence/absence headwear) or non-critical (presence/absence glasses). In order to test memory for facial features, half of the faces from each category were presented with a

red box that covered the forehead and top of the head (to test memory for headwear) while the other half were presented with a red box that covered the eyes (to test memory for glasses). On each trial participants made two judgements; a two-alternative forced choice (2AFC) regarding whether they believed that face was paired with an urban or rural context image, followed by a 2AFC judgment regarding the presence of absence of the facial feature that was covered (headwear or glasses).

On each trial the face was presented in the centre of the screen. Participants made their responses using a key press which was aligned with the alternative responses presented on the screen. The context decision “Urban” was presented on the left and associated with a ‘Z’ key press, while “Rural” was presented in the right and associated with an ‘M’ key press. This set-up was also used for the feature decision with the ‘Z’ key aligned with the response “Glasses” and “Hats” and the ‘M’ key aligned with the response “No Glasses” and “No Hats”. Participants were instructed to be as accurate as possible in this task and were given an unlimited amount of time to make their responses. A fixation cross, presented in the centre of the screen separated each trial (100ms) and breaks were provided throughout.

4.3.4.3.2 Speeded Judgement Task

This was a speeded 2AFC task which asked participants to distinguish between correct and incorrect face-location associations. On each Trial a face was presented in one of the six screen locations, 60% of the faces were presented in the correct location and 40% of the faces in the incorrect location (each face was presented twice in the task with the allocation to the correct or incorrect location randomised). The faces were presented for a maximum of 3000ms and participants were instructed to respond as accurately and as quickly as possible. Participants made a match (correct face-location pair) or a mismatch (incorrect face-location pair) judgement and made their response using a key press which was aligned with the two alternative responses presented in the screen. “Match” was presented on the left and associated with a “Z” key press, while “Mismatch” was presented on the right and associated with an “M” key press. A fixation cross, presented in the centre of the screen separated each trial (1000ms) and breaks were provided throughout.

4.3.4.4 Psychomotor Vigilance Task (PVT)

The PVT is a sustained-attention, reaction-timed task that measures the speed with which participants respond to visual stimulus. The PVT task was obtained from <http://bhsai.org/downloads/pc-pvt/> (Khitrov et al., 2014). During the task, participants were presented with a blank black screen; at random intervals, a millisecond counter began to scroll, and participants had to left click the mouse to stop the counter as quickly as possible. After clicking, the counter displayed the achieved reaction time for 1000 ms, providing the subject with feedback on performance. Inter-stimulus intervals were distributed randomly from 2 to 10 seconds, and the task lasted for a total of 3 minutes.

4.3.5 Questionnaire

At the end of the experiment participants were asked to complete a questionnaire to assess their explicit understanding of the regularities associated with each location. For each location they were asked to indicate whether they thought the presence or absence of any of the following features contributed to the location regularities: age (critical feature), face shape (critical feature), headwear (critical feature), glasses, mole, hair colour and gender (male/female judgment). Points were given for each correctly chosen critical feature that was part of the rule for each location (a maximum of 3 per location). A total maximum score, summed over the six locations, was 18 points.

4.4 Results

Data were analysed in SPSS 23. All effects that reached a significance level of $p < .1$ are reported, with effects where $p < .05$ considered significant. Bonferroni-corrected alpha levels are presented to evaluate the direction of significant interactions.

4.4.1 Sleepiness and Vigilance

Alertness measures were taken using the SSS (ratings of sleepiness) and performance on the PVT (3 participants did not complete the PVT due to task failure). Analysis of PVT performance is focused upon measures of reaction time (RT) and attentional lapses (RT > 500ms, data is presented in Table 4.1). Each measure was

analysed using an analysis of variance (ANOVA) with the between-subjects factor Group (wake, sleep) and repeated measure Session (session 1, session 2). There were no differences in the levels of rated sleepiness between the two groups ($F(1, 78) = 2.16, p = .145$) or between sessions ($F(1, 78) = 0.25, p = .622$), and no Group x Session interaction ($F(1, 78) = 1.34, p = .251$). Similarly, there were no main effects or interactions when analysing mean RT or number of attentional lapses on the PVT (RT; Group $F(1, 75) = 0.88, p = .350$, Session $F(1, 75) = 0.71, p = .402$, Group x Session $F(1, 75) = 0.63, p = .429$. Lapses; Group $F(1, 75) = 1.60, p = .210$, Session $F(1, 75) = 2.78, p = .100$, Group x Session $F(1, 75) = 1.75, p = .190$). The data therefore suggests that there were no general group differences in sleepiness or vigilance.

Table 4.1 Stanford Sleepiness Scale and Psychomotor Vigilance Task scores for each group in Session 1 and Session 2. SSS ratings are marked on a 7-point scale (1 – most alert); mean scores are presented. PVT scores represent mean reaction time (RT) and mean number of attentional lapses (RT > 500ms). Standard error of the mean is presented in brackets.

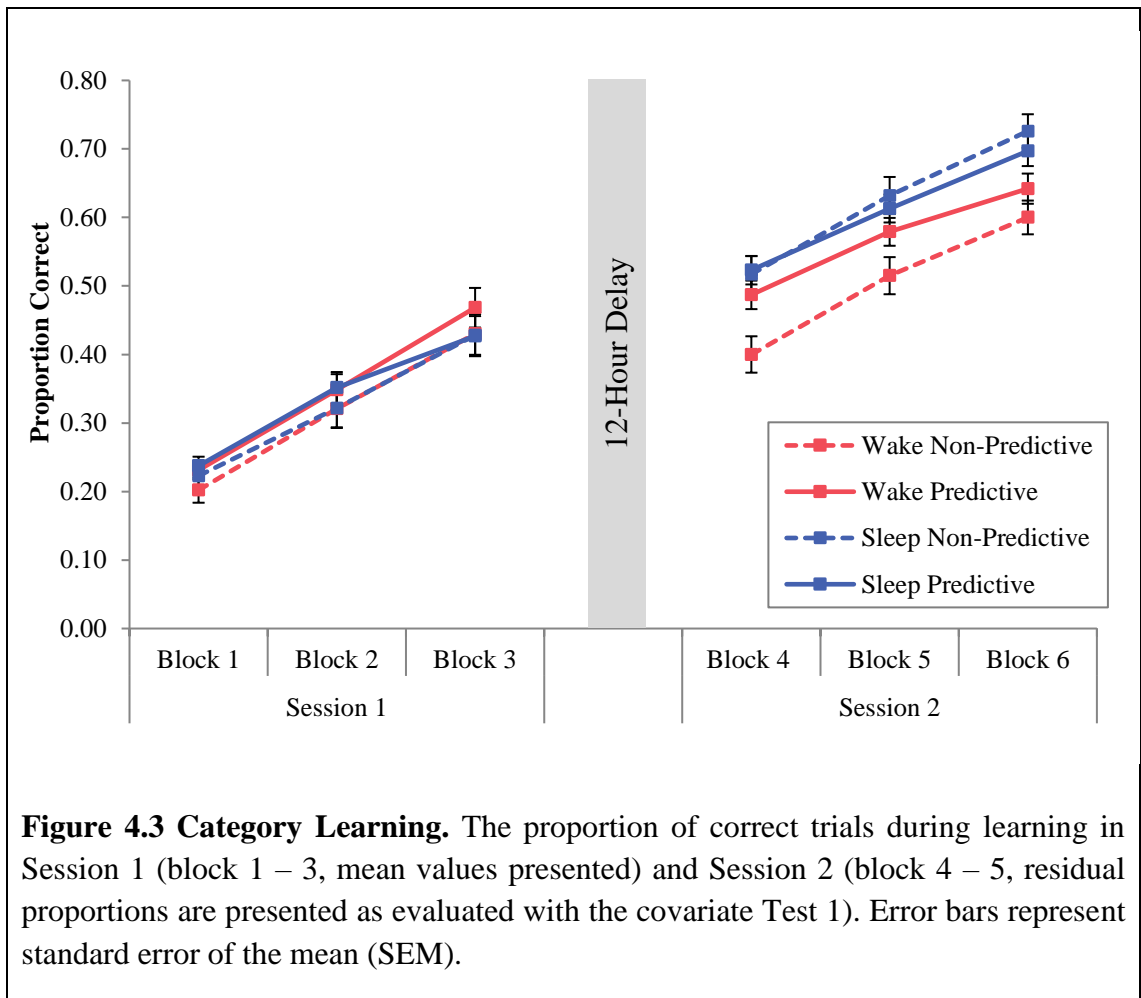
	Stanford Sleepiness Scale		Psychomotor Vigilance Task			
			Mean RT (ms)		Attentional Lapses	
	Session 1	Session 2	Session 1	Session 2	Session 1	Session 2
Wake Group	2.48 (± .13)	2.38 (± .15)	267.99 (± 4.87)	261.73 (± 5.01)	0.71 (± .22)	0.26 (± .09)
Sleep Group	2.55 (± .13)	2.80 (± .21)	270.79 (± 5.04)	270.61 (± 5.66)	0.74 (± .15)	0.69 (± .18)

4.4.2 Session 1 – Face-Location Association Task

4.4.2.1 Training Performance

Performance was measured by the number of correctly located faces across the three training blocks in Session 1. Items were separated into predictive and non-predictive associations to assess the impact of context on learning (see Figure 4.3). An ANOVA with the factors Block (block 1, block 2, block 3), Predictability (predictive, non-predictive) and Group (wake, sleep) was performed. The analysis

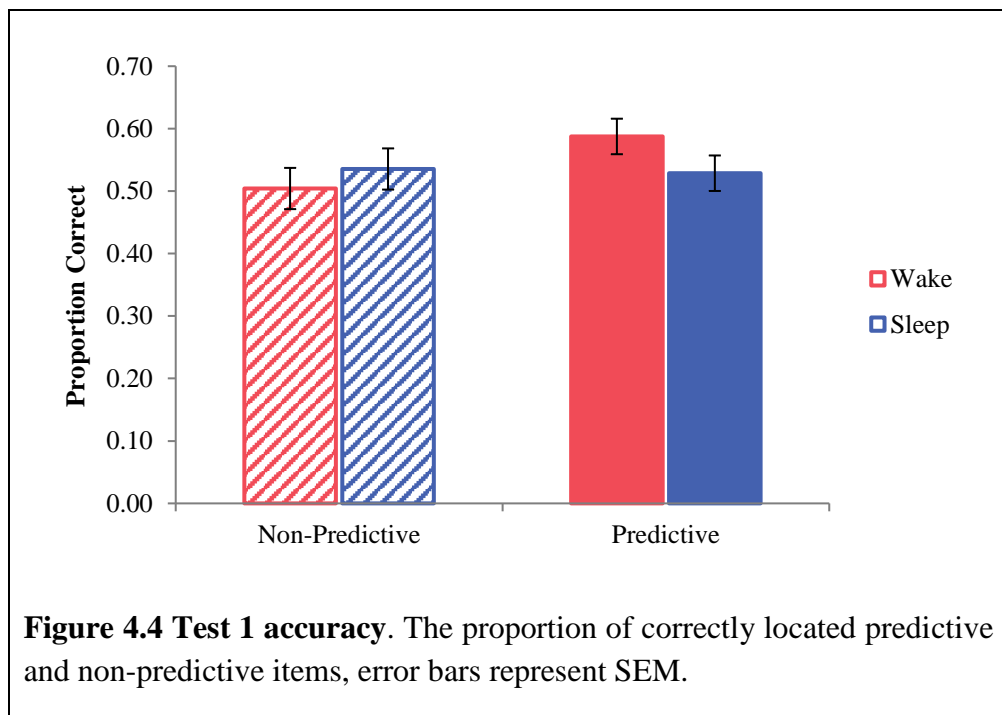
revealed a main effect of Block ($F(2, 156) = 124.92, p < .001, \eta^2 = 0.62$), with participants showing a significant improvement across training (all pairwise comparisons between successive blocks were significant, $p < .001$). There were no differences in performance between the predictive and non-predictive items ($F(1, 78) = 2.74, p = .102$) or between the two groups ($F(1, 78) = .01, p = .937$). No significant interactions were observed (all $p > .422$). The two groups therefore showed equivalent levels of learning during the first session.



4.4.2.2 Test Performance

The test provided a measure of performance in the absence of feedback, requiring participants to make a face-location judgement followed by a confidence score. The proportion of correct responses is presented in Figure 4.4. Data were analysed using a 2

x 2 ANOVA with the factors Predictability (predictive, non-predictive) and Group (wake, sleep). This analysis revealed a main effect of Predictability ($F(1, 78) = 4.01, p = .049, \eta^2 = 0.05$) and a significant interaction between Predictability and Group ($F(1, 78) = 5.55, p = .021, \eta^2 = 0.07$). Paired-samples t-tests (with a Bonferroni corrected alpha level of .025) revealed that this interaction was driven by higher accuracy for the predictive compared to non-predictive items in the wake group ($t(39) = -3.12, p = .003$). No differences were observed in the sleep group ($t(39) = 0.25, p = .806$) and there was no overall main effect of Group in the analysis ($F(1, 78) = 0.13, p = .725$). Group differences at this stage of the study were not expected given that participants had not yet completed the consolidation delay. Sleepiness and vigilance scores did not suggest differences in general alertness and therefore it is not clear what was driving this interaction. To account for these differences, performance in Test 1 was used as a covariate in Session 2 analyses.



A similar 2 x 2 ANOVA was performed on confidence scores, focusing upon mean confidence rating for correctly recalled associations (mean confidence score \pm SEM; wake: predictive = 3.40 ± 0.15 , non-predictive = 3.18 ± 0.15 , sleep: predictive = 3.32 ± 0.14 , non-predictive = $3.31, 0.12$). This analysis did not reveal a main effect of Group ($F(1,78) = 0.02, p = .897$) or Predictability ($F(1,78) = 2.52, p = .116$) and there was no

interaction between these factors ($F(1, 78) = 2.39, p = .126$). Despite differences in accuracy, confidence was comparable across groups.

4.4.3 Session 2 – Face-Location Association Task

To take into account individual differences in Session 1, mean accuracy from Test 1 was used as a covariate in Session 2 analyses. In Session 2, participants completed two tests (before and following Session 2 training). These are analysed within the same analysis of covariance (ANCOVA) to capture the impact of second session training on performance. The analysis will first focus on performance in these tests; it will then present analyses from training to give a full account of performance in the experiment.

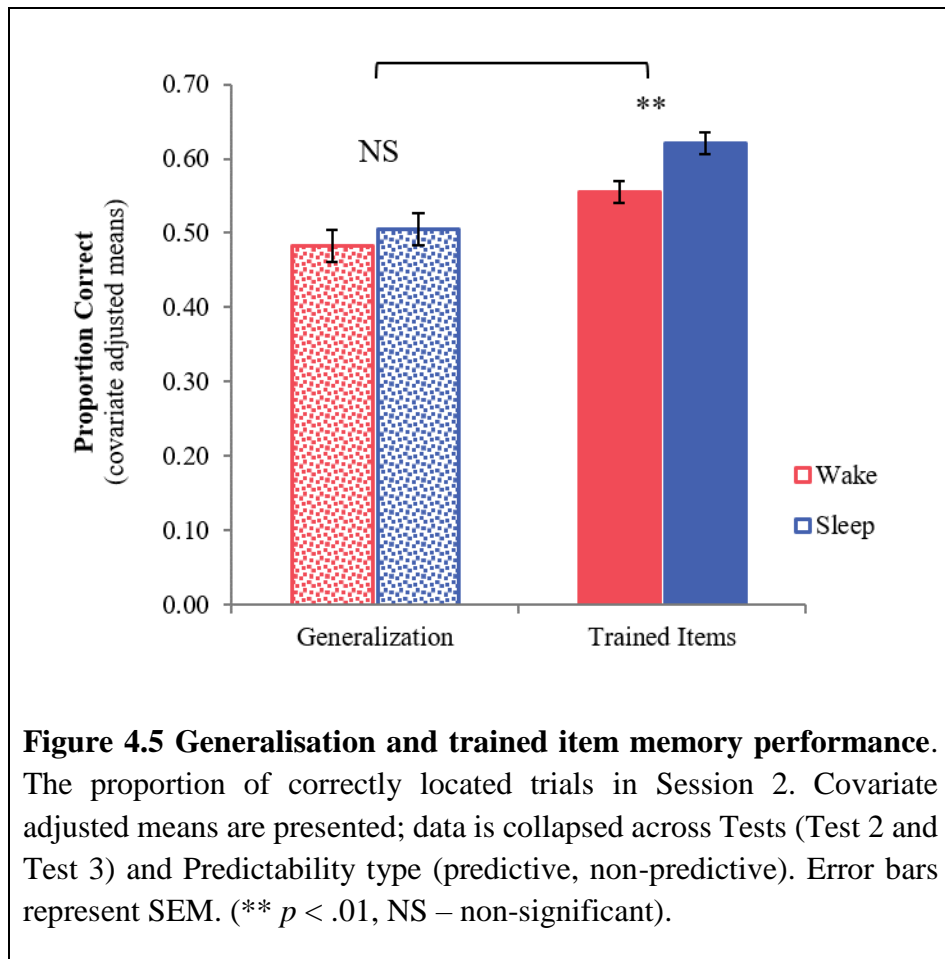
4.4.3.1 Test Performance

In the two Session 2 tests participants were presented with trained items and new items that had not been trained which we refer to as Generalisation trials. Test performance was analysed using a $2 \times 2 \times 2 \times 2$ ANCOVA with the factors Group (wake, sleep), Test (test 2, test 3), Trial Type (trained, generalisation) and Predictability (predictive, non-predictive). Accuracy scores are presented in Table 4.2. This analysis revealed a main effect of Test ($F(1, 77) = 6.03, p = .016, \eta^2 = .073$) and a main effect of Training ($F(1,77) = 4.86, p = .031, \eta^2 = .059$). As would be expected, participants were more accurate in Test 3 compared to Test 2, and were more accurate for trained compared to new items.

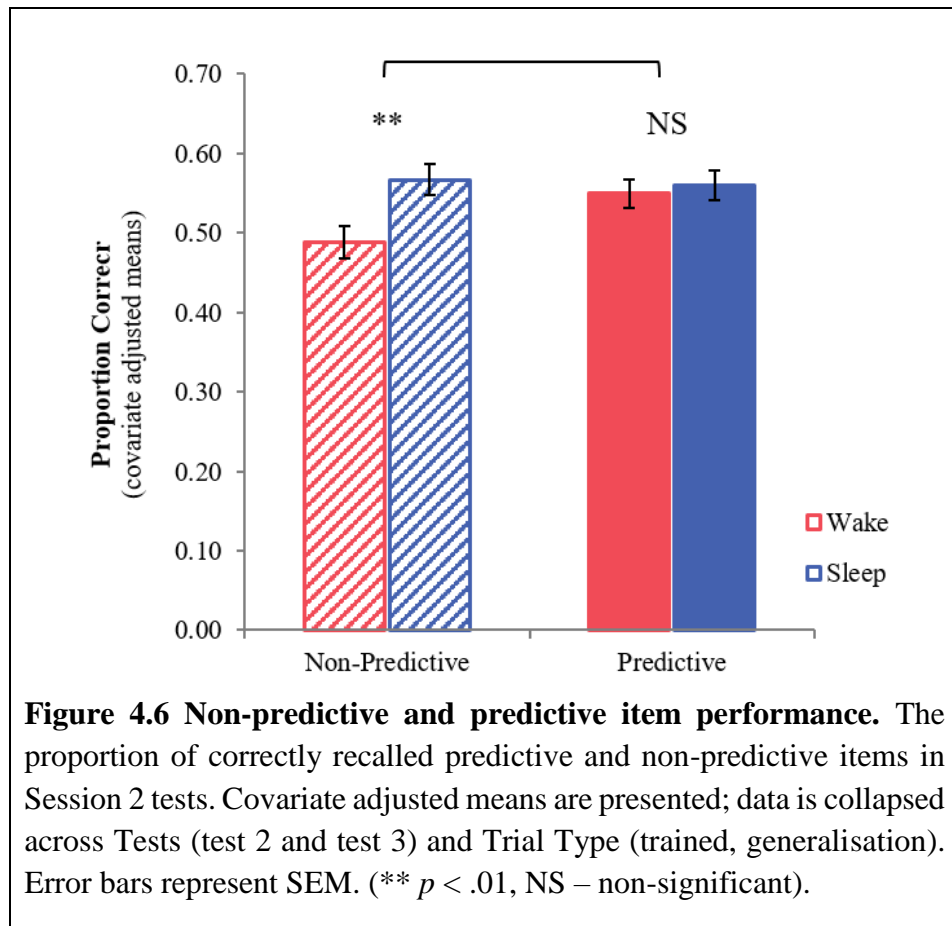
Table 4.2 The proportion of correctly recalled face-location associations in the tests completed in Session 2. Data is split to show trained and generalisation trials with predictive and non-predictive contextual information. Estimated marginal means are presented as evaluated with the covariate Test 1; standard error of the mean is presented in brackets.

