# **Associative memory in ageing:**
## Changes in anticipatory brain activity

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A dissertation submitted for the degree of
Doctor of Philosophy
of the
University College London.

Institute of Cognitive Neuroscience
University College London

2016

## Declaration

I, Jiangyi Xia, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

## Abstract

Older adults are impaired in the ability to remember, especially for the associations across different elements of an event. It has been shown that during both memory encoding and retrieval, brain activities in anticipation to an upcoming event can influence memory for that event. To explore the role of the anticipatory brain activity in associative memory processing and how it may be affected by ageing, three electroencephalography (EEG) experiments were performed with both younger and older participants. Analyses were conducted in both ERP and time-frequency domains. Experiment 1 demonstrated that unlike older adults, younger adults were able to engage encoding-related anticipatory neural mechanisms before encountering any to-be-remembered information. During retrieval, however, older adults showed a pronounced ERP anticipatory effect for associative retrieval that was not seen in younger adults. Experiment 2 provided evidence suggesting that age-related differences in anticipatory associative memory effects were due, at least partly, to inefficient encoding as a consequence of diminished processing resources in older adults. Experiment 3 further revealed that when participants switched between words and pictures in an associative recognition task, only younger adults engaged anticipatory encoding-related activity, and they were more likely to recruit material-selective anticipatory mechanisms. Older adults were able to recruit anticipatory mechanisms during retrieval but not during encoding. In conclusion, older adults are impaired in anticipatory activity for associative encoding, but they are able to recruit anticipatory neural mechanisms at retrieval possibly to compensate for poor associative encoding. Compared to younger adults,

however, they are less able to recruit these mechanisms flexibly in a goal-directed manner. The present findings advance the understanding of neural mechanisms of associative memory deficits in ageing, which may open new doors for cognitive training in ageing by targeting these mechanisms.

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# Chapter 1: Introduction

This PhD thesis aimed to investigate age-related changes in anticipatory memory-related brain activity. Memory deficits in ageing are mostly found in episodic memory, especially when the binding between different episodic features is emphasised (Mitchell & Johnson, 2009; Old & Naveh-Benjamin, 2008). Episodic memory relies a great deal on cognitive control processes during both encoding and retrieval. An important aspect of cognitive control in episodic memory is the anticipatory process prior to a memory event. A number of studies have shown that anticipatory brain activity can influence episodic encoding (e.g. Otten et al., 2006) and retrieval (e.g., Addante et al., 2010). Cognitive impairments in ageing are often linked to a decline in executive control functions (West, 1996). This would suggest that memory deficits in ageing may be partly due to deficits in cognitive control such as anticipatory activity. However, very little research has been conducted to investigate this possibility. This thesis therefore aimed to elucidate age-related changes in anticipatory memory-related activity. To this end, associative memory tasks were used in all three experiments in this thesis, as age differences in memory performance have been consistently observed in these tasks (Mitchell & Johnson, 2009; Old & Naveh-Benjamin, 2008).

An introduction to the relevant theoretical background and research methods used in this thesis will be provided in Chapter 1. Firstly, general theories of cognitive ageing will be briefly described. Following this, main functional neuroimaging methods and related research findings on episodic memory will be introduced. Structural and functional changes in the ageing brain, as well as theories on how these changes may explain cognitive ageing will then be described. Previous research findings on anticipatory brain activity will be reviewed and a brief introduction to the EEG methodology that was used in this thesis will be given. The introductory chapter closes with an outline of the research aims of this thesis. Chapters 2 and 3 are experimental chapters, with chapter 2 covering ERP analyses and chapter 3 covering time-frequency analyses. Chapter 4 summarises the findings in the context of previous literature. General implications and future directions will also be discussed

## 1.1 Memory

Memory involves the encoding, consolidation, and retrieval of information and experiences. Memory encoding refers to the initial process of forming neural representations of newly encountered information. Memory consolidation refers to the process of stabilising memory representations after its initial acquisition. Memory retrieval refers to the recovery of stored memory representations, usually triggered by external or internal cues. Human long-term memory can be divided into declarative (explicit) memory and nondeclarative (implicit) memory systems, according to the multiple-systems view (Squire, 1992). The declarative memory system is thought to consist of semantic and episodic memories, both of which can be consciously retrieved. Semantic memory involves knowledge and facts whereas episodic memory involves personal events with rich spatial-temporal contextual details (Tulving, 1983). The present thesis will focus on episodic memory.

Episodic memories are made up of multiple components of an episode, derived from perception or thoughts including perceptual, spatial, temporal, semantic, emotional, and meta-cognitive information (Mitchell & Johnson, 2009). These episodic components, or features, differentiate one event from another, and may also be called source information. Source memory (i.e., memory for episodic features bound to an event) is closely related to the concept of associative memory, referring to memory for relations formed between components or items. Associative memory is usually contrasted with item memory, which refers to memory for individual items such as words or objects, isolated from other information associated with the items during encoding.

It has to be noted that even though source memory and associative memory are closely related concepts, there may be subtle differences when they are used in the memory literature. Source memory refers to memory for the spatial-temporal context of an event, and is therefore distinguished from the event itself. However, in reality it is difficult to clearly delimit events and contexts. Consider a summer party that consists of many individual parts such as the food, the music, and the people. It cannot be readily defined which is the event and which is the source. Nevertheless, the binding across multiple components of an episode is the key for episodic memory, regardless of whether these components are regarded as events or contexts. Therefore, source memory and associative memory are used interchangeably in this thesis.

In the laboratory, episodic memory can be measured using different memory tests, usually variations of old/new memory paradigms. In a simple old/new recognition test, initially studied items (old) are presented, intermixed with unstudied (new) items. Participants have to judge whether the item (i.e., the probe) is old or new. The old/new test may not be appropriate to tap into episodic memories, because an old response can be made based on the retrieval either with contextual details (recollection) or without (familiarity). Dissociations between recollection-based and familiarity-based retrieval can be achieved using a remember/know (R/K) paradigm. In an R/K test, participants have to decide whether they remember an item with its contextual details. R responses are made if they recollect some contextual details, whereas K responses are made if they recognise the item without any contextual detail. In this paradigm, responses are based on subjective judgements of the participants, and a wide variety of contextual information may underlie an R response. A more objective measure of episodic memory is the source memory paradigm. In a source memory test, participants attempt to recollect ‘diagnostic’ contextual information if they recognise an item, i.e., experimentally created context such as the modality or the time of item presentation. Only the recollection of the diagnostic detail can be classed as correct source retrieval, although other non-diagnostic information may also be recollected. It is believed that recollection contributes more than familiarity in source retrieval. A variation of the source memory paradigm is the associative memory paradigm. Associative memory tests are similar to source tests, except that participants have to remember item-item associations instead of item-source binding. In an associative test, one item serves as the retrieval probe and the other the to-be-retrieved target. Therefore, associative memory tests usually involve one-to-one mapping between probes and targets. In contrast, source memory tests involve many-to-one mapping between probes and source. The largest age-related decline in memory performance is found using source and associative memory paradigms (Old & Naveh-Benjamin, 2008), although older adults also show impairments in R/K memory tests (Mitchell & Johnson, 2009).

Neural activity related to memory processing can be measured using the event-related approach (e.g., Donchin & Lindsley, 1969). Using this approach, neural activity in response to individual experimental stimuli or events can be separated in a time-locked fashion and then contrasted according to the classes of these stimuli or events. For example, neural activity related to memory retrieval can be measured by contrasting neural activity elicited by items that are remembered and items that are forgotten. To measure encoding-related activity, the classes of the stimuli have to be defined on the basis of later retrieval responses in a post-hoc manner. This approach has been termed the 'subsequent memory approach' (Paller, Kutas & Mayes, 1987), and successfully applied in a large number of studies (e.g., Gruber & Otten, 2010; Paller et al., 1987). The difference between neural activity for later remembered and forgotten items is termed the 'subsequent-memory effect' (SME), which is thought to be an index of successful memory formation (for review see Paller & Wagner, 2002). For source memory and associative memory, successful item-context and item-item binding can be measured by contrasting neural activity related to subsequent successful and unsuccessful source retrieval or associative retrieval.

A great deal of evidence suggests that healthy ageing is associated with disproportionate declines in source memory relative to item memory (see Mitchell & Johnson, 2009; Old & Naveh-Benjamin, 2008; Spencer & Raz, 1995 for reviews). In this thesis, neural mechanisms underlying associative memory deficits in ageing were investigated. Memory deficits in ageing may stem from more general cognitive impairments. A number of theories have been proposed to account for the effects of ageing on general cognition. In the next section, some of the most influential cognitive ageing theories will be reviewed. These theories can help us to better understand memory deficits in ageing.

## 1.2 Theories of cognitive deficits in ageing

Healthy ageing is associated with performance decline in a wide variety of real-world activities, from actors learning lines, recalling of bridge hands, to memory for conversations (see Salthouse, 1996 for a review). In the laboratory, age-related impairments have been found in many cognitive functions such as attention, executive functions, working memory (WM), and episodic memory (Park & Reuter-Lorenz, 2009; Sander, Lindenberger, & Werkle-Bergner, 2012), whereas other functions are preserved, such as verbal knowledge, implicit, and semantic memory (Jennings & Jacoby, 1993; Park et al,1996; Ballesteros, 2009). The most often reported cognitive impairment in ageing is episodic memory, when binding across different elements is involved. There have been a number of theories proposed to account for the effects of ageing on memory and cognition.

An influential theory is the processing speed hypothesis of ageing, proposing that a major factor contributing to age-related cognitive impairments is slow processing speed (Salthouse, 1996). The relationship between reduced speed and degraded cognition is thought to be mediated by two distinct mechanisms. One is that relevant cognitive operations cannot be successfully executed in the available time (limited time) and the other that the products of early processing are no longer available during later processing (simultaneity). Higher level processing requires a greater amount of simultaneously available information. Assuming that the quantity and quality of available information decay over time, a slow processing speed could be expected to negatively affect the availability of information at crucial points in time.

The problem with the speed hypothesis of ageing is that it is solely based on correlational studies, which indicate that the best overall predictor of performance across age is speed rather than accuracy. However, because it is difficult to isolate processing speed from other aspects of cognitive processing, it is not meaningful to talk about speed independent of the task in which it is assessed. In response to this kind of criticism, Salthouse has focused on the Digit Symbol Substitution Test (DSST) taken from the Wechsler Adult Intelligence Scale (WAIS). This test, however, as many other tasks, does not allow a pure measure of speed but involves strategy and working memory. Furthermore, speed measures are not always the best predictor for memory decline. For example, Baltes and Lindenberger (1997) found that the best predictors were auditory and visual sensory thresholds, which depend on accuracy rather than speed. Subsequently, they even found that grip strength was a better predictor. Thus, the authors themselves noted, correlation does not equal causation. More solid evidence is needed to support the processing speed theory of ageing. There is some evidence from neuroimaging studies. Electrical brain activity reflecting higher-order cognitive functions, as reflected in ERP components such as N2b and P3b, show prolonged latency with advancing age (Friedman, 2012). The latency of the P300, the component that has specific implication in memory processing, increases steadily in healthy ageing and becomes more severely delayed in dementia (Neshige, Barrett, & Shibasaki, 1988). Although there is no evidence of the slowing of early sensory processing, as reflected in the P50 and N1, the evidence for changes in relatively late-stage information processing is consistent with the processing speed theory of ageing.

Another important theory of ageing is the diminished processing resources theory (Craik & Byrd, 1982). This theory proposes that ageing is accompanied by a decrease in available processing resources, which limits the depth and elaboration of memory encoding and leads to a lack of specificity and distinctiveness of memory representations. This theory is based on a series of experiments, mainly from Craik and colleagues but also other groups, demonstrating the impact of reduced processing resources on memory performance (Craik & Rose, 2011). In the experiments, episodic memory performance in young adults is similar to that of older adults when processing resources are reduced by attentionally demanding concurrent tasks (e.g., Anderson, Craik, & Naveh-Benjamin, 1998; Craik & Byrd, 1982; Craik, Luo, & Sakuta, 1992). The concurrent tasks may or may not share the same representational systems as the memory tasks (e.g., memory test for words coupled with a word processing task or a number counting task), or may even be in a completely different domain such as visual-motor coordination (Shallice et al., 1994) or movement control (Lindenberger, Marsiske, & Baltes, 2000). Based on the similarity between the effects of ageing and the effects of divided attention in younger adults on memory performance, it has been proposed that age-related cognitive impairments are due to diminished attentional resources (Craik & Rose, 2011).

However, there are also experimental findings that are inconsistent with this theory. For example, Naveh-Benjamin (2000) showed that young adults who perform a concurrent task during memory encoding are impaired in memory for both related and unrelated word pair recognition to the same extent, whereas older adults differed only for the unrelated items. A series of follow-up experiments from Naveh-Benjamin’s group (e.g., Naveh-Benjamin et al., 2003,

2004) have consistently demonstrated that the patterns of memory performance in ageing and in divided attention conditions in younger adults are not entirely the same. Therefore, the difference in performance between older and younger adults cannot be attributed only to attentional differences.

Based on these differences, Naveh-Benjamin (2000) proposed the ‘associative deficit hypothesis’ of ageing, suggesting that older adults’ episodic memory impairments lie in a deficit in creating binding. Subsequent studies by the group replicated the relative preservation of recognition of information that is already bound together with a substantial deficit in binding unrelated pairs, not attributable to an attentional deficit. Naveh-Benjamin et al. (2004) studied face-name associations in younger and older adults. Age-related decrements in later face recognition and name recognition were relatively slight (4% and 2%, respectively), but the name-face associative recognition deficit was substantially greater (14%). These effects of aging were not entirely mimicked by dividing attention in young adults (e.g., Naveh-Benjamin et al., 2004). Whereas divided attention in young adults reduces item and associative recollection to the same extent, aging is associated with a disproportionate drop in memory for associative information. Naveh-Benjamin and colleagues (2004) therefore concluded that the performance decline in older adults is not caused by depleted attentional resources. It is very clear that age effects on the recall of associative memories (face and name combined) are reliably greater than effects of the demanding concurrent task.

Given the similarities between young divided-attention adults and older adults in many respects such as free recall and cued-recall (Anderson, Craik, & Naveh-Benjamin, 1998), Craik and Rose (2012) made the suggestion that divided attention in younger adults impairs frontal lobe functioning and therefore resembles ageing in this respect. Older adults, however, have an additional associative impairment as a consequence of poor hippocampal functioning (e.g., Davachi and Wagner, 2002; Raz et al., 2005; Shing et al., 2010), which is not mimicked by divided attention in younger adults.

Taken together, theories of ageing as described above have provided theoretical frameworks to show that cognitive impairments in ageing may stem from general deficits such as diminished processing resources, a slowing of processing speed, and the ability to bind multiple components together. To better understand the underlying neural mechanisms for age-related changes in cognition and behaviour, one needs to look into findings from neuroimaging studies.

## 1.3 Neuroimaging methods

A number of neuroimaging methods have been used to investigate the relationships between cognitive functions and brain activity. The most frequently used methods in cognitive ageing research are electroencephalography (EEG), magnetoencephalography (MEG), and functional magnetic resonance imaging (fMRI), which have complementary advantages in mapping functional brain activity. Although EEG is the neuroimaging method of choice in this thesis, it is necessary to look across other neuroimaging methods to obtain a fuller picture of the cognitive neuroscience of ageing.

### 1.3.1 EEG

EEG is used to record spontaneous electrical brain activity. When a couple of electrodes are placed on the scalp, electrical potentials are measured between the two electrodes, and the voltage differences over time are referred to as EEG signals (Coles & Rugg, 1995; Luck, 2015). EEG signals reflect the summation of synchronised activity from a large number of similarly oriented cortical neurons (Luck, 2015). If the directions of the neurons are random, the current flow can be cancelled out from each other. It is suggested that scalp-recorded EEG signals are mainly generated by post-synaptic potentials of cortical pyramidal neurons, which are well-aligned and synchronised (Luck, 2005). Action potentials are considered to be too brief for the field summation to occur and to be captured by EEG. Furthermore, as voltage fields fall off with the square of the distance, signals from deep structures such as the thalamus or hippocampus may not be detected on the scalp (Coles & Rugg, 1995).

The particular strength of EEG as a neuroimaging method is its excellent temporal resolution in the range of milliseconds. In human cognitive research, EEG activity is recorded while participants perform experimental tasks. EEG data are segregated into epochs, time-locked to experimental events such as the stimulus or response. Epoched data can be analysed in two approaches: event-related potential (ERP) and time-frequency analyses. In the ERP approach, segregated epochs are averaged according to experimental conditions to remove random background noise, i.e., activity not time-locked to event onsets (Coles & Rugg, 1995). The waveforms that survive this averaging process are thought to index changes, relative to a pre-event baseline, in sensory and cognitive processes that unfold over time in response to a class of events. Differences in averaged waveforms across different conditions are considered to represent differences in brain activity that can be attributed to experimental manipulations. In a well-designed study, EEG representations of distinct cognitive processes can be isolated by comparing ERPs across experimental conditions. A number of prototypical deflections, or components, in relation to certain cognitive processes can also be obtained. Such components are usually characterised in terms of their specific polarity, timing, scalp distribution and sensitivity to experimental manipulations (Coles & Rugg, 1995). These characteristics can help to interpret ERP findings in relation to the underlying cognitive processes, and to compare ERP findings across studies. Reversed polarity and differences in scalp distributions of ERP waveforms are thought to reflect qualitative differences in the underlying neural activities, which may be generated from different neural sources. In contrast, a difference in amplitudes is thought to reflect a quantitative difference in the activation of certain cognitive processes (e.g. Otten & Rugg, 2001). Differences in timing indicate an upper bound on differences in the occurrence and duration of underlying processes. For example, the well-known mid-frontal and left-parietal old/new effects, derived from comparing ERP waveforms elicited by correctly remembered items to those elicited by correctly identified new items, are dissociated by their characteristic differences in timing, scalp distribution, and sensitivity to experimental manipulations, and thought to reflect distinct retrieval processes (Rugg, 1995). Similarly, a well-known ERP component relevant to memory, the P300 component traditionally observed in ‘oddball’ paradigms and mentioned earlier in this chapter in relation to ageing, is characterised as a large positive deflection elicited by a salient stimulus around 300-900 ms after stimulus onset (Polich, 2012). Based on observations from various experimental manipulations, the P300 is thought to reflect higher-level cognitive processes such as context updating, with its amplitude associated with the amount of attentional resources devoted to a task (Donchin, 1981).

Time-frequency analyses of EEG epochs, in contrast, are used to investigate oscillatory brain activity in relation to cognitive processes. EEG can be modelled as sine waves that evolve over time, each with its own frequency. The frequencies have been separated into bands such as delta (0-4 Hz), theta (4 – 8 Hz), alpha (8 – 12 Hz), beta (13 – 30 Hz) and gamma (30 – 80 Hz) (Herrmann, Grigutsch, & Busch, 2005) and are thought to carry important information about neural and cognitive processes (e.g., Sauseng & Klimesch, 2008). The principle of the time-frequency approach is to decompose EEG signals into magnitude and phase information for each frequency, i.e., time-frequency decomposition or spectral decomposition, and to characterise changes in this information over time with respect to experimental events (Roach & Mathalon, 2008). Magnitude refers to the height of the sine wave at a given time point, which is the square root of the power that signals the strength of activity in a certain frequency. A power increase in a given frequency is interpreted as synchronisation of large neural populations in that frequency, and a power decrease is interpreted as desynchronisation (Klimesch, 1997). The phase, i.e., the direction of the sine wave, can be measured as an angle at any time point.

Like the ERP approach, time-frequency representations of each epoch are averaged across trials within the same experimental condition, and changes in power/phase information over time are used to characterise changes in brain activity in respect to each condition. However, unlike ERP analyses that only take phase-locked activity into account, time-frequency analyses represent activity either phase-locked or non-phase-locked to the events (Roach & Mathalon, 2008). For example, if EEG signals in two trials start with opposite phase angles, they will cancel each other out and lead to zero ERP activity given that they have the same magnitude. In event-related oscillations, however, power/phase representations ensure that signals of variable phases will not be averaged out. Therefore, time-frequency analyses provide useful information that is complementary to ERP analyses.

Unlike scalp EEG, intracranial EEG (iEEG) provides direct access to population activity in theoretically important cortical regions located on the brain surface (Kahana et al., 1999). Compared to scalp-recorded EEG, iEEG offers improved spatial resolution without attenuation of brain signals by the skull and scalp. iEEG also avoids muscle artefacts, including eye movements. However, due to the invasiveness of the procedure, this method in human research is limited to patients who undergo brain surgery. These patients are already suffering from epilepsy, stroke, or other neurological conditions. Therefore, it is difficult to control for confounds caused by abnormal neural activities.

### 1.3.2 MEG

Similar to EEG, MEG measures the electromagnetic field generated by synchronised activity from a large number of similarly oriented cortical neurons. Unlike EEG, MEG measures the magnetic component of the electromagnetic field, and the neurons therefore have to be oriented tangentially to the scalp surface. Scalp EEG is sensitive to both radial and tangential sources in a spherical volume conductor, whereas MEG is sensitive to tangential sources only. This means that scalp EEG can detect activity in more brain areas including activity in sulci and the top of cortical gyri, whereas MEG is most sensitive to activity originating in sulci. Also, it has been demonstrated that the scalp topography of EEG and MEG signals from the same source may be orthogonal (Reite, Teale, & Rojas, 1999). Compared to EEG, a major advantage of MEG is that magnetic fields suffer less from smearing and distortion of the skin, scalp, skull, and cerebrospinal fluid. In addition, MEG is more sensitive to superficial cortical activity as the decay of magnetic fields as a function of distance is more pronounced than for electric fields. This can be a limitation, as signals from deep structures cannot be recorded, but also an advantage, as signals can be localized with more accuracy than EEG. Similar to EEG, MEG data can be subjected to event-related field (ERF) and time-frequency analyses. As MEG signals are relatively invulnerable to distortion from the media they traverse, it is more suitable than EEG for source localisation analyses.

A particular problem with scalp-recorded EEG and MEG is the determination of the location of intracranial sources. The primary difficulty is that there may be an infinite number of possible solutions and it is often impossible to define the best or correct solution. This issue is referred to as the inverse problem. Any number of intracerebral generators might be contributing to the electrical activity recorded at a single electrode site because of volume conduction of the brain, i.e., electrical brain activity propagates through the brain tissue along the least resistant path and spreads laterally when reaching the skull (Luck, 2014). Thus, it is not possible to accurately localise the neural generators of scalp recorded activity, at least not on the basis of scalp recorded EEG alone.

### 1.3.3 fMRI

Different from EEG and MEG, fMRI uses the blood-oxygen-level dependent (BOLD) contrast, an indication of energy use by neurons, to image regional brain haemodynamic responses as a function of cognitive processing

(Huettel, Song, & McCarthy, 2009). Therefore, fMRI signals are not a direct measure of neural activity, but rather the consequence of it. The haemodynamic responses occur much more slowly than neural activity does, usually taking 4-5 s to develop after neural activity (Huettel et al., 2009). The temporal resolution of fMRI is also limited by the sampling rate, which is usually once per 1-2 s. Therefore, fMRI has poorer temporal resolution than EEG and MEG. The most important advantage of fMRI is its excellent spatial resolution, which increases with higher strength of the magnet field, and can distinguish brain structures with less than millimetre accuracy.

The slowness of the vascular response means the final BOLD signal is the summed version of the whole region's network; blood flow is not discontinuous as the processing proceeds. Also, both inhibitory and excitatory input to a neuron from other neurons sum and contribute to the BOLD signal. Within a neuron these two inputs might cancel out. Compared to EEG/MEG, fMRI has superior coverage of most of the brain. However, like EEG/MEG, fMRI cannot provide uniform coverage of the whole brain. Because fMRI is sensitive to subtle changes in the local magnetic field, including those caused by differences in brain structure such as air-filled pockets in the head (e.g., the sinuses), some regions such as the inferior frontal and temporal cortex are hard to image. These structures, however, are important for cognitive functions such as language, memory, and decision making.

fMRI data are commonly analysed on a voxel level in the framework of the general linear model (Kiebel et al., 1999), which predicts how the signal will change over time as a function of experimental events such as stimulus presentation or task performance. Using such methods, signals can be compared across experimental conditions and isolate brain activity related to cognitive processes of interest.

There are also other haemodynamic methods, such as positron emission tomography (PET), that measure changes in blood volume. However, PET is not as popular as fMRI mainly because of its invasiveness: a radioactively labelled substance has to be injected into the blood stream. PET is also poorer in spatial and temporal resolution compared to fMRI.

### 1.3.4 The relationship between neuroimaging methods

The neuroimaging methods described above may not represent the same neural activity. For example, the BOLD signal primarily reflects metabolic demands, which are driven by the number of active neurons within a population (Logothetis et al., 2001). In contrast, a power increase in EEG/MEG can reflect either an increase in the number of active neurons or an increase in the synchrony of neuronal firing. Furthermore, EEG/MEG are most sensitive to post-synaptic potentials that are generated in superficial layers of the cortex, but not those generated in deep structures such as the hippocampus. Therefore, unlike fMRI, EEG/MEG provides information with a large bias to specific neuron types.

Therefore, it is important to integrate findings across different neuroimaging methods, which can provide evidence complementary to each other. Both EEG and MEG have high temporal resolution, best suited to capture the rich temporal dynamics that underlie cognitive processes, whereas fMRI can provide information about the underlying neural generators with high spatial resolution. Nevertheless, it may be difficult to directly compare EEG/MEG findings with fMRI findings, as the time course of fMRI activity may be different from those of EEG/MEG and different types of neural activity are captured by each measure.

With a temporal resolution in the range of milliseconds, EEG is particularly useful for the study of memory because of the ease with which neural activity can be dissociated according to successful and unsuccessful retrieval, or according to whether activity occurs before or after stimulus onset. Also, the timing of different cognitive processes can be pinpointed with EEG. In the same vein, EEG investigations of cognitive ageing can provide detailed information on the timing and duration of age-related differences in neural activity contributing to memory formation and retrieval. EEG is therefore the method adopted in the experiments in this dissertation.

## 1.4 Memory-related brain activity

### 1.4.1 Encoding

In the next section, neuroimaging studies investigating neural processes of memory encoding and retrieval will be reviewed, with an emphasis on associative memory and ageing. According to the levels of processing framework (Craik & Lockhart, 1972), memory performance depends on the initial mechanisms used to encode information. Events that are deeply processed are more likely to be remembered than those receiving less elaborative encoding, leading to fewer conceptual associations with pre-existing knowledge (Craik, 2007). Insights into the neural mechanisms underlying successful memory encoding have been revealed by fMRI research. Numerous fMRI studies have identified the inferior frontal cortex (IFC) and the medial temporal lobe (MTL) as the key regions mediating successful encoding, with higher levels of BOLD activity predicting later recall (see Paller & Wagner, 2002 for a review). The left IFC is thought to reflect semantic processing (e.g., Otten & Rugg, 2001), and the MTL is likely involved in binding an item to its spatiotemporal context (Davachi, 2006).

Comparing younger and older adults in LTM encoding, Morcom et al. (2003) found that encoding-related brain areas largely overlap in younger and older adults, in particular left IFC and left hippocampal formation. In this study, recognition memory performance was matched across age by manipulating the length of delay between learning and testing. Another study (Filippini et al., 2012) found greater left ventral lateral PFC activity in older relative to younger adults when performance was matched across age. These findings suggest that older adults are able to engage neural circuits associated with semantic processing to a similar, or even greater, extent as younger adults to encode new memories. In addition, over-recruitment of the PFC, in particular the left dorsal lateral PFC and regions in the right PFC, has been found in older adults across a number of studies (see Rajah, Maillet, & Grady, 2015 for a review). Such over-recruitment has been interpreted as compensatory neural mechanisms or an inefficient use of neural resources in ageing, depending on whether signal increases are accompanied by an impairment in memory performance (further discussion can be found in later section).

In terms of associative encoding, studies showed that inter-item associations are related to left PFC activation during encoding (Hales et al., 2009; Park & Rugg, 2008, 2011). Dennis and colleagues (2008) looked at the SME for face–scene pairs in an fMRI study. They found an age-related reduction in hippocampal activity as well as bilateral dorsolateral PFC activity that were specific to the encoding of paired associations relative to the encoding of either feature alone. Similar age-related decreases in PFC and hippocampal activity have been observed for the encoding of word-word pairs (e.g., Kim & Giovanello, 2011), picture-picture pairs (Iidaka et al., 2001), and object-location binding (Mitchel, Johnson, Raye, & D'Esposito, 2000). This pattern of age differences has been linked to reduced processing resources. In a study using a divided attention task at encoding (Kim & Giovanello, 2011), it was found that reduced processing resources in young adults yield the same patterns of behavioural and neural impairments as those observed in older adults, including decreased activity in PFC and MTL regions.

Inter-regional connectivity analyses have revealed that the hippocampus and lateral PFC are functionally connected during successful associative encoding (Dennis et al., 2008). In contrast to the decreases in activity levels in each of these areas, hippocampal–PFC connectivity has been found to be stronger in older adults than younger adults. This age-related increase in hippocampal–PFC connectivity was coupled with an age-related decrease in the connectivity between the hippocampus and posterior regions (e.g., posterior cingulate, parietal cortex, and inferior temporal regions), suggesting a posterior-to-anterior shift in the areas that co-activate with the hippocampus during encoding (Dennis et al., 2008). As posterior brain regions are in part related to sensory representations, such a shift was thought to reflect that older adults' difficulty in associative encoding is to some extent driven by weak representations of sensory information, or weak connectivity from/to these sensory regions. In line with this hypothesis, studies have shown age-related impairments in sensory regions during LTM encoding, including reduced activation (Dennis et al., 2008) and reduced specificity of activation for distinct classes of information such as faces and scenes (Chee et al., 2006; Park et al., 2004; Payer et al., 2006).

The age-related increase in hippocampal-PFC connectivity might serve as a compensatory mechanism as a consequence of deficient sensory processing (Grady, 2012). Dennis et al. (2008) found that unlike those in the hippocampus and PFC, age-related deficits were equal for associative and item memory in visual representational areas in the inferior temporal cortex, i.e., the fusiform face area (FFA) and the parahippocampal place area (PPA). This suggests that older adults may have difficulty in binding features in addition to a problem of less detailed feature representations, although the relative contribution of each of these problems to older adults’ source memory difficulties remains to be determined. Taken together, the pattern of regional differences is consistent with the idea that age-related source memory deficits are due, at least in part, to age-related decrements in memory binding during encoding resulting from hippocampal dysfunction, PFC dysfunction, and changes in hippocampal–posterior functional connectivity. There may be multiple ways that PFC, MTL, and posterior regions and their functional connectivity during encoding are affected by ageing.

A number of ERP studies have investigated the SME for source memory (Cansino et al., 2010; Duarte et al., 2004; Friedman & Trott, 2000; Mangels et al., 2001; Smith, 1993). These studies usually employed the remember/know (R/K) procedure, which is thought to be an indirect measure of source memory, with ‘remember’ judgments indicating recollection, i.e., the retrieval of contextual information, and ‘know’ judgments indicating familiarity, i.e., recognition of an item without its context. Apart from Smith (1993), all of these experiments have shown that items subsequently “remembered” elicit more positive-going waveforms than items subsequently termed “know”. These SMEs are present from about 300-400 ms after stimulus onset, suggesting that neural activity from at least 300-400 ms after encountering an event determine contextual encoding success of that event.

However, R/K judgements are phenomenological in nature, resting mostly on subjective retrospection. In contrast, the source memory procedure, in which explicit retrieval of specific contextual information is required, is an objective measure of source memory. Subsequent source memory effects have also been measured directly using source memory procedures. For example, Friedman and Trott (1999) asked participants to retrieve temporal information, i.e. whether a word was presented in the first or second list during encoding. Cansino and Trejo-Morages (2008) asked participants to retrieve spatial information, i.e. in which of the four quadrants of the screen an object was presented. In Friedman and Trott’s study, there was no reliable difference in encoding activity for items whose source was correctly remembered versus forgotten. In Cansino and Trejo-Morages’ study, there was a reliable subsequent source memory effect in the form of more positive-going ERPs for items associated with correct source retrieval. There could be many reasons for the discrepancy between the two source memory studies. For example, different learning materials were used in these studies, i.e. words vs. pictures. It is possible that pictures, with much richer perceptual details than words, naturally afford elaborative encoding to a greater extent (Yonelinas, 2002) and therefore give rise to stronger subsequent source memory effects. Another important difference between the two studies is the number of to-be-remembered sources. In Friedman and Trott’s study this was two (list 1 or list 2) whereas it was four in Cansino and Trejo-Morages' study (4 quadrants on the screen). The possibility of lucky guesses in source memory was therefore higher in Friedman and Trott's study (0.5) than that in Cansino and Trejo-Morages' study (0.25). Thus, it is likely that correct source judgments in the former were mixed with a larger proportion of lucky guesses than those in the latter, which may have diluted the SME that might have emerged. In addition, the nature of the source information was different across the two studies. Temporal and spatial information might be processed differently during encoding and have different sensitivities to source retrieval. Therefore, encoding-related activity appears to be influenced by the properties of the to-be-encoded source information.

EEG activity associated with source encoding has also been found using oscillatory analyses. For example, in Summerfield and Mangels (2005), participants studied lists of words presented in one of four different font colours, and were subsequently required to recognise the words and also make source judgments on the corresponding font colours. Theta power increases over right frontal scalp sites from 400 ms after stimulus onset were found for subsequent successful source retrieval, whereas theta power increases over left frontal sites were found for subsequent item retrieval. In Staudigl and Hanslmayr's (2013) study, participants were shown words superimposed on movie clips. Memories for words were later tested with words presented on either the same or different movie clips. SMEs in theta activity were found in both conditions. In the same context condition (i.e., the same movie clip), theta power increased for subsequently remembered words. In the different context condition, the opposite effect was found with theta power increasing for subsequently forgotten words. These findings suggest that theta increases may reflect item-context binding, which enhances memory when encoding-retrieval contexts match and impairs memory when encoding-retrieval contexts mismatch.

Even fewer studies have investigated the effect of age on subsequent source memory. Studies using the R/K paradigm (e.g., Friedman & Trott, 2000) usually find an age difference in SMEs, with younger adults showing the typical positive-going SME for items given ‘remember’ responses and older adults showing no reliable SME. In Friedman and Trott’s (2000) experiment, participants studied pairs of unassociated nouns embedded in two temporally distinct lists of sentences. Memory for the nouns was later tested with old/new recognition, followed by R/K and source (list 1 or list 2) retrieval. For young adults, the SME associated with recollection was bigger than that for familiarity from about 400 ms post-stimulus, indicating that the two types of items were differentially processed at encoding. In older adults, SMEs were found for items given both ‘remember’ and ‘know’ responses. However, there was no reliable difference between these two kinds of SME. The lack of difference in SMEs associated with later ‘remember’ and ‘know’ judgments indicates that in older adults, neural processes that determine source success may not be operative at encoding. Taking the SME as an indicator for elaborative encoding (Friedman & Johnson, 2000), it is likely that older adults are impaired in elaborative encoding processes. Considering that behaviourally, younger and older participants did not differ significantly in percentages of R or K judgments, but on the percentage of R items attracting correct source judgments, it seems reasonable to assume that R judgements in older adults were based less on the amount of source retrieval than those in younger adults, possibly as a result of less elaborative encoding. Thus, older adults might be impaired in the spontaneous recruitment of elaborative encoding strategies that facilitate source memory.

Studies using direct source memory measures do not consistently demonstrate age differences in SMEs. Friedman and Trott (2000) did not find any reliable difference in encoding-related activity as a function of successful source retrieval in either age group. However, in a study using images of objects in a source memory procedure similar to that used by Cansino and Trejo-Morages (2008), Cansino and colleagues (2010) did find source-related SMEs in both young and older adults. Younger adults showed a sustained positive-going SME at the right frontal scalp sites, and older adults showed an SME that was similar in amplitude but spatially more widespread to the posterior sites. As already discussed above, there are a number of differences between these studies, such as different learning materials and experimental procedures. It is therefore impossible to pinpoint the cause of the discrepancy between their findings. It seems that in some situations younger and older adults engage similar processes during encoding, while differences emerge in other situations. There is currently insufficient evidence to determine whether and if so, how, SMEs for source memory differ across age.

In summary, previous studies suggest that brain activity during encoding influences subsequent associative retrieval as reflected in SMEs. In EEG studies, associative SMEs manifest as positive ERP deflections and theta power increases. Evidence for age differences in associative encoding-related EEG activity is inconsistent, possibly influenced by the nature and content of the encoding task. In contrast, fMRI studies have revealed age-related under-recruitment of the hippocampus and the PFC, as well as reduced hippocampal–posterior connectivity, probably due to reduced processing resources. Together with the findings that older adults are able to engage neural circuits associated with semantic processing just like younger adults, these findings indicate that older adults may have difficulty in binding episodic features as well as having less detailed feature representations. Furthermore, older adults may be impaired in spontaneous recruitment of elaborative encoding strategies that facilitate associative memory. Nevertheless, older adults may engage compensatory activity as reflected in greater PFC-hippocampal connectivity.