		Test Performance in Session 2			
		Test 2		Test 3	
		Trained Items	Generalisation	Trained Items	Generalisation
Wake Group	Predictive	.53 (\pm .01)	.47 (\pm .01)	.65 (\pm .03)	.55 (\pm .03)
	Non-Predictive	.41 (\pm .02)	.38 (\pm .02)	.63 (\pm .03)	.54 (\pm .03)
Sleep Group	Predictive	.54 (\pm .02)	.44 (\pm .01)	.70 (\pm .03)	.55 (\pm .03)
	Non-Predictive	.53 (\pm .03)	.45 (\pm .03)	.71 (\pm .04)	.58 (\pm .04)

There was no main effect of Group ($F(1, 77) = 3.54, p = .064$) or of Predictability ($F(1, 77) = 2.01, p = .161$) in the analyses however there were significant interactions between Group and Trial Type ($F(1, 77) = 4.11, p = .046, \eta^2 = .059$, see Figure 4.5) as well as Group and Predictability ($F(1, 77) = 6.96, p = .010, \eta^2 = .083$, see Figure 4.6). To assess the interaction between Group and Trial Type, t-tests assessing differences between the wake and sleep groups for trained and generalisation items were carried out using the covariate-adjusted means (tested against the Bonferroni corrected alpha level of .013). These t-tests reveal a significant difference between the two groups for trained items, with the sleep group (mean \pm SEM; 0.62 ± 0.02) outperforming the wake group (mean \pm SEM; $0.55 \pm 0.02, t(78) = 3.35, p = .001$). There were no group differences for the generalisation trials (mean \pm SEM, sleep group = 0.51 ± 0.02 , wake group = $0.48 \pm 0.02, t(78) = 0.74, p = .461$, see Figure 4.5).



Similar t-tests were performed to assess the interaction between Group and Predictability (Bonferroni corrected alpha level .013). These t-tests revealed a significant difference between the sleep and wake group for non-predictive items (mean \pm SEM; sleep group 0.57 ± 0.02 , wake group 0.49 ± 0.02 , $t(78) = 2.79$, $p = .007$). There were no group differences for the predictive items (mean \pm SEM, sleep group = 0.56 ± 0.02 , wake group = 0.51 ± 0.02 , $t(78) = 2.16$, $p = .034$, see Figure 4.6).



4.4.3.2 Training Performance

Performance between the tests in Session 2 improved significantly due to the second session of training that participants completed. Training data is presented in Figure 4.3. This data was analysed using an ANCOVA with the factors Block (block 4, block 5, block 6), Predictability (predictive, non-predictive) and Group (wake, sleep). Test 1 performance was used as covariate. This analysis revealed a main effect of Block ($F(2, 154) = 8.50, p < .001, \eta^2 = 0.10$) with participants showing a significant improvement across training (all pairwise comparisons between successive blocks were significant, $p < .001$). This analysis also revealed a main effect of Group ($F(1, 77) = 9.76, p = .003, \eta^2 = 0.11$) and a significant interaction between Group and Predictability ($F(1, 77) = 9.50, p = .003, \eta^2 = 0.11$). Overall, participants in the sleep group outperformed those from the wake group, however this was greatest for the non-predictive items (mean \pm SEM; sleep 0.63 ± 0.02 , wake $0.51 \pm 0.02, t(78) = 3.86, p < .001$). Performance for the predictive items did not significantly differ between groups (mean \pm SEM; 12-hour sleep

group = 0.61 ± 0.02 , 12-hour wake group = 0.57 ± 0.02 , $t(78) = 1.65$, $p = .103$). There was no main effect of predictability in this analysis ($F(1, 77) = 9.50$, $p = .003$, $\eta^2 = 0.11$) and all other interactions were non-significant ($p > .806$).

4.4.3.3 Follow-Up Tasks

Participants completed two follow-up tasks, one that aimed to assess memory for individual stimuli features, and one that asked participants to make speeded judgements regarding the face-location associations. As participants had now been presented with all the faces in the stimuli set, both trained and generalisation trials were combined in all subsequent analyses.

4.4.3.3.1 Features Task

The first judgement participants needed to make in the Features task was regarding the type of context image (urban or rural) that was presented with each face. Throughout the experiment, each face was only ever presented with one type of context and therefore it was possible to achieve 100% accuracy in this task; chance performance is 50%. Data is presented in Table 4.3. T-tests against chance level show that only items that belonged to locations with a predictive context were above chance level (wake; $t(39) = 5.39$, $p < .001$, sleep; $t(39) = 3.82$, $p < .001$). Items from locations with non-predictive contextual information remained at chance level (wake; $t(39) = 1.55$, $p = .128$, sleep; $t(39) = 0.09$, $p = .929$). To compare performance across groups an ANOVA with the factors Predictability (predictive, non-predictive) and Group (wake, sleep) was performed. This supported the t-test results showing a main effect of predictability ($F(1,78) = 12.02$, $p = .001$, $\eta^2 = 0.13$), however there were no Group ($F(1, 78) = 1.80$, $p = .183$) differences and no interaction effects ($F(1, 78) = 0.02$, $p = .881$).

The second part of the Features Task assessed knowledge of individual facial features that were either critical (i.e. headwear) or non-critical (i.e. eyewear) to category membership. Data is presented in Table 4.3; t-tests against chance level (0.5) reveal that groups performed significantly above chance for all trial types in this task. An ANOVA with the factors Group (wake, sleep), Predictability (predictive, non-predictive) and Feature Type (critical, non-critical) revealed only a main effect of Feature Type, with memory for critical features higher than memory for non-critical features ($F(1, 78) =$

53.34, $p < .001$, $\eta^2 = 0.41$). There was no main effect of Predictability ($F(1, 78) = 0.64$, $p = .427$) and no main effect of Group ($F(1, 78) = 0.91$, $p = .342$). All interactions between the three factors were non-significant ($p \geq .376$).

Table 4.3 Proportion of correct responses in the Feature Task assessing knowledge of individual face-context pairings and individual feature knowledge. SEM is presented in brackets.

		Feature Task Performance		
		Context Knowledge	Feature Knowledge	
			Critical	Non-Critical
Wake Group	Predictive	.55 ($\pm .01$)	.63 ($\pm .02$)	.56 ($\pm .01$)
	Non-Predictive	.52 ($\pm .01$)	.64 ($\pm .02$)	.57 ($\pm .02$)
Sleep Group	Predictive	.54 ($\pm .01$)	.63 ($\pm .02$)	.53 ($\pm .01$)
	Non-Predictive	.50 ($\pm .01$)	.61 ($\pm .02$)	.56 ($\pm .02$)

4.4.3.3.2 *Speeded Judgment Task*

Data was cleaned to remove any trials that had a reaction time (RT) larger than two standard deviations above or below the mean for each individual. For five participants this resulted in over 20% of their data being rejected and therefore they were removed from the analysis. A further participant was not included in the analyses as they did not complete this task; in total 4 participants were removed from the wake group, and 2 participants from the sleep group. Measures of accuracy focused upon the proportion of correct responses; data is presented in Table 4.4. A 2 x 2 ANOVA with the factors Group (wake, sleep) and Predictability (predictive, non-predictive) revealed no main effects of interactions (Group; $F(1, 72) = 0.005$, $p = .943$, Predictability; $F(1, 72) = 1.57$, $p = .214$, Group x Predictability $F(1, 72) = 0.99$, $p = .214$).

A similar ANOVA was performed analysing RT data, focusing upon correct trials only. The ANOVA revealed a main effect of Predictability ($F(1, 72) = 4.87$, $p = .031$) and a significant interaction between Predictability and Group ($F(1, 72) = 4.05$, $p = .048$, see

Table 4.4). This interaction is driven by faster reaction times for predictive compared to non-predictive items in the wake group; however, there were no overall Group differences for the predictive or non-predictive items ($p > .704$).

Table 4.4 Speeded judgment task; the proportion of correct responses (accuracy) and mean reaction time (ms). SEM is presented in brackets.

	Speeded Judgment Task Performance			
	Accuracy		Response Time (ms)	
	Predictive	Non-Predictive	Predictive	Non-Predictive
Wake Group	.75 ($\pm .02$)	.73 ($\pm .02$)	954 (± 66)	979 (± 64)
Sleep Group	.74 ($\pm .02$)	.74 ($\pm .02$)	970 (± 73)	968 (± 75)

4.4.4 Questionnaire

Participants could achieve a maximum of 18 points by correctly identifying the presence or absence of the three critical features for each of the six locations. Participants were able to identify ~50% of the correct features relevant for the rules (proportion correct \pm SEM; wake group – 0.55 ± 0.05 , sleep group – $0.52 \pm \text{SEM} = 0.05$). A between-subjects t-test showed there were no differences in explicit rule knowledge between the sleep and wake groups ($t(78) = 0.51, p = .610$).

To determine if explicit rule knowledge was related to item-knowledge and generalisation, we carried out correlations between accuracy on the questionnaire and performance at each test for trained and novel (Test 2 and Test 3 only) items. There was a strong correlation between explicit rule knowledge and both item-level knowledge and generalisation performance (see Table 4.5) at all three Tests in both the wake and the sleep group, suggesting that both item knowledge and generalisation performance are strongly influenced by explicit knowledge of the underlying regularity structure (Test 1 performance did not however survive a Bonferroni corrected alpha level of $p < .005$). The size of the correlation did not significantly differ between the wake and the sleep groups at any test point (all p 's $> .246$).

Table 4.5 Correlations between explicit rule knowledge, measured with the post-study questionnaire, and behavioural performance in the three categorisation tests are presented. Significance is evaluated with a Bonferroni corrected alpha level of $p = .005$ (** $p < .005$, *** $p < .001$).

Explicit Knowledge and Test Performance						
		Test 1	Test 2		Test 3	
		Trained	Trained	Generalisation	Trained	Generalisation
Wake	<i>r</i>	0.35	0.51**	0.46**	0.71***	0.63***
Group	<i>p</i>	.029	.001	.003	<.001	<.001
Sleep	<i>r</i>	0.37	0.48**	0.42**	0.55***	0.54***
Group	<i>p</i>	.016	.002	.007	<.001	<.001

4.5 Discussion

This study explored the role of consolidation on conceptual knowledge using a task that required the extraction of regularities from multiple associative representations. We found sleep-associated benefits for memory of trained face-location pairings, with enhanced performance in the sleep, compared to wake, group in the two post-consolidation tests. These sleep-associated benefits were not observed for novel trials that required the generalisation of shared features that occurred across the training set, suggesting a differential impact of sleep-associated consolidation on these two types of memory. Predictive information that co-occurred with learning had a protective influence on memory, which was marked by reduced wake associated forgetting, suggesting it supported processes of offline consolidation.

4.5.1 The Impact of Offline Consolidation on Memory

Memory for individual events requires the storage of specific memory details and the CLS suggests that these can be rapidly acquired by the hippocampal memory system that promotes pattern separation (McClelland et al., 1995). Over time and with consolidation, these aspects of memory are thought to be transferred to long-term

neocortical stores through a process of hippocampal-neocortical cross-talk which may happen preferentially during sleep (McClelland et al., 1995; Rasch & Born, 2013; Squire & Alvarez, 1995; Mirkovic & Gaskell, 2016). Neuroimaging studies confirm the involvement of the hippocampus in face-location associative memory paradigms (Sweegers et al., 2014; Takashima et al., 2009), we therefore expected to find sleep-associated consolidation benefits for trained associations and our results are in line with this prediction. A previous study using the same experimental task did not observe any differences in performance over sleep and wake intervals, however this may be due to ceiling effects in their study and the nature of sleep-associated consolidation, which may be less effective for very highly encoded material (Sweegers et al., 2014; Cairney et al., 2016; Creery et al., 2015; Stickgold, 2009). By reducing the level of encoding and pre-consolidation performance in the current study we observed the typical benefits of sleep on associative memory (Diekelmann et al., 2009).

Knowledge of shared features across memories, in contrast to the item-level representations, requires the extraction of regularities from across events and experiences; the CLS suggests that these elements of memory may be supported by slow learning neocortical networks (McClelland et al., 1995). Mirkovic & Gaskell (2016) argue that due to this systems level distinction, there may be a prioritisation process during sleep, with a preferential benefit of sleep-associated consolidation for hippocampal-reliant aspects of memory (i.e. individual item-level specifics). Elements of the representations that can be learnt by the neocortex (i.e. overlapping shared representations) may however be less sensitive and show smaller behavioural benefits of sleep. The results of the current study support this suggestion by showing comparable performance in memory generalisation, which required knowledge of the shared regularities, after wake and sleep-filled consolidation delays, despite the observed sleep-associated benefit for item-level knowledge.

Similar support is provided by Frost & Monaghan (2017) who investigated speech segmentation and grammatical rule abstraction in an artificial language task. This task provided a similar distinction as in the current study, whereby speech segmentation required knowledge of the individual lexical items, while rule abstraction required knowledge of the shared grammatical regularities. In line with the current results, Frost & Monaghan (2017) observed greater sleep-associated benefits for speech segmentation

when compared to grammatical generalisation. Interestingly, although smaller when compared to the effect for speech segmentation, they do observe a sleep-associated benefit in their measurement of generalisation, suggesting a graded benefit of sleep across the two types of representation. This result supports the argument from Mirkovic & Gaskell (2016) and suggests a sleep-associated prioritisation process, whereby aspects of memory that are likely to be encoded within the hippocampal memory system may benefit most, but not exclusively, from sleep-associated consolidation.

This graded benefit of sleep on memory can be integrated with other models of consolidation, if a distinction is made between hippocampal and neocortical memory systems. For example, the information overlap to extract (iOTA) hypothesis proposed by Lewis & Durrant (2011) suggests that reactivation of experience specific memories during sleep can result in a selective strengthening of the shared elements across representations. They suggest that this happens in combination with synaptic downscaling, in which there is a global restoration of synaptic strength (Tononi & Cirelli, 2003; 2006) resulting in the development of memory schemas (Lewis & Durrant, 2011). This type of mechanism may describe a process of memory refinement within the neocortical system, which happens separately but in coordination with processes of hippocampal memory transfer. As individual memory representations become integrated into the neocortex, a result of sleep-associated consolidation via mechanisms such as memory reactivation, greater representational overlap in the cortex, along with synaptic downscaling, may emphasise shared memory regularities and promote generalisation. Enhancements in memory generalisations following sleep may therefore be observed, given successful and 'sufficient' memory integration in the neocortex. This would support the graded view of sleep-associated benefits as proposed by Mirkovic & Gaskell (2016) and predict an initial boost following sleep in item-level memory, followed by a later benefit for generalised representations.

Although this pattern of results was not observed in the current data, it is difficult to determine, from a single study, whether the level of encoding and opportunity for consolidation was optimal for such effects to emerge. To explore the graded nature of sleep-associated consolidation, further investigation into the effect size of the difference reported in Frost & Monaghan (2017) and the consequence of multiple wake-sleep consolidation cycles (to account for the slower learning rate in the neocortex) is required.

Increasing the opportunity for consolidation in the current paradigm would offer insight into the time-course of potential sleep-associated consolidation benefits on memory generalisation.

Furthermore, to determine whether generalisation performance is sensitive to mechanisms related to sleep-associated memory reactivation, it will be important to assess the relationship between memory replay and the emergence of generalisation in future studies. This study used a 12-hour consolidation delay that spanned an evening of sleep, however sleep was not measured using polysomnography (PSG) and therefore investigations into relationships between behaviour and features of sleep were not possible. In line with previous literature, it would be predicted that behavioural changes in item-level memory would be positively correlated with the amount of time spent in slow-wave sleep (SWS) and sleep signatures such as spindles, as these have been shown to be closely linked to processes of memory reactivation (Clemens, Fabo & Halasz, 2005; Gais et al., 2002; Gruber et al., 2015; Lau, Alger & Fishbein, 2011; Lustenberger, Murbach & Tüshaus, 2015; Mölle et al., 2002; Schabus, Dang-Vu & Albouy, 2007; Schabus et al., 2004; Wilhelm et al., 2011; Kudrimoti, Barnes & McNaughton, 1999; Louie & Wilson, 2001; Sutherland & McNaughton, 2000; Wilson & McNaughton, 1994; Peigneux et al., 2004; Deuker et al., 2013). If behavioural measures of generalisation also correlated with these features of sleep, even in the absence of a behavioural sleep-associated benefit, it would implicate sleep-associated consolidation processes in the development of these shared concept-based representations.

More causal evidence could be obtained by manipulating memory replay or measuring replay more directly. For instance, the technique of targeted memory reactivation (TMR) allows individual memories to be reactivated in sleep using learning associated cues (Oudiette & Paller, 2013; Rasch et al., 2007; Rudoy et al., 2009). Employing a TMR paradigm in the current study, by introducing an auditory component to the task for example, would allow the interaction between item-level memory, generalisation and the mechanism of replay to be more closely assessed. Moreover, this task is particularly well suited to neuroimaging given that associative memory representations are strongly represented within the hippocampus (Sweegers et al., 2014; Takashima et al., 2009; Talamini et al., 2008) and a region of cortex in the fusiform gyrus i.e. the fusiform face area (FFA), which is particularly active during face processing

(Gauthier et al., 2000; Kanwisher & Yovel, 2006; Kanwisher, McDermott & Chun, 1997). By using neuroimaging techniques such as multivariate pattern analysis (MVPA) during encoding (Haxby, 2012), it would be possible to identify patterns of task related brain activity. By identifying similar patterns of activity during subsequent offline consolidation, in either quiet rest or sleep, it would be possible to quantify memory replay. Investigating the relationship between patterns of memory replay and behavioural performance offers an exciting avenue for future investigations assessing the relationship between memory reactivation and the development of concept-based representations.

4.5.2 Comparing Memory Generalisation across Studies

Within the consolidation literature, there is no ‘typical’ measure of generalisation. This reflects the broad range of instances in which generalisation is required in the real-world; however, it also contributes to the differing results regarding the impact of offline consolidation on behavioural performance. There are striking differences between the testing paradigm used in this study, and those that report sleep-associated benefits in generalisation. Typically, such studies used statistical learning paradigms, which unlike associative memory, draws upon procedural memory systems that recruit striatal learning networks in the brain (Durrant, Cairney & Lewis, 2013, 2016; Durrant et al., 2015; 2011; Frost & Monaghan, 2017; Diekelmann et al., 2009). These processes may draw upon similar processes of consolidation as declarative memory, however evidence from the broader consolidation literature suggests that procedural memory is more susceptible to sleep-associated consolidation (Diekelmann et al., 2009; Durrant et al., 2013; Rieckmann, Fischer & Bäckman, 2010). Greater susceptibility to consolidation mechanisms during sleep may therefore facilitate generalisation at a faster rate, allowing benefits to emerge after a single episode of offline sleep. Investigating the impact of longer, or multiple, consolidation periods would help to determine if these sleep-associated benefits also emerge following training in declarative memory tasks. Factors relating to the opportunity for consolidation may be able to account for the discrepancies that are observed between procedural and declarative memory tasks measuring generalisation.

To dissociate the impact of consolidation on generalisation performance from individual item representations, the current study took care to ensure that generalisation was dependent upon the extracted shared and systematic features of the stimuli by

presenting novel untrained faces. The results suggest that sleep does not provide a benefit over wakefulness for generalisation; this is however in contrast to previous reports of sleep-associated benefits for generalisation using relational memory paradigms (Ellenbogen et al., 2007; Lau et al., 2010; Lau et al., 2011). Tests of relational memory methodologically draw parallels with the current study as participants are trained on declarative paired-associates. However, these previous studies have not assessed the impact of offline consolidation on item memory and generalisation separately, making it difficult to determine the true nature of the reported generalisation benefit.

For example, Ellenbogen et al. (2007) used a relational memory paradigm in which participants learnt premise pairs (e.g. $A > B$, $B > C$, $C > D$, $D > E$, $D > F$) that had an underlying hierarchical structure (i.e. $A > B > C > D > E > F$). Generalisation required participants to make use of the underlying hierarchical information in order to make inferential judgements for non-trained pairs (e.g. $C > E$, $B > E$). They found sleep specific benefits in knowledge of the most distant elements of the hierarchy (e.g. $B > E$) suggesting that sleep played a role in binding the individual memory representations into a single hierarchical structure. Their measurement of generalisation however utilized the same stimuli from training making it difficult to determine whether these effects were driven by benefits to individual items rather than generalisation. Interestingly, Ellenbogen et al. (2007) do not report significant differences between their sleep and wake groups in memory retention for the trained premise pairs (possibly due to very high pre-consolidation accuracy), however the sleep group does show numerically higher performance. It could therefore be the case that small increments in trained item knowledge enhanced performance for the inferential pairs. When evaluating generalisation performance, it is important to consider the measures of generalisation that are taken, and the extent to which they are comparable across tasks and paradigms.

A related point to consider is that generalisation may in fact be achieved in multiple ways, utilising different memory representations and systems. There is no formal model of how the brain achieves generalisation – although we have assumed that generalisation will require processing of the shared and systematic features across memory representations. Models from the categorisation literature highlight other possible routes towards generalisation, for example exemplar theory suggests that a generalised meaning can be assigned to novel items by making comparisons with all existing representations

or ‘exemplars’ that are stored from previous experiences (Medin & Schaffer, 1978; Smith & Medin, 1981). If a novel stimulus is similar enough to an existing representation then it can be assigned the same label, allowing inferences to be made about its traits and features based on the existing knowledge (Murphy, 2016).

In line with an exemplar approach to generalisation, the correct location for a novel face in the current task could be determined by comparing it with all known faces-location associations. By this account, generalisation depends upon the strength of the trained representations and should therefore show the same benefits from offline consolidation. The results from the current experiment are not in line with this prediction, as specific sleep-associated benefits were observed only for the trained representations, suggesting an exemplar approach to generalisation may not have been used by participants in this particular paradigm. This does however highlight the importance of understanding how generalisation is achieved. Developing a greater understanding of generalisation as a cognitive process, or number of processes (for example, via neuroimaging techniques and/or computationally modelling behaviour) will be invaluable for truly characterising and understanding generalisation and the differences in consolidation related changes observed across behavioural tasks.

4.5.3 The Impact of Predictive Context Cues on Performance

A contextual image was presented with each face-location pairing and was manipulated to be predictive or non-predictive of screen location. This was included in the study to assess whether information that coincides with encoding, but is incidental to the main content of learning, would benefit post-consolidation memory performance. We expected the predictive information to support the development of memory schemas or frameworks, and in line with previous evidence (McClelland, 2013; Tse et al., 2007) that schema-congruent information would show greater assimilation and integration into long-term memory networks following offline consolidation during sleep. Interestingly, greater memory for schema-congruent information is observed in the study following consolidation; however, this is seen in the wake group and not the sleep group as predicted.

This result mirrors a benefit that was also observed in the wake group at encoding, where greater memory was observed for the associations with predictive context cues

after training. One possible interpretation of this observed benefit is that the predictive information may act as a simpler ‘rule’ for determining the location that is paired with each face. Although this would be sub-optimal as an overall strategy, it may provide a point from which predictions about category membership can be made. For example, learning that faces presented with an urban context cue are often located in the bottom left location may bias participants to select this location the next time an urban context is presented. Such a strategy would then highlight that this in fact is only true if the face has a hat, and by a process of elimination the combination of facial features could be determined. Recent evidence suggests that prediction error i.e. the degree of conflict between predictions and feedback, can drive declarative learning (Greve et al., 2017). A similar prediction-based benefit may therefore also explain the current pattern of results in the wake group at encoding.

It is not however clear why this same benefit at encoding was not observed in the sleep group. At this point in testing all procedures were comparable across groups, except for the time of day at which the test took place. In the wake group Session 1 was completed at 8.30 am, while session 1 was completed at 8.30 pm in the sleep group. In order to account for potential time-of-day effects in the experiment, measurements of sleepiness and vigilance were taken at the beginning of each session of the study and these measures did not highlight any general group differences. Other factors that may influence learning at different times of day (e.g. motivation) cannot however be avoided with this type of paradigm. This design is commonly employed in sleep research (Dumay & Gaskell, 2007; Ellenbogen et al., 2006; Fenn & Hambrick, 2015; Kurdziel & Spencer, 2016; Payne et al., 2012; Payne & Kensinger, 2011; Sonni & Spencer, 2015; Tham, Lindsay, & Gaskell, 2015; van Dongen et al., 2012) and previous studies have replicated sleep-associated benefits observed from this design using nap paradigms, where time-of-day effects can be controlled (Diekelmann & Born, 2010; Lau et al., 2011; S. Mednick et al., 2003). Although this design offers a suitable sleep and wake comparison, with maximal opportunity for sleep-associated consolidation benefits to emerge across a full night of sleep, the difference between groups at encoding does require further investigation. To determine whether the effect observed in the wake group is a genuine benefit from providing predictive contextual information, replication of this study would be required. Replication using a nap design may be optimal, given that it would allow

time-of-day effects to be controlled. Including PSG recordings of sleep would also strengthen the interpretation of results from this paradigm.

Given that there are differences at encoding in the wake group, it is difficult to determine the nature of the post-consolidation change across the predictive and non-predictive items. One clear interpretation is that better learning will lead to increased subsequent memory. An attempt to control for initial learning performance was made in the current study by using pre-consolidation performance as a covariate in the analysis, however this cannot entirely rule out the above explanation. Further investigation into the impact of the predictive and non-predictive context cues, at both encoding and consolidation is required. Although the impact of including these cues is currently unclear, this manipulation highlights how learning in the real-world may be influenced by factors that are not necessarily or directly related to the content of learning. Furthermore, factors that impact learning are likely to have consequences on subsequent memory processes, including both offline consolidation and later memory retrieval.

In the sleep group, predictive information did not appear to influence performance at encoding or following consolidation. It was predicted that sleep would facilitate second session learning for the predictive items, in line with evidence that suggests schemas facilitate quicker assimilation and integration of new information into long-term memory networks (McClelland, 2013; McClelland et al., 1995; Tse et al., 2007). There was not support for this in the data, however this type of manipulation has not been previously studied and therefore it is unclear whether the manipulation was strong enough to induce behavioural consolidation effects. Previous studies have used paired-associate type paradigms to train memory schemas (Bransford & Johnson, 1972; Tse et al., 2007), however these associations were arbitrary and did not have an underlying regularity structure. In the current study, it was possible to develop a schema representation for every location (i.e. based on the facial regularities) and therefore this may have facilitated post-consolidation learning in all conditions, masking any further benefits provided by the added predictive information. Characterising the impact of predictive information upon associative representations that do not have an underlying structure would help to determine whether this manipulation is able to induce schema type effects. Creating a stronger manipulation of predictability may be useful in future studies to determine any interaction it may have with the development of concept-based representations.

Understanding the impact of the wider learning environment is likely to play a key role for integrating theoretical models with real-world observations of conceptual memory development.

4.5.4 Conclusions

To conclude, we aimed to investigate the development of conceptual memory representations using a declarative associative memory paradigm. Our findings demonstrate that people are able to acquire multiple associative memory representations, and use these to make successful generalisations to novel stimuli. There is also evidence for a role of sleep-associated consolidation; however, this is preferential for the long-term retention of trained associative representations. As we did not observe sleep-associated benefits in measurements of generalisation, these results suggest a memory prioritisation process in sleep-associated consolidation, in line with the suggestion from Mirkovic & Gaskell (2016). The exact role of sleep in regularity extraction remains to be fully determined, however the current experiment provides data to suggest that generalisation may not always be a direct consequence of sleep-associated consolidation.

CHAPTER 5

Markers of Sensory-Motor Decoupling at Rest Relate to Better Memory Generalisation

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5.1 Abstract

There is growing evidence for offline memory consolidation; however, the nature of this processing and its contribution to individual differences in long-term memory are not well understood. Using an associative memory task, in which participants were required to learn individual face-location representations, this study investigated whether intrinsic functional connectivity measured at rest could predict behavioural measures of learning, post-consolidation item memory and memory generalisation, which required participants to extract regularity knowledge from across the individual associative

representations. Participants completed a 9-minute resting state fMRI scan and then, at a separate point in time, two behavioural testing sessions separated by a 12-hour overnight consolidation delay. The results show a relationship between post-consolidation memory generalisation and two patterns of functional connectivity. Better generalisation was associated with decoupling between: i) the anterior hippocampus and a region of motor cortex, and ii) the right fusiform face area and angular gyrus. These results suggest that decoupling between sensory-motor regions and heteromodal regions implicated in memory (i.e. anterior hippocampus and angular gyrus) may support efficient category learning, due to the represented information being abstracted away from current sensory-motor states.

5.2 Introduction

Predicting and understanding the world around us relies upon the ability to remember specific events from the past and the extraction of structure based on similarities between these experiences (Kumaran & McClelland, 2012; McClelland, McNaughton & O'Reilly, 1995). Individual episodic memories encompass associations between different elements of experiences, which may include contextual information related to the time and place an event occurred, the people encountered and associated internal attributes such as emotional feelings. As well as these individual event representations, associations can also be formed across episodes, by linking overlapping memory features or contextual elements together (Backus et al., 2016). It is these interlinked representations that may ultimately generalize to provide concept-based memory representations, capturing the broader relationships between people, places, objects and experiences (Kumaran & McClelland, 2012; Preston & Eichenbaum, 2013).

Computational models of memory suggest there are specialised 'convergence zones' in the brain which act to integrate separate memory elements into coherent representations (Damasio, 1989; Eichenbaum, 2000; Marr, 1971; McClelland, 1994). The hippocampus is a key candidate for supporting information convergence and there is a growing amount of experimental evidence to suggest it is able to acquire and maintain associative information by integrating distinct perceptual, spatial and emotional inputs into holistic memory representations (Horner et al., 2015; Azab, Stark & Stark, 2014; Chadwick et al., 2010; LaRocque et al., 2013; Moita et al., 2003; Shohamy & Wagner,

2008; Wood, Dudchenko & Eichenbaum, 1999). The hippocampus is particularly well suited to perform this function given its connectivity to modality-specific sensory-motor cortices and other higher-order heteromodal regions in the brain (Moscovitch et al., 2016).

However, differences in patterns of functional connectivity along the posterior-anterior axis of the hippocampus, may give rise to functional specialisations related to the development of item-based associations and conceptual representations respectively (Poppenk et al., 2013; Sheldon et al., 2016; Sormaz et al., 2017; Strange et al., 2014). Neuroanatomical and functional connectivity analyses have shown that posterior regions of the hippocampus are preferentially connected to perceptual regions of the posterior neocortex (Aggleton, 2012; Ranganath & Ritchey, 2012), including occipital and parietal cortices which provide visual and perceptual information for object and spatial processing (Bird & Burgess, 2008; Hüfner et al., 2011; Shipman & Astur, 2008). In contrast, anterior regions of the hippocampus show preferential connectivity to anterior heteromodal regions of the brain, including the ventromedial prefrontal cortex (vmPFC) and lateral temporal cortex extending into the temporal pole and amygdala. These regions have been associated with the processing of schemas, semantic information and social and emotional cues respectively (Moscovitch et al., 2016; Ranganath & Ritchey, 2012; Jefferies, 2013; Patterson, Nestor & Rogers, 2007; Sheldon et al., 2016; Sormaz et al., 2017; Lambon Ralph., 2017).

These connectivity patterns suggest a local-to-global framework of hippocampal function, with the posterior hippocampus preferentially processing information related to local perceptual input which is important for integrating disparate memory elements into single associative representations. The anterior hippocampus, in contrast, processes broader relations among items and links these representations to other heteromodal regions of cortex such as the anterior temporal lobes which support semantic and conceptual memory processing (Poppenk et al., 2013; Sheldon et al., 2016; Sormaz et al., 2017; Strange et al., 2014). To our knowledge, the relationship between this functional specialisation and individual differences in memory for specific events versus generalised concept-based structures has not been previously assessed. We therefore aimed to address this in the current study by assessing differential functional connectivity patterns between the anterior and posterior hippocampus during rest, and relating these patterns of

connectivity to behavioural measures of learning, post-consolidation item memory and memory generalisation.

There is growing evidence to suggest that memories are processed during offline periods, e.g. during sleep and quiet wake (Diekelmann & Born, 2010; Ellenbogen, Payne & Stickgold, 2006; Mednick et al., 2011; Stickgold, 2013; Dudai et al., 2015; Rasch & Born, 2013). A neocortical candidate for long-term memory retrieval is the Default Mode Network (DMN), which is a network of highly correlated and interacting brain regions that includes the posterior cingulate cortex, inferior parietal lobule and medial prefrontal cortex (Buckner, Andrews-Hanna & Schacter, 2008; Raichle & Snyder, 2007). The DMN may be particularly relevant for memory based experiences as it is closely connected to two memory related sub-systems in the brain: i) a dorsal-medial system, including regions of the medial prefrontal cortex and anterior temporal lobes – implicated in the representation of semantic knowledge (Lambon Ralph et al., 2017) and ii) a medial-temporal system, involving regions of the medial temporal lobes – important for episodic memory (Andrews-Hanna, Saxe & Yarkoni, 2014; Moscovitch et al., 2016; Moscovitch et al., 2016).

In addition to internally driven memory retrieval, the DMN is also associated with the decoupling of attention from perceptual input, with attention focused on internally driven and directed thought (Baird et al., 2014; Poerio et al., 2017; Schooler et al., 2011; Smallwood & Schooler, 2015). For example, DMN activity is observed strongly during mind-wandering, in which thoughts and feelings are generated independently of perceptual input, facilitating the retrieval of internally stored representations that capture memories of past episodes and conceptual knowledge (Smallwood & Schooler, 2015; Spreng et al., 2014; Spreng, Mar & Kim, 2009). The DMN is commonly found to be decoupled from sensory and perceptual brain regions (Smallwood et al., 2013) and this decoupling along with internally-driven memory retrieval may place the DMN in an ideal position for offline memory processing.

Specific evidence for a role of the DMN in offline memory processing is provided by Sneve et al. (2017) who investigated whether task-independent DMN connectivity was related to long-term memory retrieval. They measured resting state functional connectivity before participants performed an associative memory task. They then related these connectivity patterns to behavioural memory performance following either a short

(hours) or long (several weeks) consolidation interval. After several weeks (but not after the short delay) they found superior memory recall to be characterised by high synchrony within the DMN, with this activity anti-correlated with that observed within perceptual networks. Their data therefore suggest that long-term memory may benefit from processing within the DMN and perceptual decoupling during rest. As they measured resting state activity before memory encoding, their data suggests that general variations in DMN connectivity can in part explain individual differences in associative memory performance across long retention intervals.

The current study built on the findings from Sneve et al. (2017) by examining the relationship between individual differences in intrinsic connectivity measured at rest and memory generalisation (i.e., the extraction of conceptual representations) for the first time. As in Chapter 4 of this thesis, participants completed an associative memory task that required the learning of face-location associations and the retrieval of locations based on facial cues (task adapted from Sweegers et al. 2014). The faces trained in the study followed complex associative regularities such that all faces belonging to a particular location had a shared set of facial features. As a result, this paradigm allowed concept-based knowledge to be assessed by presenting novel faces that had not previously been trained, but could be accurately located by generalising the extracted regularities. Behavioural measurements of memory were taken immediately following training and again following a 12-hour consolidation delay that spanned an evening of sleep.

Given the local-to-global framework of memory processing in the hippocampus, we measured differential posterior and anterior hippocampal connectivity and assessed whether this could explain individual variation in performance. We expected anterior (over posterior) hippocampal connectivity to be related to abstract and heteromodal aspects of memory (i.e. generalisation), while posterior (over anterior) connectivity was expected to relate to item-level perceptual knowledge. As the behavioural task was reliant upon facial processing, we also examined individual differences in connectivity with the right fusiform face area (rFFA), a region of visual cortex that shows strong activity during facial processing (Gauthier et al., 2000; Kanwisher & Yovel, 2006; Kanwisher, McDermott & Chun, 1997). Sweegers & Talamini (2014) used the same face-location paradigm as the current study and found this region of cortex to be active during both memory encoding and retrieval. The rFFA therefore acts as a perceptual and task-positive

region of cortex, allowing us to assess how its intrinsic connectivity with the DMN relates to individual variation in memory.

To summarise, in this study we collected resting-state fMRI data from individuals who subsequently performed a face-location associative memory task. Behavioural performance was assessed immediately after training, and again following a 12-hour consolidation delay that spanned an evening of sleep. We assessed knowledge of the trained items, as well as the capacity to generalise concept-based regularity knowledge to novel faces. We measured differential functional connectivity from the anterior and posterior hippocampus along with connectivity with the rFFA, examining whether these connectivity patterns were able to predict individual differences in item level and concept-based associative representations.

5.3 Methods

5.3.1 Participants

This study used behavioural data from 40 participants presented in Chapter 4 (the 12-hour sleep group). A further 17 participants were recruited for the purposes of this study, resulting in a total sample size of 57 (40 female; mean \pm SD age = 20.18 \pm 1.43 years). All participants were recruited from the University of York in fulfilment of course credit or payment. They were right handed, native English speakers, had normal/corrected vision and no history of psychiatric or neurological illness. All volunteers provided informed written consent. This study was approved by the University of York Neuroimaging Centre and by the University of York Department of Psychology ethics committees.

5.3.2 Procedure

The experiment consisted of two phases; the first involved acquisition of resting state fMRI data and the second included a set of behavioural tasks to assess the development of associative and concept-based memory representations. The two phases of the study were carried out at independent time points and are described below.

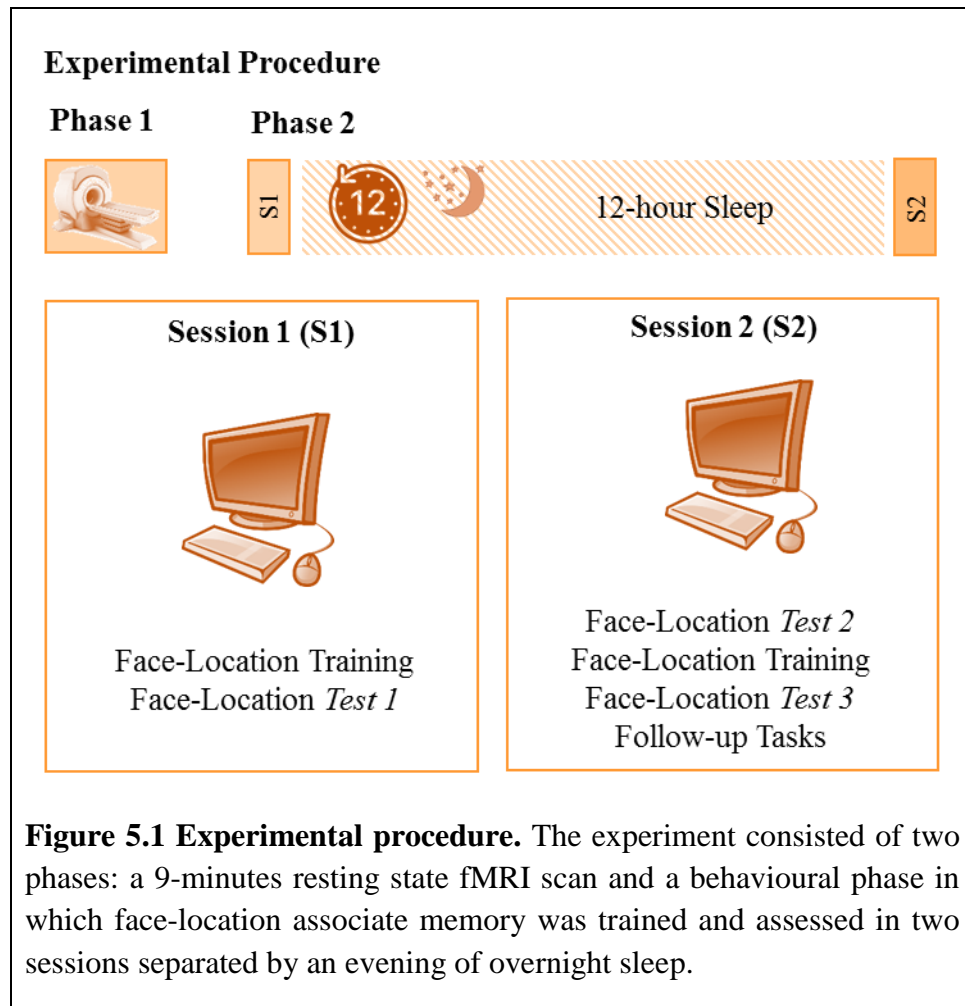
5.3.2.1 Phase 1

This first phase of the experiment required participants to undergo MRI scanning at the York Neuroimaging Centre. This was completed as part of a larger cohort study which included an hour-long MRI session that involved a number of structural scans and a 9-minute fMRI resting state scan where participants simply viewed a central fixation cross presented on a grey screen.