### 1.4.2 Retrieval-related brain activity

Numerous fMRI studies have been conducted to investigate brain activity associated with recollection (see Rugg, Johnson, & Uncapher, 2015 for a review). These studies have consistently identified a number of brain regions that are engaged when recollection is successful, including the MTL, especially the hippocampus and parahippocampal cortex, as well as other cortical regions that are connected to the hippocampus, i.e. retrosplenial, posterior cingulate, medial PFC, and the angular gyrus. Based on these studies, it has been proposed that these brain regions form a “core” recollection network, i.e. a network that is engaged for recollection regardless of the nature or the content of retrieval (e.g., Hayama, Vilberg, & Rugg, 2012; Rugg & Vilberg, 2013). Within these regions, the hippocampus is thought to play a pivotal role in episodic retrieval to reinstate patterns of activity stored during initial encoding (Rugg et al., 2015). Parahippocampal cortex, mPFC, and retrosplenial cortex are thought to be parts of an extended hippocampal system (Aggleton, 2012) that is important for the retrieval of contextual information. The angular gyrus is thought to contribute to the representation of recollected information (Vilberg & Rugg, 2012), acting as the “episodic buffer” (Baddeley, 2000) for different episodic features to be bound.

Age-related reductions in hippocampal activity during associative memory retrieval have been reported (e.g., Giovanello & Schacter, 2012; Tsukiura et al., 2011). In a study using a face-name and face-job associative memory task, Tsukiura et al. (2011) found that successful associative retrieval engaged hippocampal activity, which was greater in younger than older adults. Furthermore, in a study comparing associative retrieval and item retrieval (Giovanello & Schacter, 2012), it was demonstrated that in younger adults, hippocampal activity, as well as left vlPFC activity, was modulated by the extent to which associative processing was involved in retrieval (i.e., greater activity during associative relative to item retrieval). In older adults, however, activity in these regions did not differentiate between associative retrieval and item retrieval, suggesting an age-related impairment in the recruitment of the hippocampus and vlPFC for associative processing.

In addition to the core recollection network, other brain regions have shown age-related changes during recollection, albeit in the form of age-related over-recruitment (i.e. greater activation in older than younger adults). Compared to younger adults, older adults over-recruit some of the PFC regions during recollection, such as left dorsal lateral PFC (dlPFC) and anterior PFC (aPFC) (see Rajah, Maillet, & Grady, 2015 for a review). Age-related over-recruitment is often thought to reflect compensatory activity. For example, over-recruitment of the left dlPFC has been linked to a reliance on more abstract associative strategies to compensate for neural inefficiency in posterior brain regions such as the occipital cortex and hippocampus (Morcom, Li, & Rugg, 2007; Rajah et al., 2015). Over-recruitment of the aPFC is also thought to reflect compensation as activity in this region has been found to increase with better source memory performance (Rajah, Languay, & Valiquette, 2010). In contrast, age-related over-recruitment in other PFC regions, e.g. medial PFC, has been interpreted as reduced task-related deactivations and therefore may be detrimental to memory performance (Sambataro et al., 2010). However, more evidence is required to determine the nature of these age differences in retrieval-related brain activity.

EEG source retrieval studies using the time-frequency approach have reported greater theta power for successful than unsuccessful source retrieval over fronto-central (Gruber, Tsivilis, Giabbiconi, & Müller, 2008) and fronto-temporal (Guderian & Düzel, 2005) scalp sites. Brain source localisation analysis indicated that, for associations between faces and scenes, theta source retrieval effects are generated in a distributed network including prefrontal, MTL and visual areas (Guderian & Düzel, 2005). This is consistent with the proposal that the widespread interconnections of MTL regions provide a convergence zone for long-range interactions across distributed brain regions, supporting the interaction of different types of information that is necessary for recollection (Düzel, Penny, & Burgess, 2010). Converging evidence from iEEG studies (e.g., Watrous et al., 2013) also shows that coherence between MTL, PFC, and parietal cortex increases for correctly retrieved source information. Relatedly, theta activity during retrieval is thought to reflect the reinstatement of contextual features associated with the encoding events through projections from the hippocampus (Nyhus & Curran, 2010). Using an associative memory task, Jafarpour and colleagues (2014) found that the recollection of source information (faces and scenes) was associated with a replay of neural representations formed during encoding. This neural replay occurred between 400-550 ms after the probe (word) onset and correlated with source memory accuracy. Furthermore, a theta increase for hits compared with correct rejections was found over left-temporal channels between 250-700 ms, surrounding the time window for memory replay. These findings indicate that theta increases may be associated with neural reinstatement of contextual information during recollection.

In addition to neural reinstatement of memory traces, memory recollection also requires top-down control processes such as post-retrieval monitoring and the inhibition of irrelevant information in a goal-directed manner. Top-down control processes are also associated with theta power increases (Nyhus & Curran, 2010). During episodic retrieval, the PFC is thought to exert top-down control over the hippocampus and posterior cortex to recover memory traces (Polyn & Kahana, 2008). Theta source retrieval effects are often observed at frontal scalp sites (Gruber et al., 2008; Guderian & Düzel, 2005) and in time intervals that are in line with the post-retrieval monitoring interpretation (e.g., after 500 ms post-probe in Gruber et al., 2008). Furthermore, the magnitude of theta enhancement increases with the amount of retrieved information (Khader & Rösler, 2011). Therefore, in addition to the direct influences on the recovery of episodic memory traces, theta power may be associated with top-down control mechanisms such as post-retrieval processing. Post-retrieval monitoring involves a reactivation and manipulation of sensory representations of memory traces, which has been related to alpha power decreases (Hanslmayr, Staudigl, & Fellner, 2012). Alpha decreases are associated with recognition hits relative to correct rejections (e.g., Zion-Golumbic, Kutas, & Bentin, 2010) and usually found over posterior scalp sites such as the occipital regions (Klimesch et al., 1999). The topography of these alpha decreases varies with the type of to-be-retrieved information, e.g. left parietal effects for words and right parietal effects for faces (Burgess &

Gruzelier, 2000), and the strength of the effects varies as a function of the amount of retrieved information, i.e. larger amounts of retrieved information induce stronger alpha decreases (Khader & Rösler, 2011). Taken together, memory retrieval involves top-down control processes that may be reflected in oscillatory power changes in theta and alpha frequencies.

In the ERP approach, two retrieval effects have consistently been observed: the “left parietal” and the “right frontal” effects (e.g., Li et al., 2004; Mark & Rugg, 1998; Rugg et al., 1998; Trott et al., 1997; Wegesin et al., 2002; Wilding, 1999, 2000; Wilding & Rugg, 1996, 1997). Both effects are characterized by greater positive-going waveforms for correct source responses than for correct “new” judgments. The left parietal effect is thought to be a neural signature of recollection, because its magnitude varies as a function of the quantity and quality of the episodic information retrieved (Wilding, 2000). The right frontal effect is thought to reflect post-retrieval monitoring to form an integrated representation of a prior episode (Rugg & Wilding, 2000), or more general monitoring operations that are engaged to assess recovered information in a goal-directed way (Hayama, Johnson, & Rugg, 2008). The left parietal effect is commonly observed for episodic retrieval, whereas the right frontal effect appears more often during source retrieval compared to recognition tasks (e.g., Johnson et al., 1996; 1997; Senkfor & Van Petten, 1998; Van Petten et al., 2000; Wilding & Rugg, 1996). The right frontal effect is sensitive to the level of demands for post-retrieval monitoring (Rugg, Allan, & Birth, 2000), as well as the type of source information to be retrieved from memory (Wilding, 1999).

However, the contrast between source hits and correct rejections may not yield a putative representation of source retrieval, as it does not exclude the contribution from activity associated with item retrieval. That is, memory for contextual information in relation to an item must involve the memory for the item itself. To isolate brain activity related to source recollection alone, it would be more appropriate to compare neural activity associated with correct and incorrect source retrieval. The absence of this comparison in most previous ERP studies of source retrieval (Senkfor et al., 2002; Trott et al., 1997; Wilding, 1999; Wilding & Rugg, 1996) is mainly due to the low proportion of incorrect source responses available. The studies that did make this comparison gave inconsistent results. For example, Wilding and Rugg (1996) found a greater positive-going ERP deflection for correct than incorrect source responses spanning across the left parietal and right frontal effects. Rugg and colleagues (1996), in contrast, found the left parietal but not right frontal effect. The discrepancies between studies might be explained by differences in task requirements. In Wilding and Rugg's study, there was only one type of to-be-remembered source – male or female voices. In Rugg et al.'s study, however, each item was paired with its own source (i.e. word-pair association). As Rugg and colleagues speculated, the missing right frontal effect in their study might suggest that neural activity responsible for the effect is selectively engaged by the need to perform source discrimination. When many retrieval probes are associated with only two sources, as in Wilding and Rugg's study, presumably the need for source discrimination is greater. The left parietal effect, on the other hand, has generally been found to be sensitive to source retrieval success, i.e. greater amplitude for correct than incorrect source judgments (Wilding & Rugg, 1996; Rugg et al., 1996). In addition, it is sensitive to the strength of source memory even when item memory confidence is held constant (Woroch & Gonsalves, 2010).

It is important to note that one of these experiments employed two (Wilding & Rugg, 1996), and another three (Trott et al., 1997), successive responses. In both of these studies, the source memory judgment was the last one made. Since brain activity was recorded before the source judgment, it is possible that the actual neural activity relating to source retrieval might not be captured in the epochs analysed in these experiments, as Cycowicz and Friedman (2003) have noted. The previous studies that employed a source memory task without sequential responses reported more positive waveforms for correct than incorrect source responses (e.g., Senkfor & Van Petten,1998; Senkfor et al., 2002; Wilding, 1999). These effects could be observed at anterior (Cansino et al., 2012; Wilding, 1999), anterior central (Senkfor & Van Petten,1998), or posterior sites (Senkfor et al., 2002) depending on the nature of the source information.

Ageing research has consistently revealed that the putative recollection-based effects differ between younger and older adults. The left parietal old/new effect either becomes reduced and more right-lateralised (e.g., Dulas & Duarte, 2013; Li et al., 2002; Wegesin et al., 2002), or disappears completely (e.g., Swick, Senkfor, & Van Patten, 2006), in ageing. The right-frontal effect is generally not seen in older adults (e.g., Dulas & Duarte, 2013; Wegsin et al., 2002). A number of studies investigating the effect of age on source memory have instead reported a widespread, left-frontally or centrally focused negativity that is larger for correctly recollected old items than correct rejections regardless of whether words (e.g., Swick et al., 2006; Wegesin et al., 2002) or pictures (e.g., Dulas & Duarte, 2013; Li et al., 2004) are tested. This prominent negative-going activity starts at about 400-600 ms post-stimulus and therefore reduces or overshadows any other retrieval effects that might have presented.

A number of studies using younger adults have found a late posterior negativity (LPN), which is thought to represent neural activity related to additional search for visual information to support source recovery (see Johansson & Mecklinger, 2003 for review). Based on these studies, it has been suggested that the negative-going retrieval effects in older adults may reflect the use of alternate retrieval strategies, i.e., searching for visual information, as a consequence of greater demands on control processes required for source retrieval (e.g., Dulas & Duarte, 2013; Li et al., 2004). However, this interpretation was not supported by findings from an fMRI study (Morcom, Li, & Rugg, 2007). Using a memory paradigm similar to that used by Li and colleagues (2004), it was found that younger and older adults recruited the same left-frontal and parietal brain regions. Compared to younger adults, retrieval-related increases in neural activity were stronger and more widespread in older adults, whereas retrieval-related decreases were absent. These findings suggest that older and younger adults might recruit overlapping neural networks for source retrieval, with overall more activity engaged by older adults reflecting either compensatory or inefficient processing.

The compensatory interpretation for the retrieval-related negativity was supported by Swick and colleagues (2006) who contrasted not only healthy younger and older individuals, but also older patients with focal lesions of lateral PFC. As expected, patients were more impaired in source memory performance than healthy older adults, who in turn were more impaired than their younger counterparts. ERP results showed a left-frontally and centrally focused negativity in healthy older adults for source retrieval, which was smaller and delayed in the patients. Thus, it could be that the patients were unable to effectively recruit the compensatory mechanism that was used by healthy older adults. Furthermore, Dulas and Duarte (2013) found that when older adults were asked explicitly to pay attention to source information at encoding (presumably leading to more source information being processed), this ERP negativity was more pronounced than when they were not asked to pay attention to the source. This finding has provided the link between the ERP negativity at retrieval and the amount of source information available. The negative-going effect observed in older adults may reflect compensatory mechanisms selectively engaged to optimise source retrieval, probably when insufficient source information is available.

However, strong evidence supporting this compensatory interpretation is still lacking as no direct brain-behaviour correlation has been reported. Nevertheless, some attempts have been made towards this direction. When older adults were separated into high vs. low performing groups (Duarte et al., 2006; Friedman, de Chastelaine, Nessler, & Malcolm, 2010), the left-frontal negativity during source retrieval was found only in low-performing older adults. These findings pointed to the “dedifferentiation” interpretation (Reuter-Lorenz & Park, 2010), suggesting that low-performing older adults might recruit additional neural networks that are not specialised for source retrieval in younger adults. However, as discussed in Duarte et al. (2006), it cannot be ruled out that these networks are recruited to compensate for reduced recognition processing capacity especially in low-performing older adults. Further research is required to shed more light on the functional role of the negative-going retrieval effect observed in older adults, and whether it represents compensatory mechanisms or inefficient processing in ageing.

Very few studies have investigated source retrieval in ageing by comparing source hits with source misses. Cansino et al. (2012) showed younger and older adults images of objects on one of the four quadrants of a screen, and tested them in a one-step source memory task with the presentation location as the to-be-retrieved source. ERPs for recognised items were compared between those with correct source retrieval and those without. Both younger and older adults showed positive-going effects largest over anterior scalp regions for successful source retrieval. An age difference was found only in a late interval, 1600-2000 ms after probe onset, during which older adults showed a right-frontal effect whereas younger adults showed a frontal effect without asymmetry. No left-frontal negativity was observed in older adults, not even when comparing ERPs for correct source and correct rejection responses. The absence of the effect may be related to the encoding instructions in Cansino et al. (2012), which did not explicitly require participants to remember the source. When source memory is not emphasised, older adults might be less likely to recruit neural mechanism underlying the left-frontal negativity during source retrieval (Dulas & Duarte, 2013), possibly as a result of impoverished memory representations. Thus, the neural mechanisms underlying the left-frontal negativity may or may not be recruited by older adults depending on whether source memory is emphasized. If so, it might be suggested that the left-frontal negativity reflects control mechanisms that enhance source memory.

In summary, associative retrieval depends on neural processes related to the recovery of memory traces as well as cognitive control, which may be reflected in hippocampal and PFC activity respectively. Age differences in these processes have been found in ERPs (i.e., left-parietal and right-frontal effects) and oscillatory activity (i.e., changes in theta and alpha power). Also, some fMRI studies have revealed age differences in recollection-related brain activity, mostly in the hippocampus and the PFC. Older adults may engage compensatory activity for memory retrieval, as reflected in the over-recruitment of some PFC regions and the negative-going ERP retrieval effects. However, more evidence is clearly needed to determine the nature of these differences across age.

### 1.4.3 Encoding or retrieval?

Weighing up the existing evidence for associative information, it seems that when EEG studies are concerned, age differences in retrieval-related brain activity are more pronounced than those in encoding-related activity. When fMRI studies are concerned, however, this pattern seems to be reversed. The question arises whether associative memory deficits in ageing are more of an encoding problem or a retrieval problem. It has been proposed that associative deficits in ageing are due to the loss of encoding efficiency, as older adults are less able to encode information deeply and elaborately relative to younger adults (Craik & Rose, 2011). During episodic encoding, each event needs to be processed in relation to its specific context so that memory traces will be distinctive and more likely to be successfully remembered. It is thought that the richer the contextual information is encoded along with an event, the more likely such information will be reactivated in later retrieval. However, the older brain is thought to be less able to do so, as such elaborative encoding of episodic features requires complex control processes that are resource-demanding. In contrast, retrieval is thought to be relatively automatic and requiring few resources. Support for this hypothesis has come from studies using divided attention tasks, showing that when a secondary task is administered at encoding, subsequent retrieval performance in young participants can be reduced to levels typically seen with older participants under full attention conditions (e.g., Anderson, Craik, & Naveh-Benjamin, 1998). In contrast, secondary tasks at retrieval have little effect on retrieval accuracy. Moreover, Jennings and Jacoby (1993) showed that divided attention tasks at encoding produce the same pattern of retrieval performance in younger as older adults, i.e., intact familiarity and impaired recollection. These findings were taken to indicate preserved automatic memory processes and deficient control processes as a result of reduced attentional resources. Furthermore, a PET study (Anderson et al., 2000) demonstrated that a divided attention task during episodic encoding reduced brain activity related to encoding, i.e., activity in left PFC and MTL regions, whereas dividing attention during retrieval did not interfere with brain activity necessary for episodic retrieval. Therefore, behavioural and hemodynamic findings from divided attention studies support the hypothesis that memory deficits in ageing are due to diminished processing resources for encoding, but not retrieval.

However, as already discussed, reducing processing resources in younger adults at encoding does not produce exactly the same pattern of memory performance in ageing. Older adults have an additional deficit in associative memory that is not mimicked by divided attention, suggesting that there are other factors contributing to memory deficits in ageing. Furthermore, reducing processing resources at retrieval is not without behavioural costs. It has been shown that relative to encoding, retrieval leads to significantly poorer secondary task performance, especially for older adults (Anderson et al., 2000). Overall, secondary task performance tends to be poorer for older adults compared to younger adults, and the difference is larger at retrieval. These findings suggest that both younger and older adults prioritise retrieval over secondary tasks, and reducing processing resources at retrieval affects older adults to a greater extent than younger adults. More importantly, dividing attention during retrieval has been shown to reduce memory performance in older adults. Naveh-Benjamin, Craik, Guez, and Krueger (2005) found that although a secondary task during retrieval did not affect associative memory performance in younger adults, it reduced performance slightly but significantly in older adults. Therefore, associative retrieval is not automatic, but an effortful process that can be impaired by reducing processing resources. It appears that both encoding and retrieval demand cognitive resources, to a greater extent for older than younger adults.

Memory encoding and retrieval are sets of cognitive processes that are likely to be affected by different factors. Using a variety of divided attention tasks at encoding or retrieval, Fernandes and Moscovitch (2000) showed that retrieval can also be affected by reducing attention in young adults, but only with specific secondary tasks. When secondary and memory tasks compete for the same representational system, e.g., a verbal memory task paired with a verbal secondary task, interference would occur during retrieval. In contrast, any resource-demanding secondary tasks can cause interference during encoding. These findings demonstrate that even in younger adults, retrieval is not an automatic process. As the authors pointed out, it appears that memory encoding competes with secondary tasks primarily for general resources, whereas memory retrieval competes for representational systems. It may be inferred that encoding mostly demands general resources and retrieval processing-specific resources.

The neuroimaging findings described in the previous section suggest that healthy ageing is likely associated with changes in both associative memory encoding and retrieval. It is thus necessary to look at both encoding and retrieval when investigating associative memory deficits in ageing.

## 1.5 Cognitive neuroscience of ageing

Findings from neuroimaging studies have shed light on the mechanisms underlying age-related changes in cognition and behaviour. To better understand those findings, one needs to look into fundamental changes in the ageing brain, as well as how these changes affect cognition. In this section, main structural and functional changes of the ageing brain will be briefly introduced, and a number of cognitive neuroscience models (in particular the frontal ageing hypothesis and compensatory models of ageing) will be described. These models have been proposed to link cognitive ageing with structural and functional changes in the ageing brain by integrating research findings from psychology and the neuroscience of ageing.

### 1.5.1 Structural changes

A wide variety of structural changes in the ageing brain have been reported, including changes in grey matter such as reduced volume and thinning of the cortex, changes in white matter such as reduced integrity, changes in neurotransmitter systems, as well as the potential impact of risk factors for dementia illnesses such as Alzheimer's disease (see Grady, 2012 for a review). There is an extensive literature on reduced volume and thinning of the cortex, especially in the frontal lobes (Reuter-Lorenz & Park, 2010; West, 1996) and hippocampus and other MTL regions (Raz et al., 2005). These regions are thought to be important for associative memory, with the PFC playing a supervisory role over other brain regions including the MTL, while the MTL is responsible for binding-related processing (Giovanello & Dew, 2015). Age-related volume reduction in the frontal cortex has been shown to influence memory performance by modifying activity in other brain regions including the hippocampus (Rajah, Languay, & Grady, 2011).

In terms of white matter structure, decreases in white matter fibre density occur in various brain regions, most prominently in the frontal and especially the prefrontal cortices (Reuter-Lorenz & Park, 2010). Such changes in white matter integrity may mediate cortical activity and behavioural measures such as the speed and accuracy of task performance. For example, a longitudinal study (Persson et al., 2006) revealed that the corpus callosum white matter integrity, as well as the hippocampal volume, is reduced in older adults, and such reductions are correlated with reduced memory performance. Chen and colleagues (2009) also reported that the strength of corpus callosum integrity is positively correlated with the strength of functional connectivity in a network involving the inferior PFC and faster responses in older adults.

Studies have found age-related reduction in dopamine binding potential and receptor density, which affect reward processing (Dreher, Meyer-Lindenberg, Kohn, & Berman, 2008) and working memory performance (Bäckman et al., 2011). In a study reviewing age-related changes in dopamine functioning (Bäckman, Lindenberger, Li, & Nyberg, 2010), it was suggested that individual differences in dopamine functions are powerful mediators of age-related decline in executive functioning, episodic memory, and perceptual speed. When dopamine levels are directly manipulated, healthy older adults show enhanced episodic memory performance with increased dopamine level, albeit within a narrow dose range (Chowdhury, Guitart-Masip, Bunzeck, Dolan, & Düzel, 2012). Potential links between dopamine systems, LTM, and cognitive ageing through novelty processing have been proposed by Düzel and colleagues (2010) in a framework called 'NOvelty-related Motivation of Anticipation and exploration by Dopamine' (NOMAD). It is hypothesised that dopamine is important for attributing incentive salience towards novelty in the environment, which enhances hippocampal activation and neurogenesis that are important for episodic memory consolidation. Dopaminergic dysfunction in ageing is thought to reduce motivational salience attributed towards novelty, which in turn impairs memory.

### 1.5.2 Functional changes in spatial distributions of brain activation patterns

#### *1.5.2.1 The hemispheric asymmetry reduction in older adults (HAROLD)*

The HAROLD model was proposed by Cabeza (2002) to account for the findings that brain activity in the PFC during cognitive performance tends to be less lateralized in older adults than in younger adults. Subsequently, this model has been extended to other brain regions such as the hippocampus (e.g., Morcom, Good, Frackowiak, & Rugg, 2003). The model is supported by functional neuroimaging evidence in the domains of episodic memory encoding (e.g., Logan & Buckner, 2001), episodic retrieval (e.g., Cabeza, et al., 1997;

Grady, Bernstein, Beig, & Siegenthaler, 2002), working memory (Reuter-Lorenz et al., 2000), and inhibitory control (Nielson, Langenecker, & Garavan, 2002). For example, younger adults usually show stronger left-lateralised prefrontal activation for episodic encoding and right-lateralised prefrontal activation during episodic retrieval, whereas older adults show equivalent strength of activation across left and right PFC (Cabeza et al., 1997; Grady et al., 2002; Logan & Buckner, 2001). Furthermore, Morcom and colleagues (2003) found in an fMRI study that activity in left inferior prefrontal cortex and the left hippocampal formation was greater for subsequently recognized words in both age groups, consistent with the findings of previous studies in young adults. It is currently not clear whether such age-related hemispheric asymmetry reductions indicate additional brain activation to compensate for declined cognitive abilities (i.e. compensation), less efficient functioning of PFC regions, or reduced distinctiveness of neural representations (i.e. dedifferentiation: see Rajah, Maillet, & Grady, 2015 for further discussion). It is also not clear whether the changes are cognitive or structural in origin.

#### *1.5.2.2 The posterior-anterior shift in ageing (PASA)*

The PASA model states that ageing is related to increased activity in PFC coupled with reduced activity in more posterior regions (Davis, Dennis, Daselaar, Fleck, & Cabeza, 2008). Spreng, Wojtowicz, and Grady (2010) conducted meta-analyses assessing convergent and divergent patterns of brain activity in old and younger adults across 80 neuroimaging studies. It was found that old adults engage prefrontal regions more than young adults do across a variety of cognitive domains including perception, memory encoding, memory retrieval, and especially executive function. Young adults engage occipital regions more than old adults, particularly when performance is unequal and driven largely by perceptual functions. Furthermore, the laterality of frontal activation in older adults is influenced by their task performance. Well-performing older adults show greater left prefrontal activity whereas poor-performing older adults engage right prefrontal cortex. There is no reliable age difference in the parietal lobes, suggesting that these regions may be immune to the effects of age.

#### *1.5.2.3 Changes in functional connectivity*

Age-related changes in the spatial distribution of functional brain activation may be related to the disruption in functional connectivity between task-relevant brain regions. For example, in relation to the PASA pattern, one study (Daselaar, Fleck, Dobbins, Madden, & Cabeza, 2006) using a verbal recognition task showed reduced functional connectivity within a hippocampal-parietotemporal network but increased connectivity within a parahippocampal-frontal network in older adults. As mentioned previously, this points to a posterior-to-anterior shift in functional connectivity between task-relevant brain areas including hippocampal regions. Similarly, successful memory encoding in older adults may be mediated by PASA in the functional connectivity between MTL and other task-relevant brain regions. Studies measuring encoding-related activity for words (Dennis et al., 2008), scenes (St Jacques, Dolcos, & Cabeza, 2009) or objects (Addis, Leclerc, Muscatell, & Kensinger, 2010) consistently show weaker connectivity between MTL and posterior regions such as the occipital cortex, but stronger connectivity between the MTL and the PFC in older adults.

Weakened functional connectivity between PFC and posterior regions may be important to explain the mechanisms of cognitive ageing. For example, it may reflect the reduced ability in older adults to attend to and make use of task-related information. Although attention to specific task-related cues is associated with activation of the dorsal PFC and parietal regions in both younger and older adults, functional connectivity between these regions is enhanced in younger relative to older adults (Madden et al., 2012). Crucially, this increase is positively correlated with efficient executive control performance.

### 1.5.3 Functional changes in temporal dynamics of brain activation patterns

In addition to age-related differences in the spatial distribution of brain activation, there are also differences in temporal dynamics, as stated in the early-to-late shift in ageing (ELSA) model (Dew, Buchler, Dobbins, & Cabeza, 2012). In an fMRI study comparing older and younger adults in an executive control task (Paxton, Barch, Racine, & Braver, 2008), it was found that activity in lateral PFC associated with goal maintenance was reduced in an early time interval (during cue processing) and increased in a later interval (during probe processing) in older adults relative to younger adults. A similar early-to-late shift in ageing was replicated in an episodic retrieval study (Dew et al., 2012), not only in the PFC, but also in the MTL. Furthermore, higher functional connectivity between the left hippocampus and PFC was found during cueing than during successful probe in the young, and vice versa in older adults. These findings point to an age-related failure to engage in early, proactive processing to constrain incoming information to enhance subsequent task performance. Instead, older adults may rely on late, reactive processing elicited by the probes, as reflected in activity in posterior parietal cortex linked with bottom-up attention and activity in visual association cortex related to memory trace recovery, in addition to PFC and MTL activation (Dew et al., 2012). Thus, the early-to-late shift in ageing may reflect a delayed activation of various brain regions to compensate for poor preparation. Of particular importance to episodic memory, the connectivity between PFC and MTL has been shown to increase during the anticipation of contextual retrieval relative to item retrieval (Dobbins & Han, 2006). Thus, a reduction of the PFC-MTL connectivity in older adults during cue processing may indicate an age-related decline in the preparation for contextual retrieval, whereas increased probe-related PFC-MTL connectivity is likely to reflect post-retrieval processing of memory representations.

### 1.5.4 Frontal ageing hypothesis

As described above, age-related structural and functional changes as revealed by neuroimaging research usually involve the frontal lobes. Also, the effect of aging is pronounced on tasks require cognitive control, which is often linked to the frontal lobes. Based on these findings, the ‘frontal ageing hypothesis’ (West, 1996) claims that the pattern of cognitive deficits in ageing can be linked to structural and functional changes in the frontal lobes that develop as a result of normal ageing (Cabeza et al., 2004; Grady et al., 2006). In particular, cognitive functions that are impaired in ageing, such as episodic memory and executive functions, can be localised in the frontal lobes (Craik & Rose, 2011; West, 1996). The general idea is that older adults are less able to self-initiate appropriate strategy, which is associated with a decrease in frontally-based control mechanisms (Craik & Rose, 2011).

The frontal lobes, especially the PFC regions, are thought to play a supervisory role over other brain regions including the MTL during episodic memory processing. At encoding, the PFC it thought to organise input into the

MTL (Blumenfeld & Ranganath, 2007), and during retrieval it mediates goal-directed searching and post-retrieval monitoring processes (Cabeza, 2006). Particularly relevant to ageing, the frontal lobes are important for source memory. Focal lesions to the PFC in human subjects typically produce larger impairments in associative memory than item memory (Wheeler, Stuss, & Tulving, 1995). The patients are disproportionately impaired on cued recall and free recall than old/new recognition. Furthermore, numerous fMRI findings indicate that regions in the PFC are activated during associative memory encoding (e.g., Park & Rugg, 2008; 2011) and retrieval (Ranganath et al., 2004). It has also been suggested that PFC subregions may differentially contribute to different types of associative information (e.g., perceptual, temporal) or different cognitive processes engaged during the task (Giovanello & Dew, 2015; Ranganath, 2004).

In addition, there are age differences in PFC activity during associative memory processing. In a study of word-pair associate learning, Anderson et al. (2000) found that only young adults activated regions of the left inferior PFC whereas older adults showed relatively more activation in the inferior parietal lobes. As the left inferior PFC has been associated with semantic encoding (Buckner et al., 1999), these age-related differences are taken to indicate that older adults do not rely on semantic processing as much as younger adults do. Similar findings of age-related decreases in left inferior PFC regions have been reported by Cabeza et al. (1997) using verbal paired associates and by Dennis et al. (2008) using a source memory task. During word-pair associative retrieval, younger adults showed right-lateralised PFC activity whereas older adults showed bilateral PFC activity (Cabeza et al., 1997). Therefore, consistent with the HAROLD model (Cabeza, 2002), older adults have reduced hemispheric asymmetry during associative memory processing, suggesting a link between changes in frontal activity and impaired associative memory in ageing. Moreover, it has been demonstrated in an fMRI study (Kim & Giovanello, 2011) that depleting processing resources in young adults using a divided attention task during associative memory encoding yields the same patterns of behavioural and neural changes as observed in older adults. Thus, both age-related associative memory deficits and changes in frontal functioning can be linked to diminished processing resources.

Episodic memory relies a great deal on executive control processes, including elaboration and organization of episodic information during encoding, as well as searching for and evaluation of such information during retrieval (Mitchell & Johnson, 2009). Such executive control processes have often been associated with the PFC (e.g., Düzel et al., 2001). Previous studies also found age-related differences in PFC activity in relation to executive control in episodic memory processing. For example, Logan and colleagues (2002) reported that older adults under-recruit left PFC relative to younger adults during intentional encoding of verbal stimuli, but not during incidental encoding in a semantic task. Thus, when the same encoding strategy is engaged, age differences in PFC activity are eliminated. This suggests that the under-recruitment of left PFC is related to impairment in spontaneous use of an effective encoding strategy. Divided attention studies using neuroimaging methods also provide evidence supporting the relationship between frontal dysfunction and impaired executive functions in ageing. In a PET study in which young adults learned auditorily-presented word pairs while simultaneously performing an easy or difficult visual-motor task (Shallice et al., 1994), it was found that left dorsolateral PFC was activated during the easy task but not the difficult task. Thus, the effect of divided attention resembles the effect of ageing in reducing left PFC activity during the encoding of verbal material. Other studies (e.g., Anderson et al., 2000; Iidaka et al., 2000) reported similar results, and found significant correlations between left PFC activity and subsequent memory performance. It was thought that similar effects of ageing and divided attention on left PFC activity during encoding reflect a reduced ability to effectively engage in elaborative encoding strategies (Anderson et al., 2000).

### 1.5.5 Compensatory activity in ageing

The compensation hypothesis of ageing was proposed to account for findings from neuroimaging studies that in older adults, decreased cognitive functions often co-occur with the presence of additional brain activity (i.e., over-recruitment) that does not present in the young (e.g., Cabeza, Anderson, Locantore, & McIntosh, 2002; Grady, McIntosh, Rajah, Beig, & Craik, 1999; Reuter-Lorenz & Cappell, 2008). It is thought that older adults attempt to compensate for age-related declines in cognitive abilities by engaging additional brain activity, usually involving the frontal lobes. However, over-recruitment of neural resources is not universally found in older adults, who sometimes show equivalent or less brain activity compared to younger adults. To account for the inconsistent findings, Reuter-Lorenz and Cappell (2008) proposed the compensation-related utilization of neural circuits hypothesis (CRUNCH) and argued that the extra brain activity reflects more neural resources recruited by older adults at low levels of cognitive load. Younger adults, in contrast, do not need additional neural resources in these situations. At higher levels of cognitive load, this compensatory activity is no longer effective, resulting in equivalent or less activation in older adults. According to CRUNCH, over-recruitment in older adults is an attempt to compensate for less effective use of neural resources at low cognitive load. For example, increased activation in the frontal cortex in older adults may reflect the attempted compensation for age-related impairments in neural efficiency of posterior regions (in line with PASA), or de-differentiation of the frontal cortex (in line with HAROLD).

An alternative, but similar, account is the scaffolding theory of aging and cognition (STAC; see Park & Reuter-Lorenz, 2009; Reuter-Lorenz & Park, 2010 for reviews). STAC explains the additional brain activity using the concept of “scaffolding”, referring to a process that can occur across the life span whenever demanding processing conditions arise such as learning a new task. The key difference between STAC and other compensatory hypotheses is that the scaffolding process is a normal response, which can occur adaptively across age. According to STAC, over-recruitment of neural resources also occurs in younger adults when needed.

Despite the basic assumption that older adults engage additional brain activity to improve task performance, it is not clear how effective the compensatory activity is. The effectiveness can be measured by correlating the extent of the extra brain activation with task performance. However, the existing evidence is inconsistent and relatively scarce. For example in memory research, additional brain activity in older adults has been positively correlated with memory performance, or present in high- but not low-performing older adults in some studies (e.g., Anderson et al., 2000; Cabeza et al., 2002). In other studies, it was negatively correlated with performance (e.g., Colcombe, Kramer, Erickson, & Scalf, 2005; de Chastelain et al., 2011). The left-frontal negative ERP retrieval effect in older adults, as discussed in a previous section, may also be ineffective for memory retrieval (Nessler, Friedman, Johnson Jr, & Bersick, 2007). Such inconsistent findings somewhat undermine the compensatory interpretation of additional brain activity in ageing. For example, there has been debate about whether age-related over-recruitment of particular brain regions reflects compensation or dedifferentiation, as a positive brain-behaviour correlation is thought to support the former whereas a negative correlation is thought to support the latter (Park & Reuter-Lorenz, 2009). However, the discrepant evidence may also suggest that the attempts to compensate are not always successful. It may be argued that compensatory activity only mitigates age-related impairments to some extent, as the effectiveness of compensatory activity is likely to depend on many factors, such as the extent to which other task-related cognitive processes are compromised. For example in memory, there are multiple stages of processing during encoding, maintenance, and retrieval. If memory encoding and/or maintenance processes are severely impaired (e.g., poor-performing older adults), engaging in compensatory activity during retrieval may have little effect on memory performance. On the other hand, it is also possible that high-performing subjects are less inclined to recruit compensatory mechanisms at retrieval because these subjects rely on relatively intact encoding processes to enhance performance.

Further research is needed to provide more information about the nature and functional roles of additional brain activity in older adults. Existing evidence is inconclusive with respect to whether over-recruitment reflects compensatory or ineffective use of neural resources. If it is compensatory in nature, it is unclear whether it represents general cognitive processes such as an upregulation of attention, or task-specific processes. Furthermore, to better understand compensatory activity, more evidence is needed to specify the necessary and sufficient conditions for its occurrence.

In summary, along with structural changes in the brain, especially in the frontal lobes and MTL, ageing is associated with a number of functional changes in the spatial distribution, temporal dynamics, and functional connectivity of brain activation. These changes have been linked to age-related deficits in executive control processes, and additional brain activity, mostly in the frontal lobes, that is thought to reflect compensatory mechanisms for reduced cognitive abilities. It appears that the key in cognitive ageing relates to deficits in cognitive control and changes in the frontal lobes.

## 1.6 Anticipatory activity and memory

As discussed above, episodic memory relies a great deal on cognitive control processes, including elaboration and organization of episodic information during encoding, and goal-directed search for information during retrieval (Mitchell & Johnson, 2009). An important aspect of cognitive control during episodic memory processing is the anticipation of an upcoming event. It has been shown across a number of cognitive domains such as attention, action, perception, and emotion that brain activity just before an event can influence how the event is processed (e.g. Cunnington et al., 2003; Driver & Frith, 2000; Galli, Wolpe & Otten, 2011; Shibata et al, 2008). This is also the case for episodic encoding (e.g. Otten et al., 2006) and retrieval (Addante et al., 2010). In this section, neuroimaging studies investigating anticipatory brain activity, especially in regard to the contingent negative variation (CNV), will be briefly introduced. Then, attention will be paid to studies looking at the effect of age on such anticipatory activity. Following this, neuroimaging findings on anticipatory memory-related brain activity will be reviewed.

### 1.6.1 Anticipatory brain activity

The CNV is a well-known neural signature of anticipation, manifesting as a sustained negative ERP deflection typically observed over frontocentral scalp sites (see Brunia, van Boxtel, & Böcker, 2012 for a review). The CNV is usually elicited by a warning signal (S1) preceding an imperative stimulus (S2) that requires a quick response. The negative shift increases gradually and reaches the maximum just before stimulus onset, with a magnitude as large as 20 µV. The negative shift is thought to reflect anticipatory mechanisms that allow for more efficient processing and a quicker response to the stimulus.

Early studies of the CNV mainly used neutral warning signals as S1, and more recent studies have used instructional warning signals that contain information about the upcoming stimulus (e.g., Shibata et al., 2008). These instructional cues have been shown to elicit preparatory brain activity relevant for the processing of upcoming stimuli. For example, in a study (Shibata et al., 2008) using visual cues indicating whether colour or motion of an upcoming stimulus needs to be attended, it was found that brain regions that are selective for colour or motion processing are activated in pre-stimulus intervals. Similarly, when different categories of objects are cued, corresponding brain regions are activated before stimulus onset (Driver & Frith, 2000). Furthermore, the amplitude of the CNV is influenced by the motivation to prepare. Using instructional cues to signal the difficulty of and the amount of monetary reward for an upcoming task, Schevernels and colleagues (2014) found that the magnitudes of CNV were larger than when the upcoming task was easy. When no reward was attached to the upcoming task, there was no difference in CNV magnitudes between difficult and easy tasks. Also, response times in the tasks were faster when the differences in CNV between difficult and easy tasks were larger but only when monetary rewards were expected. These findings suggest that the CNV is an index of preparatory processing, which can be influenced by motivation and reward.

Not many studies have been conducted to investigate the effect of ageing on the CNV. The limited amount of evidence suggests that the magnitude of the CNV is generally smaller for older than younger adults, especially when the CNV is measured from frontal scalp sites (see Dustman, Shearer, & Emmerson, 1993 for a review). In an EEG study, Zanto et al. (2011) showed that young adults are quicker to respond to targets preceded by cues predictive of the timing of the target presentation, relative to targets preceded by non-informative cues. This preparatory benefit was also shown in brain activity, as reflected in larger CNV amplitude in the predictive cue condition than unpredictive cue condition. Neither the behavioural improvement nor the difference in neural activity was observed in older adults. It was suggested that older adults are unable to engage expectation-based neural processes to orient attentional resources over time, supporting an expectation deficit hypothesis of ageing. Even though there is also evidence suggesting either no age differences in the CNV (Friedman et al., 1990) or larger CNVs in older relative to younger adults (Podlesny & Dustman, 1982), a general trend in the existing literature is that older adults may be impaired in anticipatory activity, at least as reflected by the CNV.

### 1.6.2 Anticipatory encoding-related activity

Anticipatory activity before encountering an event may influence how well this event will be remembered. A number of EEG studies (e.g., Galli et al., 2011; Gruber & Otten, 2010; Otten et al., 2006) using subsequent memory paradigms have shown prestimulus anticipatory activities that benefit episodic encoding, i.e. prestimulus subsequent memory effects (PSME). Different types of PSMEs have been found using ERP analyses, for example, a negative ERP modulation over frontal scalp sites which is associated with semantic but not non-semantic processing (Otten et al., 2006), and a widespread positive ERP modulation that is associated with high reward but not low reward (Gruber & Otten, 2010). The negative-going PSME is thought to reflect the mobilisation of semantic processing resources in preparation for semantic encoding, whereas the positive-going PSME is thought to reflect emotional (Galli et al., 2011) or motivational preparation. An early engagement of such mechanisms before event onset may aid the formation of an appropriate neural context that facilitates deeper, more elaborative encoding, which leads to successful retrieval later on (Craik & Lockhart, 1972). Thus, a plausible hypothesis for the mechanisms of PSMEs would be that different prestimulus modulations reflect different preparatory processes that are cue-specific. For example, when people are cued to perform a semantic task, semantic processing resources are prepared, which facilitates subsequent semantic encoding. Similarly, when a higher reward is expected, motivation-related processing is prepared, which may be related to dopaminergic activity for reward (Gruber, Watrous, Ekstrom, Ranganath, & Otten, 2012).

Prestimulus anticipatory mechanisms are not always successfully engaged during memory encoding. For example, it has been demonstrated that PSMEs are sensitive to the level of available processing resources (Galli et al., 2011). PSMEs are evident only when sufficient processing resources are available, but not when processing resources are compromised by difficult secondary tasks during the anticipation interval. Therefore, it is likely that encoding-related anticipation is a controlled process that can be successfully engaged only when sufficient processing resources are available. This suggests that older adults might have specific impairments in the engagement of anticipatory neural mechanisms due to diminished processing resources (Craik, 2005). If so, it is possible that age-related memory deficits, e.g., deficits in source memory, are at least partly due to such impairments in prestimulus anticipatory mechanisms.

Very few studies have directly tested the effect of age on prestimulus anticipatory activities in memory encoding, but existing evidence points to an age-related deficit in anticipatory processing. As previously described, Zanto et al. (2011) have shown an age-related impairment in the ability to use predictive cues to improve performance in an attentional orienting task. This finding, together with studies (Gazzaley et al., 2008; Zanto et al., 2010) using other types of attentional orienting tasks (e.g., feature- and object-based), indicate a general expectation deficit in ageing.

The failure to engage expectation mechanisms may affect the formation of an adequate neural context for an upcoming stimulus, which in turn may affect stimulus processing and memory encoding. An fMRI study has provided evidence supporting such an encoding-related anticipatory deficit in ageing.

Bollinger and colleagues investigated prestimulus encoding-related activity in both younger (Bollinger et al., 2010) and older (Bollinger et al., 2011) adults. Predictive cues indicating the type of upcoming stimuli (faces or scenes), as well as unpredictive neutral cues, were presented before stimulus onset. Younger adults showed improved working memory and LTM performance when stimulus categories were expected relative to when they were unexpected. Older adults, in contrast, did not show these memory benefits. Consistent with the pattern of behavioural findings, fMRI data also indicated age-related deficits in the engagement of expectation mechanisms. Unlike younger adults, older adults failed to show expectation-driven activity increases in the relevant brain regions such as the fusiform face area (FFA). This inadequate prestimulus FFA modulation was significant only in a subgroup of older adults who did not show memory benefits from predictive cues, suggesting a relationship between expectation-driven sensory preparation and subsequent memory performance. Older adults also showed decreased functional connectivity between the FFA and regions in a fronto-parietal top-down control network during the expectation period. This expectation-mediated functional connectivity was positively correlated with memory performance in younger adults only. Taken together, these findings demonstrate that expecting a stimulus category could activate stimulus-specific sensory processing before stimulus onset, which enhances later memory for that stimulus. However, older adults may be impaired in such anticipatory mechanisms, which has a negative influence on both working memory and LTM. Furthermore, these encoding-related anticipatory processes are related to top-down control networks that might be malfunctioning in ageing.

Bollinger and colleagues’ studies have provided crucial evidence for age impairments in encoding-related prestimulus anticipatory processing. However, the validity of these findings has been questioned (Galli, Bauch & Gruber, 2011). In Bollinger et al. (2010, 2011), the presentation of stimuli was blocked by category, which leads to uncertainty about whether prestimulus brain activity is related to anticipation or on-going category-specific processing (Galli et al., 2011). That is, it is possible that the observed anticipatory activity is actually due to category-selective activation maintained throughout the block. Thus, it is possible that the PSMEs in fact reflect post-stimulus processing of items in the same category. If this is the case, the observed age difference might not reflect a difference in prestimulus activation of category-specific brain regions, but an age difference in the processing of a given stimulus. Therefore, a more careful experimental design is needed with a more precise delineation of prestimulus activity during encoding.

Taken together, a number of SMEs have been identified and associated with different cognitive processes. It has also been shown that successful engagement of anticipatory encoding-related activity depends on the amount of available processing resources. Older adults may be impaired in such anticipatory mechanisms, which have a negative influence on both working memory and LTM. More evidence from carefully designed experiments is needed.

### 1.6.3 Pre-probe anticipatory retrieval-related activity

Memory retrieval can be thought of as the interaction between a retrieval cue and an internal representation of memory traces (Tulving, 1983). Successful retrieval of episodic information may be influenced by anticipatory activity that guides such interactions to recover specific information. Previous research (e.g., Herron & Wilding, 2004; Johnson & Rugg, 2006) has shown that cueing subjects to retrieve specific information from memory leads to alterations in cue-elicited anticipatory brain activity before the presentation of a retrieval probe, depending on the kind of information to be retrieved. For example, Johnson and Rugg (2006) found that ERPs were more positive-going when words rather than pictures were targeted. The patterns of anticipatory activity also differ depending on whether retrieval of information is mixed or blocked in an experiment (Morcom & Rugg, 2002; Werkle-Bergner, Mechlinger, Kray, Meyer, & Düzel, 2005; Johnson & Rugg, 2006). For example, a sustained frontal ERP positivity has been found to be greater when test lists are mixed rather than blocked (Johnson & Rugg, 2006). These pre-probe brain activities have been conceptualised in terms of ‘retrieval mode’, a cognitive state that allows retrieval processes to be triggered, and ‘retrieval orientation’, a task-specific retrieval strategy that modulates the retrieval processes in a goal-directed manner (Rugg & Wilding, 2000). It has been speculated that preparatory cue-elicited brain activity reflects either an initial task set configuration, i.e., the attempt to activate the appropriate retrieval orientation, or a selective activation of memory representations for the targeted information.

An EEG study using oscillatory analyses (Addante, Watrous, Yonelinas, Ekstrom & Ranganath, 2011) has found that pre-probe brain activity, manifested as enhanced neural synchronisation in the theta range, was associated with successful retrieval of source information. Differences between source hits and source misses in theta power were found at left temporal and left parietal scalp sites from 300 ms before stimulus onset, which spread to mid-frontal sites 150 ms later. The frontal effect starting 150 ms before the onset of the retrieval probe was correlated with source memory accuracy across and within subjects, indicating that the effect directly relates to subjects’ ability to retrieve source information. Furthermore, it was found that the magnitude of prestimulus theta was related to the magnitude of post-stimulus theta. This suggests that prestimulus brain activity in anticipation of a retrieval probe may facilitate successful source retrieval. Addante and colleagues (2011) suggested that the pre-probe theta activity might reflect cortico-hippocampal interactions that serve a functional role similar to “retrieval orientation” or “retrieval mode”. Thus, it is possible that pre-probe brain activity at retrieval reflects an early activation of relevant brain networks in anticipation of the retrieval of required information (Polyn, Natu, Cohen, & Norman, 2005; Sederberg et al., 2009). This anticipatory activity may influence probe-elicited processing and facilitate episodic source retrieval.

However, a problem with Addante et al.’s (2011) study is that no preparatory cue was used to separate neural activity related to anticipation from activity related to retrieval in the preceding trial. Although retrieval probes were presented at regular intervals, it cannot be ruled out that the pre-probe theta activity reflects post-probe retrieval processing to some extent, as participants might not use the timing information to prepare for the probes. The question remains whether pre-probe retrieval-related activity can be elicited by preparatory cues, and if so, whether it is affected by ageing.

An fMRI study (Dew, Buchler, Dobbins & Cabeza, 2011) has given clues to these questions. Using a source memory task with pre-probe cues indicating whether contextual information was to be retrieved, the study found that younger adults had increased activity in the MTL during pre-probe cueing, whereas older adults showed increased MTL activity only after probe onsets. The probe-elicited hippocampal activity in older adults was correlated with the proportion of correct source hits. Functional connectivity between left hippocampus and PFC showed the same pattern of age differences. PFC activity increased during the cueing of context retrieval, relative to item retrieval (Dobbins & Han, 2006), indicating that it is critical for context retrieval preparation. Therefore, although the cue-related MTL activity was not correlated with memory performance in either age group, the results in Dew et al. (2011) were interpreted as demonstrating an age-related failure to engage in proactive processing, i.e., pre-specifying memory representations from which to match the upcoming retrieval probes, in order to improve retrieval. These findings pointed to an age-related decline in pre-probe anticipatory brain mechanisms for source retrieval.

Taken together, anticipatory brain activity can influence memory processing during both encoding and retrieval. Although previous findings indicate a general anticipatory deficit in ageing, there is currently insufficient evidence to know whether older adults are impaired in anticipatory brain activity in relation to associative memory. This question is at the heart of the current PhD dissertation. Before outlining the experiments that were conducted to address the role of anticipatory processes during encoding and retrieval of source information in younger and older adults, this introductory chapter will review the neuroimaging methodology that was employed in the experiments.

## 1.7 EEG methods

Scalp EEG was the neuroimaging method of choice to investigate the relationship between cognitive functions and brain activity in this thesis. As described earlier, EEG reflects voltage changes over time between an active site and a reference site. The amplitudes of scalp EEG signals are tiny, usually in the range of microvolts. These small signals are amplified and subjected to analog-to-digital conversion. The amplification factor used in this thesis was 20,000. The resolution of the AtoD converter was 12 bits, which means the analog EEG voltages are represented by $2^{12} = 4096$ values. The gain of an EEG recording system can be calculated by the amplification factor and the resolution of the AtoD converter (Picton et al., 2000). In the present EEG system, as the range of AtoD conversion for the signals is ±5 V, the gain of the system can be calculated as 10/20,000/4096, which is 0.122 µV/bit. The digital values are reconstructed into waveforms representing voltage changes of the analog EEG signals.

How well a continuous EEG waveform can be represented by discrete digital values depends on the sampling rate, which is the number of digital data points per second sampled from the analog EEG waveform. The higher the sampling rate, the better the reconstructed waveform. According to the Nyquist theorem, the sampling rate must be at least twice the highest frequency in the signal to avoid aliasing, a form of signal distortion where a higher frequency signal is misrepresented as a lower frequency signal due to under-sampling (Luck, 2014). Overly high sampling rates result in redundancy and unnecessarily large data files.

EEG signals are usually filtered to eliminate low frequency artefacts, e.g., skin potentials caused by sweat and breathing, and high frequency noise, e.g., electrical line noise and muscle movements. Therefore, both low-pass and high-pass filters are applied, with a low-pass filter selected to cut off noise above a certain frequency while avoiding the aliasing problem and a high-pass filter to cut off drifts slower than a selected frequency (Luck, 2005). In this thesis, online analog band-pass filters were between 0.01 Hz and 35 Hz, eliminating the 50 Hz line noise and some of the slow drifts related to artefacts. Although these settings could not completely remove muscle artefacts and task-irrelevant slow drifts, they allowed the EEG activity of interest to remain, such as slow modulations related to anticipation and ERP SMEs, as well as oscillatory activity in theta (4 - 8 Hz) and alpha (8 - 12 Hz) frequency bands. Offline digital filters were also applied, with 0.05 Hz and 20 Hz for ERP analyses and a high-pass filter at 0.5 Hz for time-frequency analyses. Even though any form of filter can lead to distortion in amplitude and latency of the signals (Luck, 2005), a zero-phase-shift filter with narrow width of the transition band was used to achieve optimal results.

As already discussed, EEG is particularly useful for the study of memory because of the ease with which neural activity associated with successful and unsuccessful memory can be compared. Furthermore, EEG is an excellent tool for dissociating brain activity before and after a stimulus because of its high temporal resolution (Otten et al., 2006; Rugg et al., 2002). Therefore, EEG is best suited for the present research purpose of investigating anticipatory memory-related brain activity. Pre-stimulus and post-stimulus memory-related EEG activities were analysed using both the ERP and time-frequency approaches. As described in that section, ERP and time-frequency analyses are based on averaging procedures to extract event-related activity from EEG epochs time-locked to a class of experimental events. To ensure an appropriate signal-to-noise ratio, in this thesis at least 16 artefact-free trials for each experimental condition were used. This is considered to be an acceptable number also used in many previous LTM studies (Picton et al., 2000).

### 1.7.1 ERP analyses

The ERP analyses in this thesis utilised the mean amplitude method to quantify ERP waveforms, i.e., averaging amplitudes in a pre-defined time interval (Luck, 2014). The advantage of this type of measurement is that it is minimally affected by noise and individual differences in the signal, but at the expense of not being able to assess latency differences across conditions. An issue with this method is how to select appropriate time windows for quantification. It is possible to use multiple narrow time windows, which somewhat remedies the problem with assessing latency differences across conditions. However, using many time windows would aggravate the multiple comparison problem and increase the risk of Type 1 errors (Kilner, 2013). In the present studies, the selection of time windows was primarily based on existing knowledge. When existing knowledge was scarce or inconsistent, care was taken not to select time windows purely based on visual inspection.

Statistical analyses of ERP data were performed using analyses of variance (ANOVA). Although effective and commonly used, ANOVAs using ERP data are particularly susceptible to the violation of the assumption of sphericity with repeated measures. This means that the variances of the differences between any two levels of an independent variable have to be equal. The consequence is an increase of the risk of Type 1 error. To avoid such risk, the Greenhouse-Geisser correction procedure (Keselman & Rogan, 1980) was used when violations of sphericity occurred. The Greenhouse-Geisser correction estimates epsilon (an index of the extent of the violation of sphericity) and this measure is used to correct the degrees of freedom of the *F*-distribution.

When electrode sites are entered into an ANOVA as a factor, significant interactions between experimental conditions and electrode sites reflect differences in ERP scalp distribution between conditions. In turn, this is thought to reflect qualitative differences in the underlying neural mechanisms of the ERP effects across conditions. However, McCarthy and Wood (1985) demonstrated that such interactions can be caused by multiplicative changes in the amplitude of a single ERP generator. It is therefore recommended that ERP data should be normalised to avoid this problem. A number of scaling methods have been proposed, with the max/min and vector methods being most effective. Max/min scaling involves identifying the maximum and minimum amplitude across all electrodes sites for each condition, subtracting the minimum value from each site and then dividing the outcome by the difference between the maximum and minimum. Vector scaling involves dividing the voltage at each electrode by the vector length for that condition. As there are unsolved interpretational problems with the vector scaling method (Urbach & Kutas, 2002, 2006; Wilding, 2006), the max/min method was used in this thesis to ensure that significant interactions involving factors of electrode site were not confounded by overall amplitude differences across conditions or groups.

### 1.7.2 Oscillatory analyses

The time-frequency approach involves the decomposition of EEG signals into magnitude and phase information in different frequencies (see Neuroimaging Methods section). This is accomplished through multiplication of the signals with a windowed transformation function (e.g., Morlet wavelet) centred on a segment of the EEG epoch, an operation known as “convolution”. By sliding this windowed function across the EEG time series, a complex number is derived at the window’s centred point for each time point. The resulting time series of complex numbers (i.e., complex coefficients) are used to derive magnitude and phase angle information. There are many methods for time-frequency decomposition, each with different temporal and frequency resolutions. In essence, the larger the time window used to estimate the complex data for a given time point, the higher the frequency resolution but poorer the temporal resolution, and vice versa. In this thesis, the method of choice was Morlet wavelet decomposition, which has been shown to strike a good balance between temporal and frequency resolutions (van Vugt, Sederberg, & Kahana, 2007). The analyses focused on theta and alpha oscillations, both of which play important roles in memory processing. The Morlet wavelet method has been shown to offer superior frequency resolution when the frequencies of interest are below 40 Hz, which is well suited for the investigation of theta and alpha oscillations (4 – 12 Hz). A fixed number of oscillation cycles (4 cycles) were used for the wavelet function for each frequency, which has been used effectively for the decomposition of theta and alpha oscillations in previous work (e.g. Gruber et al., 2013).

Although theta and alpha frequency bands are commonly defined as 4-8 Hz and 8-12 Hz respectively, the frequency boundaries can vary across studies (Klimesch, 1999). For example, Fell et al. (2011) used 4 – 7 Hz for the rhinal cortex and 3 – 7 Hz for the hippocampus when investigating encoding-related pre-stimulus theta power. Klimesch (1999) reviewed a number of studies investigating alpha activity using various frequency bands ranging from 7 Hz to 14 Hz, and suggested that due to individual differences in brain oscillations, theta and alpha bands should be adjusted for each participant using individual alpha frequency as an anchor point. To be consistent across experiments and with previous literature, in this thesis theta and alpha bands were instead defined as 4-8 Hz and 9-12 Hz respectively, chosen based on the traditional definition (Herrmann et al., 2005). The reason for choosing 9-12 Hz, instead of 8-12 Hz, for the alpha band was to avoid overlap between theta and alpha bands. Having some separation between frequency bands helps to avoid the boundary frequency being picked up twice, which may increase the chance of Type I errors (Herrmann et al., 2005; Mazaheri & Picton, 2005).

Event-related spectral perturbation (ERSP), a measure of total power, i.e., phase-locked and non-phase-locked as implemented in EEGLAB (Delorme & Makeig, 2004), was used for oscillatory analyses in this thesis. For the statistical analyses, the data were collapsed into 200 ms time bins. For each bin, mean theta power (4-8 Hz) and alpha power (9-12 Hz) were calculated for each electrode, participant, and trial. To protect against excessive Type I errors caused by multiple comparisons, permutation tests (Blair & Karniski, 1993) were used to examine the statistical differences between experimental conditions. Permutation tests are a type of resampling method, referring to repeated random sampling. When comparing two experimental conditions, data from the contrasting conditions are shuffled together and randomly divided into two equally sized samples, each representing one of the conditions, from which a *t* value is derived. This process is repeated to yield a permutation *t* distribution. The actually observed *t* value is then compared to the extreme tails of this distribution to judge whether the observed difference is significant. In this thesis, permutation tests were conducted for each electrode, each time window, and each frequency band. Thus, to further reduce the chance of Type 1 errors, only effects that spanned across at least two adjacent electrodes and two consecutive time windows were interpreted (cf. Gruber et al., 2012). More details for the permutation tests can be found in the Chapter 3.

### 1.7.3 The relationships between ERPs and oscillations

As already discussed, ERPs mainly reflect activities that are phase-locked to experimental events, while oscillations also reflect non-phase-locked activity. Thus, ERPs and oscillations are considered to be mostly independent measures that are complementary to each other (Klimesch et al., 2000) and both have been shown to play a role in memory. However, the relationship between ERPs and oscillations is currently unclear. Different models have been proposed to explain the neural mechanisms of the generation of ERPs and their relationship with ongoing oscillations (Bastiaansen et al., 2012; Sauseng et al., 2007). In the additive model, ERPs are assumed to reflect event-related activity that is superimposed on, and imbedded in, ongoing background oscillations that are completely unrelated to processing of the events. Thus, ERPs and oscillations reflect independent neural processes. In contrast, the phase-resetting model proposes that ERPs are the result of phase-resetting of ongoing oscillations induced by a stimulus, suggesting that ERPs and oscillations reflect similar neural processes.

There has been evidence supporting both models. In support of the phase-resetting model, it was found that early visual evoked ERPs such as the N1 component are accompanied by increases in inter-trial-coherence in alpha phase after stimulus onset (Makeig et al., 2002). Also, post-stimulus oscillatory power is not altered by stimulus onset relative to the pre-stimulus level (Hanslmayr et al., 2007). These findings suggest that ERPs are unlikely to reflect activity added to the background oscillations that should cause power increase, but are related to event-induced changes in phase. However, Mazaheri and Picton (2005) demonstrated that increases in inter-trial coherence also occur when simply adding an ERP to the background oscillations. Furthermore, it was found that background oscillatory power decreases at stimulus onset, which might bias the amount of changes in overall post-stimulus power (Hanslmayr et al., 2007). Thus, convincing evidence supporting the phase-resetting model is still lacking.

In support of the additive model, an intracortical EEG study using monkeys (Shah et al., 2004) showed that ERPs do not depend on the ongoing oscillations during a pre-stimulus period, although it is not yet clear whether this finding can be compared with scalp-recorded EEG in humans (Sauseng et al., 2007). Furthermore, using a phase preservation index to measure the phases of ongoing prestimulus oscillations and the phases after stimulus onset, Mazaheri and Jensen (2006) found no evidence for phase resetting of the background oscillations at the time of stimulus onset. However, as the index that was used may be biased by phase perturbations caused by additive stimulus-evoked responses (Bastiaansen et al., 2012; Sauseng et al., 2007), it cannot be used to refute the phase-resetting model unambiguously.

Despite a large body of EEG research, it has not been possible to unambiguously differentiate between these alternative models of the relationship between ERPs and oscillations. Some researchers attempted to reconcile the two models in the ‘shared generators view’ (e.g. Mazaheri & Picton, 2005), proposing that ERPs and oscillations might share the same neural generators. In this view, an ERP does not necessarily depend upon the existence of ongoing oscillations. At the same time, however, the presence of a stimulus can change ongoing oscillations to be phase-locked to stimulus onset. Furthermore, it was proposed that event-related synchronisations may occur in frequencies that are lower or higher than the ongoing oscillations while event-related desynchronisations occur in the frequencies of the ongoing oscillations. Therefore, the shared generators view accounts for findings that cannot be explained by either the phase-resetting or additive models, although further evidence is required to test this theory.

The present thesis was not designed to test any of these models. However, an understanding of the relationship between ERPs and oscillations will help to interpret EEG activity and shed more light on the underlying neural mechanisms. These models also suggest that it will be valuable to analyse EEG data in both ERP and oscillatory domains. Memory consists of multiple complex processes that vary across trials and individuals. Therefore, it is likely that both phase-locked and non-phase-locked activity contribute to memory processing. ERP and oscillatory activity can reveal distinct neural processes or changes in the same neural processes. For example, in terms of pre-stimulus encoding-related activity, previous studies have found SMEs in both ERP and oscillatory domains (Guderian et al., 2009; Otten et al., 2006). These effects differ in time, scalp distribution, and sensitivity to experimental manipulations. Therefore, combining ERP and oscillatory analyses can reveal distinct cognitive and neural processes underlying anticipatory brain activity for memory encoding. This was the approach taken in this thesis.

## 1.8 Overview of experiments and hypotheses/questions

The overall aim of this PhD thesis was to investigate the neural mechanisms of memory deficits in healthy ageing. In particular, it aimed to explore age-related changes in anticipatory brain activity in associative memory processing. The questions of interest were: whether anticipatory brain activity, i.e., pre-stimulus associative encoding-related activity and pre-probe associative retrieval-related activity, vary with age, what might have caused these changes if there are any, and the functional meaning of these changes. Three EEG experiments were conducted, two with groups of younger and older individuals (Experiment 1 and 3) and one with younger individuals only (Experiment 2). The ensuing EEG data were analysed in both ERP and time-frequency domains alongside a thorough analysis of behavioural task performance. Associative memory tasks were used to target source-related, episodic memory processes and the effects on these of ageing. Relative to memory for individual items, associative memory is more sensitive to changes in mnemonic states in healthy ageing. The tasks involved the learning of novel inter-item associations between two independent items (word pairs or picture pairs). This way, each item had its own associative information. The tasks were followed by source memory tests in which one item in a pair was presented to probe the other (Experiments 1 and 2), or in which judgments had to be made about the integrity of the pair as a whole (Experiment 3). The precise rationale underlying each experiment and the experimental hypotheses are explained in the relevant chapter. For the ease of understanding, ERP and time-frequency analyses are presented in separate Chapters (Chapters 2 and 3).

# Chapter 2: ERP analyses

## 2.1 Experiment 1: Does anticipatory associative memory-related activity vary with age?

### 2.1.1 Encoding

#### *2.1.1.1 Introduction*

As discussed in the Introduction, a number of ERP studies have shown that prestimulus anticipatory activities can benefit episodic encoding, i.e., PSMEs. There are different kinds of PSMEs depending on the types of cognitive processes involved. For example, a negative-going ERP PSME over frontal scalp sites has been associated with semantic but not non-semantic processing (Otten et al., 2006), a widespread positive-going PSME is associated with high reward but not low reward (Gruber & Otten, 2010), and a right-lateralised positive-going PSME is associated with the preparation for negative but not neutral or positive emotion (Galli et al., 2011). Therefore, the negative-going PSME is thought to reflect the mobilisation of semantic processing resources in preparation for semantic encoding, whereas the positive-going PSMEs are thought to reflect emotional or motivational preparation. Thus, it may be assumed that different prestimulus modulations reflect different anticipatory processes. Such anticipatory activity can be initiated by instructional cues indicating the kind of cognitive processes are required. For example, when people are cued to perform a semantic task, semantic processing resources are prepared, which facilitates subsequent semantic encoding. Similarly, when a higher reward is expected, motivation-related processing is prepared.

A previous study has shown that PSMEs are sensitive to the level of available processing resources (Galli et al., 2011). PSMEs are evident only when sufficient processing resources are available, but not when processing resources are compromised by difficult secondary tasks during the anticipation interval. Therefore, it is likely that encoding-related anticipation is a controlled process that can only be successfully engaged when sufficient processing resources are available. This suggests that older adults might have specific impairments in the engagement of anticipatory neural mechanisms due to diminished processing resources (Craik & Rose, 2012). If so, it is likely that age-related memory deficits, e.g., deficits in source memory, are at least partly due to such impairments in prestimulus anticipatory mechanisms.

Very few studies have directly tested the effect of age on prestimulus anticipatory activities in memory encoding, but existing evidence has pointed to an age-related deficit in anticipatory processing. It has been demonstrated that unlike older adults, young adults are quicker to respond to targets preceded by cues predictive of the timing of the target presentation, relative to targets preceded by non-informative cues (Zanto et al., 2011). This preparatory benefit in younger adults was reflected in larger CNV magnitude in the predictive cue condition relative to the unpredictive cue condition. Neither the behavioural improvement nor the difference in neural activity was observed in older adults. Therefore, older adults are thought to be impaired in the ability to engage anticipatory neural processes to orient attentional resources.

The failure to engage anticipatory mechanisms may affect the formation of an adequate neural context for an upcoming stimulus, which in turn may affect stimulus processing and memory encoding. Bollinger and colleagues (2010) have shown improved working memory and LTM in younger adults when stimulus categories could be anticipated relative to when they were unexpected. Consistently, fMRI data revealed that expectation-driven activity increased in the relevant brain regions such as the fusiform face area (FFA) when faces were expected. Furthermore, functional connectivity between the FFA and regions in a fronto-parietal top-down control network also increased during the expectation period, and this functional connectivity was positively correlated with memory performance. In a follow-up study testing older adults (Bollinger et al., 2011), it was found that anticipatory brain activity was absent in a subgroup of older adults who did not show memory benefits from predictive cues. This finding indicates a relationship between expectation-driven sensory preparation and subsequent memory performance. Considering the involvement of the fronto-parietal top-down control network, the failure to engage in encoding-related anticipatory processes may be related to a top-down control malfunctioning in ageing. This would be consistent with the frontal ageing hypothesis (West, 1996).

The aim of the present study was to investigate whether there is an age difference in neural activity associated with the successful encoding of associative source information. An associative memory paradigm was used to evaluate encoding-related brain activity before, as well as after, the presentation of the source and target information. Participants had to intentionally memorise location-object word pairs, with location words as retrieval targets and object words as probes. There are two advantages of this paradigm. Firstly, instead of the more common approach of testing a small number of sources, each target item had its own unique source, which largely reduced the probability that a correct source judgement was due to a lucky guess. Secondly, the sources and the targets were separated in time to allow an examination of anticipatory activity at different stages of associative encoding. Previous studies investigating anticipatory encoding-related activity usually look at brain activity after a cue, before the presentation of to-be-encoded item and source information. In reality, however, episodic memory involves the binding of an event to an existing context or source. For the binding of an event to its context, the anticipation just before the occurrence of the event should also be important. Therefore, in the present study for each word pair, the location word was presented first and then the object word. This design allows the separation of three associative encoding stages: (1) before the presentation of the first word (pre-location), (2) between the first and the second word (pre-object), and (3) after the second word (binding). Thus, there were two preparatory intervals before binding, i.e., pre-source preparation initiated by a neutral warning cue, and pre-binding preparation initiated by location cues.

Brain activity during encoding was contrasted for subsequently recognised items according to whether they elicited successful or unsuccessful associative retrieval. This contrast was to isolate brain activity related to the encoding of associative information, and more importantly, whether this activity was affected in ageing. Because of the novelty of the paradigm, this study was mostly exploratory. Based on the Bollinger et al. (2011) study, it was expected that younger adults are likely to show a pre-stimulus subsequent associative memory effect whereas older adults are not.

#### *2.1.1.2 Methods*

*Participants*

Twenty-six younger volunteers were recruited from the University College London student community, and 28 older volunteers were recruited from the local community and University of the Third Age through flyers. Volunteers were remunerated at £7.5/hr for participation in the experiment. Two younger and 4 older volunteers were excluded because of insufficient trial numbers due to inadequate memory performance or poor EEG quality (see EEG acquisition subsection for exclusion criteria). The final groups included in the analyses comprised 24 older adults (mean age 67.29 year, range 60-79, 12 males) and 24 younger adults (mean age 22.67 years, range 19–29 years, 10 males). All participants were right-handed and were screened via email or telephone to ensure that they had normal or corrected-to-normal vision, no history of neurological or psychiatric and were not taking psychotropic medications. The experimental procedures were approved by the University College London Research Ethics Committee. All participants provided informed written consent before participating.

*Stimuli*

Stimuli were drawn from a pool of 172 location words, i.e., words depicting locations such as ‘garden’ or ‘school’, and 258 object words (half living and half non-living such as animals and tools respectively). All words were between 3-8 letters in length and 1-350/million in written frequency (Kučera & Francis, 1967). Sixteen location words and 24 object words were drawn from the stimulus pool for practice sessions. All stimuli were visually presented in white uppercase Helvetica letters (font size 30) against a grey background at the centre on a computer monitor. A pilot study was conducted to determine the minimum number of stimuli and the length of study-test blocks to obtain sufficient trials for both associative hit and associative miss.

### *Design*

The experiment used an associative memory paradigm. Participants memorised object-location word pairs which were later tested in a way that the objects words served as retrieval probes and the locations as the to-be-retrieved associative information. All 156 location words were randomly paired with an equal number of object words to create the study list for each participant. All 234 object words were pseudorandomly assigned to 3 sets with the constraint that living and non-living objects were equal within each list. The sets were rotated across participants to ensure that each word was equally likely to be presented in the study phase or as an unstudied word in the test phase.

### *Neuropsychological testing*

Following the memory test, participants were administered a battery of eleven neuropsychological tests to assess a range of cognitive functions that may decline with age. The Mini-Mental State Examination (MMSE) was used to screen against dementia (Folstein, Folstein, & McHugh, 1975) with a cut-off score of 26/30. Long-term memory was assessed with the Verbal Paired Associates and the Word List (Immediate and Delayed) from the WMS-III. Short-term memory was assessed with the forward and backward digit span test. General cognitive functions such as processing speed and executive function were assessed using the Trail Making tests A and B, and the verbal fluency tests (letter and category) respectively. The National Adult Reading Test

(NART) – second edition was used to obtain an estimation of full-scale IQ. The geriatric Depression Scale (GDS) was also administered to both age groups.

*Procedures*

While the EEG cap was applied, the participant read and then verbally described the instructions to the experimenter to ensure a thorough understanding of the experimental procedures. Each participant was tested individually inside a quiet chamber and was instructed to minimize eye movements and muscle tension during testing. Stimulus presentation and behavioural response recording were controlled using MATLAB software on Windows PCs.

The session began with 2 short practice sessions (8 studied word pairs and 12 tested items within each session) to familiarize participants with the task procedures. The sessions could be repeated until participants felt comfortable to proceed. Data were acquired during 6 study-test blocks. Each study phase contained 26 location-object word pairs, which was followed by a test phase containing the 26 studied and 13 unstudied object words. The test phase started without delay once the participant was ready to proceed.

In the study phase, each trial began with a preparatory cue (a red exclamation mark “!”) presented for 1.9 s. After a 100 ms blank screen, a location word was presented for 1.5 s followed by a fixation cross for 500 ms, and then an object word was presented for 1.5 s. Participants were instructed to make the association between the location and the object by imaging the object in the location. They responded by pressing one of two buttons, using the left and right middle fingers, indicating whether the location-object association was easy or difficult to make. The fixation cross was visible at all times except when a stimulus was presented, and the participants were instructed to focus their eye gaze on the centre of the screen. The offset of the object word and the onset of the preparatory cue in the next trial were separated by a jittered inter-trial interval of 3-4.5s. Participants were told that the judgment was subjective, and that the task was designed to help them remember word-pair associations.

In the test phase, each trial also began with the preparatory cue, the same as that in the study phase, for 1.9 s. After a 100ms blank screen, an object word was presented for 1.5 s which was followed by the fixation cross. Participants indicated whether the stimulus was old or new and whether they could remember the source location by pressing one of four buttons, using their index fingers and middle fingers of both hands, representing ‘old/location’, ‘old/other information’, ‘old/no information’ or ‘new’. Participants were asked to respond ‘old/location’ if they could recall the location that was paired with the object at study, and to respond ‘old/other information’ if they recollected some information from the study episode but could not retrieve the location. In these two situations, participants were required to verbally report either the location or the ‘other information’ they recalled once they pressed the corresponding button. Participants were asked to respond ‘old/no information’ if recognition was devoid of associative retrieval. There was no time limit for the button response although both accuracy and speed were stressed. This self-paced design was to accommodate the variability in RT common in older adults and also maximise the accuracy of their retrieval. Once a ‘new’ or ‘old/no information’ response was made, a fixation cross was presented for 2 s before the onset of the next trial. Once an ‘old/location’ or ‘old/other information’ response was made, the fixation cross was presented for a further 4 s while participants verbalised the location or the other information they recalled. The ‘old/other information’ option was included to ensure that the comparison between association-remembered trials and association-forgotten trials would not be contaminated by the recollection of associative information other than the location (Galli & Otten, 2011). It was made sure that participants fully understood the distinctions between the four types of responses during the initial practice sessions. Response assignments for the keys associated with study and test decisions were counterbalanced across participants. EEG was recorded throughout all study-test blocks.