5.3.2.2 Phase 2

This part of the experiment was carried out in the Department of Psychology, University of York. There were two experimental sessions separated by a delay of 12-hours. Session 1 was completed at 8.30 pm, participants then slept overnight at home and returned to the university to take part in Session 2 at 8.30 am the following morning (see Figure 5.1).

In Session 1, participants completed face-location association training, followed by an immediate test (*Test 1*) which provided a measure of initial learning (Session 1 took ~ 50 minutes to complete). In Session 2, participants completed a second test (*Test 2*) which assessed memory for the previously trained stimuli and a set of novel stimuli which had not been trained and therefore acted as ‘generalisation’ trials. This was followed by a second round of training and a third test (*Test 3*) including trained and untrained stimuli. At the end of the experiment, we included a two-alternate-forced-choice features task and speeded judgement task (Session 2 took ~ 90 minutes to complete). Of these measures, we concentrate on performance in the first test which measured initial learning (*Test 1*) and performance immediately following the consolidation delay (*Test 2*), focusing on memory for trained items following overnight consolidation, plus novel trials (generalisation trials). These measures were chosen as they provide a clear measure of long-term memory, without further exposure to the stimuli and task which may have influenced behavioural measures of performance.



5.3.3 Behavioural Measures

5.3.3.1 Stimuli

5.3.3.1.1 Faces

Stimuli were taken from Sweegers & Talamini (2014) and comprised of 144 greyscale pictures of emotionally neutral faces (created using TM Software, IQ Biometrix, 2003). The faces contained a range of non-critical elements (e.g. gender, the presence of glasses, moles and dark/light hair colour) as well as three critical features that were used to generate face categories; these features were: age – young adult or aged, face shape – slender or stout and headwear – with headwear (caps, hats or headbands) or without headwear (see Figure 5.2A). To maintain perceptual distinctiveness in the stimuli the individual features were perceptually distinct across the faces (e.g. different headwear, wrinkle patterns, etc.). Six out of eight possible three-way combinations of critical

features were selected for the experiment, creating six face categories that could be characterised by a unique combination of three features. For each face category just two (out of the three) critical features sufficed to distinguish that category and this 2-feature combination did not occur in any other category. Twenty-four faces were created for each of the six categories. Each face was allocated to one of four experimental sets (containing 6 faces from each category).

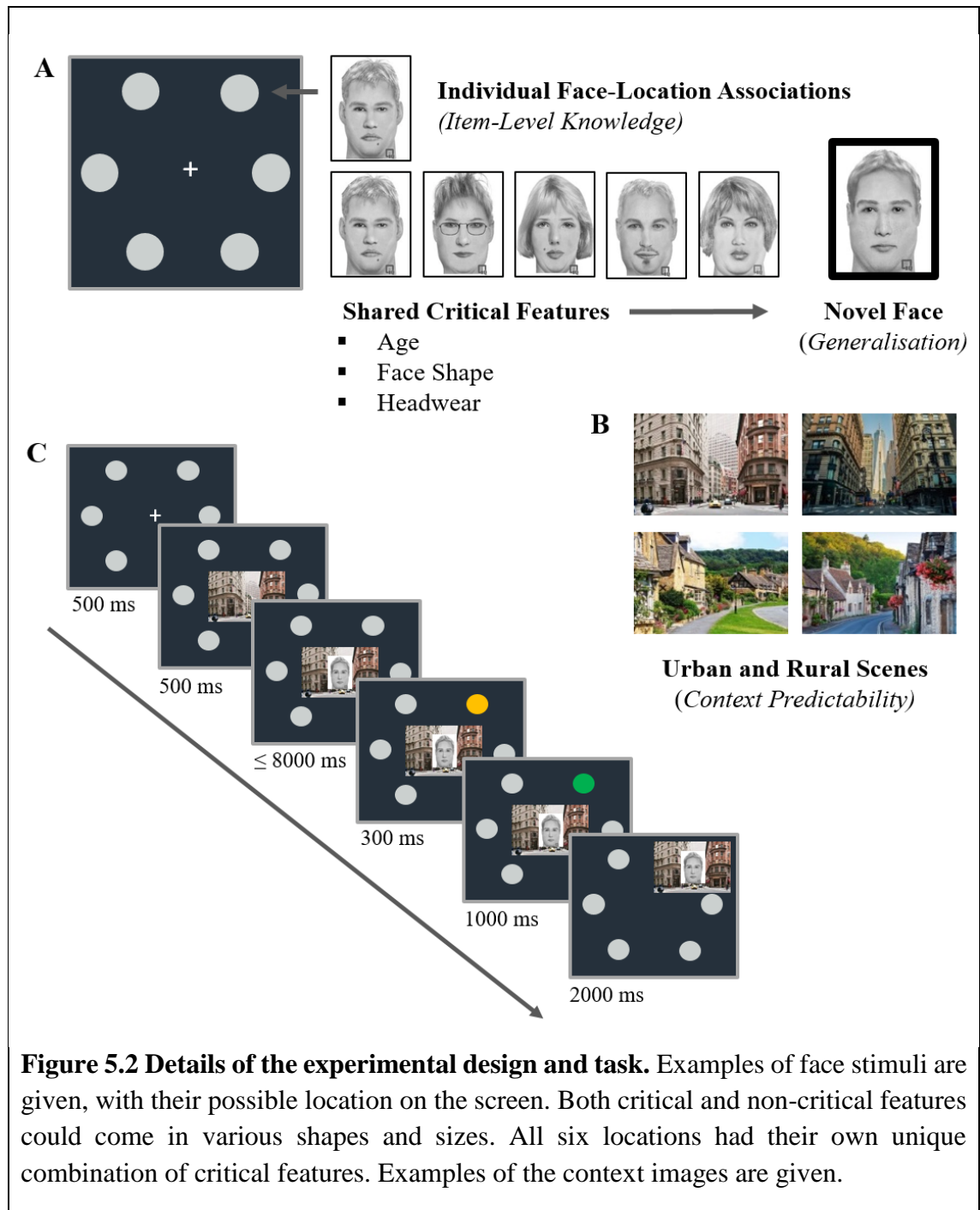
5.3.3.1.2 *Context Images*

Twenty images were selected from the internet to represent contextual scenes. The chosen images were of street scenes with buildings (see Figure 5.2B). Half of the images were taken from a city location (10 images) to generate an ‘urban’ context set, and the other half were taken from a village location to generate a ‘rural’ context set. Twenty-seven participants (independent to the main study) classified each image as belonging to the intended context, confirming the urban/rural manipulation. Similarity ratings, between every image within each context type were collected using a 7-point scale (1-very different, 7 – very similar). All images were rated as being similar (urban images; (mean \pm standard deviation) 5.26 ± 0.12 , rural images; 5.22 ± 0.15) with equivalent levels of similarity between the two context types ($t(18) = 0.58$, $p = .568$). The context images were used in the experiment to mimic real-world learning which happens in rich contextual environments. As in Chapter 4 of this thesis, context cues were set up to be predictive or non-predictive of screen location.

5.3.3.2 Stimuli Set-Up

Each face was coupled to one of six screen locations in order to create face-location associations. The faces assigned to a single location all belonged to the same category (determined by the combination of critical facial features described above). The associations to be learned therefore adhered to deterministic regularities between screen location and facial features. Each category was also assigned to a predictive or non-predictive context condition. In the predictive condition (four categories), 87% or 67% of the faces were presented with a single type of context (e.g. urban) and the remaining faces presented with the other context type (e.g. rural). This provided a predictive, but non-deterministic, cue to the face-location regularities. In the non-predictive condition (two categories), 50% of the faces from each category were presented with each context type,

making context cues completely non-predictive of the face-location regularities. The assignment of context predictability was counterbalanced such that both urban and rural contexts acted as the predictive context type, and the allocations were randomised across the six categories.



5.3.3.3 Tasks

5.3.3.3.1 *Face-Location Association Training*

In Session 1, two sets of faces were selected to be trained (72 faces in total). Participants were instructed to try to learn the individual face-location associations; to begin with they were told to guess, but to use the feedback provided with each trial to help make the correct associations. Participants were told that they could learn regularities to help them allocate the faces to the correct location, however they were not informed as to what elements of the stimuli contributed to these regularities.

Each trial began with a fixation cross in the centre of the screen with the six screen locations depicted by grey circles, which were arranged hexagonally around the centre. For each trial, a context image (randomly selected from the assigned context set for that trial) was presented in the centre of the screen for 500ms; a single face was then presented in front of this context image. The face covered only the central 20% of the context image ensuring that strong contextual information provided from buildings etc. remained clearly visible throughout the trial. Participants were instructed to use the mouse to select the screen location they believed that face to belong to. Participants were given up to 8000ms to make their responses with the selected location changing from grey to orange after being selected (300ms). If the participant made a correct response, this location changed to green (1000ms) and the face and context image moved to this location, remaining on the screen for a further 2000ms. If the participant made an incorrect response, the selected location changed to red (1000ms) and the correct location changed to green (1000ms), the face and context image then moved to the correct location and remained on the screen for 2000ms. A fixation cross presented in the centre of the screen separated each trial (1000ms) and short breaks were provided throughout (see Figure 5.2C). In each session, participants completed three blocks of training, with each face presented once in each block.

5.3.3.3.2 *Face-Location Association Test*

Participants completed tests to assess their memory of the trained associations (see Figure 5.1) The analysis in this chapter focuses upon performance following learning in Session 1 (*Test 1*) and following the consolidation delay in Session 2 (*Test 2*). Both tests

assess memory of trained items; with *Test 2* also including a set of non-trained items to measure generalisation.

The test followed the same procedures as learning; on each trial a context image (500ms) followed by a face was presented in the centre of the screen along with the six hexagonally arranged screen locations. Participants were instructed to use the mouse to select the location they believed that face to belong to (presented for up to 8000ms) and the chosen location changed from grey to orange after being selected (300ms). Participants did not receive feedback during the test, and were instead asked to provide a confidence judgement for each response. They were presented with a 5-point scale (1 – low confidence, 5 – high confidence) and were asked, using the mouse, to click on the scale to rate each response; an unlimited amount of time was given to make this confidence judgement. A fixation cross in the centre of the screen separated each trial (1000ms) and short breaks were provided throughout.

5.3.4 Functional Connectivity

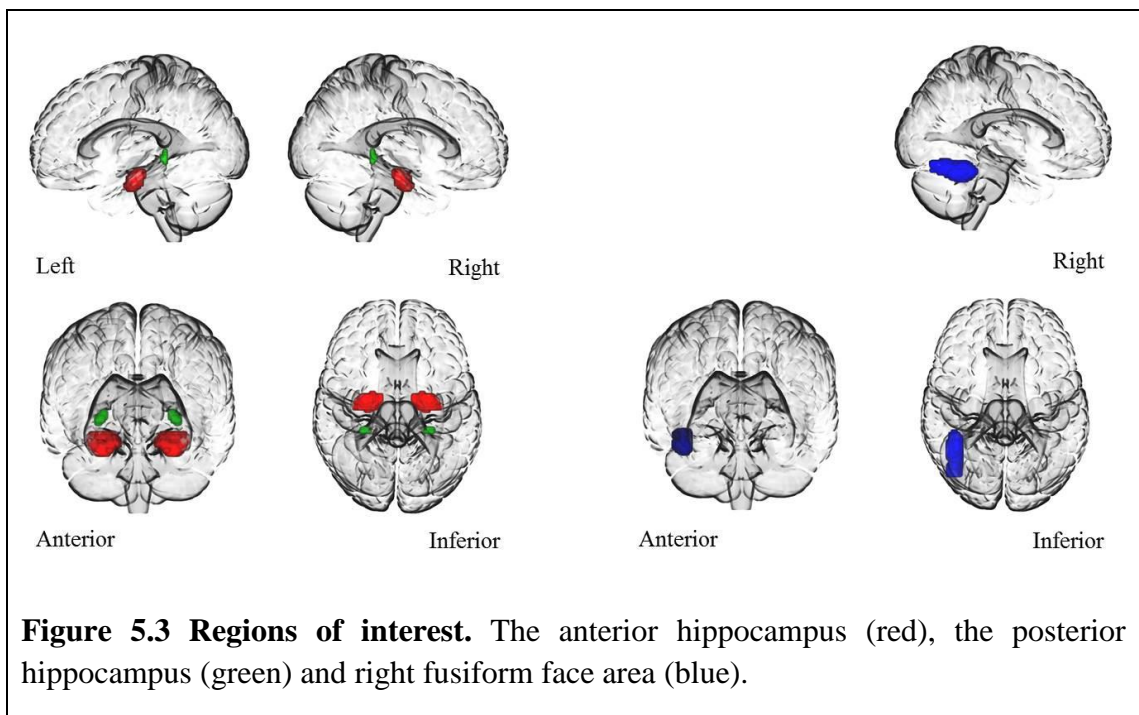
5.3.4.1 MRI Image Acquisition

Structural and functional data were acquired using a 3T GE HDx Excite MRI scanner utilising an eight-channel phased array head coil (GE) tuned to 127.4 MHz, at the York Neuroimaging Centre, University of York. Structural MRI acquisition in all participants was based on a T1-weighted 3D fast spoiled gradient echo sequence (TR=7.8 s, TE=minimum full, flip angle=20°, matrix size=256×256, 176 slices, voxel size=1.13×1.13×1 mm). Resting-state activity was recorded from the whole brain using single-shot 2D gradient-echo-planar imaging (TR=3 s, TE=minimum full, flip angle=90°, matrix size=64×64, 60 slices, voxel size=3×3×3mm³, 180 volumes). A FLAIR scan with the same orientation as the functional scans was collected to improve co- registration between subject-specific structural and functional scans.

5.3.4.2 Region of Interest and Mask Creation

Figure 5.3 illustrates the masks that we used to describe the regions of interest (ROIs) in this study. We selected anterior and posterior regions of the hippocampus based on statistical probabilistic anatomic maps in MNI space following a previously established protocol (Bernasconi et al., 2003) using anatomical landmarks described by

Duvernoy (1988). Hippocampal probabilistic maps were thresholded at a relatively conservative threshold of 60% to ensure the seed regions contained only core hippocampal voxels. To ensure perfect symmetry across hemispheres for anterior and posterior sections for the hippocampus, we first performed a binarisation of the 60% thresholded left and right anterior and posterior hippocampal masks. Following this these masks were mirrored across hemispheres using the `dimswap` command in FSL (<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Fslutils>). Finally, we multiplied the mirrored hippocampal masks together with the original hippocampal masks leaving us with equally sized, symmetrical anterior and posterior hippocampal masks across hemispheres. The rFFA mask was taken from a previous study in which face-responsive regions of interest were defined by comparing faces to scrambled faces, with peak voxels determined from group-level statistical maps (Flack et al., 2014).



5.3.4.3 Data Pre-Processing and Analysis

Resting-state fMRI: Functional and structural data were pre-processed and analysed using FMRIB's Software Library (FSL version 4.1, <http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FEAT/>). Individual FLAIR and T1 weighted

structural brain images were extracted using BET (Brain Extraction Tool). Structural images were linearly registered to the MNI-152 template using FMRIB's Linear Image Registration Tool (FLIRT). The resting state functional data were pre-processed and analysed using the FMRI Expert Analysis Tool (FEAT). The individual subject analysis involved: motion correction using MCFLIRT; slice-timing correction using Fourier space time-series phase-shifting; spatial smoothing using a Gaussian kernel of FWHM 6mm; grand-mean intensity normalisation of the entire 4D dataset by a single multiplicative factor; highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with $\sigma = 100$ s); Gaussian lowpass temporal filtering, with $\sigma = 2.8$ s.

We extracted the time series from the hippocampal (bilateral anterior and posterior) and rFFA ROI masks and used these as explanatory variables in connectivity analyses at the single subject level. In each analysis, we entered 11 nuisance regressors; the top five principal components extracted from white matter (WM) and cerebrospinal fluid (CSF) masks based on the CompCor method (Behzadi et al., 2007) and six head motion parameters. Spatial smoothing (Gaussian) was applied at 6mm (FWHM). WM and CSF masks were generated from each individual's structural image (Zhang, Brady, & Smith, 2001). No global signal regression was performed, following the method implemented in Murphy et al. (2009). The nature and interpretation of correlation in resting state analysis is a matter of a debate that is focused on a lack of clarity regarding what constitutes a correlation of zero (see Murphy et al., 2009). We therefore use the terms 'relatively strongly correlated' and 'relatively weakly correlated' to describe regions whose correlation with the seed region is increased or decreased relative to the average.

5.3.4.4 Analysis of Individual Differences in Functional Connectivity

The hippocampal masks were used to calculate differential connectivity along the anterior-posterior axis at the individual level. This map described relative differences in functional connectivity between bilateral anterior and posterior regions of the hippocampus in each voxel. This measure (i.e. 'differential' connectivity) is sensitive to regions of cortex that show strong connectivity to *either* the anterior *or* the posterior hippocampus (areas that share strong connectivity with both the anterior and posterior hippocampus would not be identified as 'significant' regions of connectivity in this

analysis). These connectivity maps therefore highlight regions of cortex that have the greatest difference in connectivity along the anterior-posterior axis of the hippocampus.

The spatial and functional characteristics of this map, along with the rFFA group map, were quantified by comparing the unthresholded functional connectivity activation profiles to previous studies using the Neurosynth decoder (<http://www.neurosynth.org/decode/>). This quantifies the functional terms most commonly associated with each spatial map, performing a quantitative reverse inference regarding the most likely associated functions (see Yarkoni et al. (2011) for further details). To produce our word clouds, we manually extracted the top ten task descriptions (based on frequency) for each unthresholded z map, manually excluding the names of brain regions or MRI methods.

Connectivity patterns were then related to individual variations in behaviour using two multiple regression models in which the hippocampal differential connectivity and rFFA connectivity were the dependent variables, and z-scored accuracy on the three memory measures (learning, post-consolidation item memory and generalisation) were the explanatory variables. To ensure that general individual differences in learning and/or consolidation did not drive performance in our three measures, we used covariate adjusted means. Our post-consolidation item measure included initial learning performance as a covariate and the generalisation measure included both learning and post-consolidation item memory as covariates. We also included mean frame displacement (Power et al., 2014) in our group level regressions to rule out spurious effects related to motion artefacts. These analyses were carried out using FMRIB's Local Analysis of Mixed Effects (FLAME1). For all significant effects, we then computed the correlation between the connectivity measure and performance across individuals. To control for multiple comparisons, we used a cluster-forming threshold of $Z = 2.6$ and controlled our Type I error rate at an alpha value of $p < .025$ in order to take account of the number of voxels in the brain as well as the two different regression models we conducted (Eklund, Nichols & Knutsson, 2016).