After all six study-test blocks had been completed, participants were given a short questionnaire to assess (1) whether they had tried to memorise the word-pairs, (2) whether they have paid attention to every word pair, (3) what strategies they had used to memorise the word-pairs, (4) what strategies they normally use to remember, (5) what they did when they saw the warning stimulus at study, and (6) what they did when they saw the location words. Following this, the EEG cap was removed and participants relaxed while having their hair washed. Finally, they completed the neuropsychological tests when they were ready.

The EEG session, including application of the electrode cap and running of the task (excluding the neuropsychological testing), lasted approximately 2.5 hours for each younger subject and 3 hours for each older participant as it took longer for the older participants to learn and complete the task.

### *EEG acquisition*

EEG was recorded with sintered silver/silver-chloride electrodes from 37 scalp sites using Easycap (montage 10 at www.easycap.de/easycap/e/electrodes/13_M10.htm) referenced online to a midfrontal site corresponding to Fz in the 10/20 system. Vertical and horizontal eye movements were recorded bipolarly from electrodes above and below the right eye and at the outer canthus of each eye, which were used to correct trials contaminated by eye-movement artifacts. Impedance was tested and reduced to below 5kΩ before recording. On-line, signals were amplified, bandpass filtered between 0.01 and 35 Hz (3dB roll-off), and digitized at 500 Hz with 12-bit resolution. Off-line, the data were digitally filtered between 0.05 and 20 Hz (96 dB roll-off, zero phase shift filter).

Even though the prime interest was pre-stimulus anticipatory activity, binding-related activity after object word onset was also computed for completeness. Activity elicited by neutral warning cues, location words, and object words were aligned independently to the onset of each event, allowing each to be analysed separately. Epochs of 2560 ms duration surrounding cues and probes, starting from 100 ms before their onset were extracted and down-sampled to 100 Hz. Event-related potentials (ERPs) were computed for each participant at each electrode site for stimuli later given different responses, baseline corrected to the 100 ms before event onset. Trials with non-blink eye-movement artifacts, muscle tension, analog-to-digital saturation and drifts exceeding ±50 µV were excluded from the averaging process. Blink artifacts were minimized via estimating and correcting their effects using a regression method (Rugg, Mark, Gilchrist, & Roberts, 1997). The data were then re-referenced to an average mastoid reference (re-instating the online reference Fz as a site of interest). Grand-average ERPs were derived for each electrode site by averaging across subjects according to response categories. To ensure a good signal-to-noise ratio, a minimum of 16 artefact-free trials per condition was set as the criterion for a subject to be included.

### *Behavioural analyses*

Between-subject *t*-tests were performed on neuropsychological test scores to examine performance differences between older and younger individuals in each test. For encoding task performance, mixed-model ANOVAs were computed on both the proportions of easy and difficult responses and reaction times (RTs) to examine whether the two groups differed in subjective judgement of task difficulty, and whether they spent different amounts of time processing the easy and difficult items.

Memory performance was initially assessed for accuracy with Pr value and response bias with Br values (Snodgrass & Corwin, 1988), computed as follows: Pr = H – FA; Br = FA/(1-Pr), where H refers to the proportion of recognition hit (collapsing across old/location, old/other information, and old/no information responses for old items) and FA to the proportion of the recognition false alarm. The analyses of associative memory performance mainly focused on two critical response categories: associative hit and associative miss, measured as the percentages of all old items for which correct associative information was retrieved (old/location response with correct location reported) or no source retrieved (old/no information response).

In addition, as the ability to spontaneously use associative strategies is crucial for associative memory in older individuals, the effect of associative strategies was evaluated according to participants' answers to the questionnaire (see Procedures). The numbers of strategies used to memorise the word pairs were compared across age groups using a between-subject *t*-test. Across-subject correlations were computed to assess the relationship between the number of strategies and memory performance for each group.

### *ERP analyses*

As the experiment aimed to identify neural correlates of associative memory, averaged ERPs were formed for two critical conditions, subsequent associative hit and subsequent associative miss, for each of the three encoding intervals, i.e., pre-location, pre-object, and binding. Associative hit refers to recognised old words (objects) for which the associative information (locations) was remembered, and associative miss refers to recognised old words for which the associative information was forgotten. Item recognition memory was not analysed, as pilot work was done purposely to foster a high level of recognition for the retrieval probes. This ensured that sufficient numbers of trials were generated for both associative hits and associative misses, albeit at the expense of trial numbers for recognition misses (i.e., old items misclassified as new).

### *Associative encoding-related anticipatory activity*

EEG data from all 24 older and 24 younger participants were included in the analyses. For neutral warning cue-elicited activity (pre-location), the average numbers and ranges (in parentheses) of artefact-free trials for associative hit and associative miss were 81(37-124) and 42(20-85) for the older group and 43(17-110) and 54(23-100) for the younger group respectively. For location word-elicited activity (pre-object), the average numbers and ranges of artefact-free trials for associative hit and associative miss were 83(49-125) and 43(23-86) for the younger group and 45(21-118) and 55(17-107) for the older group respectively.

Statistical comparisons of the mean amplitude differences in size, time, and scalp distribution across the two critical conditions were tested using ANOVAs.

For both pre-location and pre-object activities, statistical analyses were conducted including 28 electrodes (Figure 1), which allowed a balanced partition of four quadrants out of the maximum number of electrode sites available in the current montage. This symmetrical hemisphere by anteriority partitioning has been successfully used to assess encoding-related activity to capture the anterior-posterior variation and left-right asymmetry in scalp topography (Galli et al., 2011). The selection of electrodes was performed to limit the total number of comparisons but also to allow the examination of the effects observed in previous studies.

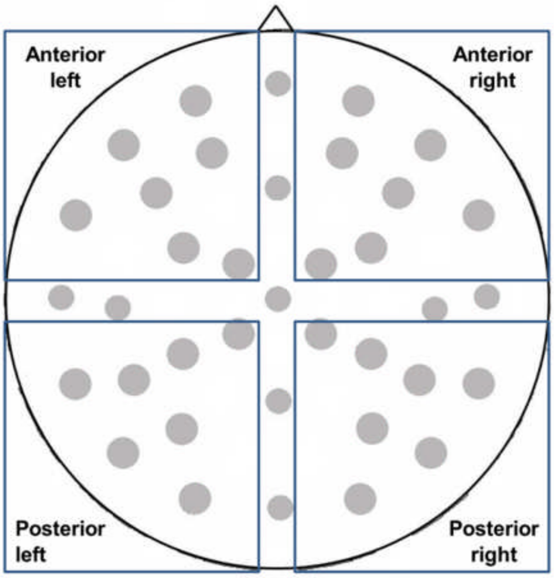


**Figure 1. Schematic illustration of the 37 recording electrode sites with the 28 sites used for the ERP analyses marked by 4 squares as in 4 quadrants.**

To best capture the pre-probe associative retrieval effect, mean amplitudes were measured from 200 ms after cue onsets, and evenly divided into two continuous latency intervals: 200-1100 ms (early) and 1100-2000 ms (late). The latency before 200 ms was not included as it is thought to reflect primarily the sensory processing of stimuli, which was not of interest to the current study.

Also, studies of early ERP components (e.g., P50, N1, and P2) generally do not find age-related sensory deficits (Friedman, 2012). The early/late continuous latency separation was used to measure the development and change in amplitude and scalp distribution over time of such sustained effects as memory-related anticipation. It was also expected that such effects would be larger in the late interval when the probes were about to appear.

Initial mixed-model ANOVAs were conducted incorporating factors of age (older/younger), memory (subsequent associative hit / subsequent associative miss), latency (two intervals), anteriority (anterior/posterior), hemisphere (left/right), and site (7 sites). Significant interactions including latency and memory would suggest that SME varied across the two intervals, and therefore warrant separate analyses for each of the two latency regions. The effects of interest were those involving the factor of memory (i.e., pre-probe associative retrieval effects), especially age-related differences on such effects (i.e., interactions involving age and response).

*Binding activity*

EEG data from all 24 older and 24 younger participants were included in the analyses. The average numbers and ranges (in parentheses) of artefact-free trials for associative hit and associative miss were 83(51-119) and 41(16-81) for the younger group and 43(18-117) and 57(25-105) for the older group respectively.

Again, statistical comparisons of mean amplitude differences across the two critical conditions were tested using ANOVAs including 28 electrodes partitioned into four quadrants. For the binding interval, mean amplitudes were measured from 300 ms after object word onset, and divided into two continuous latency intervals: 300-900 ms (early) and 900-1600 ms (late). ERP subsequent memory effects often manifest as sustained effects starting from about 300 ms (for reviews see Friedman & Johnson, 2000). Furthermore, SMEs may not represent a single uniform cognitive process but consist of different components that change with age. For example, Johnson et al. (2013) used an early/late segregation of the encoding epoch and found that the two intervals were not equal in terms of their effects on memory when interrupted.

Initial mixed-model ANOVA was conducted incorporating factors of age (older/younger), memory (subsequent associative hit / subsequent associative miss), latency (2 regions), anteriority (anterior/posterior), hemisphere (left/right), and site (7 sites). The rationale for the partition in latency regions can be found in the next section. Significant interactions including latency and memory would be followed up with separate analyses for each of the two latency regions. Again, the effects of interest were those involving the factors of memory and age. For the latency intervals during which significant age differences in subsequent associative memory effects emerge, subsidiary within-group ANOVAs were performed to investigate these effects within each group. This analysis approach first identified significant age differences in subsequent associative memory effect, and then looked to see whether SMEs emerged within each group during those latency intervals. Greenhouse-Geisser corrections for violations of the sphericity assumption were applied when appropriate for factors with more than two levels, as indicated by the adjusted degrees of freedom.

Analyses of scalp distribution were performed to determine whether significant intertactions between site and experimental conditions were simply due to overall amplitude differences rather than differences in the underlying neural mechanisms between conditions. The purpose was to assess the extent to which the observed scalp topography differences represented distinctive underlying neural generators and cognitive processes across groups and conditions. ERP data were rescaled using the max/min method (McCarthy & Wood, 1985) applied to difference scores (associative hit – associative miss) for each age group including all 37 electrodes. Both the maxi/min and the vector length scaling methods have been used in the literature, but the max/min method was selected in the current study to avoid the interpretational problems that have been hotly debated (Urbach & Kutas, 2002, 2006; Wilding, 2006). Significant differences between the topographies of different conditions and age groups were verified by ANOVAs conducted on the rescaled data.

In addition, across-subject correlations were computed to assess the relationship between ERP effects and memory performance for both recognition accuracy and associative hits. Because correct source retrieval is typically related to the strength of recognition memory (Yonelinas, 2001), it is possible that SMEs influence recognition memory in general rather than being specific to associative retrieval, especially in older adults. The correlation analyses were done to elucidate the functional role of these effects, and to shed more light on neural mechanisms of associative encoding impairments in ageing.

#### ***2.1.1.3 Results***

*Neuropsychological Test Scores*

Performance on the neuropsychological tests is summarized in Table 1. All participants scored 27 or above on the MMSE, and therefore are unlikely to suffer from dementia. Older adults spent less time in formal education than the younger adults. They also showed the typical pattern of age-related impairments and preservations, including lower scores on tests for long-term memory, processing speed, and executive functions, but higher scores in estimated crystallised intelligence using the NART compared to younger adults.

**Table 1. Subject characteristics and scores on neuropsychological tests for the 2 age groups.**

| | Older Group | | Younger Group | | |
|---|---|---|---|---|---|
| | *Mean (SD)* | *Range* | *Mean (SD)* | *Range* | *p* |
| Years of education | 15.1 (3.1) | 9-20 | 16.7 (2.4) | 13-22 | .044 |
| MMSE | 29.0 (0.9) | 27-30 | 29.5 (0.9) | 27-30 | *ns* |
| Verbal Paired Associates | 22.0 (7.9) | 6-32 | 28.9 (2.8) | 20-32 | <.001 |
| Word List (Immediate) | 33.8 (7.1) | 22-45 | 41.4 (4.3) | 33-48 | <.001 |
| Word List (Delayed) | 8.5 (2.9) | 3-12 | 10.3 (1.7) | 5-12 | .011 |
| Digit Span (backward + forward) | 20.5 (4.2) | 14-30 | 22.3 (4.0) | 16-28 | *ns* |
| Verbal Fluency – Letter | 43.5 (12.6) | 23-89 | 46.6 (9.4) | 30-67 | *ns* |
| Verbal Fluency – Category | 28.5 (6.4) | 22-48 | 37.5 (5.0) | 29-47 | <.001 |
| Trail Making Part A (s) | 36.2 (9.2) | 21-54 | 22.6 (6.7) | 11-38 | <.001 |
| Trail Making Part B (s) | 89.2 (34.7) | 34-199 | 56.2 (21.3) | 23-114 | <.001 |
| NART (FSIQ-estimate) | 119.0 (6.8) | 105-131 | 110.8 (6.5) | 95-122 | <.001 |
| GDS (short form) | 3.0 (3.8) | 0-13 | 2.7 (4.0) | 0-15 | *ns* |

### *Task performance*

At encoding, participants judged whether each word-pair was easy or difficult to associate. Encoding task performance is summarised in Table 2. Mixed-model ANOVAs were computed on both the proportions of response and RTs with factors of age (older/younger) and difficulty (easy/difficult). For the proportions, there was a significant main effect of difficulty ($F(1, 46) = 8.79$, $p = .005$) but no significant age × difficulty interaction. For RTs, there was a significant main effect of age (*F*(1, 46) = 13.65, *p* = .001) but no main effect of difficulty or age × difficulty interaction. These results suggested that the two groups were similar in their opinions on task difficulty and that easy and difficult word-pairs were given similar amount of time to encode.

**Table 2. Encoding task (word-pair association judgement) performance for the two age groups.**

| | Proportion (SD) | | Response Time (ms) | |
|---|---|---|---|---|
| | Easy | Difficult | Easy | Difficult |
| Older | 0.41 (0.22) | 0.57 (0.21) | 2586 (986) | 2620 (1099) |
| Younger | 0.40 (0.18) | 0.59 (0.18) | 1736 (522) | 1745 (486) |

At test, means and SD of Pr values were 0.77 (0.13) for older subjects and 0.89 (0.08) for younger subjects. A between-subject *t*-test suggested that this difference was statistically significant (*t*(46) = 3.81, p < .001). Mean and SD of Br values were 0.41 (0.23) for older adults and 0.41 (0.33) for younger adults, which were not significantly different from each other.

Associative memory performance for the two groups is summarised in Table 3, showing the percentages and RTs of different response categories. Mixed-model ANOVAs were computed on both the proportions of responses and RTs with factors of age (older/younger) and response (associative hit/associative miss). For the proportions, there was a main effect of age (*F*(1, 46) = 18.61, *p* < .001), a main effect of response (*F*(1, 46) = 7.36, *p* = .009), and a significant interaction (*F*(1, 46) = 29.52, *p* < .001). Of interest here is the significant interaction between age and response, confirming that older adults made relatively more associative misses whereas younger adults made relatively more associative hits. As for the RTs, there was a main effect of age (*F*(1, 46) = 10.62, *p* = .002) and a main effect of response (*F*(1, 46) = 24.90, *p* < .001), but not an interaction between age and response. These results confirmed that older adults were slower than younger adults across the two response categories, and both age groups were slower to make associative misses than associative hits. The similarity across age groups in the relationship between associative hit RT and associative miss RT is important for the present investigation, indicating that between-group differences in neural correlates of associative memory retrieval are unlikely to reflect merely RT differences.

**Table 3. Associative memory performance for different response categories for the two age groups**

| | Associative hit | Other information* | Associative miss | Miss | Correct rejection |
|---|---|---|---|---|---|
| Response Percentages | | | | | |
| Old | 35.3(15.6) | 2.9(4.3) | 45.5(14.9) | 12.1(7.2) | 89.2(10.2) |
| Young | 59.8(10.6) | 4.3(4.7) | 29.4(11.7) | 4.7(2.5) | 93.4(8.0) |
| RT (ms) | | | | | |
| Old | 3177(1246) | 5674(3718) | 4010(2051) | 2505(880) | 1731(519) |
| Young | 1749(498) | 3750(2532) | 2863(1818) | 2111(988) | 1263(435) |

*** Seven older and five younger participants did not make any ‘Other information’ response.**

Mean number of strategies used to memorise the word pairs was 2.71 (range: 1-4) by younger subjects and 1.96 (range: 0-4) by older subjects, and the between-group difference was significant (*t*(46) = 2.74, p = .005). Correlation tests showed that the number of strategies did not significantly correlate with memory performance in either age group, possibly due to the narrow range of the number of strategies.

### *ERPs*

Encoding-related ERPs elicited by subsequent accurate associative retrieval and no associative retrieval were compared between groups to find age-related differences in subsequent associative memory effects. Figure 2(A) illustrates the grand-average ERP waveforms at a right-frontal electrode site for the two age groups at pre-location, pre-object, and binding intervals during encoding. In the pre-location and the pre-object intervals, the waveforms almost overlap across the two conditions for both age groups. In the binding interval, ERPs for subsequent associative hits are more positive-going than associative misses for both age groups. Consistent with previous research (e.g., Duarte et al., 2004; Friedman et al., 1996), the positive-going effects emerge at about 300 ms post-stimulus and persist until about 1600 ms. For both groups, the effects tend to be larger over the anterior sites relative to the posterior sites (Figure 2B). It appears to be right-lateralised in older but not younger adults. In line with many previous studies (e.g., Li et al., 2004; Wegesin et al., 2002) the general morphology of the waveforms differ markedly between younger and older adults, particularly over the frontal scalp. These differences may be caused by cerebral atrophy or other age-related changes in brain structure, as they are not affected by any experimental manipulation (Rugg & Morcom, 2005). Nevertheless, it is interesting that a major morphological difference is that waveforms in younger adults were more negative-going between around 300-600 ms post-stimulus compared to those in older adults. The timing of this effect is consistent with the

N400 component, which has been related the processing of meaning, especially in language comprehension (Kutas & Federmeier, 2011).

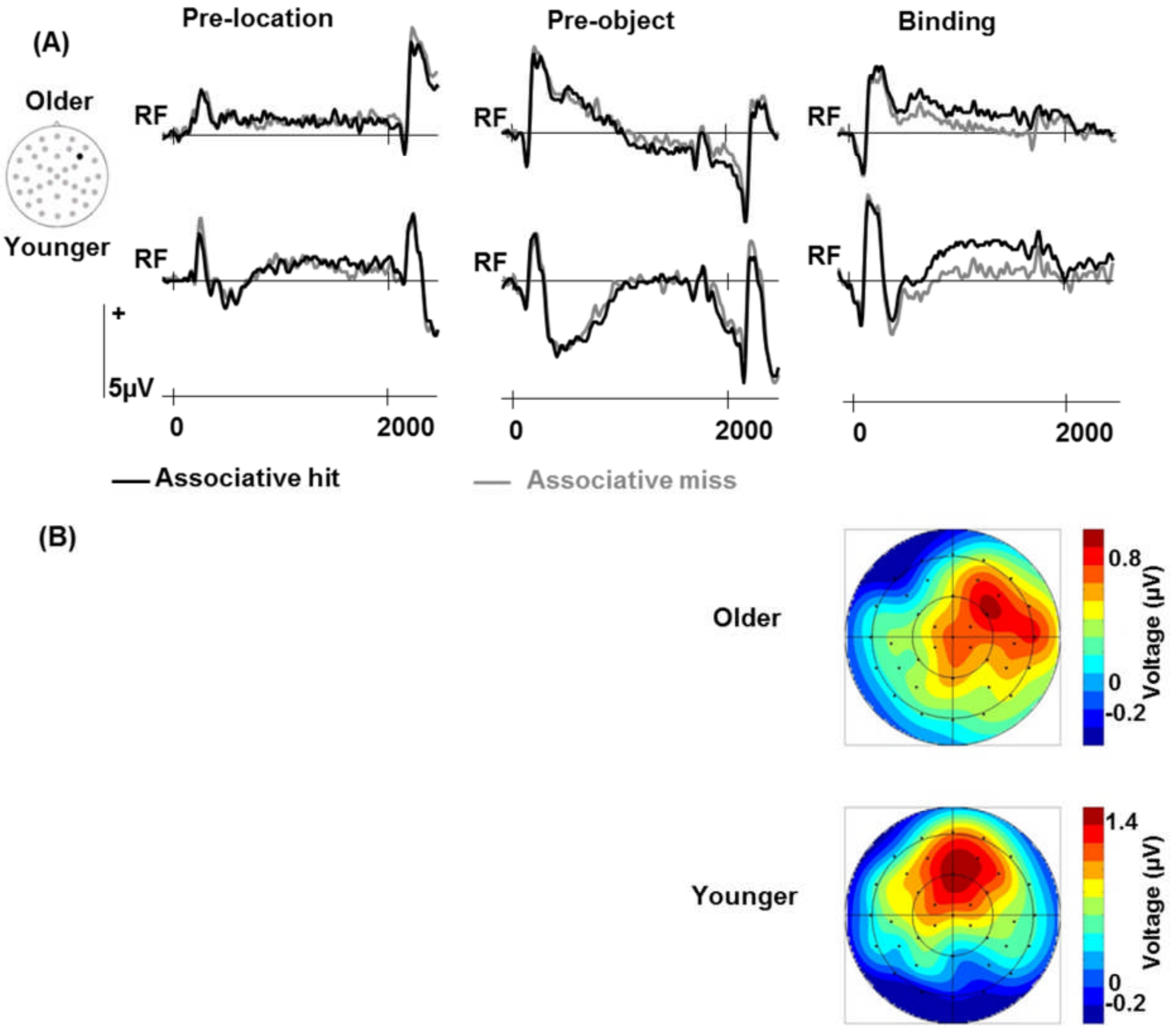


**Figure 2. Subsequent associative memory effects. (A) Grand-averaged ERPs for the two age groups elicited by neutral warning cue (left), location word (middle), and object word (right) according to whether they were associated with accurate associative retrieval or no associative retrieval. The insert indicates the location of the displayed right frontal electrode (site 22 from Montage 10; www.easycap.de/easycap/e/electrodes/13_M10.htm). (B) Voltage spline maps for the two groups showing the scalp topographies of the ERP subsequent associative memory effects (associative hit – associative miss) in the 300-1600 ms time window. The maps are range scaled.**

*Anticipatory pre-binding activity*

Confirming visual inspections of Figure 2, mixed-model ANOVAs incorporating the factor of latency interval did not reveal any significant effect involving the factor of memory (all *Fs* < *.06*, all *ps* > .74), suggesting that there was no anticipatory subsequent associative memory effect in the two pre-binding intervals.

*Binding activity*

Mixed-model ANOVAs incorporating the factor of latency interval revealed a significant memory × interval × site interaction (*F*(3.9,181.1) = 3.75, *p* = .006). However, this interaction did not survive after data scaling (*F*(4.1,190.8) = 1.20, *p* = .314. These results suggest that subsequent associative memory effects do not differ qualitatively across the latency regions. Therefore, the two latency regions were combined for subsequent analyses.

In the 300-1600 ms interval, a mixed-model ANOVA revealed a significant main effect of memory (*F*(1,46) = 5.97, *p* = .018), a significant memory × hemisphere interaction (*F*(1,46) = 4.72, *p* = .035), and a significant memory × hemisphere × anteriority interaction (*F*(1,46) = 5.35, *p* = .025). These results indicate that there is a significant subsequent associative memory effect across age. The memory × hemisphere interaction reflected a positive-going subsequent associative memory effect that was larger over the right-hemisphere (0.65 µV) relative to the left-hemisphere scalp sites (0.39 µV). Subsidiary ANOVAs were conducted for the right- and left-hemisphere sites separately. The results showed that for the right-hemisphere sites, there was a significant main effect of memory (*F*(1,46) = 7.86, *p* = .007) and a significant memory × anteriority interaction (*F*(1,46) = 4.93, *p* = .031), reflecting a positive-going subsequent associative memory effect that was larger over the right-anterior (0.85 µV) relative to the right-posterior sites (0.45 µV). No significant effect of interest was found for the left-hemisphere scalp sites (all *Fs* < 3.48, all *ps* > .069).

Taken together, words with subsequent successful associative memory retrieval elicited more positive-going ERPs during encoding than words with no associative retrieval. Across the groups, this effect showed a significant right asymmetry in scalp distribution. It was also larger over right-anterior relative to right-posterior sites. There was no age difference in this subsequent associative memory effect.

To further substantiate the functional significance of the subsequent associative memory effect and ageing, across-subject correlations were computed to assess the relationship between the ERP effect and memory performance. Because source hits are typically associated with confident item recognition (Yonelinas, 2001), it is possible that the effects currently observed influenced subsequent recognition accuracy rather than accurate associative memory retrieval. The ERP effect for each age group was computed by taking the difference in mean amplitude between subsequent associative hits and associative misses across four electrodes where the effect appeared to be largest (sites 22, 10, 3, 4 for the older adults and sites 8, 7, 3, 1 for the younger group). Pearson product moment correlation coefficient tests revealed that in older adults, there was no significant correlation between the ERP effect and associative memory performance ($r$ = .32, $p$ = .128) or Pr ($r$ = .36, $p$ = .087), although the latter was approaching significance. In younger adults, there was a significant correlation between the ERP effect and associative hits ($r$ = .41, $p$ = .047), but not between the ERP effect and Pr ($r$ = .15, $p$ = .494). However, this significant correlation in younger adults was partly driven by an outlier in the ERP voltage value (defined as more than twice the interquartile range less than the first quartile, see Figure 3). After removing this outlier, the correlation between the ERP effect and associative memory performance was no longer significant, but still approaching significance (r=.37, p=.085).

As the subsequent associative memory effect in older adults was spatially widespread, correlation tests were also computed using the mean difference amplitude across all 37 electrodes. The results showed that for older adults, there was a significant correlation between the ERP effect and Pr (*r* = .41, *p* = .047) but not associative memory performance (*r* = .35, *p* = .09). No significant correlation was found for younger adults (both *r* < .41, *p* > .20).

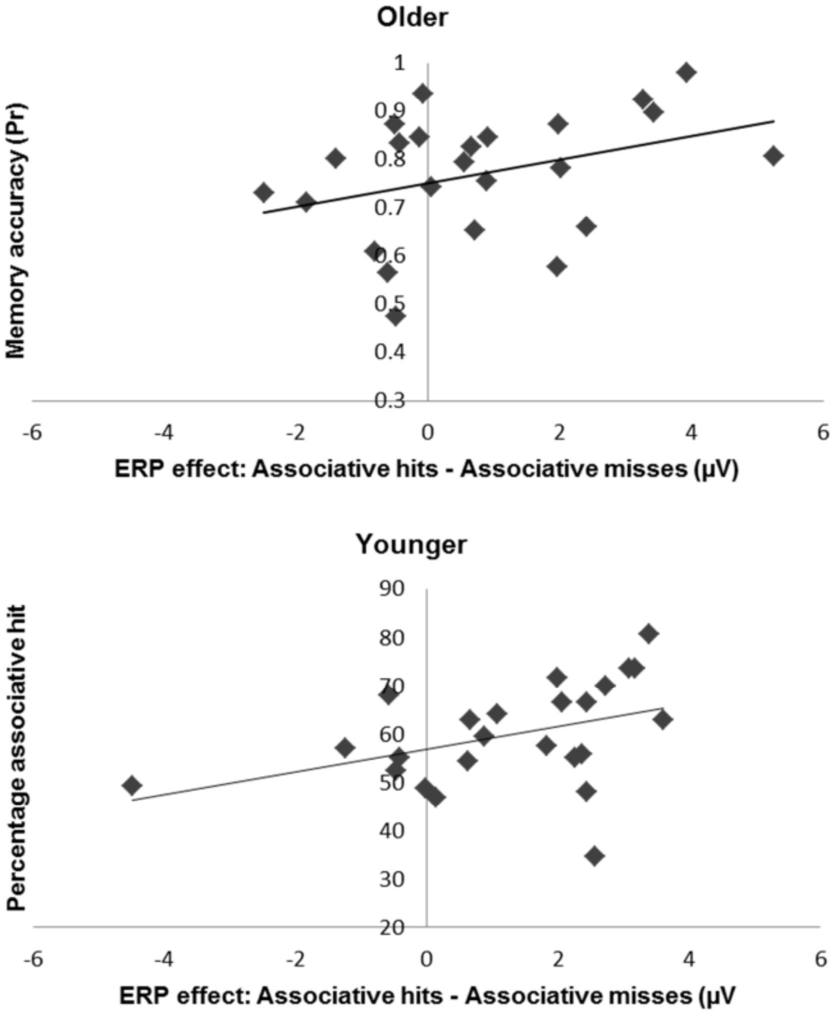


**Figure 3. Scatterplots showing the relationship between ERP subsequent associative memory effect (averaged over the 300-1600 ms time window after object-onset across the 4 frontal electrode sites where the effects were observed in the grand-average waveforms) and memory performance (Pr for older and percentage associative hit for younger adults).**

### *2.1.1.4 Discussion*

The primary interest of this study was the influence of age on associative encoding-related anticipatory activity. Behavioural analyses showed that younger adults outperformed older adults in both recognition accuracy (Pr) and associative hits. As expected, the age difference in associative hits was greater than that in recognition accuracy, which was consistent with the 'associative deficit hypothesis' (Naveh-Benjamin, 2000). This pattern of performance difference is unlikely to be due to an age difference in perceived task difficulty, as older and younger participants did not differ in their subjective judgements on task difficulty for associative encoding. Both older and younger participants spent similar amounts of time on word pairs judged as easy and those judged as difficult, suggesting that equivalent amounts of effort were made to process both easy and difficult items.

#### *Anticipatory encoding-related activity*

Different from previous studies investigation the PSME, the present study used a two-step encoding preparation, i.e., a neutral warning cue followed by a source (location) stimulus before the presentation of the target (object) stimulus. The ERP analyses did not reveal any PSME following either the neural warning cue or the location words in either age group, suggesting an absence of the expectation-driven prestimulus neural processing that influences associative encoding. The lack of PSME in ERP before source was not surprising considering that there was no encoding task implemented following the location word. Even though participants had to memorise the location words, it could be that participants did not engage in deep processing of the location words. Instead, they might simply hold the location words in working memory, and did not engage in deep semantic processing until both location and object words were presented. If this was the case, neutral warning cues could not initiate the neural processing for laying down an encoding context.

It was somewhat surprising that there was no PSME in ERPs during the pre-binding interval, especially in younger individuals. It could be that differential encoding processing for successful associative memory does not start until both items are presented. That is, pre-binding neural activity is not critical for associative encoding. However, a previous study (Otten et al., 2009) using the remember/know paradigm has reported a difference in the magnitude of PSMEs for later remembered and known items. Although not statistically significant, the PSME for remembered items appeared to be larger than that for known items. If this difference was real, it would suggest that prestimulus brain activity may influence subsequent source memory performance, given that the remember/know procedure permits a true measure of source memory.

Another possible explanation is that if participants were holding the location word in working memory during the pre-binding interval, they might not be able to effectively engage binding-related anticipatory processes due to a high level of working memory load. A previous study has shown that the PSME in ERP is subject to whether there were sufficient processing resources (Galli et al., 2012). Prestimulus encoding-related activity can be successfully engaged only when there are sufficient processing resources. By separating the source and item in time, the current paradigm might have introduced a high level of processing demands during the pre-binding interval, which could have interfered with pre-binding anticipatory neural mechanisms that facilitate associative memory.

Furthermore, a difference between the present study and previous PSME studies is the ‘blocked’ design used in the present study, i.e., the same encoding task and the same type of stimuli were used throughout a study block. Previous PSME studies mostly used an intermixed design where different encoding requirements or materials were randomly intermixed in a trial sequence (e.g., Otten et al., 2006, Otten et al., 2010; Gruber & Otten, 2010; Galli et al., 2011). This difference gives rise to the question whether PSMEs reflect task switch processing. If prestimulus activity reflects the mobilization of semantic resources to form a neural context for encoding, it is possible that in the present study, the encoding context was maintained throughout the study trials. As a consequence, prestimulus brain activity was not differentially engaged for items associated with successful or unsuccessful source memory. A piece of evidence against this hypothesis was that prestimulus brain activity affects encoding in both stay (the preceding trial and the current trial belong to the same category) and switch (the preceding trial belongs to a different category) trials (Otten et al., 2010). If prestimulus activity does reflect task switching, PSMEs should be evident only for switch trials. However, the possibility remains that PSMEs could only be found when there is a requirement to switch across trials. When the type of upcoming trial is unpredictable, it would be more efficient to set up the ‘encoding orientation’ on a trial-by-trial basis. Further investigation should be carried out to test this hypothesis.

Taken together, the present study did not find the prestimulus encoding-related activity for associative memory in either older or younger adults. It could be that the PSME is insensitive to associative memory, but there are also a number of factors that could have affected the results. Further investigation is still needed to reach a firmer conclusion on whether prestimulus brain activity affects associative memory during encoding, and how it might change in ageing.

### *Post-stimulus subsequent associative memory effects*

The present study showed that brain activity after word onset was predictive of subsequent associative memory performance. There was a sustained positive-going subsequent associative memory effect across age. Similar SMEs have been consistently found in numerous previous studies (see Friedman & Johnson, 2000; Paller & Wagner, 2002 for reviews), and were thought to reflect deep, elaborative semantic processing. The present finding, in line with previous research, indicated that younger adults engaged in the kind of elaborative processing that enhanced subsequent associative memory. Importantly, older adults also engaged similar associative encoding-related activity. Even though the SMEs in the two age groups appeared to have different scalp distributions by visual inspection, i.e., right-lateralised in older but not younger adults, this difference was not statistically significant.

Previous studies have shown that the SME as a function of episodic retrieval success was absent in the older adults (Friedman et al., 1996; Friedman et al., 1999; Friedman & Trott, 2000). In terms of SMEs in source memory, previous studies either failed to find any reliable effect in either age group (e.g., Friedman & Trott, 2000) or found SMEs that were equivalent in amplitude but different in topography in older adults (Cansino et al., 2010). As discussed in the Introduction, the discrepancy amongst studies may be caused by a number of factors including the use of different learning materials and different source memory paradigms. The present study used verbal learning material, which was similar to that in Friedman and Trott (2000), but the subsequent source memory effect found in the current study did not emerge in Friedman and Trott's study. The discrepancy between studies might be related to the difference in the source memory tasks. In Friedman and Trott (2000), participants had to remember whether an item was presented in the first or the second study list, whereas in the current study, each item had its unique source information. This means that the possibility of lucky guesses in source memory was much lower in the current study (1/156) than in Friedman and Trott's (1/2). It is highly unlikely that the associative hits in the current study were diluted by lucky guesses, and therefore represent a “purer” measure of associative source memory.

A related factor is the explicit use of associative encoding strategies in the current study. Participants in the present study were required to use an encoding strategy that emphasises inter-item association (i.e., they had to imagine the object interacting with the location). A previous study (Weyerts, Tendolkar, Smid, & Heinze, 1997) has shown that only word pairs encoded associatively elicited a reliable SME in a recognition memory task, whereas those word pairs encoded non-associatively did not. Thus, it is possible that when associative learning strategy is explicitly required, both age groups, especially younger adults are able to engage in the kind of elaborative processing that enhance subsequent associative retrieval.

Even though brain-behaviour correlations did not reach the critical significance level, the pattern of the correlations may shed more light on the nature of the age difference in subsequent associative memory effects. There was a trend that in older adults, the SME was more closely associated with recognition accuracy (Pr) than with subsequent associative memory performance, whereas in the young, the SME was correlated with associative memory performance. This suggested that younger adults were able to engage in the kind of encoding activity that selectively enhanced associative encoding, but older adults engaged in less specific encoding activities that benefit recognition memory in general. The current findings indicate that relative to the young, older adults are less able to adopt novel effortful learning strategies to enhance associative encoding. This is consistent with previous findings that when trained to use learning strategies, younger adults benefit more when novel associative operations are required, which are too difficult for older adults (Luo, Hendriks, & Craik, 2007).

In a previous source memory encoding study using pictures of objects, Cansino et al. (2010) found an SME in older adults that was similar in amplitude but different in topography to that found in younger adults. The topography of the SME in older adults was more wide-spread over the posterior scalp sites than that in younger adults. Analogous findings of additional encoding-related brain activity in ageing have also been reported in fMRI studies using pictorial stimuli. For example, Gutchess and colleagues (2005) found that older adults had more activation than younger adults in the middle frontal cortex but less activation in the parahippocampus during the encoding of pictures of complex scenes. In the present experiment, however, there was no reliable age difference in SMEs in either amplitude or topography. Such discrepancy might be related to a difference in learning materials. Compared to words, pictures are richer in visual details and highly meaningful in everyday life, and therefore tend to elicit deep, elaborative encoding naturally without effortful control processing required. As a consequence, pictures are usually better remembered than words (e.g., Craik & Schloerscheidt, 2011) and age differences in memory performance are reduced when pictorial learning material is used (Luo et al., 2007). It is likely that additional neural activity is engaged by older adults when pictures are processed, which may reflect compensatory processing in ageing.

For example, in Gutchess et al.’s (2005) study, it was found that frontal activity and parahippocampal activity were negatively correlated during encoding of items that were later remembered. The authors speculated that prefrontal activation might compensate for age-related declines in medial-temporal activity. Thus, there might be encoding deficits in ageing for both verbal and pictorial stimuli, but additional frontal activity might be engaged to compensate for such deficits for pictures but not words.

It is interesting that in the current study, the SME in older adults appeared to be right-lateralised, which is somewhat similar to the SMEs found in younger adults in previous studies when pictures of objects were used as learning material (Duarte et al., 2005; Cansino et al., 2010). Some fMRI studies also demonstrated that during memory encoding, left-lateralised brain activation was associated with the processing of verbal information, whereas right or bilateral activation was associated with the processing of pictorial information (Kelley et al., 1998; Wagner et al., 1998). It could be that in the current study, older adults relied more on visual imagery to bind the word-pairs during encoding, which was what they were instructed to do. Young adults, on the other hand, were more flexible and able to use a variety of different strategies to memorise the word-pairs. This was supported by the age difference in self-reported number of encoding strategies, with younger adults using significantly more encoding strategies (mean = 2.71) than older adults (mean = 1.96). In addition, the SME in older adults was extended further into the posterior scalp areas relative to that in younger adults. This additional posterior activation is consistent to that reported by Cansino et al. (2010), who interpreted it as a representation of age-related neural inefficiency of source memory encoding. In the present study, the pattern of the brain-behaviour correlation suggested that the widespread SME was more likely to reflect compensatory processing in ageing. It is possible that the activity over posterior sites was related to sensory aspects of the visual imagery processing. Nevertheless, the topography of the SMEs did not differ significantly across the groups, suggesting that there was no qualitative age difference in brain activity for associative encoding of word pairs. Further research is needed to elucidate whether the right-lateralized brain activity is related to age or to mental imagery during associative encoding of verbal material.

The absence of a qualitative difference in SME between age groups suggests that older adults activated similar brain networks for associative encoding as their younger counterparts. The similarity in neural activation across age resembles the fMRI finding for recognition memory (Morcom et al., 2003) that older adults engage much of the same neural circuits as younger subjects to encode new memories. However, overall ERPs across associative hits and associative misses were more negative-going in younger adults compared to older adults between around 300-600 ms post-stimulus, conforming with the N400 component that is related to semantic processing (Kutas & Federmeier, 2011). A smaller N400 effect has been found in older relative to younger adults (Federmeier & Kutas, 2005) when comparing predictable with unpredictable final words in sentences. The sentences in the predictable final-word condition were strongly constrained and provided richer contextual information, as compared to the sentences in the unpredictable final-word condition. The age-related changes in N400 were thought to reflect age-related impairments in the ability to use contextual information to guide semantic processing. Similar findings have been reported by Gunter and colleagues (1995, 1998), who also demonstrated that the magnitude of the N400 effect was positively correlated with recall performance (Gunter, Jackson, & Mulder, 1998). Thus, it is possible that in the present study, older adults were less able to form a rich semantic context for encoding. However, as explained above, caution is needed when interpreting the differences in ERP morphology across age. Further evidence is needed to examine the relationship between semantic elaboration at encoding and associative retrieval.

Previous research has pointed to an age difference in temporal dynamics of episodic memory encoding. Nessler et al. (2007) tested both younger and older adults for semantic encoding, and found a negative-going ERP effect related to semantic processing over left inferior prefrontal (LIPFC) scalp sites in a 300-1400 ms post-stimulus interval. In the first half of this interval (before 800 ms), the effect was evident in both younger and older adults, albeit larger in the young. In the second half (from 800 ms), however, the effect was completely absent in older adults. Both of these age differences were associated with significant decrements in subsequent recognition performance in older adults. Another study (see Friedman & Johnson, 2000) also found an early/late segregation of the SMEs, with the early part sensitive to the semantic attributes of the stimuli whereas the late part directly correlated with the amount of episodic information retrieved. The present study, however, found no evidence for the difference between the early and late part of the SME. It is possible that in the present study, older adults were able to engage in semantic elaboration and episodic encoding processes, which might overlap temporally and/or spatially across the scalp.

In conclusion, the present study showed that neural correlates of associative encoding during inter-item binding are statistically indistinguishable across age.

For both older and younger adults, similar neural processes that determine associative memory success were operative during binding. Older adults might be impaired in the kind of elaborative processing for associative encoding. This impairment was possibly related to the inability to flexibly engage in associative encoding strategies, which taxes heavily on processing resource. An unexpected finding is that pre-stimulus activity did not modulate associative encoding in either age group. Further investigation is needed to shed more light on anticipatory activity during associative encoding.

### 2.1.2 Retrieval

#### *2.1.2.1 Introduction*

In addition to deficits at encoding, age-related memory decline may also be due to retrieval impairments. Episodic retrieval involves the interaction between a retrieval probe and an internal representation of memory traces (Tulving, 1983). Successful recovery of specific information requires cognitive control processes to guide this interaction in a goal-directed manner. Control processes may be exerted after, but also before the encountering of a retrieval probe. As already described in the Introduction chapter, numerous ERP studies (e.g., Herron & Wilding, 2004; Johnson & Rugg, 2006) have shown that cueing subjects to retrieve specific information from memory leads to alterations in cue-elicited brain activity before the presentation of a retrieval probe depending on the kind of information to be retrieved. The patterns of anticipatory activity also differ depending on whether it is in the mixed or blocked condition (Morcom & Rugg, 2002; Werkle-Bergner et al., 2005; Johnson & Rugg, 2006). These pre-probe anticipatory brain activities have been interpreted in terms of ‘retrieval orientation', i.e., a tonically maintained task-specific retrieval strategy that modulates the retrieval processes in a goal-directed manner (Rugg & Wilding, 2000). It was speculated that such pre-probe activity reflects either an initial task set configuration or a pre-activation of memory representations for the targeted information. However, evidence for a direct effect of the ERP pre-probe anticipatory activity on memory retrieval is lacking.

An EEG study using the time-frequency approach (Addante et al., 2011) has provided such evidence. It was found that pre-probe oscillatory brain activity in the theta range was associated with successful retrieval of source information. The magnitude of pre-probe theta was related to the magnitude of post-probe theta. Together with findings from other studies that pre-probe brain activity at retrieval may reflect an early activation of relevant brain networks in anticipation of the retrieval of required information (Polyn et al., 2005; Sederberg et al., 2009), The Addante et al. (2011) study suggests that anticipatory activity may influence probe-elicited processing and facilitate episodic source retrieval.

It is presently unclear whether anticipatory retrieval-related activity is affected by ageing. An fMRI study (Dew et al., 2011) has given some clues to this question.  Using instructional cues signalling whether source or item retrieval was to be performed, it was found that only younger adults showed increased activity in the MTL during pre-probe cueing for source retrieval. In contrast, older adults only showed increased MTL activity for source retrieval after the probe onset. Functional connectivity between left hippocampus and PFC showed the same pattern of age differences. Together with the finding from another study (Dobbins & Han, 2006) that PFC activity increases during the cueing of context retrieval relative to item retrieval, it was thought that PFC activity is also critical for context retrieval preparation. Therefore, the results in Dew et al. (2011) were interpreted as demonstrating an age-related failure to engage in anticipatory processing in a proactive manner. Such impairment in ageing might be related to cognitive control deficits as reflected in changes in PFC activity. These findings pointed to an age-related decline in pre-probe anticipatory brain mechanisms for source retrieval. However, as the cue-elicited pre-probe activity was uncorrelated with memory performance in either age group in Dew et al. (2011), it is unclear whether such activity was directly related to source retrieval.

In terms of post-probe retrieval, a number of ERP studies have reported a widespread, left-frontally and/or centrally focused negativity for successful episodic retrieval, specific to older adults (e.g., Dulas & Duarte, 2013; Li et al., 2004; Swick et al., 2006; Wegesin et al., 2002). This prominent negative-going activity starts at about 400-600 ms post-stimulus and therefore reduces or overshadows other retrieval effects such as the mid-frontal and left-parietal effects that might have presented. This negative-going retrieval effect is thought to reflect the use of alternate retrieval strategies by older adults, i.e., searching for visual information, as a consequence of greater demands on control processes for source retrieval (e.g., Dulas & Duarte, 2013; Li et al., 2004). Such a compensatory interpretation was supported by Swick et al. (2006) who tested healthy younger and older adults, as well as older patients with focal lesions of lateral PFC in a source retrieval task. It was found that in healthy older adults, there was a left-frontally and centrally focused negativity for source retrieval, and this effect was smaller and delayed in the patients. This finding indicates that patients with PFC impairments are less able to recruit neural mechanisms underlying the left-frontal negative-going retrieval effect as their healthy counterparts do. Furthermore, the left-frontal negativity has been related to the amount of source information available for retrieval. Dulas and Duarte (2013) demonstrated that the left-frontal negativity emerged only when older adults were explicitly asked to pay attention to source information at encoding, compared to when they were not. Therefore, the ERP negative-going retrieval effect by older adults may reflect compensatory mechanisms selectively engaged to optimise source retrieval, depending on the amount of source information available. Dulas and Duarte's findings also suggest that the recruitment of such compensatory mechanisms is influenced by whether source memory is emphasized. It is possible that the left-frontal negativity reflects cognitive control processes related to the search for source information when source memory is emphasized. If so, neural mechanisms underlying the left-frontal negativity might also interact with other control mechanisms at retrieval, such as pre-probe anticipatory mechanisms.

The main aim of this experiment was to investigate the effect of age on anticipatory retrieval-related activity. There is currently not enough evidence to show whether older adults are able to engage anticipatory activity, or even whether such activity affects retrieval in younger adults. In the present study, post-probe retrieval-related activity was also analysed to find out how it changes with age and whether it was influenced by anticipatory activity during retrieval. As described in the encoding section, the associative memory paradigm in the present study emphasised the association between item (object) and source (location) to maximise the associative memory effects. Also, because each item was associated with its unique source, the probability of correctly recovering associative information due to "lucky guesses" was very small.

A one-step response procedure, i.e., old/new and source decisions indicated in one response, was used to best capture neural activity related to associative retrieval (Cycowicz & Friedman, 2003). The critical contrast was between successful and unsuccessful associative retrieval, so that brain activity for associative retrieval was isolated. More importantly, age-related differences specific to associative retrieval-related brain activity could be examined, albeit at the expense of item memory.

It was predicted that associative memory performance should be better in younger than older adults. For probe-elicited activity, younger adults were expected to show left-parietal and right-frontal effects for associative retrieval, whereas older adults would show different effects, most likely the left-frontally and centrally focused negativity (Dulas & Duarte, 2013; Li et al., 2004; Swick et al., 2006; Wegesin et al., 2002). Based on findings from Addante et al. (2011) and Dew et al. (2011), older adults might have a deficit in anticipatory brain activity, reflected in the reduction or absence of pre-probe associative retrieval-related effects that might be observed in younger adults.

#### ***2.1.2.2 Methods***

Information about participants, design, and procedures, can be found in the encoding section.

##### *ERP analyses*

Averaged ERPs were formed for two critical conditions, associative hits and associative misses. Both pre-probe anticipatory brain activity and retrieval-related activity after probe onset were analysed. Activity elicited by preparatory cues and retrieval probes were aligned independently to the onset of each event, allowing each to be analysed separately. Epochs of 2560 ms duration surrounding cues and probes, starting from 100 ms before their onset were extracted and down-sampled to 100 Hz. ERPs were computed for each participant at each electrode site for the two critical conditions, baseline corrected to the 100 ms before event onset.

*Pre-probe associative retrieval-related activity*

For anticipatory cue-related analyses, one older subject was excluded due to insufficient (< 16) artefact-free trials. EEG data were taken from 23 older and 24 younger participants. For the remaining 23 older and 24 younger subjects, the average numbers and ranges (in parentheses) of artefact-free trials for associative hits and associative misses were 43 (18-111) and 57 (23-107) for the older group and 81 (44-122) and 39 (16-70) for the younger group. Statistical analyses were conducted including 24 electrode sites (Figure 4), to characterise scalp distribution according to anteriority (anterior/posterior) and site (12 sites). The anterior/posterior partition was done because pre-probe preparatory ERP effects were mostly found at the frontal electrode sites (e.g., Johnson & Rugg, 2006).

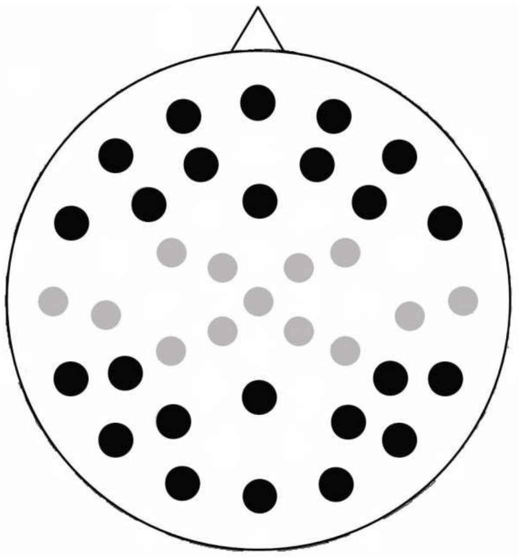


**Figure 4. Schematic illustration of the 37 recording electrode sites and the black dots depicting the 24 sites used for the ERP analyses.**

Mean amplitudes were quantified using two continuous latency intervals: 200-1100 ms (early) and 1100-2000 ms (late), same as those used to measure anticipatory encoding-related activity. Here too, the use of early/late continuous latency separation was to capture the development and change of anticipatory memory-related activity over time. It was also expected that such effects would be larger in the late interval when the probes were about to appear. Therefore, initial mixed-model ANOVAs were conducted incorporating factors of age (older/younger), response (associative hits/associative misses), latency (two regions), anteriority (anterior/posterior), and site (12 sites). Significant interactions including latency and response would suggest that the associative retrieval effect varies between the two latency regions, which warrant separate analyses for each of the two intervals. The effects of interest were those involving the factor of response (i.e., pre-probe associative retrieval effects), particularly age-related differences on such effect (i.e., interactions involving age and response). Significant age-related differences were followed up by subsidiary within-subject ANOVAs for each age group separately. Analyses of scalp distribution were also performed using the same method as for encoding-related analyses. Significant differences between the topographies of different conditions and age groups were verified by ANOVAs conducted on the rescaled data. The Greenhouse-Geisser correction for nonsphericity was used when appropriate, as indicated by the adjusted degrees of freedom.

Additional analyses were conducted to further substantiate the functional significance of the pre-probe effect in memory retrieval and ageing. Firstly, across-subject correlations were computed to assess the relationship between pre-probe ERP effect and memory performance. Secondly, a number of analyses were done to rule out the possibility that the pre-probe effect reflected the influence of speech from preceding trials. This step was necessary as verbal responses were required at retrieval, which led to the problem that associative hits could be preceded by proportionally more speaking trials relative to associative misses. This was important especially for older adults, who tended to give lengthier answers relative to younger adults.

Furthermore, ERP waveforms elicited by cues were collapsed across all valid trials regardless of whether the subsequent retrieval probes were old words or new words. This was done to assess the difference between groups in overall cue-related preparatory activity. To this end, all 37 electrode sites were included in a mixed-model ANOVA with factors of age (older/younger) and site (37).

### *Post-probe associative retrieval-related activity*

For probe-elicited activity, EEG data from all 24 older and 24 younger participants were included in the analyses. The average numbers and ranges of artefact-free trials for associative hits and associative misses were 46(17-105) and 61(25-107) for the older group and 84(48-125) and 43(15-83) for the younger group.

Same as those for post-stimulus encoding, statistical analyses were conducted including 28 electrodes partitioned into 4 quadrants (Figure 1). A similar partition has been used in previous research of source retrieval and ageing (e.g., Cruse & Wilding, 2009; 2011; Wang et al., 2012). Mean ERP amplitudes were measured in three separate latency intervals: 300-600 ms, 600-900 ms, and 900-1200 ms. These intervals have been used in previous studies investigating age-related change in retrieval (Trott et al., 1999; Swick et al., 2006; Wegesin et al., 2002). They were slightly prolonged than those traditionally used to capture the well-known old/new effects, e.g., mid-frontal (300-500 ms) and left-parietal (500-800 ms) effects, to accommodate age-related delay in the timing of these components as well as the additional negative-going effect found in older adults. A later time window from 1200 ms was not included due to potential contamination from the effect of speech preparation, which manifested in the grand-average ERP waveforms as a large late positive-going deflection in the younger group.

Initial mixed-model ANOVAs were computed incorporating factors of age (older/younger), latency (3 intervals), memory (associative hits/associative misses), anteriority (anterior/posterior), hemisphere (left/right), and site (7 sites). Significant interactions including latency and response were followed up with further mixed-model ANOVAs including the 1st and the 2nd intervals, or the 2nd and the 3rd intervals to determine whether each interval can be separated from the adjacent one. If so, further ANOVAs were conducted for each latency region separately. For the intervals during which significant age differences in associative retrieval effect emerge, subsidiary within-group ANOVAs were performed for each age group separately. Again, significant differences in topographies were verified by ANOVAs conducted on rescaled data.

In addition, across-subject correlations were computed to assess the relationship between the amplitudes of post-probe ERP effects and memory performance, as well as the relationship between pre-probe and post-probe ERP effects. These were done to examine how the pre-probe and post-probe activities might interact and influence associative memory retrieval, and to shed more light on neural mechanisms of the impairments in ageing.

#### ***2.1.2.3 Results***

Behavioural results have been reported in the encoding section, therefore only ERP results are reported in this section.

*Pre-probe associative retrieval-related activity*

Grand-average ERP waveforms elicited by cues preceding retrieval probes that led to accurate associative retrieval versus those led to no associative retrieval are shown in Figure 5 for the frontal (FPz) and posterior (Oz) electrode sites representing the anterior/posterior partition. In older adults, the waveforms diverged early after cue onset with the waveforms preceding retrieval probes that led to successful retrieval of associative information being more negative-going than those with which the associative information was forgotten. In line with previous research (e.g., Johnson & Rugg, 2006), this effect built up gradually during the cue-probe interval and reached its maximum just before probe onset. It showed a widespread scalp distribution and was largest over the anterior frontal electrode sites. In younger adults, the effect started later from around 1000 ms after cue onset and was much attenuated.

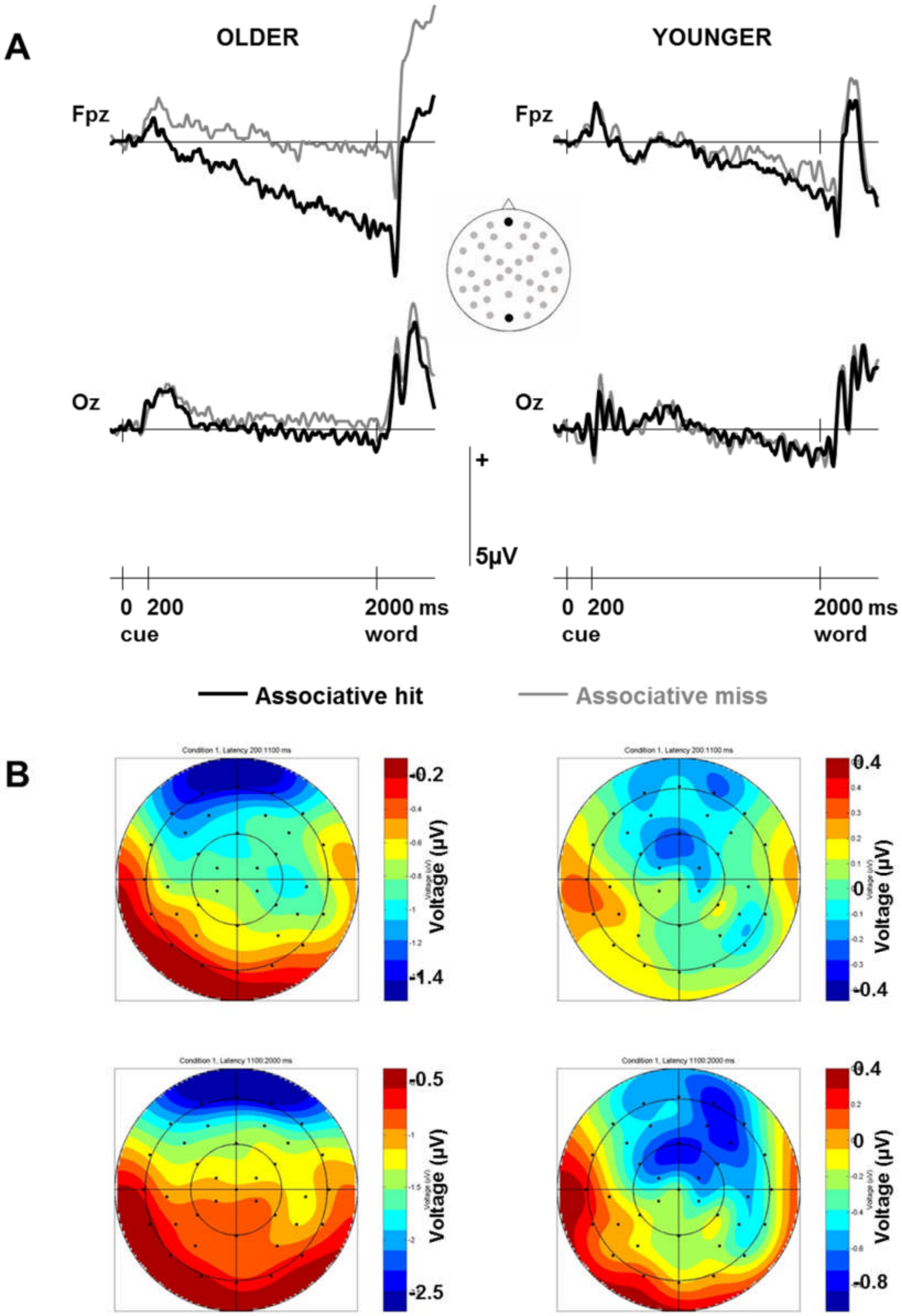


**Figure 5. Pre-probe brain activity related to associative retrieval. (A) Grand-average ERPs of the two groups elicited by retrieval cues according to whether they were followed by words that elicited accurate associative retrieval or no associative retrieval. The insert indicates the locations of the 2 representative electrodes (site 35 and 43 from Montage 10; www.easycap.de/easycap/e/electrodes/13_M10.htm; equivalent to site Fpz and Oz of the 10-20 system). (B) Voltage spline maps for the older and younger groups showing the distribution of the difference between cue-related activity preceding associative retrieval and no associative retrieval in the 200-1100 ms and 1100-2000 ms intervals. The maps are range scaled.**

The initial mixed-model ANOVA incorporating the factor of latency interval revealed a significant main effect of response (*F*(1, 45) = 8.08, *p* = .007) and a significant response × interval interaction (*F*(1, 45) = 5.41, *p* = .025), suggesting that pre-probe associative retrieval effects differed across the two latency intervals. Subsidiary mixed-model ANOVAs for each interval revealed that in the early interval, there was a significant main effect of response (*F*(1, 45) = 4.40, *p* = .042), a response × group interaction (*F*(1, 45) = 4.38, *p* = .042), and a response × anteriority × site interaction (*F*(3.9, 176.0) = 3.87, *p* = .005). The response × group interaction reflected that the associative retrieval effect (associative hits – associative misses) was more negative-going in older (-0.83 µV) than younger (0 µV) adults. Subsidiary within-group ANOVAs revealed that for older adults, there was a significant main effect of response (*F*(1, 22) = 6.33, *p* = .02). No significant effect was found for younger adults (*F*s < .41, *p*s > .53).

In the late interval, there was a significant main effect of response (*F*(1, 45) = 9.37, *p* = .004), a response × anteriority interaction (*F*(1, 45) = 7.84, *p* = .008), and a response × anteriority × site (*F*(4.4, 198.2) = 4.05, *p* = .003). The response × anteriority interaction reflected that across the groups, the associative retrieval effect was more negative-going over anterior (-1.21 µV) than posterior (-0.48 µV) sites. Taken together, results from individual latency interval analyses showed that in the early interval, there was a negative-going pre-probe associative retrieval effect in older adults only, whereas in the later interval the effect was found across the age groups and larger over the anterior than the posterior sites.

To further substantiate the functional significance of the pre-probe effect in memory retrieval and ageing, across-subject correlations were computed to assess the relationship between the pre-probe ERP effect and memory performance. As shown in Figure 6, older adults are much more heterogeneous than younger adults as a group in terms of the magnitude of the ERP effect. Given the large neural as well as behavioural inter-individual variability in older adults, it might be expected that there was a relationship between the pre-probe ERP effect and memory performance in older adults. The pre-probe ERP effect was quantified using the 200-2000 ms interval over the 12 anterior scalp sites. Although an age difference was found only in the early interval, the pre-probe effects across both groups were larger in the later interval over anterior sites. Also, additional within-group ANOVAs (results not reported) suggested that there was no reliable difference in pre-probe retrieval effects between the two intervals in either group. Therefore, the difference in mean amplitude between associative hits and associative misses during 200-2000 ms after cue onset was correlated with Pr as well as the percentages of associative hits for each group separately. For the correlation between the ERP effect and Pr (Figure 7), Pearson product moment correlation coefficient tests showed a significant correlation in the older group ($r = .60$, $p = .003$), indicating that the larger the ERP effect, the poorer the memory accuracy. No significant correlation was found in the younger group ($r = .08$, $p = .70$). For the correlation between the ERP effect and the percentages of associative hits, the pattern of results was unchanged (older: $r = .43$, $p = .043$; younger: $r = .12$, $p = .581$). The pattern of correlations might reflect the difference in the magnitude of the ERP effect across the groups. Correlation analyses were also performed to assess the relationships between the pre-probe ERP effect and RTs for associative hits, and the results suggested that the pre-probe associative retrieval-related activity did not affect later RT (r < .08, p > .73 in each group).

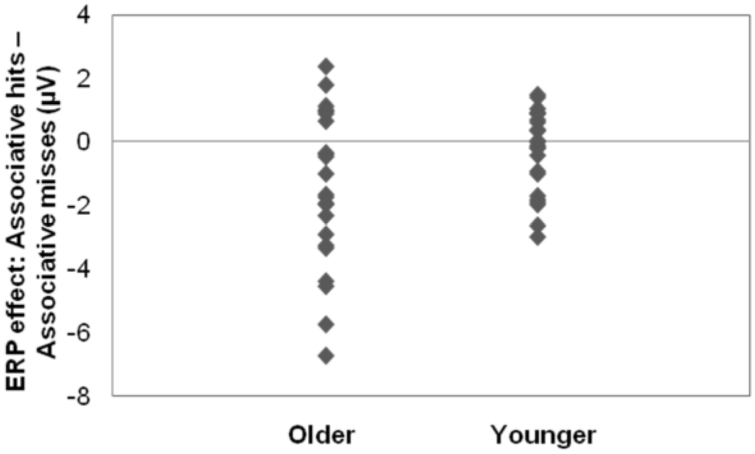


Figure 6. Scatterplot showing the amplitudes of the pre-probe ERP effect (averaged over the 200-2000 ms interval after cue-onset across the 12 frontal electrode sites) for the 23 older and 24 younger participants.

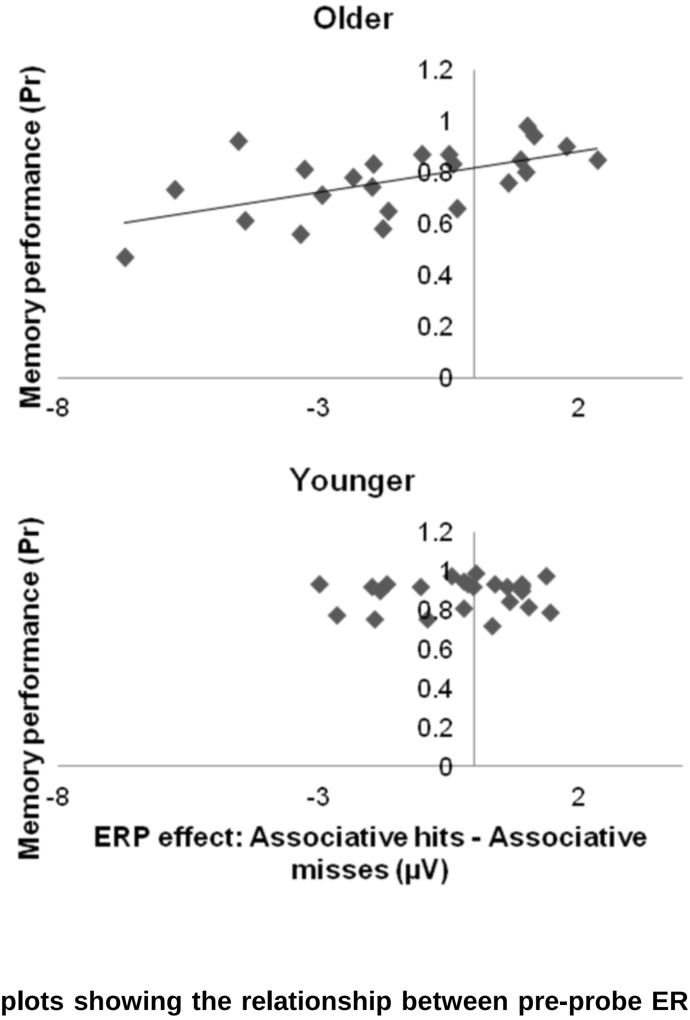


Figure 7. Scatterplots showing the relationship between pre-probe ERP effect (averaged over the 200-2000 ms time window after cue-onset across the 12 frontal electrode sites) and memory performance (Pr) for the older group (above, *N* = 23) and the younger group (below, *N* = 24).

As verbal responses were required at retrieval, and older adults tended to give lengthier answers relative to younger adults, it is possible that the pre-probe effect in older adults reflects the influence of speech from preceding trials. It might be that associative hit trials were preceded by proportionally more speaking trials relative to associative misses, and the preparation to speak selectively affected associative hit trials. To rule out this possibility, group-averaged ERPs were computed using only trials that were preceded by non-speaking trials in older adults (on average 28% of associative hit trials and 22% of associative miss trials respectively). The patterns of ERP waveforms closely resembled those shown in Figure 5. A within-subject ANOVA incorporating factors of response, anteriority, hemisphere, and site identical to that reported above revealed a main effect of response ($F(1, 22) = 8.41$, $p = .008$), a response by anteriority interaction ($F(1, 45) = 5.40$, $p = .030$), and a response by anteriority by site 3-way interaction ($F(4.1, 91.3) = 3.70$, $p = .007$). These results closely resembled the overall effects in older adults. In addition, older participants were separated into two subgroups according to whether a larger proportion of associative hits or a larger proportion of associative misses was preceded by speaking trials. Cue-elicited ERPs were averaged for each subgroup, and ERP waveforms of both groups showed similar patterns to those shown in Figure 5. Taken together, it is unlikely that the pre-probe effect in older adults reflected the influence of speech in response to preceding trials.

Finally, grand-average ERP waveforms were collapsed across all valid trials regardless of whether the subsequent retrieval probes were old or new words. This overall cue-related preparatory activity is illustrated in Figure 8, showing the waveforms at three midline electrode sites as well as the scalp distributions of voltage amplitudes for the two groups. The waveforms of older adults showed positive deflections over the central scalp cites and reversed polarity at the right-frontal sites. The waveforms of younger adults also showed the negative deflections at the right-frontal sites but not the positive deflections over the central sites. In younger but not older adults, there appeared to be sustained negative-going ERP deflections over frontocentral scalp sites resembling the CNV, a well-known neural signature of anticipation (Brunia et al., 2012). Over the central sites, The time course of the divergence between the two groups appeared to be in line with the pre-probe associative retrieval effect, started early after cue onset and gradually built up before the probe onset. Results of a mixed-model ANOVA with factors of age (older/younger) and site (all 37 sites) showed a significant main effect of age ($F(1, 45) = 6.12$, $p = .017$) but not the interaction between age and site ($F(3.2\ 143.8) = 2.49$, $p = .059$), suggesting that there was no reliable age difference in scalp distributions of the overall cue-related preparatory activity.

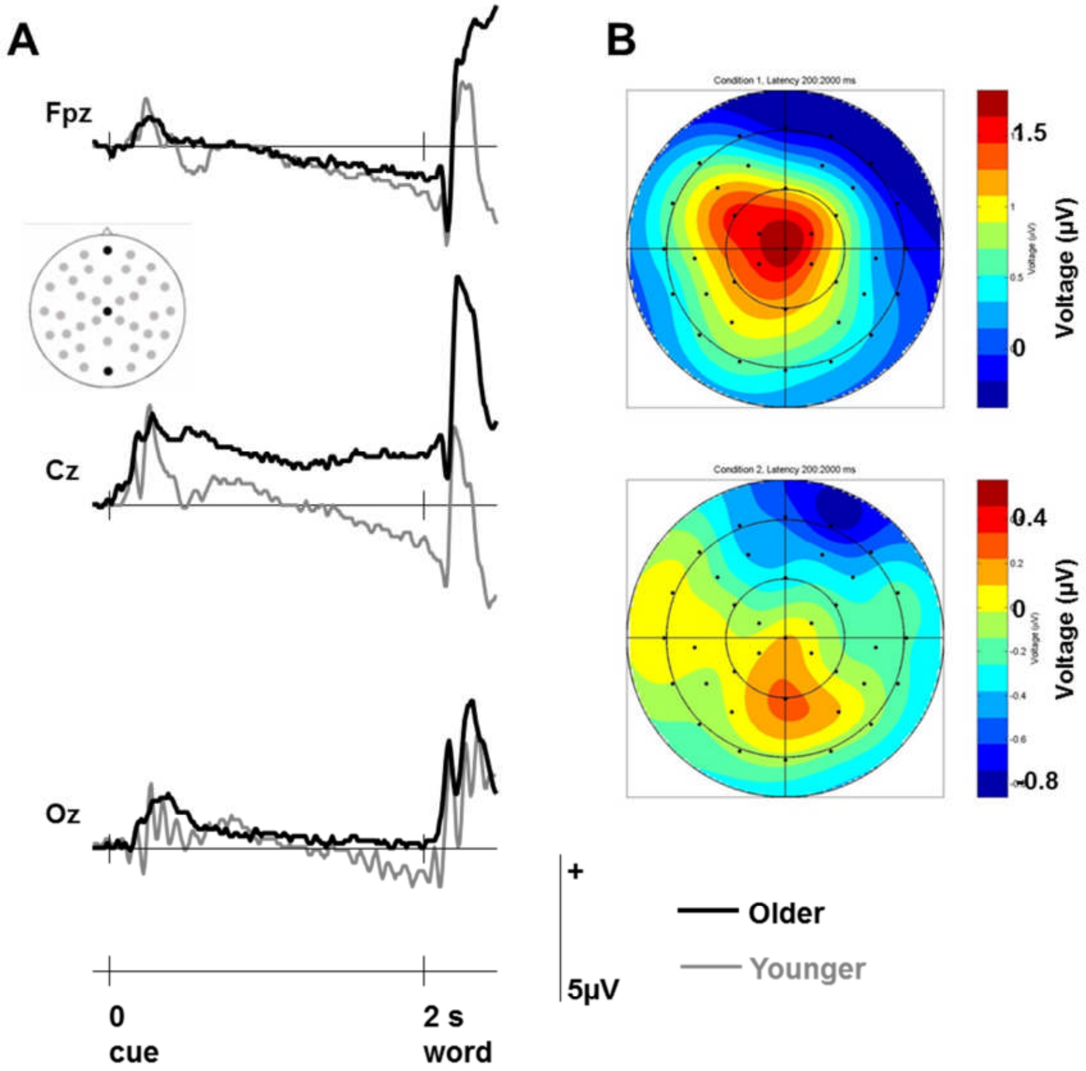


**Figure 8. Pre-probe brain activity across all trials. (A) Grand-average ERPs of the two groups elicited by retrieval cues regardless of whether the following words were old or new. The insert indicates the locations of the 3 midline electrodes (equivalent to Fpz, Cz, and Oz of the 10-20 system). (B) Voltage spline map showing the distribution of amplitude in older (upper) and younger (lower) individuals in the 200-2000 ms interval after cue onset. The maps are scaled to the same range across groups.**

### *Post-probe associative retrieval-related activity*

Figure 9 shows ERP waveforms elicited by retrieval probes lead to associative hits and associative misses respectively. Visual inspections of the waveforms revealed pronounced age differences. In younger adults, the waveforms differ from around 300-400 ms post-stimulus, with those related to associative hits more positive than those for associative misses. This effect was larger over fronto-central and left parietal sites. From around 1200 ms there was a wide spread positive-going effect that was largest over frontal sites, which might reflect speech preparation. In contrast, in older adults the waveforms related to associative hits were more negative-going than those for associative misses. This negative shift started as early as 200 ms after probe onset over frontal sites, and turned into a wide spread effect from about 500-600 ms that built up gradually and was largest over the left and central sites.