5.4 Results

5.4.1 Behavioural Results

5.4.1.1 Face-Location Training

Performance was measured as the number of correctly located faces across the three training blocks and distinguished between items presented with predictive and non-predictive contexts (see Table 5.1). An ANOVA with the factors Block (block 1, block 2, block 3) and Predictability (predictive context, non-predictive context) was performed and revealed a main effect of Block ($F(2, 112) = 85.61, p < .001, \eta^2 = 0.61$), with participants showing a significant improvement across training (all pairwise comparisons between successive blocks were significant, $p < .001$). There were no differences in performance between the predictive and non-predictive items ($F(1, 56) = 2.41, p = .126$) and no interaction between these factors ($F(2, 122) = 0.40, p = .671$). Consequently, the two Predictability conditions were collapsed in all subsequent analyses.

Table 5.1 The proportion of correctly located faces during learning in Session 1. Standard error of the mean (SEM) is presented in brackets.

	Face-Location Training Performance		
	Block 1	Block 2	Block 3
Predictive	.24 ($\pm .01$)	.35 ($\pm .02$)	.44 ($\pm .02$)
Non-Predictive	.22 ($\pm .02$)	.31 ($\pm .02$)	.47 ($\pm .03$)

5.4.1.2 Post-Training Performance

Accuracy rates from *Test 1* (measured immediately following initial training) and *Test 2* (immediately following the consolidation delay) are presented in Table 5.2. *Test 2* assessed knowledge of trained items and new items that we refer to as Generalisation trials. A paired-samples t-test showed accuracy to be significantly greater for trained compared to generalisation trials in this test ($t(59) = -7.06, p < .001$).

Table 5.2 The proportion of correctly recalled face-location associations *Test 1* and *Test 2*. For *Test 2* data is shown separately for trained items and novel generalisation trials. Standard error of the mean is presented in brackets.

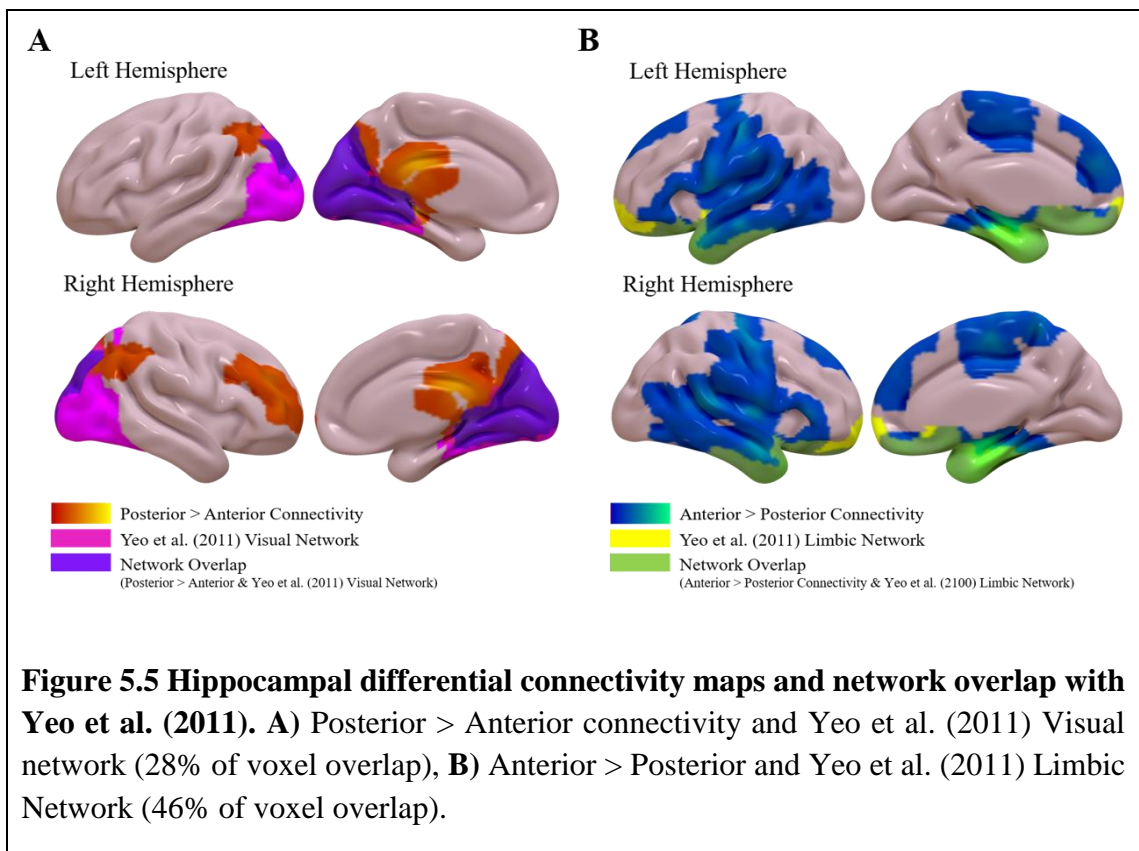
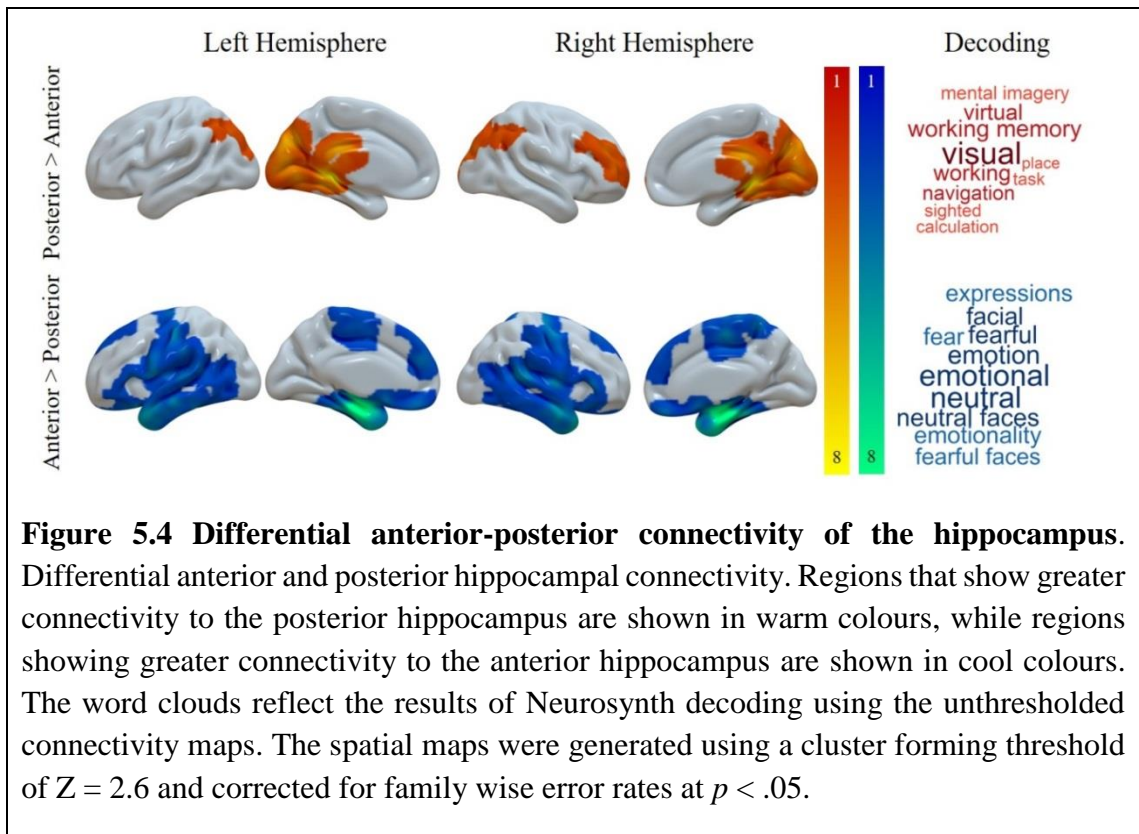
Face-Location Test Performance		
Trained Items		Generalisation
<i>Test 1</i>	<i>Test 2</i>	<i>Test 2</i>
.50 (\pm .02)	.49 (\pm .02)	.40 (\pm .02)

5.4.2 Functional Connectivity

5.4.2.1 ROI: Hippocampus

5.4.2.1.1 *Differential Connectivity and Meta-Analytic Decoding*

Figure 5.4 presents differential connectivity maps comparing the anterior and posterior hippocampus. Posterior regions showed relatively stronger connectivity to dorsolateral prefrontal cortex, fusiform gyrus and medial occipital cortices (indicated by warm colours). Neurosynth decoding of the spatial posterior > anterior hippocampal map produced terms related to vision and spatial processing in memory, e.g. visual, sighted, working memory and navigation. A number of these regions (28% of voxels) fall within the visual cortical network described by Yeo et al. (2011; see Figure 5.5A), supporting a relationship between posterior regions of the hippocampus and visual processing. Anterior regions showed relatively stronger functional connectivity to medial prefrontal cortex, lateral temporal regions, posterior lateral prefrontal cortex and regions of the mid-cingulate cortex (cool colours). Terms related to emotion, fear, faces and expressions were produced by Neurosynth decoding of the anterior > posterior hippocampal map, and these regions (46% of voxels) largely fell within the limbic cortical network described by Yeo et al. (2011; see Figure 5.5B). These differential connectivity patterns therefore support the suggestion that the anterior and posterior hippocampus have functional specialisations.

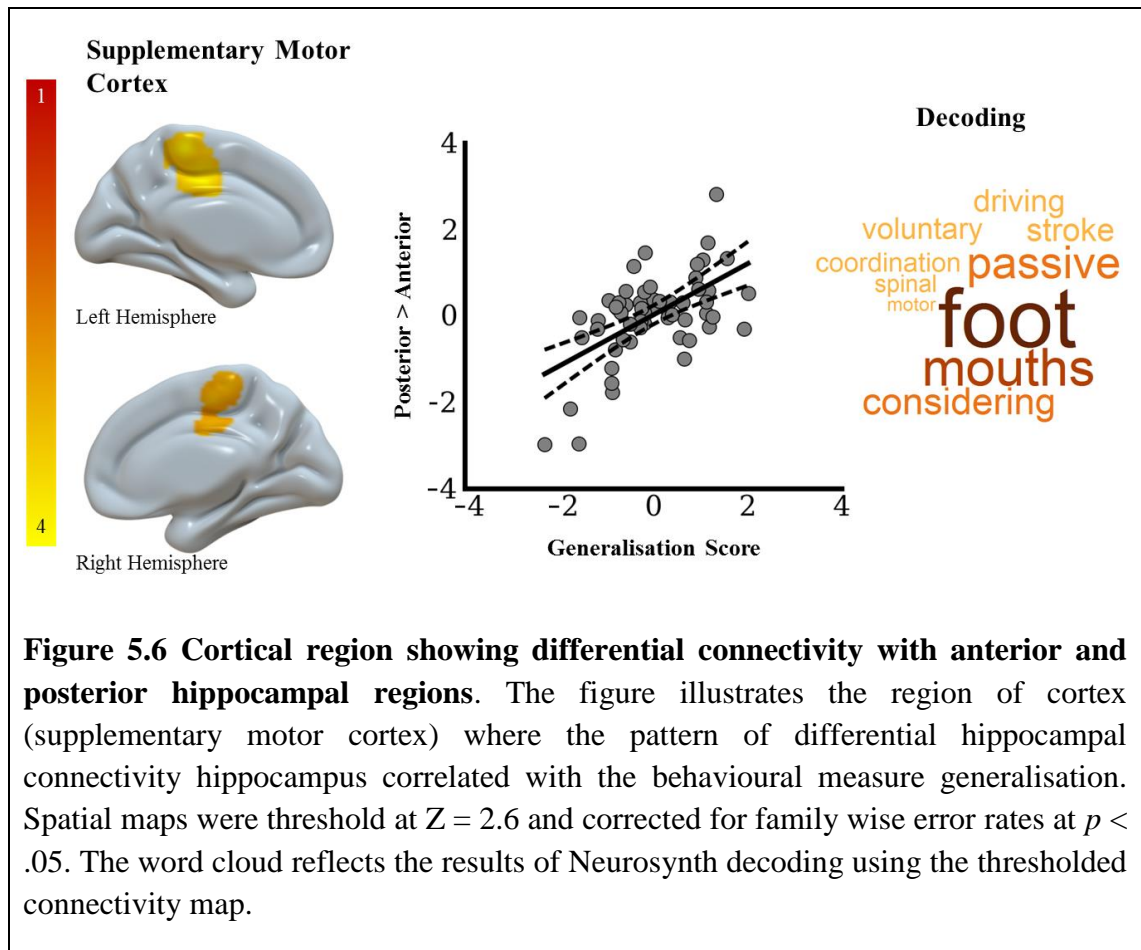


5.4.2.1.2 Hippocampal Variation in Connectivity and Task Performance

Having characterised the differences in functional connectivity between the anterior and posterior hippocampus, we then assessed how individual differences in this pattern of differential connectivity related to behavioural measures of learning, post-consolidation item memory and generalisation. The accuracy of each participant, from each measure, was included as an explanatory variable in a multiple regression analysis, with differential hippocampal connectivity as the dependent variable. This analysis produced a significant result related to our behavioural measure of generalisation and a cluster in the bilateral paracentral and supplementary motor cortices (see Figure 5.6 and Table 5.3). Neurosynth decoding of this cluster showed a role in motor processing, and produced terms such as foot, mouth and coordination (see Figure 5.6). Connectivity with this motor cluster correlated positively with individual differences in posterior > anterior hippocampal activity. When connectivity was related to behavioural performance, better generalisation was observed when there was stronger posterior over anterior hippocampal connectivity (see Figure 5.6).

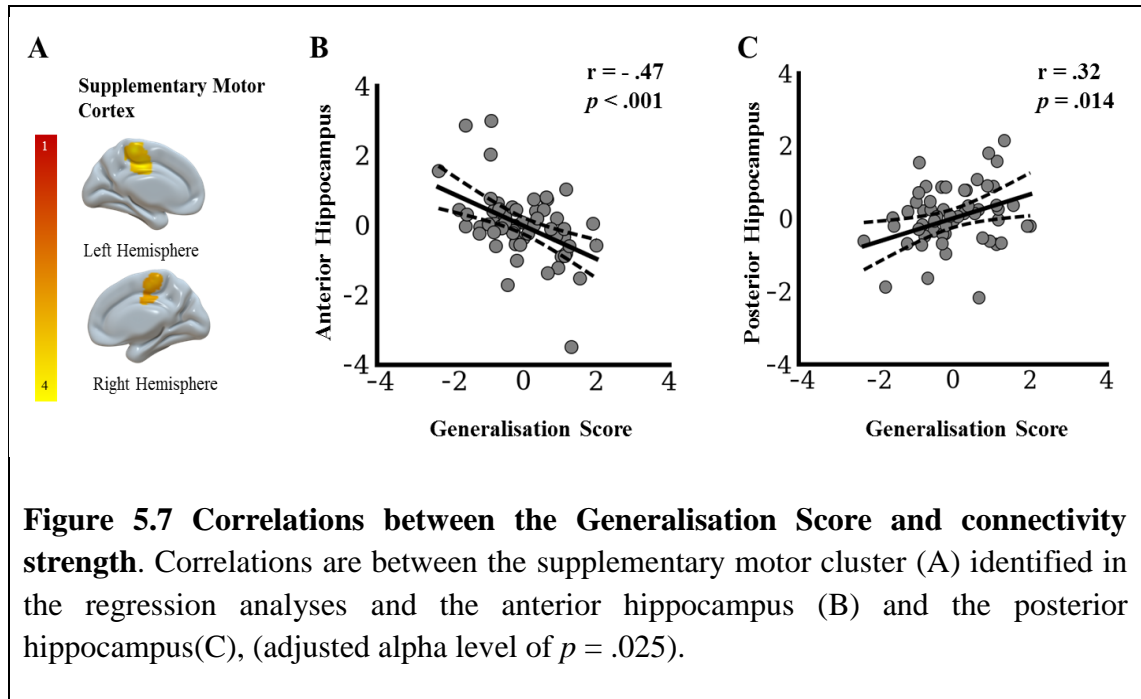
Table 5.3 Cluster of activity that has a differential correlation with posterior > anterior hippocampus and the behavioural measure of Generalisation.

ROI: Hippocampus							
Hem	Connectivity	Z	X	Y	Z	Total Voxels	<i>p</i>
Anterior > Posterior & Generalisation Score						545	.009
L	Cingulum	4.49	-4	-18	42		
L	Paracentral Lobule	4	-4	-30	60		
R	Supplementary Motor Area	3.58	2	-20	50		
R	Paracentral Lobule	3.17	6	-26	60		



To facilitate the interpretation of this connectivity pattern, and to establish the contribution of anterior and posterior hippocampal connectivity to this effect, the β connectivity values from the separate anterior and posterior hippocampal connectivity maps were extracted and correlated with generalisation performance (see Figure 5.7). This showed a strong negative correlation between generalisation performance and connectivity of the medial motor cluster and the anterior hippocampus ($r = -.47, p < .001$, adjusted alpha level of $p = .025$). This pattern of data suggests that the posterior > anterior hippocampal effect described above, was driven by strong decoupling between the anterior hippocampus and this region of motor cortex, supporting the view that decoupling between heteromodal memory regions and sensory-motor networks may support memory processing. There was also a weaker positive correlation between behavioural generalisation performance and posterior hippocampal connectivity (see Figure 5.7C; $r = .32, p = .014$, adjusted alpha level of $p = .025$), which may relate to the perceptual processing of features that contribute to regularity knowledge. No significant

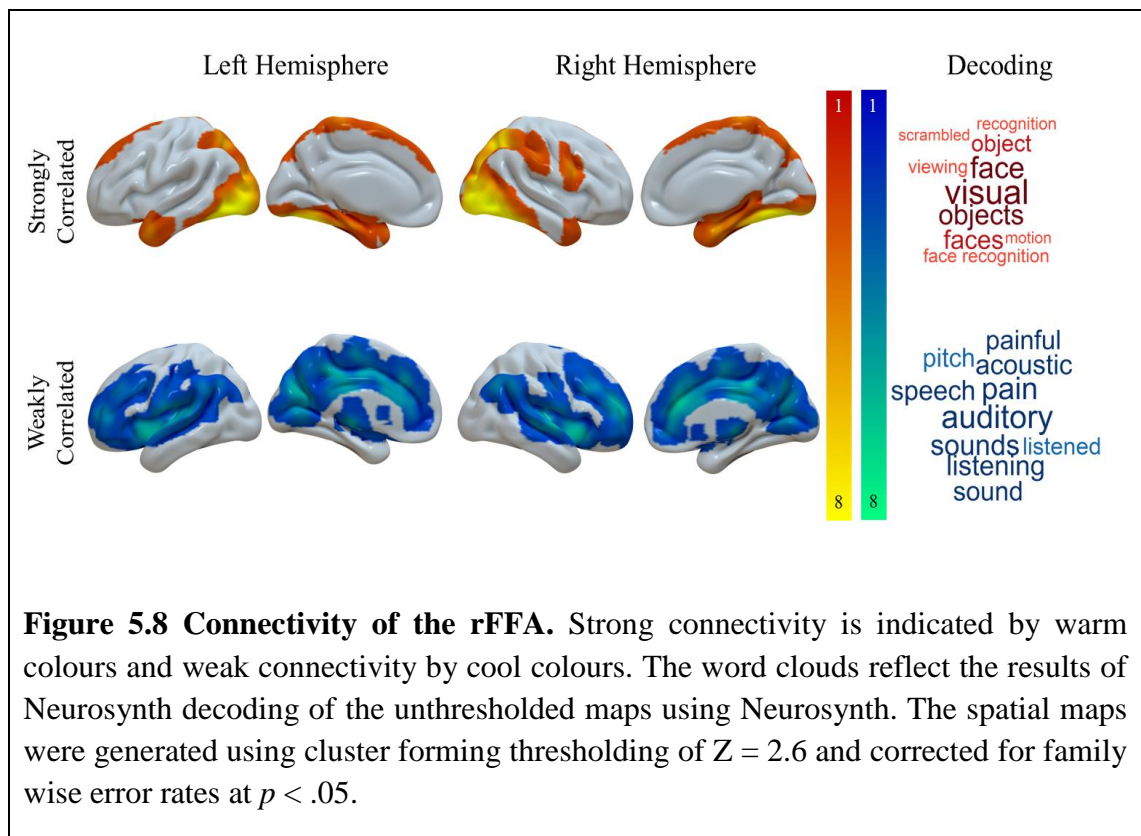
effects were observed related to the behavioural measures of learning or post-consolidation item memory.