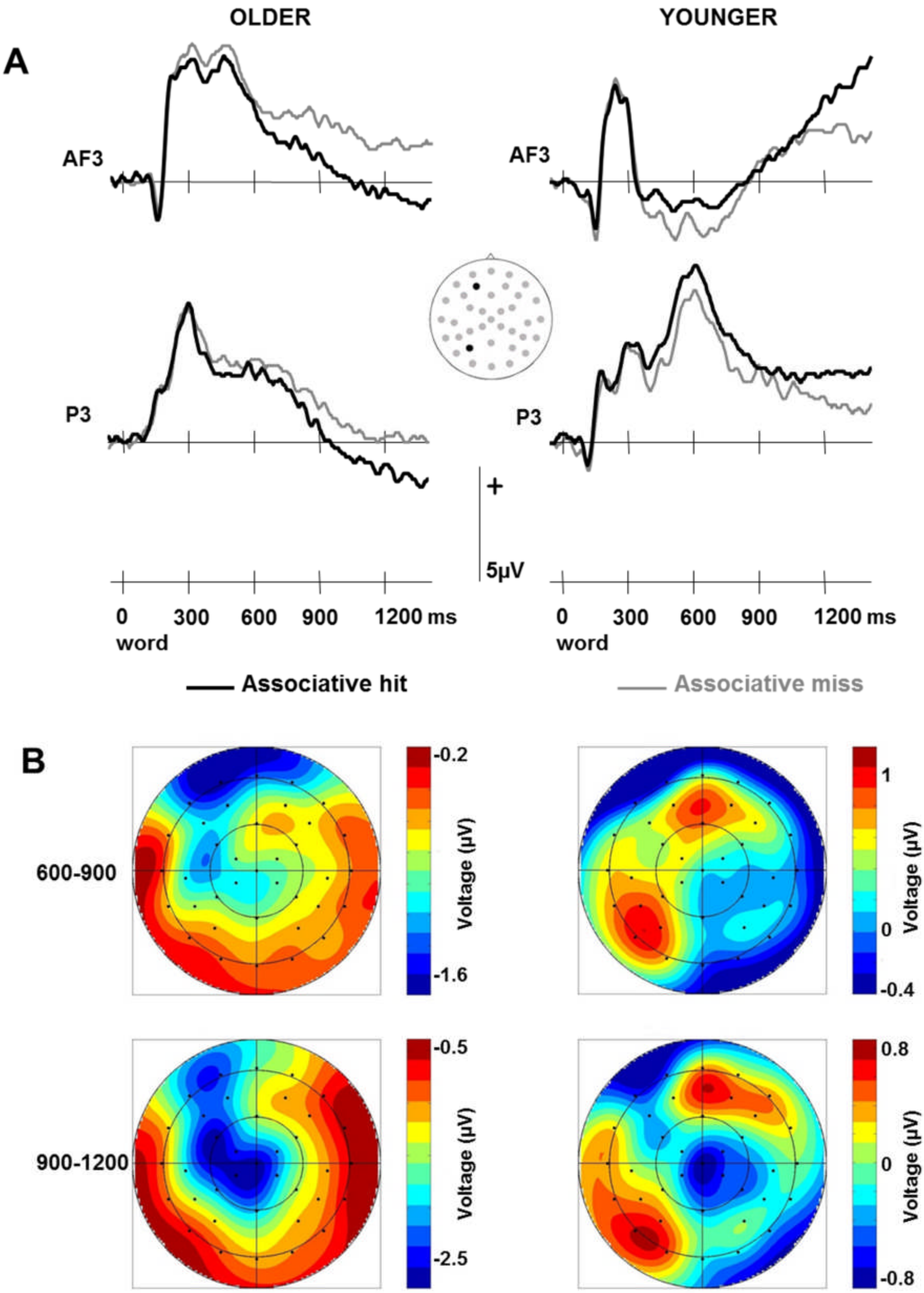


**Figure 9. Post-probe brain activity related to associative retrieval. (A) Grand-average ERPs of the two groups elicited by retrieval probes according to whether they elicited accurate associative retrieval or no associative retrieval. The insert indicates the locations of the 2 representative electrodes (site 34 and 29 from Montage 10; <u>www.easycap.de/easycap/e/electrodes/13_M10.htm</u>; equivalent to site AF3 and P3 of the 10-20 system). (B) Voltage spline maps for the older and younger groups showing the scalp topographies of the ERP associative retrieval effects (associative hit – associative miss) in the 600-900 ms (upper row) and 900-1200 ms (lower row) intervals. The maps are range scaled.**

Initial mixed-model ANOVAs incorporating the factor of latency interval revealed significant response × interval interactions between the first and the second latency regions (*F*(1,46) = 6.76, *p* = .013) and also between the second and the last latency regions (*F*(1,46) = 8.09, *p* = .007). Furthermore, significant response × interval × site interactions were also found both between the first and the second intervals (*F*(3.5,159.2) = 4.79, *p* = .002, after data scaling: *F*(3.2,145.6) = 4.18, *p* = .006) and between the second and the last intervals (*F*(3.1,141.3) = 5.89, *p* = .001, after data scaling: *F*(3.0,139.8) = 3.30, *p* = .022). These results suggested that associative retrieval effects differed qualitatively across the latency intervals. Therefore, separate ANOVAs were carried out for each interval separately.

In the 300-600 ms interval, there was no significant effect of interest as revealed in a mixed-model ANOVA. In the 600-900 ms interval, a mixed-model ANOVA revealed a significant response × group interaction (*F*(1,46) = 4.10, *p* = .049), indicating an age difference in associative retrieval effect in this latency region. The difference (associative hit – associative miss) was negative in older adults (-0.84 µV) and positive in younger adults (0.36 µV). In the 900-1200 ms interval, a mixed-model ANOVA revealed a significant main effect of response (*F*(1,46) = 5.84, *p* = .020) and a response × group interaction (*F*(1,46) = 5.38, *p* = .025), indicating an overall negative-going associative retrieval effect that was larger in older adults (-1.52 µV) than younger adults (-0.03 µV). Therefore, subsidiary within-subject ANOVAs were conducted for each age group separately in the last two latency regions (results shown in Table 4).

**Table 4. Significant within-group ANOVA results for the post-probe ERP associative retrieval effects.**

| Time Interval (ms) | Analysis | Effect | *df* | *F* | *p* |
|---|---|---|---|---|---|
| 600-900 | Older | RS × AP × HM | 1, 23 | 3.58 | .017 |
| | Younger | RS × AP × HM | 1, 23 | 14.72 | .001 |
| 900-1200 | Older | RS | 1, 23 | 8.54 | .008 |
| | | RS × HM | 1, 23 | 16.66 | <.001 |
| | | RS × AP × HM | 1, 23 | 7.09 | .014 |
| | Younger | RS × AP × HM | 1, 23 | 15.11 | .001 |

RS = response; GP = group; HM = hemisphere; AP = anterior/posterior

In the 600-900 ms interval, significant interactions as shown in Table 4 were followed up with subsidiary analyses. In older adults, within-subject ANOVAs were conducted for anterior and posterior scalp sites separately. Over anterior sites, there was a significant response × hemisphere interaction ($F(1,23) = 3.86$, $p = .041$), reflecting a negative-going effect that was larger over left-anterior (-1.20 µV) than right-anterior (-0.79 µV) sites. In younger adults, subsidiary ANOVAs were conducted for anterior and posterior sites separately. A significant response × hemisphere interaction was revealed over posterior sites ($F(1, 23) = 10.68$, $p = .003$), reflecting a positive-going effect that was larger over left-posterior sites (0.75 µV) than right-posterior sites (0.06 µV).

In the 900-1200 ms interval, significant interactions as shown in Table 4 were followed up with subsidiary analyses. In older adults, within-subject ANOVAs were conducted for the left-hemisphere and the right-hemisphere scalp sites separately. There was a significant main effect of response over the left-hemisphere sites ($F(1,23) = 11.48$, $p = .003$) and a significant main effect of response over the right-hemisphere sites (*F*(1,23) = 5.55, *p* = .027), reflecting an overall negative-going effect that was larger over the left-hemisphere (-1.85 µV) than the right-hemisphere (-1.20 µV) sites. Similarly, significant main effects of response were found over the anterior (*F*(1,23) = 5.84, *p* = .024) and posterior (*F*(1,23) = 11.88, *p* = .002) sites, with the effect larger over the anterior (-1.69 µV) than posterior (-1.36 µV) sites. In younger adults, subsidiary ANOVAs were conducted for anterior and posterior sites separately. A significant response × hemisphere interaction was revealed over posterior sites (*F*(1, 23) = 4.72, *p* = .041), reflecting a positive-going effect over left-posterior sites (0.95 µV) and a negative-going effect over right-posterior sites (-0.32 µV).

Taken together, results from within-group analyses suggested that in older adults, there was a left-lateralised negative-going associative retrieval effect larger over frontal and central sites. This effect was more pronounced in the 900-1200 ms interval. In younger adults, there was a positive-going effect over left-parietal sites in both intervals. The frontal positivity, however, might be insensitive to analyses using the 4-quadrant partition. There was no evidence of a qualitative difference in scalp topographies between the age groups, as there was no significant response × group × site interaction in the mixed-model ANOVAs.

Correlation analyses revealed no significant correlation between the ERP effects and associative memory performance (Pr and associative hits) for either age group (all |*r*| < .10, *p* > .63). Also, no significant correlation was found between the ERP effects and RTs for associative hits or associative misses (all |*r*| < .32, *p* > .09) for either group. In addition, post-probe ERP effects were not correlated with the pre-probe ERP effects found in older adults (all |*r*| < .26, *p* > .23). The electrodes selected to quantify the effects were: left-frontal sites (site 35, 49, 50 from Montage 10; www.easycap.de/easycap/e/electrodes/13_M10.htm) for older adults and left-parietal sites (site 29, 30, 45 from Montage 10) for younger adults. These sites were chosen as the associative retrieval effects were most evident over left-frontal and left-parietal sites in older and younger adults respectively.

#### *2.1.2.4 Discussion*

As reported in the encoding section, both Pr and associative hits were more superior in younger adults than older adults, with the age difference greater in associative hits than Pr. Response biases (Br) were equivalent across age groups, suggesting that the associative memory paradigm was successful in eliminating the potential confound of response bias that is inherent in ageing research of memory (Pidgeon & Morcom, 2014). With a strong emphasis on associations, older adults appeared to have resorted to associative information to guide their responses.

The ‘other information’ response category attracted small but non-zero proportions of responses in both younger and older participants, suggesting that it was used successfully in diverting non-critical associative retrieval (the retrieval of information associated with the object words during encoding other than the location words) away. Therefore, the contrast between associative hits and associative misses was unlikely to be diluted by the retrieval of different types of associative information.

*Pre-probe associative retrieval*

The ERP results supported that anticipatory brain activity before a retrieval probe contributes to successful retrieval of associative information. The waveforms preceding probes that lead to successful associative retrieval were more negative-going than those preceding probes that were recognised but without associative retrieval. The effect was spatially widespread and largest over prefrontal scalp sites. It was only observed in older adults, particularly in those who performed poorly in the associative memory test. The magnitude of the ERP effect increased with the degree of memory impairment across older participants.

Previous studies investigating cognitive control in retrieval have found that older adults are impaired in memory-related anticipation (Dew et al., 2011; Morcom & Rugg, 2004), which is in stark contrast with the present findings. One potentially important difference is the experimental design, i.e., blocked design in the current study and intermixed design in previous studies. In an intermixed design, pre-probe anticipatory operations have to be reset on a trial-by-trial basis according to different instructional cues. Under this condition, older adults may be disadvantaged due to the high level of cognitive control required. In a blocked design, however, older adults may be more able to engage in anticipatory mechanisms when no additional switch cost is required. The current findings are important to demonstrate that older adults may employ retrieval-related anticipation to a larger extent relative to younger adults, at least under some circumstances. This is inconsistent with the theories of proactive-to-reactive shift in ageing (Paxton et al., 2006) and the ELSA model (Dew et al., 2011).

So what is the functional role of the pre-probe neural activity in associative retrieval? To answer this question, it was first needed to eliminate any extraneous factors that might affect the results. One such factor is the differential influence of speech from preceding trials, which, however, has been demonstrated to be unlikely to result in the observed effect in older adults. Another possibility is that the activity reflects fluctuations in attention or general alertness in anticipation to upcoming probes. It could be that older adults were unable to maintain an adequate level of attention throughout the test session due to limited attentional resources. Furthermore, it was found that preparing for fearful events gave rise to sustained stimulus-preceding negativity, with a fronto-central scalp distribution (Böcker, Baas, Kenemans, & Verbaten, 2001) that was similar to, but more restricted than, the effect found in the present study. It is possible that older adults in the present study were more emotionally strained than younger adults, which led to fluctuations in attention and mobilisation of processing resources. However, this interpretation implies that heightened attention preferentially benefits the retrieval of associative information but no other decisions such as the identification of new items (waveforms for correct rejections were not reported here but they did not show a negative-going ERP deflection). Furthermore, if the present effect reflected the fluctuation of attention, it should be expected that the amplitude of the effect correlates with RTs for associative hits across participants. However, this was not the case (see Results).

The currently observed pre-probe effect is very similar in both polarity and scalp distribution to the PSMEs reported by Otten and colleagues (Otten et al., 2006; Otten, Quayle, & Puvaneswaran, 2010). In those studies, frontal negative-going ERP waveforms were predictive of subsequent memory success but only in tasks requiring semantic processing of the stimuli. The effects were interpreted as goal-directed mobilisation of semantic processing resources in anticipation of upcoming stimuli. In the present study, the goal was to recall a specific kind of information that was associated with a given retrieval probe, i.e., the location word. Thus, a plausible account for the present pre-probe effect is that it reflected the adoption of a control process in favour of semantic processing of a retrieval probe to facilitate the recovery of goal-directed information. Nevertheless, the negative correlation between the pre-probe effect and associative memory performance is difficult to explain.

Pre-probe activity might modulate retrieval through a mechanism of neural reinstatement of category-specific contextual details (i.e., location) experienced at encoding, which can be activated prior to the presentation of retrieval probes (Polyn et al, 2005). This interpretation is akin to the concept of ‘retrieval orientation’, i.e., a tonically maintained retrieval set that can influence probe-processing in order to optimise the recovery of goal-related information (Herron & Wilding, 2006). Previous studies have shown that retrieval orientations can be initiated by instructional cues on a trial-by-trial basis (Herron & Wilding, 2004; 2006; Johnson & Rugg, 2006), but the study that found a pre-probe retrieval effect used a blocked design without instructional cues (Addante et al., 2011). In contrast to the present finding, Addante et al. found a positive correlation between pre-probe brain activity and source memory performance. Considering the different design used in Addante et al.’s study, e.g., only young participants were recruited and the use of encoding manipulations as to-be-retrieved source, it is likely that the pre-probe theta activity reflects a different type of pre-probe processing. Regardless of the underlying neural and cognitive mechanisms for the pre-probe retrieval effects across the two studies, it is clear that pre-probe neural activity plays an important role in the successful retrieval of associative information.

However, the question arises why younger adults in the present study did not engage the pre-probe activity as did older adults. The lack of the effect in the young may again be related to the blocked design currently employed. Studies using younger adults have shown that when the retrieval of episodic information is required, preparatory cue-elicited effects only appear in intermixed conditions (Herron & Wilding, 2006; Johnson & Rugg, 2006). Thus, it is possible that the currently observed frontal effect is specific to ageing. Considerable evidence has shown that over-recruitment of the prefrontal cortex is a common feature of ageing (Davis et al., 2008), which may serve a compensatory role in memory. The compensatory interpretation, however, is difficult to reconcile with the negative correlation between the ERP effect and memory performance. The negative correlation between increased neural activity and poor performance is not uncommon in the ageing literature. Increased activation in the PFC has been correlated with poor memory performance during both encoding (de Chastelaine et al., 2011) and retrieval (Persson et al., 2011). According to de Chastelaine et al. (2011), this contradiction might be resolved with the ‘partial compensation’ hypothesis. It was proposed that the additional PFC activation is an adaptive mechanism that compensates for the failure of neural systems that should be responsible for the ongoing task, but the additional activation in itself contributes little to memory performance. Therefore, a larger PFC activation in older individuals indicates a larger impairment in the neural system that supports associative memory. The partial compensation interpretation is further supported by findings that age-related brain volume reduction in the PFC accounted for the over-recruitment of the PFC during associative memory retrieval (Kalpouzos, Persson, & Nyberg, 2012).

Although the compensatory interpretation implies that the present effect might be age-specific, the current data do not completely rule out the possibility that the effect is related to poor associative memory. As shown in Figure 7, younger adults were much more homogeneous both in brain and behaviour, and their memory performance was better than older adults. This proposal is consistent with a previous study demonstrating that greater demands on pre-probe preparatory processing were reflected by a sustained negative-going ERP effect at the frontal scalp sites (Johnson & Rugg, 2006). It has been shown that the PFC was selectively engaged by the demands to retrieve weakly rather than strongly encoded source information (Kuo & Van Petten, 2006). Therefore, it remains possible that younger adults might also engage the pre-probe activity to the same extent as currently observed in older individuals once the task is made sufficiently difficult for them. A follow-up experiment was conducted to examine whether the effect is an intrinsic feature of ageing or related to poor performance by manipulating the level of memory performance in younger adults (see Experiment 2).

Taken together, the present findings point to a critical role of pre-probe anticipatory activity in associative memory retrieval. In older adults, particularly poor-performing individuals, the probability that a probe will lead to recollection of associative information is influenced by neural activity leading up to the event. The individual difference suggests that additional neural mechanisms might be recruited by poor performers in compensation for their weak memory. An important question for the follow-up study is whether the effect is specific to ageing or memory performance.

*Post-probe associative retrieval*

The age groups showed different associative retrieval effects in the two later latency regions. In the case of younger adults, there was a positive-going effect over left-parietal sites in both intervals. In older adults, there was a left-lateralised negative-going associative retrieval effect over frontal and centro-parietal sites. This effect was more pronounced in the 900-1200 ms interval.

*The left-parietal effect*

In line with previous studies (e.g., Rugg, et al., 1996; Wilding & Rugg, 1996), a left-parietal effect was found for associative retrieval in younger adult. This finding highlighted the importance of the left-parietal effect in associative memory retrieval, as it was sensitive to the recovery of associative information independent of item recognition. Although the strength of item memory could not be measured in the current study, it has been found previously that the left-parietal effect varies with the strength of source memory while the strength of item memory is held constant (i.e., high-confident item recognition) (Woroch & Gonsalves, 2010). Therefore, the present finding supported the notion that the left parietal effect represents the quantity and quality of the episodic information recollected (Wilding, 2000), at least in younger adults. However, the magnitude of the left parietal effect did not co-vary with associative memory performance across subjects, indicating that there is no linear relationship between performance level and the extent of neural activation underlying the left parietal effect.

In older individuals, the left parietal associative retrieval effect was absent. Similarly, previous studies found the left parietal old/new effect to be either reduced (e.g., Li et al., 2002; Wegesin et al., 2002) or absent (e.g., Swick et al., 2006), possibly due to an overlapping left frontal and central negativity. In the present study, the timing of the left fronto-central negative-going effect started early, overlapping not only the right-frontal but also the left-parietal effect. One possibility was that older individuals engaged in completely different neural networks for associative retrieval, reflected by the left-lateralised negative-going effect over frontal and central scalp areas. Alternatively, it could be that the left-parietal effect in older individuals was masked by the overwhelming negative-going effect, consistent with the lack of qualitative difference in ERP topographies between the age groups.

A right-frontal effect can also be observed in the present study. This effect, however, was insensitive to the statistical analyses using the 4-quadrant scalp partition. Using a different method including 9 electrode sites partitioned into factors of hemisphere (left/middle/right) and location (frontal/central/parietal), a significant right-frontal effect for associative retrieval could be found in the 900-1200 ms interval (not reported). Using a word-pair associative memory task, Rugg et al. (1996) did not find the right-frontal effect for successful associative retrieval. The authors argued that the right-frontal effect would present only when there was a strong need for post-retrieval monitoring and source discrimination, e.g., when only two different sources were used, as in most of the source memory studies (e.g., Wilding & Rugg, 1996). Furthermore, Rugg et al. used an incidental learning task in which participants had to learn all 128 word-pairs before memory retrieval. Consequently, associative retrieval performance was poorer compared to that for younger adults in the present study (average associative hits: 36% in Rugg et al.’s study and 59.8% in the present study). Thus, the right-frontal effect may vary depending on the degree of reliance on post-retrieval verification or monitoring. It could be that in the present study, post-retrieval monitoring was required to make a correct response from a large amount of associative information available during retrieval. Therefore, the right-frontal effect may not necessarily vary with the levels of recollection, but rather depends on whether post-retrieval evaluation processes are required. Consistent with previous research (e.g., Dulas & Duarte, 2013; Wegesin et al., 2002), the right-frontal effect was absent in older adults, possibly as a consequence of the pronounced negative-going effect during the later time windows.

### *Left-frontal central negativity*

The pronounced negative-going associative retrieval effect in older adults was similar to the left frontally and centrally focused negativity commonly observed in older individuals for source memory retrieval (e.g., Dulas & Duarte, 2013; Li et al., 2004; Swick et al., 2006; Wegesin et al., 2002) contrasting source hits with correct rejection. One study comparing source hits with source misses, however, did not find the negative-going effect in older adults (Cansino et al., 2012). As already discussed, the absence of the effect in Cansino et al.'s study could be due to the encoding instructions that did not explicitly require participants to remember the source information. In the present study, the associative nature of the memory task was emphasised. Participants were informed about, and practiced associative encoding and retrieval. Even though source hit rates were similar between the current study (35.3%) and Cansino et al. (39.6%), older adults in the present study were superior in source retrieval considering that the possibility of lucky guesses was much higher in Cansino et al. (0.25) than that in the current study (0.006). Thus, the left-frontal negativity is more likely to present when associative memory is emphasised.

It is interesting that in older adults, both pre-and post-probe ERP effects were negative-going, spatially wide-spread with a frontal focus. The question arises whether the post-probe negative-going ERP effect is a continuation from, or under the influence of, the pre-probe effect. If this was the case, the pre- and post-probe effects could be expected to correlate with each other, in line with the finding in Addante et al. (2011). In the present study, however, no significant correlation was found between the two effects.

It may be argued that the negative-going effect in older adults simply reflects the RT differences, as RTs were longer in older relative to younger adults. This is unlikely for two reasons: firstly, the patterns of RT difference for the critical contrast (associative hit vs. associative miss) were similar between the age groups (see Results); and secondly, previous studies have found similar negative-going ERP source retrieval effect with age, even when RTs were equivalent across age (e.g., Li et al., 2004). It has to be noted that in the present experiment the RTs are very long, especially in older adults (i.e., on average 3.2 s for associative hits and 4.0 s for associative misses). As an indicator of the complexity of information processing, long RTs suggest that multiple complex neural processes are involved in retrieval performance. Consequently, the relationship between the RTs and the ERPs is complicated and difficult to interpret. Nevertheless, at present there is no evidence to suggest that the negative-going retrieval effect in older adults is simply a consequence of long RTs.

Previous studies (Duarte et al., 2006; Friedman et al., 2010) found that the negative-going source retrieval effect is related to the level of performance, i.e., only poor-performers, but not good-performers, in older adults displayed the effect. It was therefore thought that cognitive processes underlying this effect were not specific to ageing, but to the level of performance. This is not the case in the present study, as both good- and poor-performers showed similar negative-going ERP effects, and there was no correlation between the ERP effect and memory performance. Furthermore, even when memory performance was equated across age, a similar negative-going ERP effect of source retrieval also emerged (Li et al., 2004). It is therefore unlikely that the effect was, at least not entirely, due to performance differences. It is possible that the effect is specific to the recovery of associative source information in ageing. In some circumstances, only poor-performing older adults need to engage neural mechanisms underlying this effect. In other circumstances, perhaps when source retrieval is difficult as in the present study, both high- and poor-performing older adults engage these mechanisms to optimise performance.

Using a group of young adults, Addante, Ranganath, and Yonelinas (2012) have also found a wide-spread negative-going associative retrieval effect when contrasting source correct with source incorrect ERPs. The topography of the effect is similar to the effect currently found in older adults except that it was more evident over right posterior sites than the current finding. It is important to note that in Addante et al’s study, this negative-going associative retrieval effect was found for retrieval probes that were recognised with low confidence. The authors provided an interpretation that it reflects a form of “contextual familiarity”, which can be independent of either item familiarity or item-context association. This is in line with the ‘Convergence, Recollection, and Familiarity Theory’ (CRAFT), which is based on the “Binding Item in Context” (BIC) view that episodic memories reflect the binding of item and contextual information (Montaldi & Mayes, 2010). According to CRAFT, it is possible to weakly activate the contextual information upon encountering a studied item even when the recall of item-context association (i.e., recollection) fails. This is a plausible account for the effect in Addante et al.’s study, in which only two types of source information were used. Participants could have relied on familiarity to make source judgements. In the current study, however, it would be too difficult to give the correct associative information without recovering the item-context association as the associative information was unique to each item.

Another possible neural account of the effect proposed by Addante and colleagues was that it reflects a controlled search via top-down executive control mechanism. This interpretation is akin to that for the LPN, although it was considered to be a separate effect for a number of reasons: 1) it was topographically more widespread than the LPN, 2) it started earlier from 200-400 ms, and 3) LPN is either insensitive to source accuracy (Herron, 2007) or even larger for inaccurate source retrieval (Wilding, 1999). The temporal and spatial dynamics of the effect in the present study are similar to that in Addante et al. (2012), starting at about 300 ms over frontal sites, and becoming increasingly stronger and more widespread overtime. These characteristics are consistent with the controlled search interpretation, with the early negativity over frontal sites representing top-down control and the later widespread negativity representing goal-directed search. It is possible that these activities were engaged by older adults to compensate for weak memory representations, corresponding to less confident recognition in Addante et al.’s study, possibly as a result of insufficient encoding.

In conclusion, the present findings indicate that compared to younger adults, older individuals engage in different neural activity for successful associative retrieval. This effect has often been observed in the elderly during source retrieval. The novel finding is that before encountering a retrieval probe, older adults recruit neural mechanisms that influence the likelihood of successful retrieval of associative information related to that probe. Both pre- and post-probe associative retrieval effects may reflect compensatory neural mechanisms in ageing. While the post-probe effect possibly represents a controlled search processing when the retrieval of source information is emphasised, the pre-probe effect represents the engagement of additional neural mechanisms by poor-performing older adults in compensation for weak memory representations or weak associations between those representations.

## 2.2 Experiment 2: Are age differences in anticipatory memory-related activity related to poor memory?

### 2.2.1 Introduction

In light of the negative-going pre-probe associative retrieval ERP effect found in the first study, this study aims to further elucidate the nature of this effect. In the first study, the effect was only found in older adults, and the magnitude was negatively correlated with memory performance. Thus, it is possible that neural activity underlying this effect was engaged as a result of poor memory. However, it is not clear whether this effect is specific to the level of memory per se, or specific to older age but also vary with their memory ability. Both of the assumptions suggest that extra neural networks are recruited by older adults in an attempt to compensate for declined memory abilities, but different predictions can be made based on each assumption. If the effect is specific to the level of memory, it may be expected that younger adults will show a similar effect when their memory is impaired. In contrast, if it is an intrinsic feature of ageing, the effect will not emerge in younger adults regardless of their memory performance. The former interpretation is in line with the scaffolding theory of ageing (STAC) (Park & Reuter-Lorenz, 2009; Reuter-Lorenz & Park, 2010), claiming that additional brain activity can be engaged across age in the face of increasing task demands, such as increasing retrieval difficulty caused by impoverished encoding. The latter, in contrast, suggests that the additional activity is only engaged by older adults to compensate for the failure of neural systems that should be responsible for the task, and this activity makes little contribution to retrieval performance (de Chastelaine et al., 2011).

In the first study, the pre-probe associative retrieval effect was statistically indistinguishable across age in the late (1100-2000 ms) interval, suggesting that younger adults might also have recruited similar anticipatory neural mechanisms as older adults did. This hypothesis could not be tested in the first study, because the memory performance was superior in younger adults than older adults, and the range of individual variation was limited between younger adults. Therefore, the present study is intended to mimic memory performance of older adults in a group of younger adults to see whether the same pre-probe associative retrieval-related effect will emerge.

According to the diminished processing resources theory of ageing (Craik & Byrd, 1982), memory deficits in older adults are due to a reduction of available resources for memory processing (e.g., Craik & Byrd, 1982). Using divided attention tasks at encoding to decrease the amount of processing resources, studies showed that memory retrieval in healthy young adults can be reduced to the levels typically seen in healthy older adults under full attention conditions (e.g., Anderson et al., 1998). Furthermore, the pattern of memory impairments induced by a concurrent task at encoding (i.e., intact familiarity and degraded recollection, respectively) is consistent with that found in older adults using the same materials under full attention condition (Jennings & Jacoby, 1993).

In addition, neuroimaging studies provide evidence supporting the link between reduced processing resources at encoding and memory deficits in ageing. PET studies (Anderson et al., 2000; Fletcher, Shallice, & Dolan, 1998) and an fMRI study (Uncapher & Rugg, 2005) showed that divided attention during encoding significantly reduces activity in PFC and MTL, which are critical for episodic memory formation. Furthermore, brain activation in left inferior PFC in younger adults under divided attention decreases to the same level as observed in older adults under full attention (Anderson et al., 2000). The reduced left inferior PFC activity was thought to reflect reduced ability to engage in elaborate encoding processes as a result of both ageing and attentional resource depletion. Furthermore, EEG studies (Curran, 2004) demonstrated that dual-tasking at encoding leads to attenuated left-parietal old/new effect during retrieval while the mid-frontal effect remains intact, suggesting that diminishing processing resources at encoding selectively affects recollection but not familiarity. At both encoding and retrieval, the patterns of effects induced by reducing processing resources at encoding in younger adults resemble the patterns found in older adults.

In relation to associative memory, divided attention tasks have also been widely used to test the hypothesis that age-related associative deficits are caused by reduced processing resources at encoding. Converging evidence from neuropsychological studies (e.g., Glisky, Rubin, & Davidson, 2001) and neuroimaging studies (e.g., Park & Rugg, 2011) suggests that that frontal lobe functioning is crucial for binding together items and their contexts. Also, age-related shrinkage of frontal lobes is also related to deficits in strategic control processes (Raz, Gunning-Dixon, Head, Dupuis, & Acker, 1998). It is therefore likely that older adults' poor memory for associations may be due to poor frontal functioning, possibly related to the inability to use appropriate encoding strategies in a flexible manner. Interruption of frontal functioning by divided attention tasks should lead to impairments in associative memory similar to that in ageing.

Such evidence has indeed been found in a number of studies (e.g., Castel & Craik, 2003; Craik, Luo, & Sakuta, 2010; Kilb & Naveh-Benjamin, 2007). For example, Castel and Craik (2003) found that younger adults in the divided-attention condition performed more poorly than younger adults in the full-attention condition, with the deficit in associative information being greater than the deficit in item information. This pattern of memory impairments was similar to that observed in older adults under full attention conditions. However, as younger adults under divided attention conditions are usually impaired in both associative memory and item memory to similar extents, it is unlikely that memory deficits in older adults can be attributed solely to reduced processing resources at encoding (Kilb & Naveh-Benjamin, 2007). Nevertheless, both divided attention and ageing are associated with a loss of available processing resources that may reflect inefficient frontal lobe functioning.

Reducing processing resources at encoding may lead to the recruitment of compensatory brain activity at retrieval. Johnson and colleagues (2013) used tone discrimination tasks to disrupt semantic encoding of visually presented words in healthy young adults. Memory was tested with an old/new recognition task, which was followed by free recall. The results showed that concurrent tasks at encoding led to characteristic features of ageing at retrieval: reduced subsequent episodic recognition and recall, reduced recollection-related ERP activity, i.e., left-parietal effect, and the presence of “compensatory” brain activity, i.e., decreased ERP amplitude over left-frontal scalp sites during the retrieval of words encoded in the dual-task condition relative to those in the single-task condition. Based on the positive correlation between the size of the ERP amplitude reduction over left-frontal sites and recognition accuracy, it was concluded that the underlying brain activity is compensatory in nature, reflecting individual differences in retrieval ability and retrieval strategies. It is tempting to relate this left-frontal negativity reported by Johnson et al. (2013) to the left-frontal negative-going source retrieval effect frequently observed in older adults (see Friedman, 2013). If they reflect the same underlying neural mechanisms, it would mean that both younger and older adults recruit these mechanisms during retrieval to compensate for poor encoding.

The aim of the present study was to test whether the negative-going pre-probe associative retrieval effect as observed in older adults in the first study also emerges in younger adults when their associative memory is impaired. If it does, it would suggest that poor associative memory is responsible for the recruitment of neural mechanisms giving rise to the pre-probe retrieval effect. Finding such a link between poor associative memory and the pre-probe retrieval effect would shed light on the nature of age-related differences in associative memory, as well as the ‘compensatory’ theory of ageing.

To this end, healthy young adults were asked to perform an associative encoding task similar to that in the first study either under divided attention or full attention condition. In the divided attention condition, participants had to perform a concurrent auditory digit monitoring task in addition to associative encoding. It was expected that reducing processing resources by dual-tasking would disrupt memory encoding and affect subsequent behaviour and ERP measures of associative retrieval (Castel & Craik, 2003; Johnson et al., 2013). If young adults show a pre-probe associative retrieval effect similar to that found in older adults under dual-task conditions, it would suggest that the effect is related to poor memory and thus support the STAC model. In contrast, if no such effect is found even when their memory levels are equivalent to those found in older adults, it would suggest that the pre-probe effect is likely to be specific to older adults.

To be able to compare the effects of dual-task manipulation to those of older adults in the first study, the same associative memory paradigm was used in the present study. Stimuli and experimental procedures were also kept as close as possible to those used previously. Both encoding- and retrieval-related activities were analysed as in the first study, except for prestimulus encoding-related activity. Because prestimulus encoding-related activity was insensitive to subsequent associative retrieval in the first study, it was decided that the cue-stimulus interval at encoding could be shortened (prestimulus encoding-related activity not analysed) to save time. Again, the critical contrast was between associative hits and associative misses.

### 2.2.2 Methods

#### ***Participants***

Twenty-nine volunteers were recruited from the University College London student community. They were remunerated at £7.5/hr for participation in the experiment. Four volunteers were excluded because of insufficient trial numbers due to inadequate memory performance or poor EEG quality. The remaining 25 participants (mean age 22-96 year, range 18-31, 14 males) contributed to the final data set. All participants were right-handed and were screened via email to ensure that they had normal or corrected-to-normal vision, no history of neurological or psychiatric conditions and were not taking psychotropic medications. The experimental procedures were approved by the University College London Research Ethics Committee. All participants provided informed written consent before participating.

#### ***Material***

Stimuli were drawn from a pool of 256 location words and 384 object words (half living and half non-living), including all the words used in the first study plus additional ones. All words were between 3-12 letters in length and 1-350/million in written frequency (Kučera & Francis, 1967). Sixteen location words and 24 object words were drawn from the stimulus pool for practice sessions. All words were visually presented in white uppercase Helvetica (font size 30) against a grey background at the centre on a computer monitor.

In the digit-monitoring task, a sequence of 360 single digits (0-9) was created for each participant. The digits were spoken by a male voice. Seventy-two ‘4’s were contained in each sequence, serving as the targets. The digits were randomised with the constraint that no three ‘4’s were presented consecutively. The lags between targets ranged from 0 to 8 digits, with a mean lag of 4 digits.

### ***Procedure***

Data were acquired in 8 study-test blocks, half of which were single-task encoding blocks and the other half were dual-task encoding blocks. The two types of blocks were intermixed in ‘abab’ or ‘baba’ sequences. Half of the participants started with a dual-task block while the other half started with a single-task block. Each study phase contained 30 location-object word pairs, which was followed by a test phase containing all studied and 15 unstudied object words.

The associative memory paradigm was similar to that in the first study. One major difference was that in the present study phase, the location word and object word in each pair were presented simultaneously with the location word above and the object word below the central point of the screen. This was done mainly to shorten the duration of each trial and to keep the length of the whole experiment within 3 hours. For the same purpose, the duration of the neutral warning cue at encoding was also shortened.

In the study phase, each trial began with a preparatory cue (a red exclamation mark) presented for 0.4 s. After a 0.1 s blank screen, a location-object word-pair was presented for 1.5 s followed by a fixation cross for 4-4.5 s, during which participants performed the location-object binding task. In the dual-task condition, the digits were spoken at a rate of 1 digit every 2 s shortly after the preparatory cue onset. For each trial, the onset of the preparatory cue and the onset of the first digit were separated by a jitter of 0.5-1 s to desynchronise the presentation of the digits across trials. This was done to make sure that

ERP encoding-related activity was not confounded by the effect of digit processing. Participants counted how many ‘4’s they heard throughout the block, in addition to memorising the word-pairs, and gave their answers verbally at the end of each block. Participants were told to divide their attention evenly on the two tasks. They were given practice sessions for both single-task and dual-task conditions before starting the experiment.

In the test phase, each trial began with a preparatory cue (a red question mark) presented for 0.4 s, followed by a 0.1 s blank screen and then the fixation cross for 1.4 s followed by a 0.1 s blank screen. An object word was then presented for 1.5 s which was followed by the fixation cross. Identical to the first study, participants gave a button press without time limit indicating ‘old/location’, ‘old/other information’, ‘old/no information’ or ‘new’ responses, and verbalised their answers following ‘old/location’ and ‘old/other information’ responses. A major difference from the first study was that participants were required not to speak until they saw a signal (“—SPEAK—“), which was presented 2 s after the ‘old/location’ or ‘old/other information’ response was made. This was done to minimise the effect of speech on neural activity for retrieval. EEG data were recorded throughout the associative memory task.

### ***Behavioural analyses***

For encoding task performance, within-subject ANOVAs were computed on both the proportions of easy and difficult responses and RTs to examine whether participants’ subjective judgement of task difficulty and time spent on processing easy and difficult items differed across the two experimental conditions. Memory performance was assessed using within-subject *t*-tests comparing the two conditions for recognition accuracy (Pr) and response bias

(Br) (Snodgrass & Corwin, 1988). For associative retrieval, within-subject ANOVAs were computed on percentages and RTs of associative hits and associative misses to see whether associative retrieval differed across the two conditions.

### ***EEG acquisition and ERP analyses***

EEG acquisition and pre-processing procedures were identical to those in the first experiment. Brain activities elicited by word-pairs during encoding and by neutral warning cues and object words during retrieval were aligned to the onset of each event respectively. Epochs of 2048 ms duration were extracted, starting from 100 ms before each event onset, and down-sampled to 125 Hz. Artifact rejection and ERP computation methods were the same as those in the first study. EEG data from all 25 participants were included in the analyses.

#### *Post-stimulus associative encoding-related activity*

Averaged ERPs were formed for stimulus-elicited activity according to subsequent associative hits and subsequent associative misses in the single-task condition and the dual-task condition respectively. The average numbers and ranges of artefact-free trials for associative hits and associative misses were 63 (29-85) and 32 (17-56) in the single-task condition and 37 (18-51) and 49 (26-64) in the dual-task condition.

Within-subject ANOVAs were performed including 28 electrodes as used in the first study (Figure 1) to capture the anterior-posterior variation and left-right asymmetry in scalp topography of SMEs. The 28 electrodes were subjected to ANOVAs with factors of hemisphere (left/right), location (anterior/posterior), and site (7 positions), in addition to the experimental factors of condition (single-task/dual-task) and memory (subsequent associative hit/subsequent associative miss). In line with the first study, ERPs were quantified in 2 continuous time intervals: 300-900 ms and 900-1600 ms. Thus, initial within-subject ANOVA was conducted incorporating the factors of condition, memory, interval, hemisphere, location, and site. Significant interactions including latency and memory would suggest that SMEs varied across the two intervals, and therefore warrant separate analyses for each of the two latency regions. The effects of interest were those involving the factor of memory (i.e., pre-stimulus associative subsequent retrieval effects) or the factor of condition. Significant interactions involving these factors were followed up with subsidiary within-subject ANOVAs to further elucidate those effects.

Analyses of scalp distribution were also performed using the same method as that in the first study. Significant differences between the SME topographies in different conditions were verified by ANOVAs conducted on the rescaled data. The Greenhouse-Geisser correction for nonsphericity was used when appropriate, as indicated by the adjusted degrees of freedom.

### *Pre-probe associative retrieval-related activity*

Averaged ERPs were formed for cue-elicited activity related to associative hits and associative misses in the single-task condition and the dual-task condition. The average numbers and ranges of artefact-free trials for associative hits and associative miss were 62 (29-100) and 30 (16-52) respectively in the single-task condition, 36 (16-68) and 43 (25-63) respectively for the younger group.

Consistent with the first study, mean amplitudes were quantified using two continuous latency intervals: 200-1100 ms (early) and 1100-1948 ms (late).

Here too, the use of early/late continuous latency separation was to capture the development and change of anticipatory memory-related activity over time. It was expected that such effects would be larger in the late interval when the probes were about to appear. In line with the first study, analyses were performed using 24 electrode sites partitioned into anterior and posterior locations (Figure 4). Thus, initial within-subject ANOVAs were conducted incorporating factors of condition, response, interval, anteriority (anterior/posterior) and site (12 sites). The effects of interest were those involving the factor of response (i.e., pre-probe associative retrieval effects) and the factor of task condition. Significant interactions were elucidated with subsidiary within-subject ANOVAs accordingly. Again, analyses of scalp distribution were also performed and the Greenhouse-Geisser correction for nonsphericity was performed.

Based on the finding from the first study that the magnitude of the pre-probe associative memory effect was correlated with both recognition accuracy and percentage associative hits in older adults, cross-subject correlations were also computed to assess the relationship between the pre-probe ERP effect and memory performance in both Pr and percentage associative hits in the current experiment.

*Post-probe associative retrieval-related activity*

For probe-elicited activity, averaged ERPs were formed for associative hits and associative misses in the single-task condition and dual-task condition. The average numbers and ranges of artefact-free trials for associative hits and associative misses were respectively 61 (33-100) and 30 (16-57) in the single-task condition and 35 (17-67) and 46 (30-63) in the dual-task condition.

Identical to the first study, statistical analyses were conducted including 28 electrodes partitioned into 4 quadrants. ERPs from these electrodes were measured in 4 separate latency intervals: 300-500 ms, 500-800 ms, 800-1200 ms, 1200-1948 ms. The first 3 corresponded to the 3 intervals used in the first study but with adjustments. The 3 intervals in the first study were selected based on ageing research to accommodate the timing of associative retrieval effects in older adults. As only younger adults were tested in the present study, the temporal partitions were in line with those traditionally used to measure the well-known old/new effects, i.e., the mid-frontal (300-500 ms), left-parietal (500-800 ms), and right-frontal (800-1200 ms) effects. In the first study, the late interval from 1200 ms was not included due to potential contamination from the effect of speech preparation. In the present study, however, the speech effect was controlled by inserting a 2 s interval between the button-press response and the verbal responses (see Procedures). Thus, the late 1200-1948 ms interval could also be analysed.

These time windows were subjected to the initial within-subject ANOVA incorporating factors of condition, response, interval, hemisphere, location, and site. Although these intervals have often been used to measure old/new retrieval effects, it is not known whether they are suited to capture effects for associative retrieval, which have not been well defined in the literature. Significant interactions involving the factor of response and the factor of condition were elucidated with subsidiary within-subject ANOVAs. Analyses of scalp distribution were also performed using the same method as reported in the first study. Significant differences between the topographies of different conditions were verified by ANOVAs conducted on the rescaled data. The Greenhouse-Geisser correction for nonsphericity was used when appropriate, as indicated by the adjusted degrees of freedom.

### 2.2.3 Results

#### *Memory performance*

At encoding, participants judged whether each word-pair was easy or difficult to associate. Encoding task performance is summarised in Figure 5. Within-subject ANOVAs were computed on the proportions of response and RTs with factors of condition (single-task/dual-task) and difficulty (easy/difficult). There was only a significant main effect of condition for RT (*t*(24) = 5.37, p = .03), with mean RT in the single-task condition (2346 ms) higher than that in dual-task condition (2210 ms).

**Table 5. Encoding task performance for the two conditions.**

| | Proportion (SD) | | Response Time (ms) | |
|---|---|---|---|---|
| | Easy | Difficult | Easy | Difficult |
| Single-task | 0.53 (0.20) | 0.46 (0.19) | 2300 (771) | 2392 (853) |
| Dual-task | 0.51(0.22) | 0.45(0.22) | 2179 (752) | 2241 (847) |

At test, mean and SD of Pr values were 0.81 (0.12) for the single-task condition and 0.69 (0.13) for the dual-task condition. Within-subject *t*-test revealed that recognition accuracy was significantly higher in the single-task than the dual-task condition (*t*(24) = 8.56, p < .001). Mean and SD of Br values were 0.40 (0.29) for the single-task and 0.41 (0.23) for the dual-task conditions, which were not significantly different from each other.

Associative retrieval in the two conditions is summarised in Table 6, showing the percentages and RTs of different response categories. Within-subject ANOVAs were computed on both percentages and RTs of responses with factors of condition (single-task/dual-task) and response category (associative hit/associative miss). For percentage of responses, there was a main effect of condition (*F*(1, 24) = 38.55, *p* < .001), a main effect of response (*F*(1, 24) = 7.10, *p* = .014), and a significant interaction between them (*F*(1, 24) = 148.43, *p* < .001). The significant interaction confirmed that participants made more associative hits and fewer associative misses in the single-task condition compared to the dual-task condition. As for the RTs, there was a main effect of response (*F*(1, 24) = 10.97, *p* = .003) and a significant interaction (*F*(1, 24) = 20.44, *p* < .001). These results confirmed that participants were slower to make responses for associative misses than for associative hits, with the difference more pronounced in the single-task condition.

**Table 6. Associative memory performance for different response categories for the two age groups**

| | Associative hit | Other information* | Associative miss | Miss** | Correct rejection |
|---|---|---|---|---|---|
| Response Percentages | | | | | |
| Single-task | 57.1(13.8) | 4.4(3.3) | 28.3(8.6) | 8.8(6.2) | 91.3(8.7) |
| Dual-task | 33.4(10.8) | 5.0(4.7) | 43.9(7.6) | 16.1(10.0) | 86.3(10.6) |
| RT (ms) | | | | | |
| Single-task | 2750(1134) | 7458(6.87) | 4379(1751) | 2469(3119) | 1554(552) |
| Dual-task | 3466(1843) | 7931(7572) | 3674(1472) | 2123(817) | 1579(495) |

***** Two participants in the single-task condition and two in the dual-task condition did not make the ‘Other information’ responses.
******One participant in the single-task condition did not have any missed items.

## *ERPs*

### *Post-stimulus subsequent memory effect*

Grand-averaged ERPs elicited by word-pairs were computed according to subsequent accurate associative retrieval and no associative retrieval in each condition. Figure 10 illustrates the ERP waveforms at 9 electrode sites in the two conditions respectively. ERPs for subsequent associative hits and subsequent associative misses start to diverge at around 300-400 ms from stimulus onset. In the single-task condition, waveforms for subsequent associative hits are slightly more negative-going than those for subsequent associative misses initially and become more positive-going around 300-400 ms later. This positivity lasts until around 1600 ms, and focuses over the frontal sites, extending also to the left temporal sites. A similar pattern can be observed in the dual-task condition, except that waveforms for subsequent associative hits are consistently more positive-going than those for subsequent associative misses, although the magnitude of this positivity is smaller between around 300-900 ms interval relative to the later interval. Comparing the overall morphology of waveforms across conditions, an obvious difference is that waveforms in the single-task condition are more negative-going around 300-700 ms post-stimulus compared to those in the dual-task condition. The timing and scalp distribution of this effect is consistent with the N400 component, which has been related to semantic processing (Kutas & Federmeier, 2011).

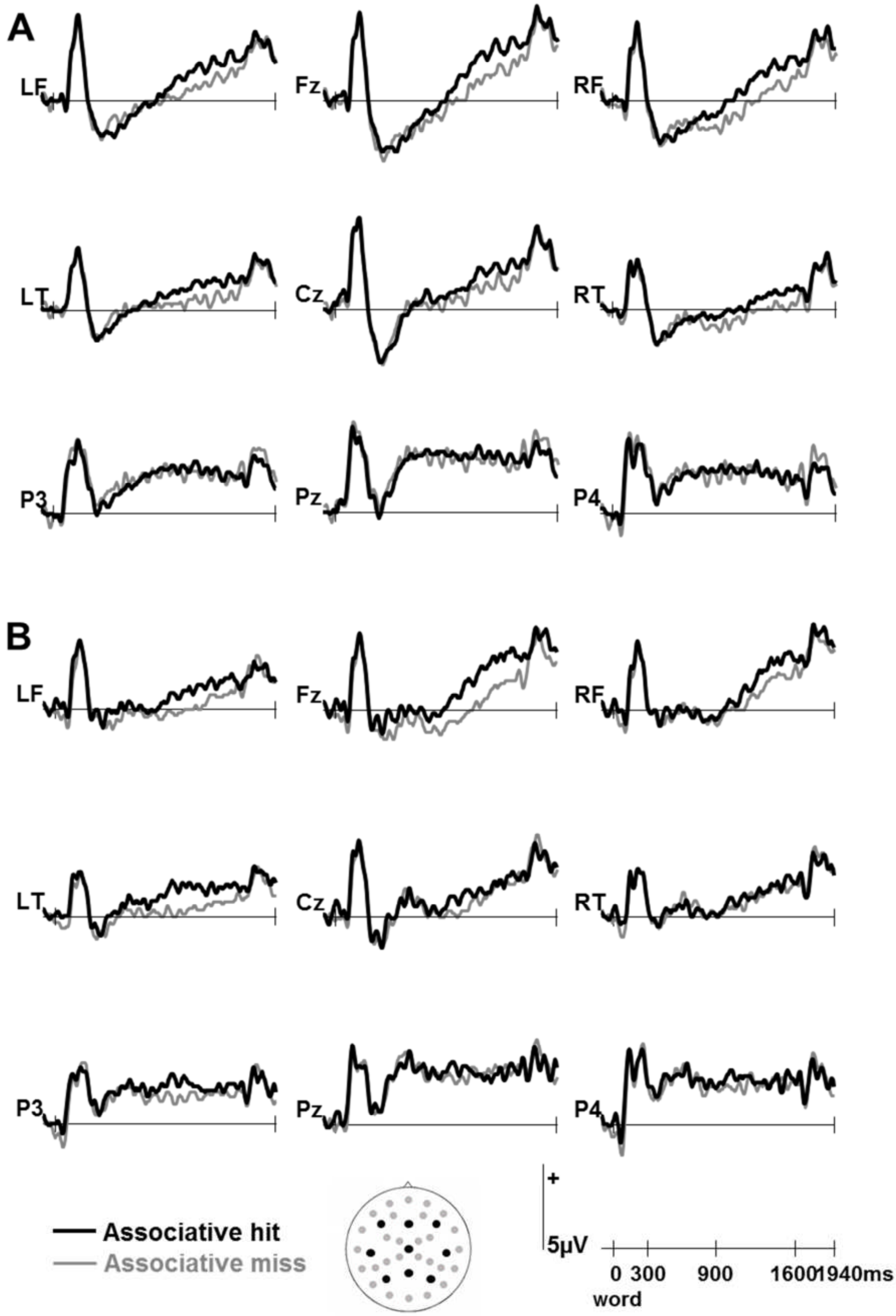


Figure 10. Grand-average ERPs elicited by word-pairs during encoding according to whether they were associated with subsequent accurate subsequent associative retrieval or no associative retrieval in (A) single-task condition and (B) dual-task condition. The insert shows the locations of the 9 electrode sites across frontal, centro-temporal, and parietal regions.

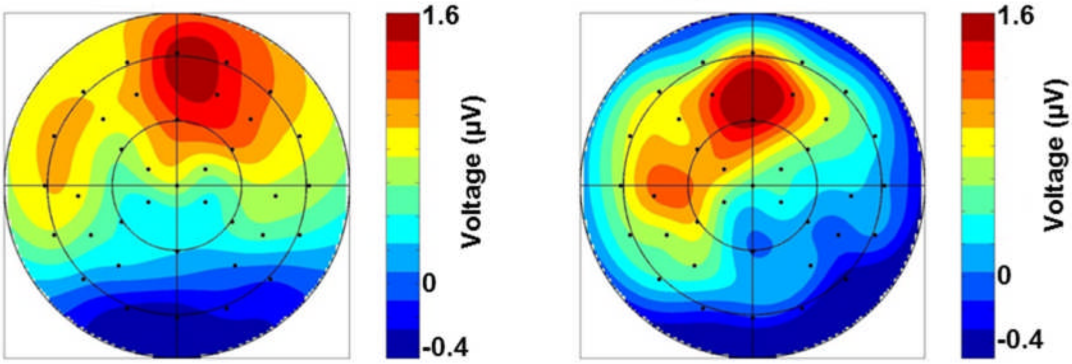


**Figure 11. Voltage spline maps for the single-task (left) and dual-task (right) conditions showing the scalp topographies of the ERP subsequent associative memory effects (subsequent associative hits – subsequent associative misses) in the 900-1600 ms post-stimulus interval when subsequent associative memory effects are reliable. The maps are range scaled.**

The initial within-subject ANOVA incorporating the factor of latency interval revealed a significant memory × interval interaction (*F*(1,24) = 14.16, *p* = .001) reflecting a larger subsequent associative memory effect in the late interval (0.33 µV) than the early interval (0.27 µV), a significant condition × interval interaction (*F*(1,24) = 5.11, *p* = .033) reflecting a larger difference between the two conditions in the early interval (-0.66 µV) than the late interval (-0.01 µV). Subsidiary within-subject ANOVAs were performed for each interval separately.

In the 300-900 ms interval, there was a main effect of condition (*F*(1,24) = 6.05, *p* = .022) which was not modulated by memory, reflecting that waveforms in the single-task condition were more negative-going than those in the dual-task condition (-0.11 µV and 0.56 µV respectively). Significant effects involving the factor of associative memory were found only in the 900-1600 ms interval.

In the 900-1600 ms interval, there was a significant main effect of subsequent memory (*F*(1,24) = 6.05, *p* = .022), a significant memory ×

anteriority interaction (*F*(1,24) = 4.83, *p* = .038), and a significant memory × anteriority × site interaction (*F*(2.3,56.0) = 4.00, *p* = .019). The results indicated that in the late interval, waveforms for associative hits were more positive-going than those for associative misses (1.66 µV and 1.08 µV respectively), and this effect was larger over the anterior than posterior sites (associative hits – associative misses: 0.90 µV and 0.27 µV). There was no significant difference between the single-task and dual-task conditions.

### *Pre-probe associative retrieval-related activity*

Grand-average ERP waveforms elicited by pre-probe cues that led to associative hits and those leading to associative misses are shown in Figure 12 for representative frontal (FPz) and posterior (Oz) electrode sites. In both single-task and dual-task conditions, the waveforms diverge around 300-400 ms after cue onset with the waveforms related to associative hits more negative-going than those related to associative misses. This effect focuses over the prefrontal sites and becomes larger in magnitude from around 1100 ms, persisting to the end of the epoch. The magnitude of the negativity appears to be larger in the single-task condition than the dual-task condition in the later interval from 1100 ms.

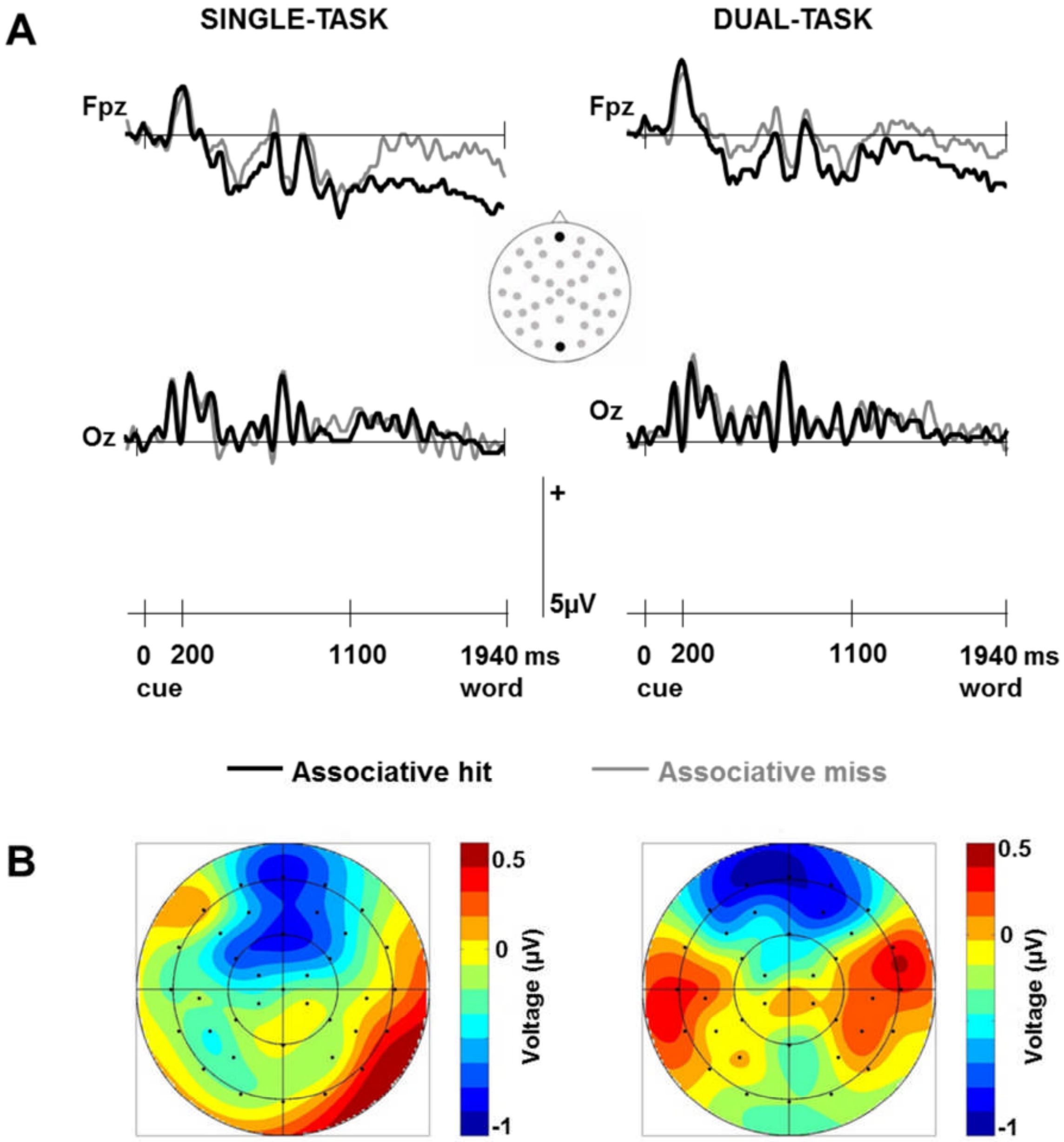


**Figure 12. Pre-probe brain activity related to associative retrieval. (A) Grand-average ERPs of the two conditions elicited by retrieval cues according to whether they were followed by words that elicited accurate associative retrieval or no associative retrieval. The insert indicates the locations of the 2 electrodes (site 35 and 43 from Montage 10; www.easycap.de/easycap/e/electrodes/13_M10.htm; equivalent to site Fpz and Oz of the 10-20 system). (B) Voltage spline maps for the single-task and dual-task conditions showing the distribution of the difference between cue-related activity preceding associative retrieval and no associative retrieval in the 1100-1940 ms interval. The maps are range scaled.**

The initial within-subject ANOVA including the factor of time interval revealed no significant interaction involving response and interval, indicating no qualitative difference between the two intervals. Therefore, subsidiary within-subject ANOVA was conducted over the whole 200-1948 time interval. There was a significant response × anteriority interaction (*F*(1,24) = 4.59, *p* = .043), indicating that the negative-going associative retrieval effect was larger over anterior sits relative to posterior sites. Subsidiary within-subject ANOVAs were conducted for the anterior and posterior sites separately. A significant response × site interaction was found for the anterior (*F*(4.2, 99.9) = 3.25, *p* = .014) but not posterior (*F*(4.0, 95.3) = 0.75, *p* = .557) sites, consistent with visual inspections that the effect was largest over the anterior sites. However, there was no significant interaction involving the condition factor.

Across-subject correlations were computed between the pre-probe ERP effects (average across prefrontal sites 50, 35, 36 in the second interval where the effects were largest) and memory performance in percentage associative hits (Figure 13) and Pr for the two experimental conditions separately. There was no significant correlation using either percentage associative hits (single-task: *r* = .06, *p* = .79; dual-task: *r* = -.16, *p* = .44) or Pr (single-task: *r* = .06, *p* = .79; dual-task: *r* =.03, *p* = .88).

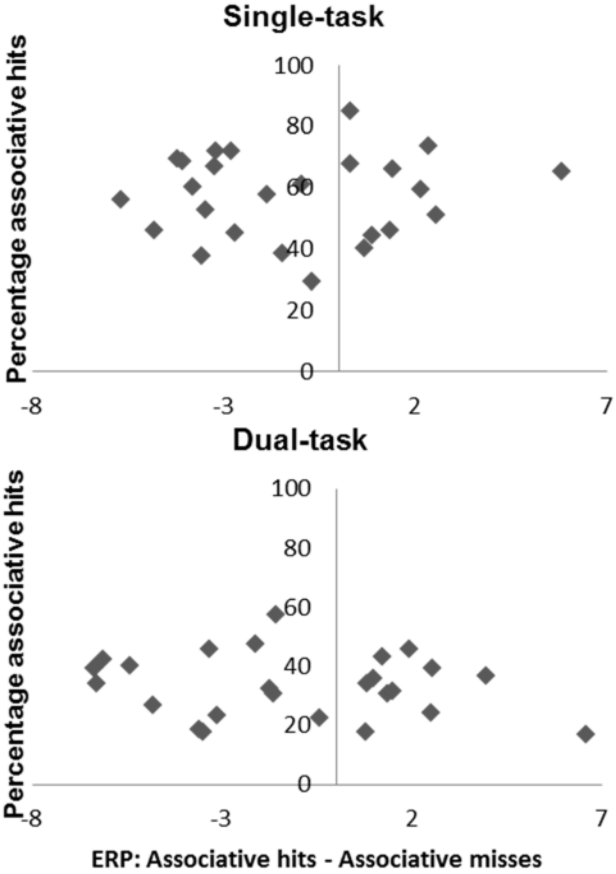


**Figure 13. Scatterplots showing the relationships between pre-probe ERPs, averaged over the 200-1940 ms time window after cue-onset across the 3 prefrontal electrode sites (sites 50, 35 and 36 from Montage 10; www.easycap.de/easycap/e/electrodes/13_M10.htm; equivalent to site Fp1, Fpz and Fp2 of the 10-20 system) and percentage associative hits across participants in the single-task (above) and the dual-task (below) conditions.**

### *Post-probe associative retrieval-related activity*

Figure 14 illustrates the grand-average waveforms elicited by retrieval probes for associative hits and associative misses. Across the two conditions, waveforms diverge from around 300-400 ms, with those related to associative hits more positive-going than those related to associative misses. This positive shift is widespread and becomes more focused over left-parietal electrode sites from around 500-600 ms. From around 1200 ms, this positivity becomes increasingly larger in magnitude, most evident over right frontal as well as posterior sites. This late positivity appears to be more prominent in the single-task condition than the dual-task condition.

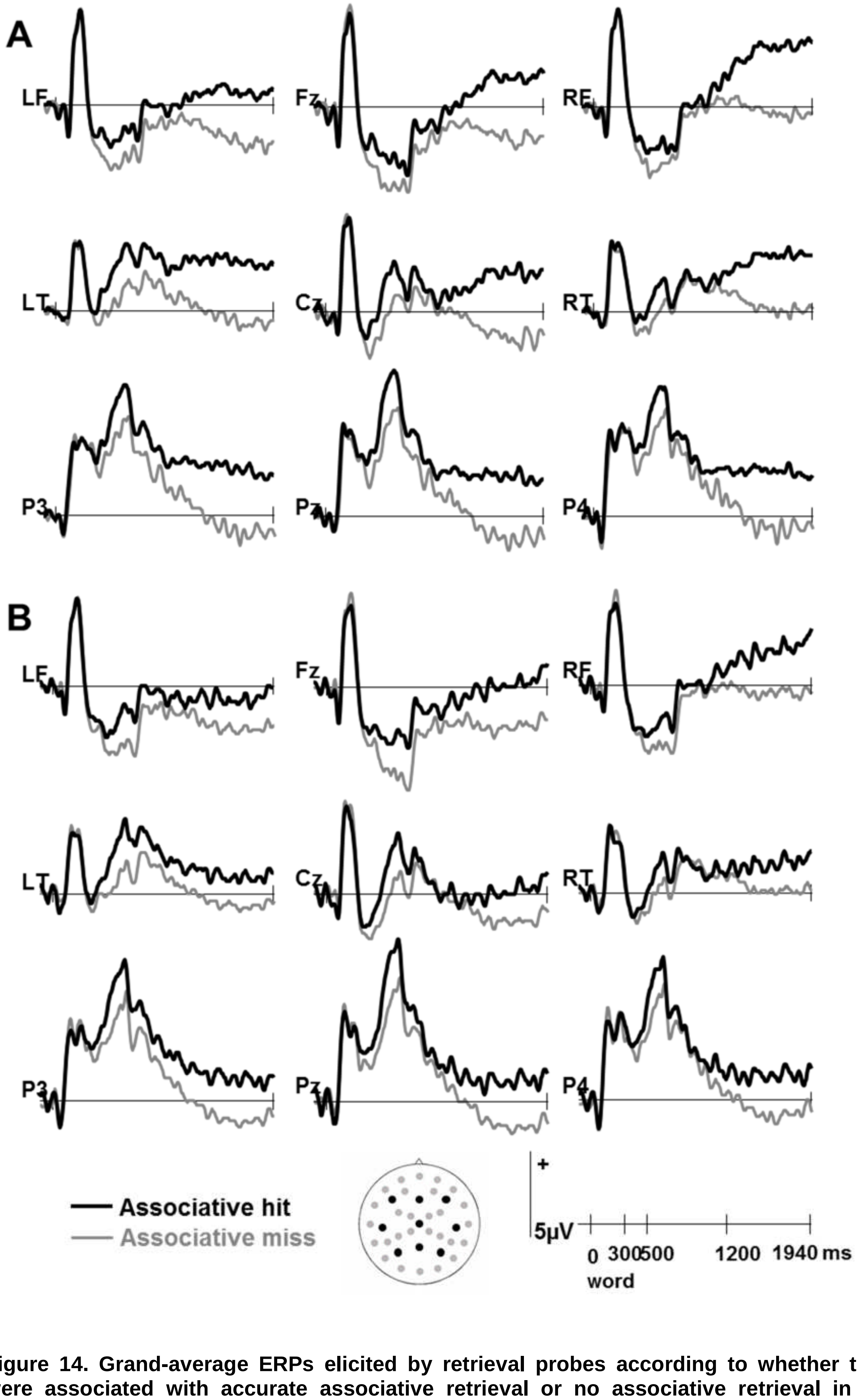


Figure 14. Grand-average ERPs elicited by retrieval probes according to whether they were associated with accurate associative retrieval or no associative retrieval in (A) single-task condition and (B) dual-task condition. The insert shows the locations of the 9 electrode sites across frontal, centro-temporal, and parietal regions.

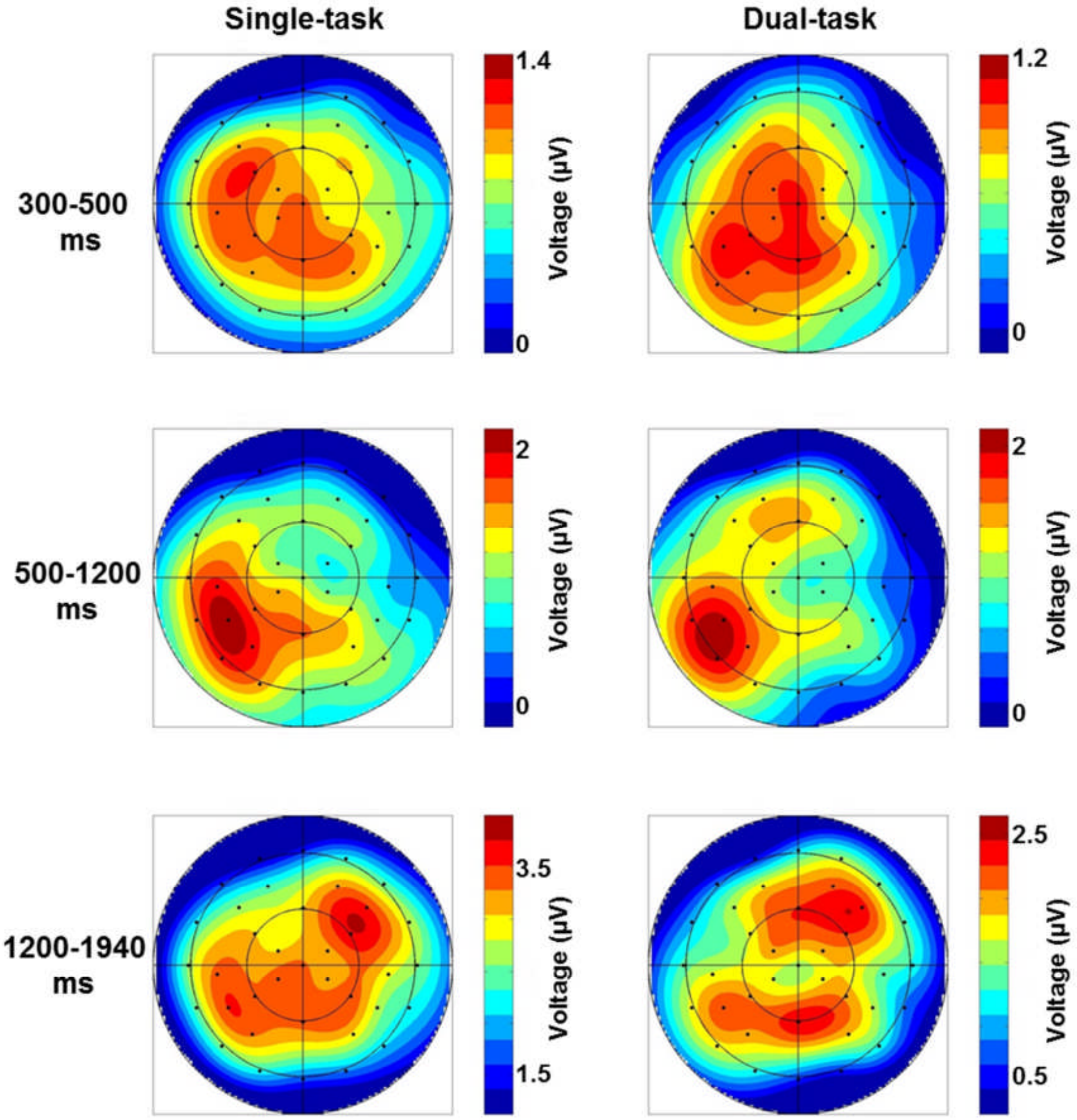


**Figure 15. Voltage spline maps for the single-task (left) and dual-task (right) conditions showing the scalp topographies of the ERP associative retrieval effects (associative hits – associative misses) in the 3 post-probe intervals. The maps are range scaled.**

Initial within-subject ANOVA including time intervals revealed significant response × interval interactions between the 1st and the 2nd intervals ($F(1, 24) = 12.33$, $p = .002$) and between the 3rd and the 4th intervals ($F(1, 24) = 27.24$, $p < .002$), but not between the 2nd and the 3rd intervals ($F(1, 24) = 4.09$, $p = .055$). Therefore, the second and the third intervals were combined for the subsidiary analyses. Subsidiary within-subject ANOVAs were conducted for the 300-500 ms, 500-1200 ms, and 1200-1948 ms intervals separately, including 28 sites partitioned into 4 quadrants as explained in the Methods. Significant results are presented in Table 7.

**Table 7. Significant ANOVA results for the post-probe EPR associative retrieval effects.**

| Time Interval | Condition | Effect | *df* | *F* | *p* |
|---|---|---|---|---|---|
| 300-500 ms | Overall | RS | 1, 24 | 15.28 | .001 |
| 500-1200 ms | Overall | RS | 1, 24 | 9.84 | .004 |
| | | RS × AP | 1, 24 | 4.95 | .036 |
| | | RS × HM | 1, 24 | 9.49 | .005 |
| | | RS × AP × HM | 1, 24 | 4.71 | .004 |
| 1200-1948 | Overall | RS | 1, 24 | 20.04 | <.001 |
| | | CC | 1, 24 | 8.12 | .009 |
| | | RS × AP × HM | 1, 24 | 19.21 | <.001 |

Note: no other effect of interest was significant (all F < 1.7, all p > .21)
RS = response; HM = hemisphere; AP = anterior/posterior; CC = condition

In the 300-500 ms interval, the main effect of memory was not modulated by the scalp distribution factors, reflecting a widespread positivity across the two conditions.

In the 500-1200 ms interval, the response × anteriority interaction reflected a larger associative retrieval effect over posterior (1.30 µV) than anterior sites (0.78 µV). The response × hemisphere interaction reflected larger effect over left-hemisphere (1.33 µV) than right-hemisphere sites (0.75 µV). Subsidiary ANOVAs revealed that for anterior sites, there was a main effect of response ($F(1, 24) = 4.36$, $p = .048$) and a response × hemisphere × site interaction ($F(3.3, 78.4) = 4.76$, $p = .003$). The 3-way interaction was further elucidated as a main effect of response ($F(1, 24) = 6.69$, $p = .016$) and a response × site interaction ($F(2.4, 58.3) = 7.45$, $p = .001$) over the left anterior sites, as well as a response × site interaction over the right anterior sites ($F(2.7, 64.4) = 8.12$, $p < .001$). For posterior sites, there was a main effect of response ($F(1, 24) = 15.68$, $p = .001$), a response × hemisphere interaction ($F(1, 24) = 29.56$, $p < .001$), and a response × hemisphere × site interaction ($F(3.2, 77.8) = 6.87$, $p < .001$). The response × hemisphere interaction reflected a larger effect over left-posterior (1.70 µV) than right-posterior sites (0.90 µV).This 3-way interaction was further elucidated as a main effect of response ($F(1, 24) = 26.54$, $p < .001$) and a response × site interaction ($F(2.1, 51.2) = 3.46$, $p = .036$) over the left posterior sites, as well as a main effect of response ($F(1, 24) = 6.88$, $p = .015$) over the right posterior sites. These results reflected a widespread positivity that was largest over left-posterior sites across the two conditions.

In the 1200-1900 ms interval, the response × anteriority × hemisphere interaction was followed up with subsidiary ANOVAs computed for anterior and posterior sites separately. For anterior sites, there was a main effect of response ($F(1, 24) = 12.90$, $p = .001$) and a significant response × hemisphere interaction ($F(1, 24) = 5.78$, $p = .024$) which reflected a larger effect over right-anterior (2.44 µV) than left-anterior sites (1.85 µV). For posterior sites, there was a main effect of response ($F(1, 24) = 24.50$, $p < .001$) that was not modulated by the hemisphere factor. These results reflected a widespread positivity with a right asymmetry over anterior sites across the two conditions. The main effect of condition reflected that the waveforms across response categories in the single-task condition were more positive than those in the dual-task condition (0.92 µV and 0.17 µV respectively).