5.4.2.2 ROI: Right Fusiform Face Area (rFFA)

5.4.2.2.1 Connectivity and Meta-Analytic Decoding

Figure 5.8 presents maps showing functional connectivity patterns with the rFFA seed. The rFFA was strongly connected to medial occipital cortex and inferior and medial temporal regions (indicated by warm colours). Neurosynth decoding of the unthresholded map produced terms related to vision, faces, objects and recognition. The rFFA showed relatively weaker connectivity with the left cingulum, superior temporal cortices, medial frontal regions, the right angular gyrus and bilateral thalamus (cool colours). Terms related to sound perception and pain were produced by Neurosynth decoding of the unthresholded connectivity map (see Figure 5.8).



5.4.2.2.2 *rFFA Variation in Connectivity and Task Performance*

To investigate individual differences in memory and rFFA connectivity, scores of learning, item memory and generalisation performance were included as explanatory variables in a regression analysis, with rFFA connectivity as the dependent variable. This regression model produced a significant result that also related to our behavioural measure of generalisation, and highlights a cluster in the right angular gyrus (see Figure 5.9 and Table 5.4). Neurosynth decoding of this cluster produced terms such as autobiographical, default network and episodic, emphasising its role in memory processing (see Figure 5.9). Relatively weaker connectivity between the rFFA and this region of angular gyrus was associated with greater generalisation performance. Like the previous result, this finding suggests that behavioural generalisation performance benefitted from greater decoupling between heteromodal regions linked to memory (i.e. the angular gyrus) and activity in sensory-motor regions (e.g. visual cortex). No significant effects were observed related to the behavioural measures of learning or post-consolidation item memory.

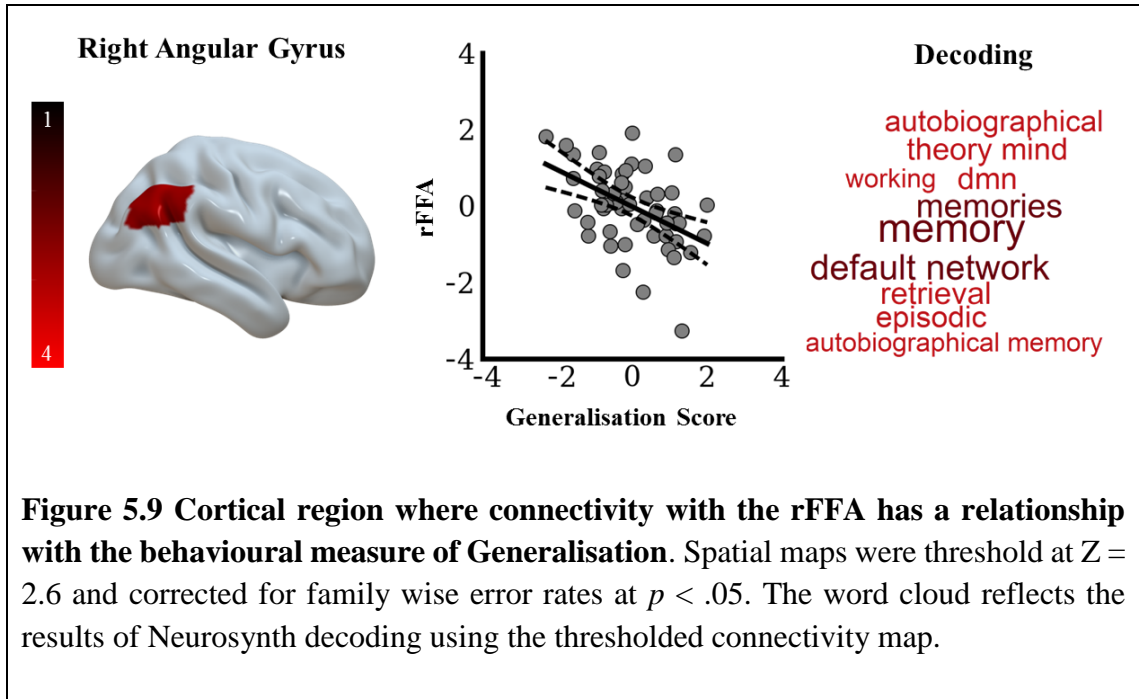


Table 5.4 Cluster of activity that showed connectivity to the rFFA and a relationship with the behavioural measure of Generalisation.

ROI: rFFA							
Hem	Connectivity	Z	X	Y	Z	Total Voxels	<i>p</i>
	rFFA & Generalisation Score					426	.025
R	Angular Gyrus	4.05	52	-60	46		
R	Angular Gyrus	3.91	54	-66	36		
R	Angular Gyrus	3.80	52	-70	34		
R	Inferior Parietal Lobule	3.72	58	-56	42		
R	Angular Gyrus	3.69	54	-64	40		
R	Inferior Parietal Lobule	3.08	58	-48	46		

5.5 Discussion

This study characterised individual differences in the intrinsic connectivity of the hippocampus and fusiform cortex and linked these patterns to behavioural measures of

learning, post-consolidation item memory and generalisation. Our results are consistent with the view that decoupling between heteromodal and sensory-motor regions of cortex is implicated in long-term memory processing. More specifically, we found this pattern of intrinsic connectivity to predict better memory generalisation, a measure that required the extraction of shared structure from across multiple associative representations and was therefore related to the development of concept-based representations. Both of the significant clusters identified in our analysis fit this pattern: generalisation was better in participants who showed weaker connectivity between a region of medial motor cortex and anterior relative to posterior hippocampus, and when there was weaker connectivity between the rFFA and angular gyrus. These results therefore highlight patterns of connectivity during rest, which may facilitate the capacity to extract concept-based memory representations from individual learning episodes.

Both the hippocampus and angular gyrus have been shown to support memory processing and are believed to integrate different elements of experience into holistic memory representations (Horner et al., 2015; Margulies et al., 2016; Seghier, 2013). The hippocampus is a key candidate for associative learning (Backus et al., 2016; Horner et al., 2015; Staresina et al., 2016) and previous studies have suggested a functional specialisation along the anterior-posterior axis (Poppenk et al., 2013; Sheldon et al., 2016; Sormaz et al., 2017; Strange et al., 2014). Posterior regions have been implicated in fine-grained ‘local’ and perceptual processing (Doeller, King & Burgess, 2008; Hassabis et al., 2009; Poppenk et al., 2013; Bird & Burgess, 2008; Hübner et al., 2011; Shipman & Astur, 2008), while anterior regions have previously shown strong connectivity to ventromedial prefrontal cortex and anterior temporal lobe regions involved in semantic memory and ‘global’ or gist processing (Jefferies, 2013; Patterson, Nestor, & Rogers, 2007; Sheldon et al., 2016; Sormaz et al., 2017; Poppenk et al., 2013). The relationship between anterior hippocampal connectivity, and the behavioural measure specifically of generalisation in this study, fits well with the suggestion of gist-based regularity processing in the anterior hippocampus.

The angular gyrus is also a multimodal association area or ‘convergence zone’, and has been implicated in a wide range of higher-order cognitive functions, e.g. numerical cognition, theory of mind, conflict resolution, autobiographical memory retrieval and semantic processing (for a review see Humphreys & Lambon Ralph, 2015 and Seghier,

2013). It is located at the junction between occipital, temporal and parietal lobes and is therefore well-suited for memory integration (Tomasi & Volkow, 2011). In terms of conceptual memory processing, the angular gyrus has been linked to the online retrieval of semantic information across modalities (Binder & Desai, 2011; Binder et al., 2009; Davey et al., 2015; Fernandino et al., 2016; van der Linden et al., 2017), with neuroimaging evidence showing greater activity during the retrieval of multimodal versus unimodal experiences (Bonnici et al., 2016; Yazar, Bergström & Simons, 2017). The convergence of task-related activity in the angular gyrus has also been observed in the weather prediction task, in which participants were required to make predictions about novel stimuli on the basis of feature combinations (Wagner et al., 2015). Interestingly, Wagner et al. (2015) only found significant angular gyrus activity after a 24-hour delay (and not when tested immediately); suggesting that feature integration in this region may be supported by offline memory consolidation.

An integrative role for the angular gyrus was also observed during online memory retrieval in a variation of the face-location paradigm used in the current study (Sweegers et al., 2014). Greater connectivity between the FFA and angular gyrus was observed specifically for the retrieval of trials in which screen location was predicted by regularities related to facial features (when compared to non-regularity trials). Like the result reported by Wagner et al. (2015), this effect was only observed for items trained 24-hours before testing. In conjunction with the current data, this pattern of angular gyrus activity therefore suggests that conceptual memory performance may be related to: i) the ability to decouple connectivity between heteromodal and perceptual regions of cortex during offline memory processing, and ii) the ability to re-couple these regions when perceptual details are task-relevant. Assessing online and offline connectivity in the same participants within a single study would be a natural extension to the current study, and add strength to this suggestion.

Both the hippocampus and angular gyrus share strong links with the DMN (Margulies et al., 2016). This network is thought to support memory retrieval and cognitive states which are largely independent of the current environment, and therefore requires attention to be directed away from the external world, i.e. perceptual decoupling during mind-wandering (Smallwood et al., 2013; Binder et al., 2009; Spreng et al., 2014; Spreng, Mar & Kim, 2009; Engen, Kanske & Singer, 2016; Rugg & Vilberg, 2013).

Heteromodal regions of the DMN show maximal distance from sensory and motor cortices in the brain, both in terms of their patterns of connectivity and in their position along the cortical surface (Margulies et al., 2016), suggesting that they are ideal candidates for perceptually-decoupled and internally-driven cognition. This suggestion is consistent with our findings, in which long-term memory generalisation can be predicted from the level of decoupling between heteromodal regions of the DMN (i.e. the hippocampus and angular gyrus) and sensory-motor regions during rest.

Similar results are reported by Sneve et al. (2017), who provide evidence to suggest that long-term memory performance is related to processing within the DMN and perceptual decoupling during rest. Sneve et al. (2017) found perceptual decoupling to be related to individual differences in paired-associate item memory. This contrasts with the findings from the current study somewhat, as we did not observe a relationship between perceptual decoupling and our measure of post-consolidation item-memory, instead we found a specific relationship with memory generalisation. Although these results appear inconsistent, Sneve et al. (2017) did not use a typical paired-associate memory paradigm; instead participants were asked to make semantic judgements regarding everyday objects, such as “Can you eat it?”. In the later test of memory, participants were required to remember the associated question for a given object and were therefore retrieving an association that related to pre-existing semantic knowledge. As a result, in their task it is therefore difficult to dissociate arbitrary object-question associations from the influence of semantics. The current study separated these effects and found perceptual decoupling to specifically benefit the conceptual components of memory. Conceptual representations require information integration across multiple features and episodes (Patterson, Nestor, & Rogers, 2007; Lambon Ralph et al., 2017). Reducing the level of perceptual input may limit the level of item-specific detail in each memory representation, which in turn may facilitate the extraction of shared regularities across experiences. Future research investigating the relationship between memory integration and perceptual decoupling is required to explore this idea.

In this study, we did not observe a significant relationship between intrinsic connectivity during rest and our behavioural measure of learning. This is somewhat intriguing given that previous studies have shown hippocampal connectivity patterns to predict memory performance in other memory tasks (e.g. topographical memory and

semantic memory; Sheldon et al., 2016; Sormaz et al., 2017). However, it should be noted that Sormaz et al. (2017) did not observe a relationship between differential hippocampal connectivity and performance using a word paired-associate paradigm, which arguably draws the closest parallels to the task used in the current study. One possible explanation may relate to the overall sensitivity of the measure, with paired-associate recall offering a relatively coarse measure of memory performance in comparison to ‘relatedness judgement’ and ‘category fluency’ tasks (Sheldon et al., 2016; Sormaz et al., 2017). Further investigation into factors such as memory sensitivity will be important to clearly determine the relationship between intrinsic connectivity and individual differences in behaviour.

The primary advantage of seed-based correlational analyses is that it is a direct approach, which shows the network regions that are most strongly connected with a seed region or ROI, providing a relatively straightforward and interpretable result (Cole et al., 2010). This technique does however impose anatomical restrictions on the measurement of network connectivity and may under-represent the data. Fundamentally, there are as many possible ‘networks’ to be derived as there are possible seeds and therefore interpreting any single connectivity pattern as distinct may be over-simplistic (Cole et al., 2010). It will be important in future work to complement the findings from this study with larger samples which would allow whole-brain connectivity patterns and their relationship with behaviour to be assessed. Furthermore, supporting these connectivity-based analyses with task-based fMRI data would reinforce the relationship between brain connectivity and behaviour. A possible extension of the current study would be to include task-based fMRI before and following opportunities for consolidation, allowing patterns of brain connectivity to be related to changes in task-relevant brain activity over time. Such an approach would allow firmer conclusions to be made regarding the relationship between network connectivity in the brain and behaviour.

This study used seed-based analyses to investigate individual differences in the functional connectivity of the hippocampus and rFFA (Buckner et al., 2013; Cole, Stephen, & Christian, 2010); consequently, we cannot exclude the possibility that differences in other brain regions would also be related to memory performance in our task. Nevertheless, the two significant results that we observed are consistent and fit a general pattern in which decoupling of heteromodal regions allied to the DMN, with

sensory/motor cortex, supports the generalisation of experience and the formation of concepts.

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CHAPTER 6

GENERAL DISCUSSION

This thesis investigated the impact of offline consolidation on conceptual memory representations. Research has shown that memories benefit from periods of offline consolidation, with mechanisms during sleep driving consolidation-related improvements in memory performance (Rasch & Born, 2013). However, in this thesis we provide evidence to suggest that not all memory representations benefit equally from these offline processes, with concept-based representations showing no immediate benefit following time for consolidation (Chapter 2 and Chapter 4) or a delayed benefit from offline consolidation during sleep which occurred only in conjunction with further post-consolidation training (Chapter 3). Using dual-session behavioural memory paradigms across a number of delay conditions, polysomnography (PSG) and resting state functional connectivity analyses, the work in this thesis has extended current understanding for the role of offline consolidation in the development of conceptual memory representations and raised important questions for future work. This discussion considers the representation of concept-based memories and integrates the work from this thesis with current models of semantic memory. It then goes on to examine the role of offline consolidation in the development of these conceptual memory representations and the extent to which the findings from this thesis fit with current models of memory consolidation, highlighting key issues that have yet to be addressed by the literature.

Finally, methodological considerations for further investigation into conceptual memory and consolidation are discussed along with directions for future research in this area.

6.1 Summary of Findings

In Chapter 2 of this thesis we aimed to investigate the formation of abstract cross-modal conceptual memory representations using an information-integration categorisation task (Ashby & Gott, 1988; Ashby & Valentin, 2005). This task required participants to integrate auditory and visual information into category exemplars and abstract statistical regularities regarding the underlying category structure. To assess the impact of offline consolidation on the development of these representations we compared memory performance across a short 15-minute and a long 24-hour consolidation delay. The results from Chapter 2 showed that participants were able to successfully integrate cross-modal perceptual information into coherent representations and acquire knowledge of the abstract cross-modal category structure. Unlike previous studies (Djonlagic et al., 2009; Hennies et al., 2014), we did not observe a 24-hour consolidation benefit on memory when performance was measured using the category training task. However, when memory was assessed in a speeded variation of the categorisation paradigm, a 24-hour benefit was observed. The speeded categorisation paradigm arguably placed greater demands on automatic implicit memory mechanisms, and therefore the results support previous studies that also report consolidation-related benefits for memory integration in more ‘implicit’ paradigms (Durrant et al., 2011; Ellenbogen et al., 2007; Hennies et al., 2014). The results from Chapter 2 support the suggestion that offline consolidation may play a role in processes of cross-modal integration and regularity extraction.

In Chapter 3 we explored the different contributions from periods of sleep and wakefulness in the development of these abstract cross-modal category representations. Initially we carried out two 12-hour delay comparisons that spanned either an evening of sleep or daytime wakefulness. We then went on to run a 15-minute control comparison and a 12-hour sleep group in which sleep was measured using PSG. This allowed us to investigate the relationship between sleep-associated behavioural benefits in memory and specific features of sleep. We developed the testing paradigm used in Chapter 2 in order to dissociate the impact of offline consolidation from post-consolidation learning and any effects that may be related to re-exposure to task stimuli. To do this, we introduced a test

of category knowledge that was carried out in the absence of feedback immediately before and after the consolidation delay. Participants were then provided with further category training and a final categorisation test at the end of the second session.

The results from Chapter 3 show sleep-associated consolidation benefits in cross-modal category knowledge; this was not however observed immediately following the consolidation delay, but seen after post-consolidation learning in session two. The results therefore suggest that processes of consolidation during sleep facilitated the integration of new information into memory stores. This finding is in line with the CLS account of consolidation (McClelland et al., 1995), which suggests that new information will be assimilated into memory at a quicker rate if it is consistent with pre-existing knowledge. Paired-associate memory was also assessed in this study and in line with previous literature, sleep-associated benefits were observed. In addition, this memory benefit correlated with the percentage of time spent in NREM sleep, suggesting a role for sleep in the memory effect (although it should be noted that this correlation did not survive stringent Bonferroni correction rates). We did not observe any correlations between behavioural performance in the categorisation task and features of sleep; the specificity of the observed behavioural benefit from sleep is therefore unclear. The findings in Chapter 3 suggest that the benefit of sleep on memory is not unitary when individual declarative item-based memories and concept-based memories are assessed. In line with previous literature (Diekelmann, Wilhelm & Born, 2009; Plihal & Born, 1997; Rasch & Born, 2013; Tucker et al., 2006) we observed sleep-associated benefits in associative declarative memory; however the benefit of sleep on the cross-modal concept-based representations emerged only following further training on the categorisation task.

To further investigate the differing impact of sleep on item-level associative memories and concept-based representations, in Chapter 4 of this thesis we introduced a face-location associative memory task (adapted from Sweegers et al., 2014), in which regularity structures could be extracted from individual associative representations. This allowed item- and concept-based knowledge to be measured within the same testing paradigm. The separate contribution of sleep and wake on memory was assessed, as well as the impact of post-consolidation learning. As real-world conceptual representations do not develop in isolation, but across many memory episodes and in different contextual situations, we also introduced a predictive context manipulation in this task. This was

included to capture co-occurring features of the environment that are typically present during memory encoding, and to assess how these influence both learning and processes of consolidation.

As in previous chapters, in Chapter 4 we found a differential effect of sleep on item- and concept-based representations. We found sleep-associated benefits for individual associative representations; however in tests of concept-based knowledge, which required the classification of novel stimuli that had not been trained but followed the same underlying category structure, we did not observe any sleep-associated changes in performance. For these concept-based representations, sleep benefits were also not observed following further training on the task, suggesting that the sleep-associated post-consolidation training benefits observed in Chapter 3 did not extend to this associative memory paradigm. The differential impact of sleep-associated consolidation on item- and concept-based memory representations fits with predictions set out by Mirkovic & Gaskell (2016), who extended the CLS account of consolidation to suggest that the benefit of sleep may be related to the dependence of memory representations on hippocampal and neocortical memory systems. Our results are in line with their suggestion of a prioritisation process during sleep, whereby elements of a memory that depend strongly upon the hippocampus (i.e. item-level specifics) are preferentially consolidated and show stronger benefits from sleep in comparison to the shared structure extracted from across memory representations (i.e. shared regularities).

The aim of Chapter 5 was to investigate intrinsic brain connectivity during rest and assess its relationship to individual differences in item- and concept-based behavioural performance in the memory paradigm used in Chapter 4. In this analysis, we focused upon differential connectivity between the anterior and posterior hippocampus and connectivity with the right fusiform face area (rFFA). The hippocampus is strongly implicated in the processing of associative representations; however, functional specialisations along the posterior-anterior axis of the hippocampus suggest that the anterior regions may be particularly well suited for processing gist-like memory representations, important for conceptual memory processing, while posterior regions may be better suited to finer grained associations at the item-level (Poppenk et al., 2013; Sheldon et al., 2016; Sormaz et al., 2017). The rFFA is strongly implicated in face processing and was therefore behaviourally relevant as a task-specific region of interest.

The findings from Chapter 5 suggest that the processing of concept-based representations is facilitated by perceptual decoupling during rest between heteromodal regions of cortex related to the default mode network (DMN; i.e. anterior hippocampus and angular gyrus) and sensory-motor regions of cortex. These results are in line with the suggestion that concept-based memories are processed within modality convergence zones, with the anterior hippocampus and angular gyrus highlighted as important regions for memory integration and generalisation. Furthermore, these results highlight a functional role for the DMN in conceptual memory development, which may have important implications for future investigations into the role of quiet wake in memory processing.

6.2 Processing Conceptual Representations in the Brain

Real-world conceptual and semantic memories are incredibly complex and require the integration of information from across all modalities to provide knowledge structures that represent our experiences (Patterson, Nestor & Rogers, 2007). The information-integration categorisation task used in Chapters 2 and 3 of this thesis allowed two important aspects of conceptual memories to be assessed; i) the integration of cross-modal representations and ii) the abstraction of statistical regularities to form category structures. The demands of this task closely align with the hub-and-spoke framework of semantic memory, which suggests that the formation of modality-invariant multi-dimensional representations results from interactions between a transmodal hub located in the anterior temporal lobes (ATLs) and modality-specific spokes (Lambon Ralph, 2013; Pobric, Jefferies & Lambon Ralph, 2010; Lambon Ralph et al., 2017). The hub is thought to integrate information from the modality-specific representations in order to extract statistical relationships between and across memories (Lambon Ralph et al., 2017). As such, the transmodal hub may play an important role in the integration of visual and auditory dimensions used in the categorisation task. We do not have data to directly support the link between our categorisation task and the hub-and-spoke model (e.g. neuropsychological or neuroimaging evidence); however the task draws parallels with a similar conceptual memory task that does implicate the ATLs in conceptual memory processing (Hoffman, Evans & Lambon Ralph, 2014).

Hoffman, Evans & Lambon Ralph (2014) studied the acquisition of new concepts in semantic dementia patients who have cortical damage centered on the ATLS. Their task involved the assignment of abstract visual stimuli to one of two categories, where the stimuli conformed to a family resemblance structure. Like in our categorisation task, this underlying structure was not present in any individual stimulus and therefore knowledge of it required the extraction of features from across multiple category exemplars. Hoffman et al. (2014) found that semantic dementia patients were unable to integrate information from across exemplars and instead relied heavily upon individual features to make their category judgements. Their data therefore suggests that the integration of distinct memory features into coherent concepts requires input from the ATLS, highlighting a central role for this region in the development of conceptual memory representations and supporting the hub-and spoke model of semantic memory.

The cross-modal categorisation task used in this thesis would provide an opportunity to extend the finding from Hoffman et al. (2014) to investigate the interaction between cross-modal memory integration and modality-specific representations in the brain. In particular, this task would allow the hub-and-spoke model (Patterson et al., 2007; Lambon Ralph et al., 2017) to be assessed and contrasted with ‘embodied’ accounts of semantics, which suggest that knowledge is grounded within sensory and motor regions of the brain (Binder & Desai, 2011; Martin, 2007; Pulvermüller, Shtyrov & Ilmoniemi, 2005). Advances in neuroimaging, e.g. distortion corrected functional magnetic imaging (Binney et al., 2010) and analysis techniques, e.g. multivariate pattern analysis (MVPA, Haxby, 2012), would allow the emergence of integrated representations to be measured, and the dependency between the integrated and modality-specific representations to be assessed. The categorisation paradigm, although very abstract and simplistic, provides a unique opportunity to study the development of conceptual representations over time, where initial memory encoding and subsequent memory exposure can be experimentally manipulated and controlled. In combination with neuroimaging techniques, these tasks have the potential to offer a great deal of insight into the processes responsible for the development of integrated concept-based representations in the brain.

The hub-and-spoke model places a strong emphasis upon the ATLS as a transmodal ‘hub’ of semantics, however other regions of cortex show similar heteromodal processing capacities and these regions may also play a role in processing conceptual knowledge

(Binder & Desai, 2011; Lambon Ralph et al., 2017). In Chapter 5 of this thesis we found evidence to suggest a role for the anterior hippocampus and angular gyrus in the generalisation of associative regularities. Both of these regions have been implicated in memory integration (Backus et al., 2016; Horner et al., 2015; Staresina et al., 2016; Binder & Desai, 2011; Binder et al., 2009; Fernandino et al., 2016; van der Linden et al., 2017) and the associative memory task used in this thesis may play to their processing strengths. The hippocampus is a key candidate for processing associative information, with evidence to suggest that it is able to acquire and maintain associative memories by integrating distinct perceptual inputs into holistic representations (Horner et al., 2015; Azab, Stark & Stark, 2014; Chadwick et al., 2010; LaRocque et al., 2013; Moita et al., 2003; Shohamy & Wagner, 2008; Wood, Dudchenko & Eichenbaum, 1999). Similarly, neuroimaging data from healthy adults and data from patients with neurodegenerative disease implicate the angular gyrus in the combinatorial aspects of semantics (Price et al., 2016; Lambon Ralph et al., 2017; Binder & Desai, 2011). In line with this previous literature, the results from Chapter 5 suggest that the anterior hippocampus and angular gyrus may play a key role in the integrative and combinatorial aspect of conceptual memory processing. Our data therefore provides support for ‘convergence zones’ in the brain and a role for these regions in conceptual memory processing.

By having a set of rigid category rules, however, the associative memory task may not have captured the more flexible nature of real-world concepts. For example, the concept of ‘birds’ needs to be particularly flexible for successful integration of knowledge about ‘penguins’ which do not fly or have typical bird-like features such as feathers. The associative memory task could be easily adapted to study this more flexible nature of real-world conceptual knowledge by including irregular instances of category membership, i.e. presenting face-location associations that do not conform to the ‘rule’ structure. It would then be possible to obtain a measure of concept flexibility by assessing over- and under-generalisations, allowing the impact of this irregular category information to be assessed. Understanding the interplay between feature integration, regularity extraction and concept flexibility will be extremely important for understanding the representation of complex conceptual knowledge and the processes that contribute to their development.

6.3 The Role of Memory Consolidation in Conceptual Memory Development

The main aim of this thesis was to assess the role of offline consolidation on the development of conceptual memory representations. We have presented findings from three studies that directly address this question, and provide consistent results showing that, unlike associative representations, concept-based memories do not show immediate behavioural sleep-associated consolidation benefits. In the following sections we discuss the role sleep may play in memory processing. We then discuss how individual associative memories and concept-based representations may be differentially influenced by offline consolidation. We use the CLS model to highlight key issues that have yet to be addressed in order to provide a full explanation for the role of consolidation in the development of both item and concept-based long-term memory representations.

6.3.1 Sleep-Associated Consolidation

The standard model of systems-level consolidation proposes that new memories depend upon the hippocampus to bind individual modality-specific memory features across the neocortex into an integrated and coherent memory representation. Over time and with covert reactivation of hippocampal-neocortical connections, there is believed to be a progressive strengthening of connectivity between the cortical modules and a concurrent reduction in dependence on the hippocampus. As a result, memories become integrated within long-term memory stores and this has two complementary benefits for memory; the hippocampus maintains its encoding capacity ready for future learning, while the gradual integration of knowledge into long-term stores reduces the risk of catastrophic interference and memory ‘overwriting’ (Frankland & Bontempi, 2005). The Active Systems Consolidation (ASC) model extends this view to propose that the redistribution of memories is driven specifically by slow oscillations, sharp-wave ripples and sleep spindles occurring during NREM sleep (Frankland & Bontempi, 2005; Walker, 2009).

In this thesis, we provide two examples of sleep-associated consolidation benefits on memory; these were demonstrated in the paired-associate task in Chapter 3 and for individual trained associative representations in Chapter 4. In line with a specific role for

processes during NREM sleep, in Chapter 3 we found the paired-associate memory benefit to correlate with the amount of time participants spent in NREM sleep (although this correlation did not survive stringent Bonferroni correction rates). We were therefore able to replicate the typical sleep-associated benefits that have been previously reported within the consolidation literature, which allowed us to make comparisons between these typical effects, and the impact of offline consolidation during sleep on the development of conceptual memory representations.

Unlike these declarative item-level associative representations, we did not find any post-consolidation benefits of sleep on concept-based knowledge immediately after the delay in the experiments presented in this thesis. This pattern of results suggests that the impact of sleep on memory is not unitary across all memory types, but may be selective. Indeed, the idea of selective sleep-associated consolidation mechanisms is not new, for instance sleep-associated consolidation has shown to be greater for: explicit compared to implicit trained skills (Fischer et al., 2006; 2002; Song, Howard & Howard, 2007; Walker et al., 2003), emotional compared to neutral material (Bennion, Payne & Kensinger, 2015; Cairney et al., 2014; Hu, Stylos-Allan & Walker, 2006; Payne et al., 2009); memories that have relevance for the future (Baran, Daniels & Spencer, 2013; van Dongen et al., 2012; Wilhelm et al., 2011) and memories that fall within an optimal level of encoding strength i.e. when encoding strength is neither too high nor too low (Stickgold, 2009). The finding that sleep does not show a behavioural benefit for concept-based representations is however particularly intriguing, given that concept-based representations are derived from individual experiences.

6.3.2 The CLS Model of Consolidation

The CLS theory extends the standard model of consolidation and suggests that the hippocampus and neocortex play distinct roles in representing memories (McClelland et al., 1995). These separate roles solve a trade-off between remembering specific experiences (e.g. where you left your keys), which benefit from separate representations for each event, and the extraction of regularities across experiences (e.g. where you would typically expect to find your keys), which benefit from overlapping memory representations. It is the cross-talk between these two systems during offline periods that is hypothesised to facilitate consolidation (McClelland et al., 1995). Importantly, the CLS

proposes that the two systems interact through ‘interleaved memory reactivation’, and this may facilitate both the consolidation of specific events and the abstraction of shared structure from across experiences. In the following sections we will discuss the extent to which our findings support the CLS model and highlight existing questions that remain to be addressed.

6.3.2.1 When Does Interleaved Memory Reactivation Happen?

The CLS model suggests that new knowledge is gradually integrated into neocortical memory systems during offline periods and that this is initiated by memory reactivation in the hippocampus (Kumaran et al., 2016). Hippocampal replay is thought to be an important process of offline consolidation during sleep, with evidence to suggest that specific features of sleep play an active role in instigating reactivation events e.g. sharp-wave ripples (Molle, 2006; Ramadan, Eschenko & Sara, 2009; Rasch & Born, 2013; Roux et al., 2017). Memory replay during sleep has been closely tied to behavioural memory benefits within the declarative domain and causal evidence for the role of replay in consolidation has been provided by techniques such as targeted memory reactivation (TMR), whereby auditory induced reactivations have been shown to selectively benefit individual memory representations (Rasch et al., 2007; Rudoy et al., 2009; Oudiette & Paller, 2013; Batterink & Paller, 2017; Cairney et al., 2014; 2016; Cousins et al., 2014; Creery et al., 2015; Fuentemilla et al., 2013; Lehmann et al., 2016; Oyarzún et al., 2017; Schouten et al., 2017; Schreiner & Rasch, 2017, 2015; Tamminen, Lambon Ralph & Lewis, 2017; van Dongen et al., 2012).

However, the CLS does not suggest that consolidation-related replay is specific to sleep, and therefore replay events during other offline periods, for instance during quiet wake, may also contribute to the consolidation of new memories (Mednick et al., 2011). The results from Chapter 5 of this thesis suggest that quiet wake may provide conditions suitable for consolidation by decoupling attention from perceptual input and allowing processing to be driven internally within the Default Mode Network (DMN). During this state, spontaneous and internally driven memory retrieval may act to replay new and existing memories, facilitating the process of interleaved memory replay as proposed by the CLS. We did not behaviourally examine the impact of quiet wake on memory performance in the experiments carried out in this thesis, however previous literature does suggest that quiet wake, in comparison to active wake, facilitates long-term memory

stabilisation (Craig et al., 2015; 2016; Dewar et al., 2012; 2014). A causal role for memory replay in wake has been provided by Oudiette et al. (2013) who were able to selectively improve memory performance by cueing memories using TMR during wake. Interestingly, in their paradigm, cueing was not carried out during quiet wake, as they did not want participants to be explicitly aware of the cued material which may lead to active memory rehearsal. Instead they replayed the cues while participants completed a challenging working memory task. Their findings therefore support the suggestion that diverting perceptual encoding demands away from long-term memory systems during wake, may allow processes of consolidation to take place.

The CLS model also suggests that for consolidation to happen without causing interference with pre-existing knowledge, new material should be replayed and interleaved with existing known representations, allowing new memories to gradually influence neocortical connection weights (Kumaran & McClelland, 2012; McClelland et al., 1995). Offline periods may provide optimal conditions for interleaved memory reactivation as memory retrieval of known information can be accessed without online encoding demands. However, this type of memory reactivation may also be achieved during online memory encoding given the correct circumstances. For example, in both the paradigms used in this thesis, participants were presented with large numbers of category exemplars, followed by explicit category feedback in an interleaved fashion i.e. category exemplars were randomly intermixed. This created a circumstance in which perceptual input could drive a large number of reactivation events, which may facilitate online consolidation processes, allowing the shared structure from among the exemplars to be extracted by neocortical learning systems without the need for offline consolidation.

Assessing memory generalisation immediately after training would allow the amount of concept-based learning that had occurred during training to be assessed in these paradigms. This measurement was purposefully avoided in the studies reported in this thesis as we wanted to avoid drawing attention to this aspect of the testing paradigm which may have subsequently influenced processes of offline consolidation (Baran, Daniels & Spencer, 2013; van Dongen et al., 2012; Wilhelm et al., 2011). This however would be an important point to address in the future and may provide strong evidence to suggest that online regularity extraction is possible, given that the circumstances during encoding permit interleaved replay of category exemplars.

The extent to which this type of online consolidation may happen within the real-world is questionable given that the typical presentation of category exemplars is much slower, with the number of exemplars gradually increasing over time. For example, the development of a ‘dog’ concept may be initially derived from pictures of dogs in books and a small number of family pets, encountering a large variety of dogs will be a slow and gradual process. Although further evidence for online memory consolidation is required, an interesting consideration for future work would be to assess whether there are different behavioural consequences of consolidation in these two states (i.e. online and offline). One potential difference may be the flexibility of the representation; offline memory replay may provide access to all previous exemplars of a concept, resulting in reactivation with a large number of experiences and therefore the development of highly flexible conceptual representations. In contrast, online consolidation may be much more rigid with goal-directed or perceptually-directed replay, which results in a concept structure that is restrained by input. It could be imagined that in a behaviourally relevant situation, the quick extraction of a rigid representation may outweigh the benefits of a more flexible representation that could be developed over time e.g. learning to avoid quicksand on a beach. These ideas are speculative; however, identifying whether there are different behavioural consequences of online and offline consolidation would increase our current understanding of the role of consolidation in the development of conceptual representations.

6.3.2.2 Which Memories are selected for Reactivation?

Memory replay may happen across a number of states; however, it is not known whether all memories undergo reactivation, or if there is a ‘selection’ process. There is evidence to suggest that sleep-associated memory replay may be biased towards rewarding events (Bendor & Wilson, 2012), suggesting a prioritisation process for the consolidation of information that is of future relevance. A prioritisation process that takes into account the specific goals of the individual would be particularly adaptive, and there are a number of factors which may influence the significance of individual experiences, e.g. reward (Breton & Robertson, 2014; Diekelmann, Wilhelm & Born, 2009; Oudiette et al., 2013) or emotion (Cairney et al., 2014; Hu, Stylos-Allan & Walker, 2006). The results from Chapter 4 also suggest that consolidation mechanisms during sleep may be

selective; however, this selectivity may depend upon the system that the memory is more strongly reliant upon, rather than the content of the representation.

The findings from Chapter 4 suggest that sleep may benefit individual associative representations, but not concept-based knowledge. This result was interpreted in line with the predictions set out by Mirkovic & Gaskell (2016) who extended the CLS account to suggest that aspects of a memory representation that rely strongly on the hippocampus (i.e. item-level specific details) may be prioritized for consolidation, over aspects that have support from the neocortex (i.e. shared regularity structure). In Chapter 4, we discussed the idea that behavioural benefits from offline consolidation may emerge for concept-based regularity knowledge, however only following sufficient integration of new information. We related this idea to the information overlap to abstract (iOTA) hypothesis proposed by Lewis and Durrant (2011), which suggests that concept-based regularity knowledge may benefit from the gradual strengthening of shared overlapping representations as a result of sleep-associated memory replay. This is proposed to happen in combination with other sleep-associated processes such as synaptic downscaling, which facilitates a global restoration of synaptic weight and acts to preserve the relative strength across representations and networks. By this account, memory replay during sleep may progressively strengthen the shared structure from across experiences, and these networks may subsequently maintain their relative strength in relation to non-shared information. Sleep-associated benefits for shared concept-based knowledge may therefore emerge over longer time-scales and be related to the amount of item-level integration.

Support for this idea is provided by Lutz et al. (2017) who used a visual Deese-Roediger-McDermott (DRM) paradigm to investigate the abstraction of gist. Like the result from Chapter 4, they found that compared to wake, sleep enhanced memory for single items following a 10-hour sleep delay, but did not influence measures of gist abstraction. When memory was assessed a year later, significant gist knowledge was observed, however this was only in participants who slept immediately after encoding. Lutz et al. (2017) suggest that sleep may strengthen episodic memories in the short-term, but facilitate long-term gist abstraction. It would be interesting across longer time-scales to assess whether sleep-associated benefits at the item-level lead to later concept-based benefits following sufficient memory integration.

One approach to assess the relationship between item- and concept-based knowledge with the mechanism of memory reactivation would be to externally manipulate reactivation during sleep and assess the subsequent impact on memory. Batterink & Paller (2017) have shown that reactivation of individual items during sleep, manipulated experimentally using TMR, improves grammatical generalisation, suggesting that item-level replay can lead to the abstraction of grammatical rules. However, in their study, Batterink & Paller (2017) only tested participants' grammar knowledge using novel phrases that had not been trained prior to sleep; they were therefore unable to assess the differential impact of reactivation on trained versus generalised knowledge. If an auditory component was introduced to the face-location associative task used in Chapter 4 of this thesis, this paradigm would lend itself well to assess the contribution of reactivation on item and concept-based knowledge via a TMR paradigm. Furthermore, it would allow the interplay between item and concept-based knowledge and the role of reactivation as a mechanism of consolidation to be explored.

6.3.2.3 Is there an Interaction between Sleep and Wake?

As previously discussed, an important aspect of real-world concepts is that they develop across multiple experiences and events that are separated in time. For example, you may develop a 'birthday party' concept (e.g. cake, balloons, games etc.) however the individual memories that contribute to this concept (i.e. birthday parties) may only occur a few times per year, leading to the very gradual integration of information over a long timescale. The impact of time between events therefore needs to be accounted for when understanding the development of concept-based representations in the long-term.

Originally, the CLS proposed that the assimilation of new information into the neocortex is a slow and gradual process (McClelland et al., 1995). However new simulations, which extend those originally reported, demonstrate that new information that is consistent with existing neocortical knowledge structures can be learned rapidly and without interference (McClelland, 2013). This has since been supported by a number of behavioural observations, the most influential presented by Tse et al. (2007). They showed that the development of neocortical schema representations for flavour-place associations in rats, developed gradually over time, in line with the idea of a slow learning neocortical system (McClelland et al., 1995). However, following the consolidation of these initial representations, new traces showed rapid assimilation and hippocampal-

independence after a single exposure, suggesting that the previously consolidated knowledge had accelerated memory integration. This provides evidence to suggest that the consolidation of information may accelerate the integration of new and consistent representations by shifting memory processing in favour of neocortical over hippocampal systems (McClelland, 2013).

In an attempt to capture this role for time in concept development and any potential schema-related benefits, we introduced post-consolidation training into the behavioural experiments in this thesis. Incorporating further training after the initial post-consolidation test is not typical within the consolidation literature, and therefore this manipulation offered an interesting insight into the interaction between consolidation and subsequent learning. In Chapter 3, our findings were consistent with a schema-related benefit and suggest that processes during sleep had facilitated memory consolidation and the development of category representations, which allowed new and consistent information to be assimilated into long-term memory networks at a quicker rate (McClelland et al., 1995; McClelland, 2013; Kumaran et al., 2016; Tse et al., 2007; van Kesteren et al., 2013). The impact of sleep-associated consolidation on category knowledge may therefore be qualitatively different to its impact on memories in the declarative domain.

The SLIMM (Schema-Linked Interaction between Medial prefrontal and Medial temporal regions) framework suggested by Van Kesteren et al. (2012) offers a mechanism to explain how prior knowledge may influence the encoding of new information. The model extends the standard two-stage model of system-level consolidation and introduces a third component – the medial prefrontal cortex (mPFC). The model proposes that the mPFC acts to detect congruency between new information and existing knowledge during encoding. If new information is congruent, the SLIMM model suggests that the mPFC inhibits activity in the hippocampus, and allows information to be directly assimilated into neocortical networks. This framework is therefore in line with our suggestion in the previous section, whereby certain circumstances during wake may facilitate online integration of information to the neocortex (online consolidation). The results from Chapter 3 expand on the SLIMM model to suggest that sleep-associated consolidation may support the mPFC congruency judgement by facilitating the development of concept-based representations. A relationship between offline consolidation during sleep

and mPFC activity during subsequent encoding would provide strong support for their combined role in the schema related memory consolidation benefit.

One limitation of the data presented in Chapter 3 is that there was only an association with sleep, with no evidence to suggest that specific features of sleep (e.g. sleep spindles) contributed to the schema effect, as would be predicted by the CLS if consolidation was driven by memory reactivation. Further research is required to address the causal role of sleep in the presented results; this could be achieved using PSG recordings of sleep in conjunction with sleep manipulation techniques such as TMR (Rasch et al., 2007; Rudoy et al., 2009). In addition, to truly determine whether this is a schema effect, whereby new and crucially ‘consistent’ information shows swifter neocortical assimilation, it would be important to assess the rate of integration for non-consistent and incongruent category information. This would be an important manipulation to add support to our interpretation of the data.

The results from Chapter 3 suggest that there is interplay between processes of consolidation during sleep and subsequent memory encoding and integration of new information. When considering the development of conceptual representations, it may therefore be insufficient to assess the role of wake- and sleep-associated processes as separate entities, and important instead to consider them as a cycle of events, whereby processes during one state (e.g. consolidation during sleep) may facilitate processes in the other (e.g. new encoding and integration during wake). Investigating the impact of wake and sleep cycles on concept-based representations over longer time-scales e.g. multiple days and weeks, would be an interesting extension to the studies presented in this thesis and would further extend our current understanding of the interplay between these states.

6.3.2.4 What Information Contributes to Concept Knowledge?

In Chapter 4, we wanted to capture the more complex nature of conceptual memories by assessing the impact of co-occurring information that was predictive of category knowledge but did not contribute to the concept directly i.e. it was not diagnostic of category membership. To do this, each category exemplar was presented with a context cue that was either predictive or non-predictive of category membership. We found greater memory for category items presented with predictive contextual cues; however, this was specific to the delay group containing wake and not sleep. Unfortunately, it is

not clear if this is a wake-associated consolidation benefit, or if this effect is driven by pre-delay performance, in which the wake group (and not the sleep group) also showed a benefit for items with predictive information. One possible interpretation of the learning-related benefit observed for the predictive items may be linked to prediction-based learning. In the predictive condition, context cues increased the amount of information that could be used to derive predictions for the correct category response. Greve et al. (2017) provide data to suggest that prediction error i.e. the degree of conflict between predictions and feedback, can drive declarative learning, and therefore this may have also influenced learning in our task. It is not however clear why this would be observed only in the wake group. This may be explained by time-of-day effects (discussed in more detail below) however further investigation is required to determine the cause of this group difference.

The idea that context cues may support prediction-based learning does however highlight the fact that the nature of the concept developed may be driven by learning strategy. In the studies presented in this thesis we did not actively manipulate the learning strategy employed by participants, i.e. they were informed that category membership could be determined by rules, but they were not instructed to try to derive the rules in a particular way. Although this may reflect the varied nature in which information is encoded in the real-world, strategy-related differences may account for individual variation in our data. Assessing the type of strategies employed by participants would be an important area of future work, allowing a clearer understanding of the type of processes involved in concept learning and development. Furthermore, assessing the impact of informed versus non-informed knowledge of potential rules and/or underlying structure may also prove to be important. For instance, it may be the case that informing participants of category rules in our studies promoted ‘rule-finding’, and therefore these studies may not capture all aspects of concept development.

The CLS does not make predictions as to the information that is assimilated into a concept. The data from Chapter 4 of this thesis would suggest that elements of the environment that are not diagnostic of category membership, but can provide useful information, may be integrated into the concept and have a later influence on memory processing. This type of mechanism would be adaptive in the long-term, whereby the integration of the wider context may increase the flexibility of the overall representation.

Much further investigation is required to determine what elements of the environment contribute to conceptual knowledge, and the factors present during encoding that may influence their integration.

6.4 Methodological Considerations for Studying Concept Development

Previous literature addressing the role of consolidation in the development of conceptual memory representations have varied in the type of experimental paradigm, stimuli, measure of generalisation and their approach to assessing knowledge over time. This diverse approach is reflective of the complex nature of conceptual representations and the wide array of information they represent. However, greater consideration over experimental variation in the literature may allow a clearer understanding as to the development of conceptual representations. These methodological considerations are discussed below.

6.4.1 Experimental Paradigm, Stimuli and the Measure of Concept Knowledge

Due to the complex nature of conceptual memory representations, there is an experimental trade-off between capturing concept complexity and gaining a clear measure related to the underlying mechanisms and processes. In Chapter 2 and 3 of this thesis we reduced the ‘concept’ to two simple cross-modal dimensions. This allowed us to investigate the integration of very basic and abstract information from different modalities, and the extraction of statistical regularities. Furthermore, the abstract nature of the stimuli allowed us to measure concept development from initial encoding, without the influence of pre-existing semantic information. Assessing the impact of learning and consolidation on these representations therefore provided some understanding as to the impact of consolidation on the fundamental mechanisms contributing to the development of concept-based representations.

To build upon these abstract representations, in Chapter 4 we introduced an associative memory task that had three ‘critical’ concept features, but the overall complexity of the stimuli was increased by using faces which involved a number of

different features e.g. eye shape, nose shape, hair style etc., and drew upon a certain level of pre-existing semantic information. For instance, although the faces and their categories were all unknown to participants, categorising faces is quite a natural task and participants would have pre-existing knowledge as to the kinds of features that are typically shared across individuals (e.g. age – young/old) and those which are considered unique (e.g. nose shape). The stimuli were realistic and were able to capture elements of real-world categorisation that the two-dimensional abstract stimuli could not, however it is possible that factors related to pre-existing knowledge may have influenced learning and consolidation. An ideal stimulus set would allow the complexity of completely novel stimuli to be manipulated, such that both the basic mechanisms and the broader realistic representations could be simultaneously investigated.

The paradigm used to train concept knowledge may also lead to different behavioural outcomes when the contribution of offline consolidation is assessed. Within the consolidation literature more generally, differences in sensitivity to the benefits of sleep are observed, with statistical learning paradigms showing memory improvements following sleep, and declarative memories typically showing memory stabilisation (i.e. reduced forgetting when compared to wake; Diekelmann, Wilhelm & Born, 2009). In line with this distinction, the benefit of sleep on concept-knowledge appears to be influenced by the type of training paradigm. Studies that have used statistical learning paradigms typically report sleep-associated consolidation benefits after a single sleep episode, (Durrant, Cairney & Lewis, 2013; 2016; Durrant et al., 2015; 2011; Frost & Monaghan, 2017), while declarative training paradigms do not show these same immediate benefits (e.g. our results from Chapter 4 and Mirkovic & Gaskell, 2016; Sweegers & Talamini, 2014).

Given that representations trained via statistical learning paradigms may be more sensitive to sleep generally, it may be that memory generalisation can progress at a faster rate, which allows benefits to emerge after a single episode of consolidation. In Chapter 4, we suggest that the impact of offline consolidation on conceptual representations may be slower to emerge if sleep prioritizes the consolidation of more hippocampal aspects of a memory representation. To provide a full account of the role of consolidation in the development of concept-based representations, it may therefore be important to distinguish between types of learning. This, in conjunction with assessing the time-course

of consolidation benefits, will be important for establishing and predicting the type of consolidation-related changes a memory may show in the real-world.

A final point to consider relates to the measure of concept-knowledge that is taken. In the experimental paradigms in this thesis we aimed to assess the contribution of concept knowledge to novel instances of the concept. This is one of the fundamental advantages of storing conceptual information in the real-world, as they allow existing knowledge to drive successful interactions during new situations. The differential impact of consolidation on item- and concept-based knowledge has not always been dissociated in the literature (Ellenbogen et al., 2007; Lau, Tucker & Fishbein, 2010; Lau, Alger & Fishbein, 2011) and the results from Chapter 4 of this thesis suggest that this may be an important factor when determining the exact contribution of sleep on item- and concept-based representations. Future studies that make a clear distinction between these two types of representation will allow the interactions between the memory types to be assessed, and the mechanisms responsible for their development over time to be determined.

6.4.2 Assessing the Role of Consolidation

Further investigation into the processes that drive consolidation and their impact on conceptual memory development is required. In the studies presented in this thesis, the different contributions from wake and sleep were assessed over time intervals that naturally contained wakefulness (i.e. across the day) and sleep (i.e. overnight). This type of paradigm was chosen to maximize the potential for sleep-associated benefits to be observed, given that the sleep opportunity spanned an entire evening of overnight sleep. This is a commonly employed paradigm in sleep research and offers a clear sleep/wake comparison (Dumay & Gaskell, 2007; Ellenbogen et al., 2006; Fenn & Hambrick, 2015; Kurdziel & Spencer, 2016; Payne et al., 2012; Payne & Kensinger, 2011; Sonni & Spencer, 2015; Tham, Lindsay & Gaskell, 2015; van Dongen et al., 2012). There are however confounds related to this paradigm, namely time-of-day effects related to circadian and homeostatic pressures (Borbely & Achermann, 1999) and differences in levels of interference across the different delays. Care was taken to account for these potential confounds, with potential-time-of-day effects assessed using explicit measures of sleepiness (i.e. using the Stanford Sleepiness Scale, Hoddes et al., 1973) and implicit

measures of vigilance (i.e. using a psychomotor vigilance task, Khitrov et al., 2014). In the studies presented in the thesis, we did not observe any group differences in these measures, suggesting that any group behavioural effects were not driven by general differences in sleepiness and/or vigilance. However future investigations may wish to avoid these confounds.

One way to remove potential time-of-day effects is to assess memory using afternoon nap paradigms, in which memory is trained and assessed over a 90-minute period of sleep, typically carried out in the afternoon. This is a natural extension to studies that have investigated the effects of consolidation over longer timescales and provides a good opportunity to replicate sleep-associated benefits in the absence of circadian confounds (Diekelmann & Born, 2010; Mednick, Nakayama & Stickgold, 2003). Although nap studies remove time-of-day group differences, they do have limitations related to the amount, and type, of sleep obtained during the nap. A 90-minute period is typically sufficient for participants to complete a full cycle of sleep and therefore waking after this time typically reduces effects of sleep inertia (i.e. fatigue that is often reported if woken from deep sleep). However, due to the nap taking place in the afternoon, the type of sleep obtained across participants is varied and strongly influenced by sleep pressure (Dinges, 1986; Ellenbogen et al., 2006). Participants with a small amount of sleep pressure may spend very little time in deep NREM sleep and a large amount of time in REM sleep, while those with a large amount of sleep pressure may spend the majority of the 90-minute cycle in NREM sleep (Knoblauch et al., 2002). The quality and type of sleep obtained across naps may therefore have a large impact on the relationships that are observed when associated with behavioural measures of memory. The strengths and weaknesses of these paradigms should be considered when investigating and/or replicating effects of sleep-associated consolidation on memory.

Factors related to the level of interference cannot be avoided in wake versus sleep paradigms. However, strong evidence for specific sleep-associated benefits (rather than 'less interference' across sleep) can be observed if sleep is measured using PSG and relationships are found with features of sleep, for example number of sleep spindles and/or time spent in a specific sleep stage. Measuring sleep using PSG recordings is a natural extension to the study presented in Chapter 4 of this thesis and would help to determine the relationship between the behavioural effects observed and sleep

physiology. If a relationship with NREM sleep or sleep spindles was observed (i.e. features implicated in memory reactivation), it would strengthen our claims that sleep has a specific influence on memory processing.

In addition, techniques that are able to manipulate sleep provide causal evidence for a role of sleep in memory processing and mechanisms of consolidation. There are currently two paradigms that have been shown to actively promote memory consolidation by manipulating sleep: TMR (Rasch, et al., 2007; Rudoy et al., 2009) and closed-loop stimulation, (CLOs, Ngo et al., 2013). Both of these techniques have been shown to manipulate features of sleep related to memory reactivation, including sleep spindles and slow oscillatory activity (Cairney et al., 2015; 2014; Ngo et al., 2015; 2013; Oudiette & Paller, 2013). They therefore provide robust evidence for a specific role of sleep in memory consolidation. Developing similar methods to target consolidation during wakefulness would similarly allow its role in memory processing to be determined. Understanding the underlying mechanisms driving consolidation is one of the main goals of memory consolidation research.

6.4.3 Investigating Resting State Connectivity and Consolidation

This study reported in Chapter 5 used a seed-based correlation (SCA) analysis to investigate whole brain voxel-wise functional connectivity with the hippocampus and rFFA. The SCA technique has proven useful for revealing the connectivity properties of many seed areas and is a popular technique used in the literature by many groups (Buckner et al., 2013; Cole, Stephen & Christian, 2010). The primary advantage of SCA is that it is a direct approach, which shows the network regions that are most strongly connected with a seed region or region of interest (ROI), providing a relatively straightforward and interpretable result. Although a popular technique, SCA analysis imposes anatomical restrictions on the measurement of network connectivity and may under-represent the data. Fundamentally, there are as many possible ‘networks’ to be derived as there are possible seeds and therefore interpreting any single connectivity pattern as distinct may be over-simplistic (Cole et al., 2010). It will be important in future work to complement findings from Chapter 5 with larger samples which would allow whole-brain connectivity patterns and their relationship with behaviour to be assessed.

Other caveats of investigating resting state functional connectivity include the interpretability of anti-correlated networks and the nature of causal relationships. The observation of inverse temporal relationships between systems in both the presence and absence of tasks is thought to be functionally relevant (Fox et al., 2005; Fransson, 2005; Zuo et al., 2010). However, whether these between-network relationships are truly ‘negative’, or the consequence of the analysis procedure (e.g. pre-processing procedures necessary to correct for global non-neuronal physiological noise) is still debated, with no current consensus (Chang & Glover, 2009; Fox et al., 2009; Van Dijk et al., 2010; Weissenbacher et al., 2009). In the future it will be important to identify factors that influence the nature and strength of these relationships and their impact on behaviour. The data from the Chapter 5, along with task-related brain activity from others (e.g. Sweegers et al. 2014) suggest that there may be network interactions across cognitive states, i.e. sensory-motor networks appear coupled with regions of the DMN during online tasks and decoupled during rest. Further research is required to determine the nature and dependency of this coupling. For example, does the DMN suppress activity within sensory-motor networks during rest and vice-versa during task performance? Combining resting state and task-based fMRI with other methodologies such as transcranial magnetic stimulation (TMS) may provide invaluable insights into these network-dependencies and their functional relevance in the future (Cole et al., 2010).

6.5 Directions for Future Research

The research in this thesis has provided some key insights into the development of conceptual memory and the impact of offline consolidation on these representations. Throughout this discussion, a number of avenues for future research have been highlighted, these have related to the representation of conceptual knowledge in the brain, the mechanisms of memory consolidation and the interaction between consolidation processes during sleep and wake. The main ideas derived from the work in this thesis are summarised below.

Firstly, further investigation is required into the brain basis of conceptual knowledge and how consolidation impacts these representations. There is strong support for the hub-and-spoke model of semantic memory (Patterson, Nestor & Rogers, 2007; Lambon Ralph et al., 2017) and the paradigms used in this thesis are suitable for future

work assessing key aspects of this model, particularly the integration of cross-modal memory features into coherent conceptual representations. In line with the CLS view of consolidation, there should be a division of labour across hippocampal and neocortical memory systems, with concept-based representations showing greater reliance upon neocortical networks and item-specific memory details reliant upon the hippocampus. Using functional neuroimaging, it may be possible to characterise this system-level distinction, and by assessing how these representations change over time, it may be possible to trace the development of concept-based representations.

In accordance with the CLS, and the predicted division of labour between memory systems (Mirkovic & Gaskell, 2016), it would be predicted that individual items would show a hippocampal to neocortical shift in dependence over offline consolidation and this has indeed been shown in previous neuroimaging studies (Takashima et al., 2009). However, the retrieval of concept-based knowledge, when assessed through tasks requiring concept-based generalisations for example, may show recruitment of heteromodal integration regions across the cortex (e.g. the angular gyrus and ATLS) and with consolidation and subsequent learning you may expect a strengthening of this neocortical representation. Such a finding would provide strong support for the reliance of item- and concept-based representations on different memory systems, and may help to explain the differential impact of offline consolidation on the two types of memory.

A second direction for future study would be to build upon the resting state connectivity results reported in Chapter 5, to assess patterns of resting state connectivity that are time-locked to memory encoding and retrieval, allowing state-dependent relationships between long-term memory processing and rest to be investigated. Using neuroimaging techniques such as MVPA it would be possible to determine memory specific patterns of activity during memory encoding. Investigating whether these same patterns of activity are also observed during quiet rest, along with a relationship with behavioural memory improvements, would provide strong support for the mechanism of memory reactivation in long-term memory processing during wake. Similar methods could also be used during offline consolidation i.e. during sleep, and in conjunction with PSG sleep recordings, which would allow features of sleep to be temporally related to neuroimaging evidence of memory reactivation; this would provide robust evidence of memory reactivation as a mechanism of memory consolidation.

In addition, this would allow the interaction between item- and concept-based representations to be assessed and related to the mechanism of replay. In Chapter 4, we suggest that there may be a prioritisation process during sleep in which item-level details may be preferentially consolidated over knowledge of shared-structure (Mirkovic & Gaskell, 2016). In line with mechanisms described by the iOTA model (Lewis & Durrant, 2011), we suggest that the benefit of sleep on concept-based representation may emerge following sufficient integration of item representations and in conjunction with processes such as synaptic downscaling. By measuring replay events, it would be possible to determine how the degree of item-level replay impacts upon concept-knowledge over time. We would predict concept knowledge to show a linear relationship with memory replay, suggesting that the integration of new memories into neocortical networks, via memory reactivation, facilitates the abstraction of shared structure and development of conceptual representations.

6.6 Conclusions

This thesis investigated the impact of offline consolidation on the development of conceptual memory representations. Conceptual memory was assessed using a cross-modal information-integration categorisation task and an associative memory task that required the extraction of regularities to form concept-based representations. Results from the categorisation task suggest that offline consolidation during sleep supports the assimilation of new and category-congruent information into long-term memory networks. Evidence from the associative memory task suggests that there may be a prioritisation process of offline consolidation during sleep, whereby item-level memories show preferential consolidation and associated sleep benefits, in comparison to concept-based representations. Together, these results suggest that processes of offline consolidation during sleep do not provide immediate boosts in conceptual knowledge, but subtle benefits may emerge when measured in combination with further post-consolidation learning and when the memory systems supporting the representation are considered. An investigation into intrinsic brain connectivity during rest suggests that general variations in connectivity can in part explain individual differences in long-term memory performance, with decoupling between heteromodal and sensory-motor regions supporting memory generalisation and the formation of concepts. This thesis provides new insights into the role of consolidation on the development of conceptual memory representations and has raised important questions for future research.

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