### 2.2.4 Discussion

The purpose of the present study was to use a secondary task at encoding to mimic the memory performance of older adults in the first study. At encoding, RTs were slower in the single-task condition than the dual-task condition regardless of subsequent associative retrieval success, indicating that participants spent less time processing the word-pairs as a result of having to juggle between the two tasks in the dual-task condition. At retrieval, as expected, participants correctly recognised more old items and made more associative hits in the single-task condition than in the dual-task condition. The pattern of performance resembles that in the first study between younger and older adults. Comparing across studies, the percentage of associative hits is similar between the dual-task condition in the present study and older adults in the previous study (33.4 vs. 35.3), and between the single-task condition in the present study and younger adults in the previous one (57.1 vs. 59.8), suggesting that the secondary task was successful in reducing the level of associative retrieval. In contrast, the levels of recognition accuracy dropped below those in the first study. Pr in the dual-task condition is lower than that in older adults in previous study (0.69 vs. 0.77; $t(47) = 2.35$, $p = .023$), and single-task Pr is also below the level for younger adults in the first experiment (0.81 vs. 0.89; $t(47) = 2.64$, $p = .011$). Thus, the overall recognition accuracy is lower in the current study, which may be due to participants having to learn more word-pairs (240 in the current study and 156 in the first study) or that the paired words were presented simultaneously instead of in a sequential manner (hence less time available for each word-pair). The difference in task difficulty between the two studies is also reflected in RTs during retrieval. The RTs across associative retrieval responses in the single-task condition were longer than those in younger adults in the first study, and the RTs in the dual-task condition were similar to those in older adults. Nevertheless, the dual-task manipulation in the present study was successful in reducing associative memory performance in young adults, and the pattern of memory impairments was comparable to that observed in older adults, i.e., larger decline in associative than recognition memory.

### ***Post-stimulus subsequent memory effect***

Consistent with findings from the previous study, as well as many other studies investigating SMEs (see Friedman & Johnson, 2000 for a review), a positive-going subsequent associative memory effect was larger over the anterior scalp sites. While the effect in the previous study was sustained across the early and late intervals, the present effect was reliable only in the 900-1600 ms interval. The timing difference may be explained by the difference in the procedures. In the previous study, words were presented one at a time, i.e., the location word followed by the object word. In the present study, however, the location word and the object word in each pair were presented together, which presumably took participants more time to process. This is also reflected in behaviour in that RTs for associative judgments were longer in the single-task condition in the present study compared to those in younger adults in the previous study, indicating a difference in task difficulty across the two studies. Thus, binding-related activity contributing to associative retrieval might have occurred later in the present study than that in the previous study.

It is somewhat surprising that there was no significant difference in subsequent associative memory effect between the single-task and the dual-task conditions, suggesting that reducing processing resources during encoding did not affect binding-related brain activity. This seems contradictive to the findings that divided attention tasks during encoding lead to altered brain activity (Nessler et al., 2007) as well as large interference in memory (Fernandes & Moscovitch, 2000). As already discussed in the previous chapter, there may be an early/late segregation of the SMEs, with the early part sensitive to the semantic attributes of the stimuli and the late part closely related to episodic encoding (Friedman & Johnson, 2000; Nessler et al., 2007). It is possible that the secondary task in the present study interfered with semantic elaboration in the early part of encoding but not with episodic/associative encoding in the late part, and therefore did not affect the subsequent associative memory effect.

In the 300-900 ms interval, the ERPs in the single-task condition were more negative-going than those in the dual-task condition, regardless of subsequent associative memory success. This finding also supported the possibility that the secondary task at encoding affected semantic processing of the word-pairs. The timing of this effect is consistent with the N400 component, which has been considered a marker for semantic processing, especially in language comprehension (Kutas & Federmeier, 2011). It may be that participants in the single-task condition processed the meaning of the word-pairs to a greater extent than they did in the dual-task condition. This N400 difference between conditions may be related to the finding in a PET study (Anderson et al., 2000) that a divided attention task during encoding reduces associative memory, and brain activity in left-prefrontal and medial-temporal lobe regions. This effect echoes with the age-related difference in ERP morphology in the previous study. ERPs for younger adults were also more negative-going than those for older adults around 400 ms post-stimulus, which suggests an age-related deficit in semantic encoding.

Taken together, ERP results show that performing the concurrent task during encoding is likely to preferentially impair semantic processing of the items but not inter-item binding. Nevertheless, associative encoding also suffers from impaired semantic processing, as reflected in reduced associative hits in the dual-task condition. Thus, dual-tasking affects overall memory performance, but neural correlates of binding seem to be an all-or-non phenomenon. As proposed by Kilb and Naveh-Benjamin (2007), older adults may have specific deficits in associative encoding, in addition to deficits in semantic encoding.

### ***Pre-probe associative retrieval***

As expected, the pre-probe associative retrieval-related ERP effect in the dual-task condition in the present study is similar to that in older adults in the previous study. They are both sustained negative-going effects with a focus over the prefrontal electrode sites, although the present effect is smaller in magnitude and more constrained in scalp distribution as compared to the effect observed in older adults in the previous study. The similarity between the two suggests that the pre-probe anticipatory mechanisms can be recruited by both older and younger adults to support associative retrieval. Furthermore, the timing of the effect is consistent with the findings from the first study. In the first study, it was found that the group difference of the effect is reliable only in the early latency interval of the pre-probe epoch, suggesting that younger adults may also engage the pre-probe activity in the late interval. This is in line with the present finding that the effect is reliable only in the late interval. This timing difference of the effect across age suggests that younger adults may be more efficient in recruiting anticipatory neural mechanisms that facilitate associative retrieval.

An unexpected finding is that the effect also occurred in the single-task condition, even though the level of associative performance, as measured by the percentage of associative hits, was significantly higher in the single-task condition than the dual-task condition. Together with the absence of cross-subject correlations between the magnitude of the pre-probe associative retrieval effect and the percentage of associative hits, the present findings show that unlike in older adults, the extent of neural activation responsible for the pre-probe effect is unrelated to the strength of associative memory in younger adults.

Why can the effect be present or absent in younger adults across the two studies using similar associative memory paradigms? One explanation is that the effect occurs when greater effort is needed to recover associative information, for example when overall memory strength is weak. Comparing memory performance in the present study to the first study, recognition accuracy was lower in the present study. It may be that participants in the present study needed to recruit additional neural mechanisms to counter the reduction in overall memory strength. If this is the case, however, it is difficult to explain why the magnitude of the effect is not correlated with the strength of memory (Pr) across subjects, as observed in the previous study. Alternatively, it could be that by intermixing the single-task and dual-task conditions, participants were able to optimise their associative retrieval across the conditions by recruiting pre-probe anticipatory mechanisms. This interpretation implies that the pre-probe anticipatory activity is a kind of retrieval strategy that can be used in a flexible way to enhance associative retrieval. Therefore, the possibility remains that poor associative memory is responsible for the recruitment of anticipatory neural mechanisms reflected in the pre-probe associative retrieval effect. In the light of the present findings, future research should consider a between-group design to further test this hypothesis.

### ***Post-probe associative retrieval***

Consistent with findings from younger adults in the first study, positive-going associative retrieval effects were found across the latency intervals in the present study. The early effect at 300-500 ms coincides temporally with the traditional mid-frontal old/new effect, but has a more posterior focus in scalp distribution relative to the typical mid-frontal effect (e.g., Nessler et al., 2001; Rugg et al., 1998; Tsivilis et al., 2001). A similar centro-parietal focused old/new effect has been reported for the recollection of words, whereas those for the recollection of objects and faces are more frontal focused (e.g., Finnigan, Humphreys, Dennis, & Geffen, 2002; Olichney et al., 2000; Galli & Otten, 2011; Yick & Wilding, 2008). It is possible that these effects in the same time window represent similar cognitive processing, i.e., familiarity, that vary with different materials. Therefore, the present associative retrieval effect at 300-500 ms possibly represents the strength of familiarity that is stronger for items related to associative hits than those related to associative misses.

The 500-1200 ms post-probe interval is dominated by a positive-going effect with a left-parietal focus, similar to the left-parietal old/new effect that is typically found in the 500-800 ms interval (e.g., Rugg & Curran, 2007). The difference in the length of the time window may be related to the nature of the effect. A previous EEG study (Cansino & Trejo-Morales, 2008) measuring source retrieval effects (source hits vs. source misses) also reported that the effects across the two intervals (470-800 ms vs. 800-1200 ms interval) did not differentiate from each other. It is not clear how to interpret the difference in the duration of the left-parietal effect, because differences in retrieval effects across latency intervals have not been routinely tested in previous studies. Nevertheless, together with findings from the first study and previous research (e.g., Woroch & Gonsalves, 2010), the present study demonstrates that the left-parietal effect varies with associative retrieval. These findings support the notion that the left-parietal effect reflects the quantity and quality of the episodic information recollected (Wilding, 2000), at least in young adults.

The left-parietal effects in the present study do not vary between single-task and dual-task conditions. This finding is at odds with findings from previous studies (Curran, 2004; Johnson et al., 2013) that the left-parietal effect is reduced following dual-task encoding relative to single-task encoding. A crucial difference in the present study is the memory task, i.e., an associative memory task as compared to recognition tasks used in previous studies. It is possible that when associative retrieval is emphasised as in the present study, neural processes for recollection are recruited regardless of the strength of encoding.

The late post-probe interval after 1200 ms is dominated by a right frontal positivity, in addition to the posterior positivity. The right-frontal effect is thought to reflect post-retrieval verification or monitoring processing (e.g., Rugg & Wilding, 2000), which does not always predict the accuracy of associative source retrieval (e.g., Rugg et al., 1996; Senkfor & Van Petten, 1998). The present study replicated the finding in the first study that the right-frontal effect is related to associative retrieval success, and further demonstrated that this relationship is not affected by dual-tasking at encoding. As discussed in the Introduction chapter, the functional role of the right-frontal effect may vary with the nature of the memory task. The present finding suggests that when associative memory is emphasised, as in the present associative memory paradigm, participants rely on post-retrieval monitoring processes to recover associate information even when memory encoding is undermined by reduced processing resources.

In the present study, there is no hint of the negative-going associative retrieval effect observed in older adults in the first study. The absence of the negative-going post-probe effect, together with the presence of the negative-going pre-probe effect, supports the dissociation between these two effects. In line with Johnson et al. (2013), ERPs for successful retrieval in the dual-task condition were more negative-going than those in the single-task condition. This negativity in the dual-task condition was interpreted by Johnson and colleagues as additional neural processes engaged by participants to recover episodic information in compensation for impoverished encoding.  However, as there is no interaction between condition and retrieval response in the present study, i.e., ERPs for both associative hits and associative misses are more negative-going in the dual-task condition, this negativity cannot be equated to the negative-going associative retrieval effect found in the first study. Thus, the present study offers no evidence to support the hypothesis that the left-frontal negativity as observed in older adults reflects neural mechanisms recruited to compensate for poor memory representations, as argued by Duarte et al. (2006) and Friedman et al. (2010). A previous study (Addante et al., 2012) has demonstrated that under certain circumstances, i.e., when the level of recognition confidence for retrieval probes is low, a similar negative-going source retrieval effect can also be found in young adults. However, if the negative-going effect is driven by low levels of recognition confidence, it is surprising that it does not occur in the present study as words studied in the dual-task condition should be recognised with less confidence than those studied in the full attention (Curran, 2004; Yonelinas, 2001). Currently, there is insufficient evidence to draw a firm conclusion on whether the left-frontal negativity observed in older adults during source retrieval represents compensatory mechanisms for poor memory.

In conclusion, the present study is important in that it demonstrates that younger adults also recruit pre-probe anticipatory neural mechanisms, possibly as a result of the secondary task manipulation imposed during memory encoding. These mechanisms are recruited strategically to optimise associative retrieval. This finding supports the STAC model, which argues that compensatory activity is an adaptive mechanism that can be recruited across the life span to achieve task goals in the face of specific task difficulty (Park & Reuter-Lorenz, 2009; Reuter-Lorenz & Park, 2010). In addition, the present findings provide insights into the nature and timing of the “compensatory” processes used by older adults during associative memory processing.

## 2.3 Experiment 3: Age differences in anticipatory memory-related activity when target materials are intermixed

### 2.3.1 Encoding

#### *2.3.1.1 Introduction*

In the first study, prestimulus brain activity during encoding did not predict subsequent associative memory success in either age group. As already discussed, a number of factors may have affected the presence of PSMEs in the first study. One possible factor is reduced processing resource before object word onset as a consequence of participants having to maintain the location word in working memory. Another possibility is that neural mechanisms underlying PSMEs are not engaged in a ‘blocked’ design as used in the first study. Previous PSME studies (e.g., Galli et al., 2011, 2012, 2013; Otten et al., 2006, 2009) used at least two types of encoding tasks or stimuli which are intermixed in a study block. For example, participants were cued on each trial to make either a semantic or orthographic judgement on the upcoming word (Otten et al., 2006), or shown items in either the visual or auditory modality, or required to process pictures of different valences (Galli et al., 2011). Therefore, PSMEs are thought to reflect a task-set configuration, i.e., setting up a different neural context for encoding on a trial-by-trial basis (Otten et al., 2006), similar to the concept of ‘retrieval orientation’ (e.g., Herron & Wilding, 2004). Although PSMEs may be observed in both stay and switch trials (Otten et al., 2009; Padovani et al., 2013), it remains possible that prestimulus encoding-related activity is only engaged when different types of tasks or stimuli are intermixed so that it is needed to set up a different task-set on a trial-by-trial basis. The present study therefore aimed to further investigate the underlying mechanisms of associative PSMEs, by testing whether they emerge when frequent switches between different classes of study material are required.

When different classes of study materials are randomly intermixed, successful encoding can be predicted by prestimulus activity that is common to different materials, i.e., material-invariant PSMEs. Otten et al. (2009) found that a negative-going, frontally distributed ERP modulation before stimulus onset predicts later recollection of both visually and auditorily presented words. An fMRI study using similar study materials also reported material-invariant PSMEs in MTL regions including the hippocampus (Park & Rugg, 2010). This kind of PSME was interpreted in terms of general semantic preparation across modalities, which can be engaged in a flexible manner to facilitate memory formation.

In addition to PSMEs for single study items, a recent fMRI study (Addante, de Chastelaine, & Rugg, 2015) contrasted prestimulus encoding-related brain activity for word–word and picture–picture associations elicited by preparatory cues signalling the type of upcoming item pair. PSMEs common to both classes of material were identified in several cortical regions, including bilateral prefrontal and parietal cortex, insula, and posterior cingulate cortex, as well as the hippocampus. This finding is consistent with those from other studies investigating PSME for single items (e.g., Adcock et al., 2006; Park & Rugg, 2010). These regions overlap with cortical regions comprising a distributed network that support cognitive control functions, such as the adoption and maintenance of task-sets in a goal-directed manner (e.g., Cole et al., 2013). Thus, Addante et al. argued that the material-invariant PSMEs may reflect differential engagement of these control processes in response to prestimulus preparatory cues. These findings demonstrated that similar to single item encoding, inter-item association is also influenced by prestimulus neural activity, which may reflect task-set reconfiguration according to different encoding requirements on each trial.

Interestingly, these material-invariant PSMEs were negatively correlated with associative recognition accuracy across individuals (Addante et al., 2015). Thus, echoing the finding in the first study regarding the pre-probe associative retrieval effect, greater magnitudes of prestimulus associative encoding effects may also predict worse associative memory. Furthermore, the nature of this negative correlation is not uniform across the cortical regions and hippocampus. It was found that PSMEs across the cortical regions are positively correlated with associative false alarms, whereas the hippocampal PSMEs are correlated negatively with associative hits. Assuming that associative false alarms occur when familiarity of each of the two items is strong while recollection of the association between them is weak, cortical PSMEs may reflect processes that support single item encoding, which may operate in parallel with other encoding processes that support inter-item binding. Cognitive processes underlying the hippocampal PSMEs, on the other hand, are more difficult to decipher. By definition, PSMEs are associated with successful associative encoding, but the magnitude of the hippocampal PSME decreases with the likelihood of effective inter-item association across subjects. It was speculated by the authors that hippocampal PSMEs may reflect neural processes that are task-irrelevant, such as distracting thoughts or the retrieval of irrelevant information, but that also activate the hippocampus. The engagement of these processes therefore reduces available hippocampal resources for the encoding of study items. However, this interpretation does not explain why these processes are specifically associated with associative hits. Also, it is difficult to reconcile this idea with the lack of a negative relationship between post-stimulus hippocampal SMEs and memory performance, as pointed out by the authors.

In Addante et al.'s study, material-selective PSME was found for picture-pairs only, in bilateral fusiform cortex and intraparietal sulcus that overlapped with cortical regions selectively activated by pictures. This finding supports the proposal that memory encoding can benefit from "pre-activation" of material-selective cortical regions (Adcock et al., 2006; Otten et al., 2006; Park and Rugg, 2010), even though the lack of word-specific PSME is difficult to explain. However, these material-specific prestimulus SMEs did not overlap with corresponding poststimulus SMEs, which is inconsistent with the "pre-activation" proposal as successful memory encoding does not depend on those pre-activated material-selective regions. Such a dissociation between pre- and post-stimulus effects is at odds with findings from attention studies (see Driver & Frith, 2000), which indicate that a pre-stimulus attentional cue leads to both prestimulus activation of domain-selective cortical regions and enhancement of the poststimulus response in the same regions. It was therefore proposed that poststimulus effects depend on a raised prestimulus baseline (Driver & Frith, 2000). This proposal, however, is not supported by findings from memory studies such as Addante et al. (2015). Addante et al.'s findings indicate that memory encoding can benefit from "pre-activation" of material-selective cortical regions, at least for picture pairs, but poststimulus encoding activity does not critically dependent on these regions.

The aim of the present study was to test whether associative PSMEs emerge when frequent switches between different classes of study material are required, in line with the typical experimental design for PSMEs. If material-invariant PSMEs emerge under such conditions, it would suggest that the effect reflects task-set configuration that has to be set up anew on each trial. In comparison, material-selective PSMEs may reflect pre-activation of cortical regions selectively activated for the processing of specific materials. In either case, PSMEs can be expected to decline with ageing. Using an executive control task, Paxton et al. (2006) have shown that unlike younger adults, older adults are unable to take advantage of cue information to benefit performance. Consistent with the pattern of behavioural findings, a subsequent fMRI study (Paxton et al., 2008) demonstrated that activity in lateral PFC associated with goal maintenance was reduced during cue processing in older adults. In addition to deficits in cognitive control, older adults are also less able to show pre-activation of material-selective brain regions in expectation of studying certain classes of material (Bollinger et al., 2011)

The present study employed an associative memory paradigm similar to that used in Addante et al. (2015). This kind of associative memory paradigm was first used by Humphreys (1976), who asked subjects to learn unrelated word pairs and later tested them using word pairs in three categories: the intact pairs (word pairs in their original pairing as during encoding), the recombined pairs (both words were studied but not paired together during encoding), and new pairs (both words were unstudied). Participants had to decide whether the pair was seen previously, and whether the two words were seen together. Associative recognition accuracy was computed as the difference between correct recognition of intact pairs (associative hits) and incorrect categorisation of recombined pairs as intact pairs (associative misses). As both intact and recombined pairs contained studied words, it was thought that successful associative recognition could not be based on memory for individual items, but on memory for the association between them. In the present paradigm, participants learned picture-picture pairs and word-word pairs that were randomly intermixed in an incidental memory task. Pre-stimulus cues were presented before each study pair signalling whether the upcoming pair comprised words or pictures. Memory for the study pairs was tested with an associative recognition test, during which studied items were presented either in their original pairing (intact) or different pairing (rearranged), along with pairs of new items. An advantage of this paradigm is that participants cannot just rely on the strength of item memory. Instead, the association between items is needed to correctly identify intact and rearranged pairs. The critical contrast is between intact pairs that are correctly identified as “intact” (associative hits) and intact pairs that are incorrectly judged as “rearranged” (associative misses). Thus, associative memory is isolated without being confounded by the strength of item memory. In addition, item pairs were presented simultaneously in the present study to reduce working memory load in the prestimulus interval, which may have affected the emergence of PSMEs in the first study. In line with the first study, both pre- and post-stimulus brain activity are analysed.

#### *2.3.1.2 Methods*

*Participants*

Twenty-six younger volunteers were recruited from the University College London student community, and 29 older volunteers were recruited from the University of the Third Age through flyers. Volunteers were remunerated at £7.5/hr for participation in the experiment. Two younger and 5 older volunteers were excluded because of insufficient trial numbers (i.e., 16) due to inadequate memory performance or poor EEG quality. The final groups included in the analyses comprised 24 older adults (mean age 67 year, range 60-75, 6 males) and 24 younger adults (mean age 23.63 years, range 19–35 years, 6 males). All participants were right-handed and were screened via email or telephone to ensure that they had normal or corrected-to-normal vision, no history of neurological or psychiatric conditions and were not taking psychotropic medications. The experimental procedures were approved by the University College London Research Ethics Committee. All participants provided informed written consent before participating.

### *Stimuli*

Stimuli were drawn from a pool of 720 grey-scale pictures of everyday objects (e.g., tools, food, animals, and plants) and their corresponding names, selected from a commercial photo-objects database. Grey-scale pictures, instead of colourful pictures, were used to minimize perceptual differences between pictures and words. All of the names were single words between three and eleven letters in length. Forty-eight items were used for practice and the rest of the items were used for the real task. For each participant, half of the 672 items were randomly selected to be presented as pictures and the other half as words. Pictures and words were randomly paired to form 168 picture-picture pairs and 168 word-word pairs.

For encoding, 252 pairs (half words and half pictures) were randomly selected and intermixed to form a study list for each participant. For retrieval, 168 studied pairs were presented in their original pairing (‘intact’) and 84 were repaired so that each item within a pair was studied but in different pairings (‘rearranged’). Intact and rearranged pairs were intermixed with 84 new pairs (half words and half pictures) to form the test list. The pairs were presented at the centre of a computer monitor, with one item above and the other below the central point. Words were presented in Helvetica size 30 and the size of each picture was 122x76 pixels. The picture size was smaller than that in previous fMRI studies (e.g., Park & Rugg, 2010) to minimize eye movements which are more problematic for EEG analyses. Each picture pair subtended a visual angle of 2.3° horizontally and 3.2° vertically, and word pairs were 1-4.2° horizontally and 1.8° vertically in size. Pilot studies were conducted to determine the minimum number of stimuli needed to obtain sufficient number of trials for ERP analyses.

A potential confound was that there might be a difference in perceptual fluency between intact and rearranged pairs, as the presentations of intact pairs were identical across encoding and retrieval phases whereas the presentations of rearranged pairs were not. To remove the influence of perceptual fluency on associative memory, for both intact and rearranged pairs each item was always presented in a different position at test from its position at study. That is, items presented above the centre of the screen during the study phase were presented below during the test phase, and vice versa. This procedure was to ensure that participants could not rely on perceptual familiarity to recognise the intact pairs.

### *Procedures*

An incidental associative memory paradigm was used in the present experiment. Participants were first given the written instructions for the study phase, which they read and then verbally described to the experimenter to ensure a thorough understanding. They were then given 2 short practice sessions (8 word/picture pairs within each session) to familiarize participants with the procedures.

For the study phase there were 6 blocks of 42 (half picture, half word) pairs. Each trial began with a preparatory cue signalling whether the upcoming study pair comprised pictures or words (“P” for pictures and “W” for words, Helvetica font size 46, colour red). The instruction was to attend to each cue and prepare accordingly for the upcoming stimuli. The cue was presented for 1.9 s, followed by a 100 ms blank screen. A picture or word pair then appeared on the screen for 1.5 s, followed by a fixation cross. Participants were required to judge “which item would fit inside of the other” and to respond by pressing one of two buttons, using the left and right index fingers, corresponding to the top or the bottom item respectively. Responses were to be made within 4.5-6 s from item pair onset, before the next trial began. Participants were told to make the judgments as quickly as possible without sacrificing accuracy.

After the study phase, participants were given instructions for the test phase. Two short practice sessions, each consisting of 8 word/picture pairs studied in the practice sessions plus 4 new pairs, were administered. For the test phase there were 8 blocks of 42 item pairs. The procedures were similar to those in the study phase except that participants had to judge whether each item pair had been studied in the same pairing (intact), had been studied but in different pairings (rearranged), or had not been studied (new). Participants responded by pressing one of the 3 buttons using the index finger, middle finger, or ring finger of their right hand. The buttons were counterbalanced across participants. Responses had to be made within 5-6.5 s from item onset. To minimise guessing, participants were instructed to respond “rearranged” when uncertain about the pairing between the items, and respond “new” if uncertain about whether they had seen the items. Response assignments for the keys associated with study and test decisions were counterbalanced across participants. EEG was recorded throughout all study-test blocks.

The EEG session, including electrode cap application and the memory task, lasted approximately 2 hours for each younger subject and 2.5 hours for each older participant. Following the EEG session, participants completed the neuropsychological test battery that was used in the first study. One of the tests, Verbal Paired Associates, was removed from the battery as the form and nature of this test overlapped with those of the experimental task.

### *EEG acquisition and analyses*

Online EEG acquisition procedures were identical to those in the first study. Activity elicited by preparatory cues and item pairs was aligned separately to the onset of each event. Epochs of 2048 ms duration were extracted, starting from 100 ms before each event onset, and down-sampled to 125 Hz. For pre-stimulus activity, artifact rejection and ERP computation methods were the same as those in the first study.

For post-stimulus activity, analyses were performed using the EEGLAB Toolbox (Delorme & Makeig, 2004) and the ERPLAB Toolbox (Lopez-Calderon & Luck, 2014) for Matlab. These software packages were used to minimise eye-movement artifacts that could not be successfully removed using the in-house package as in previous studies. Eye-movement artifacts were greater in the present study, especially in older adults, because two words or pictures were presented simultaneously in each trial. To remove these artifacts, filtered and epoched EEG data were decomposed into temporally independent components using infomax ICA implemented in the EEGLAB Toolbox. Components related to blink or other types of eye movements, as well as muscle tension and other artefacts such as analog-to-digital signal saturation were identified by visual inspection according to their spatial and temporal characteristics (for more information see Delorme, Fernsler, Serby, & Makeig, 2006) and manually removed. Epochs with drifts exceeding ±50 μV were also identified using the *pop_rejtrend.m* function implemented in EEGLAB and manually rejected. ERP averaging and plotting were done using the ERPLAB toolbox.

### *Behavioural analyses*

For the encoding task, RTs to study pairs were analysed with a mixed-model ANOVA incorporating the factors of group (older/younger) and material (word, picture) to see whether older and younger participants spent different amounts of time at encoding for word pairs and picture pairs. For the memory test, associative memory was assessed with recognition accuracy (Pr) and response bias (Br) (Snodgrass & Corwin, 1988). Pr was computed as (pHit – pFA), the proportion of associative hits minus the proportion of associative false alarms, which was measured as rearranged pairs wrongly identified as ‘intact’. This measure was based on the assumption that associative false alarms occur when the items comprising a rearranged pair are recognised while the association is forgotten. Br was computed as pFA/1-(pHit-pFA).

Mixed-model ANOVAs incorporating the factors of group (older/younger), and material (word, picture) were conducted on Pr and Br. In addition, a mixed-model ANOVA was conducted on RT data incorporating the factors of group, material, and response (associative hit/associative miss) to see whether RTs differed between groups and conditions.

### *ERP analyses*

To identify neural correlates of subsequent associative memory effects, ERP analyses were based on contrasts between brain activities associated with ‘intact’ pairs that were correctly identified as intact (associative hits) and intact pairs that were incorrectly judged as rearranged (associative misses).

### *Prestimulus anticipatory activity*

Average ERPs were formed for cue-elicited activity related to subsequent associative hits and associative misses for words and pictures separately. In younger adults, the average numbers and ranges of artefact-free trials for associative hits and associative misses were respectively 38 (19-61) and 26 (15-46) for pictures and respectively 44 (18-66) and 23 (13-49) for words. In older adults, the average numbers and ranges of artefact-free trials for associative hits and associative misses were respectively 32 (16-59) and 33 (18-52) for pictures and respectively 38 (19-58) and 26 (16-40) for words. All participants had at least 16 artefact-free trials for each category, except one younger participant who had 15 associative miss trials for picture cues and another younger participant 13 associative miss trials for word cues.

Mixed-model ANOVAs were performed including 28 electrodes as used in the previous studies. The 28 electrodes were subjected to ANOVAs with factors of hemisphere (left/right), location (anterior/posterior), and site (7 positions), in addition to the experimental factors of group, material, and memory (subsequent associative hit / subsequent associative miss). In line with the first study, ERPs were quantified in 2 continuous time intervals: 200-1100 ms and 1100-1948 ms. An initial mixed-model ANOVA was conducted incorporating the factors of interval along with all other factors to determine whether prestimulus activity varied across intervals. Significant interactions including latency and memory would be followed up with separate ANOVAs for each latency region incorporating the factors of material, memory, hemisphere, location, and site. The effects of interest were those involving the factor of memory (i.e., associative PSMEs) and the factor of material (i.e., material-selective anticipation). Significant interactions involving these factors were followed up with subsidiary within-subject ANOVAs to further elucidate those effects.

As there was no significant effect involving subsequent memory (see Results), scalp distribution analyses were performed on scaled data using the max/min method (McCarthy & Woods, 1985) applied to difference scores between the 2 types of material (picture-word) across associative hits and associative misses for each age group including all 37 electrodes. Significant differences in topography of different materials were verified using ANOVAs conducted on the rescaled data.

In younger adults, there appeared to be a positive deflection that peaked at around 160-170 ms which was larger following word cues than picture cues (Figure 18). Additional analyses were performed to evaluate this early material-specific difference. To this end, mean amplitudes were measured between 140–180 ms surrounding the peak time using all 37 electrode sites in younger adults. Mean amplitudes were contrasted between picture cues and word cues irrespective of memory performance using within-subject ANOVA including factors of material, hemisphere, location, and site. The Greenhouse-Geisser correction for nonsphericity was used when appropriate, as indicated by the adjusted degrees of freedom.

*Poststimulus associative encoding-related activity*

Averaged ERPs were formed for item-elicited activity related to subsequent associative hits and associative misses for words and pictures separately. In younger adults, the average numbers and ranges of artefact-free trials for associative hits and associative misses were respectively 42 (23-66) and 28 (17-38) for pictures and respectively 48 (24-66) and 24 (16-50) for words. In older adults, the average numbers and ranges of artefact-free trials for associative hits and associative misses were respectively 36 (18-61) and 37 (19-54) for pictures and respectively 44 (24-64) and 26 (16-43) for words.

In line with the previous studies, ERPs were quantified in 2 continuous time intervals: 300-900 ms and 900-1600 ms. An initial mixed-model ANOVA was conducted incorporating the factors of material (pictures/words), memory (subsequent associative hit / subsequent associative miss), interval (early/late), hemisphere (left/right), location (anterior/posterior), and site (7 positions). Significant interactions including latency and memory would suggest that SMEs vary across the two intervals, and therefore warrant separate mixed-model ANOVAs for each latency region. The effects of interest were those involving the factor of memory (i.e., associative PSMEs). In contrast to prestimulus analyses, effects involving material but not memory, i.e., material-selective processing of item-pairs, are not of interest in post-stimulus analyses. Significant interactions were subjected to subsidiary within-subject ANOVAs to further elucidate these effects.

Analyses of scalp distribution were also performed using the same method as reported in the first study. Significant differences between the topographies of different conditions were verified by ANOVAs conducted on the rescaled data. The Greenhouse-Geisser correction for nonsphericity was used when appropriate, as indicated by the adjusted degrees of freedom.

### *2.3.1.3 Results*

*Neuropsychological Test Scores*

Performance on the neuropsychological tests is summarized in Table 8. All participants scored 27 or above on the MMSE, and the pattern of results from between-group comparisons was largely consistent with that in the first study except for the following differences. Older adults did not differ from younger adults in the time they spent in formal education, and they did not show the impairment in word list recall (delayed), a test for long-term memory.

**Table 8. Subject characteristics and scores on neuropsychological tests for the two age groups.**

| | Older Group | | Younger Group | | |
|---|---|---|---|---|---|
| | *Mean (SD)* | *Range* | *Mean (SD)* | *Range* | *p* |
| Years of education | 16.2 (2.7) | 11-20 | 16.5 (2.0) | 14-20 | *ns* |
| MMSE | 28.9 (1.0) | 27-30 | 29.3 (0.6) | 28-30 | *ns* |
| Word List (Immediate) | 36.5 (6.1) | 22-47 | 42.2 (4.0) | 33-48 | <.001 |
| Word List (Delayed) | 9.0 (2.9) | 2-12 | 10.2 (1.5) | 7-12 | *ns* |
| Digit Span (backward + forward) | 21.4 (3.8) | 17-29 | 21.8 (4.0) | 15-28 | *ns* |
| Verbal Fluency - Letter | 45.3 (13.6) | 23-76 | 48.8 (9.3) | 35-67 | *ns* |
| Verbal Fluency-Category | 29.5 (5.4) | 19-39 | 36.2 (6.1) | 21-50 | <.001 |
| Trail Making Part A (sec) | 34.1 (10.0) | 20.7-56.6 | 21.1 (6.9) | 10.7-39.2 | .001 |
| Trail Making Part B (sec) | 87.8 (38.4) | 44.1-198.7 | 56.3 (20.3) | 27.3-99.5 | <.001 |
| NART (FSIQ-estimate) | 120.5 (6.3) | 101-129 | 109.0 (8.5) | 86-120 | <.001 |
| GDS (short form) | 1.2 (1.6) | 0-7 | 1.4 (1.7) | 0-6 | *ns* |

*Behavioural results*

At encoding, mean RTs (SDs) of younger adults were 1781 ms (672 ms) for pictures and 1866 ms (709 ms) for words, and those of older adults were 2260 ms (775 ms) for pictures and 2454 ms (871 ms) for words. A mixed-model ANOVA revealed significant main effects of material ($F(1,46) = 15.04$, $p < .001$) and group ($F(1,46) = 6.07$, $p = .018$), confirming that participants spent less time on the picture-pairs than the word-pairs across the groups, and older adults were slower to respond than younger adults across the materials. There was no interaction between these two factors.

Recognition performance is presented in Table 9 as mean percentage responses of younger and older adults to intact, rearranged, and new picture-pairs and word-pairs respectively. Associative recognition accuracy (Pr) was .38 (.17) for pictures and .42 (.17) for words in younger adults; and .20 (.13) for pictures and .27 (.11) for words in older adults. The mixed-model ANOVA revealed main effects of group ($F(1,46) = 16.68$, $p < .001$) and material ($F(1,46) = 15.9$, $p < .001$), confirming that associative recognition accuracy was higher in younger adults than in older adults, and higher for words than for pictures. There was no significant interaction between group and material ($F(1,46) = 0.54$, $p = .47$). Response bias (Br) was .22 (.12) for pictures and .32 (.16) for words in younger adults; and .28 (.17) for pictures and .31 (.15) for words in older adults. The mixed-model ANOVA revealed a main effect of material ($F(1,46) = 7.59$, $p = .008$), confirming that response bias was significantly more liberal for words than it was for pictures across age.

As test, mean RTs (SDs) of younger adults were 2103 ms (456 ms) for associative hits and 2795 ms (702 ms) for associative misses of pictures, and

2085 ms (504 ms) for associative hits and 2989 ms (1189 ms) for associative misses of words. Mean RTs (SDs) of older adults were 2978 ms (854 ms) for associative hits and 3598 ms (1543 ms) for associative misses of pictures, and 3065 ms (836 ms) for associative hits and 4602 ms (2298 ms) for associative misses of words. A mixed-model ANOVA revealed significant main effects of material ($F(1,46) = 10.33$, $p = .002$), memory ($F(1,46) = 34.75$, $p < .001$), and group ($F(1,46) = 14.53$, $p < .001$), as well as group × material ($F(1,46) = 5.39$, $p = .025$), material × memory ($F(1,46) = 13.55$, $p = .001$), and material × memory × group ($F(1,46) = 5.29$, $p = .026$) interactions. Significant main effects confirmed that participants responded faster to pictures than to words and faster to associative hits than associative misses, and older adults were slower to respond than younger adults overall. Post-hoc *t*-tests revealed that RTs for words were significantly longer than for pictures in older adults ($t(23) = 3.08$, $p = .005$) but not younger adults ($t(23) = 1.01$, $p = .32$), RTs did not differ significantly between pictures and words for either associative hits or associative misses (*t*s < .35, *p*s > .23), whereas in older adults, the material-selective RT difference was significant for associative misses ($t(23) = 3.41$, $p = .002$) but not for associative hits ($t(23) = .83$, $p = .413$).

**Table 9. Mean percentage responses (SD) to each type of retrieval probes for the two age groups**

| | | Response | Older | Younger |
|---|---|---|---|---|
| Picture | Intact pairs | Intact | 43.1 (14.4) | 51.5 (15.1) |
| | | Rearranged | 43.4 (11.7) | 36.1 (10.2) |
| | | new | 13.3 (9.6) | 12.3 (9.7) |
| | Rearranged pairs | Intact | 22.9 (15.3) | 13.9 (8.3) |
| | | Rearranged | 58.3 (14.9) | 65.3 (15.1) |
| | | new | 18.7 (14.4) | 18.7 (12.8) |
| | New pairs | Intact | 7.4 (9.2) | 0.9 (1.7) |
| | | Rearranged | 26.7 (10.9) | 24.8 (15.1) |
| | | new | 65.9 (15.7) | 71.9 (16.1) |
| Word | Intact pairs | Intact | 50.3 (12.1) | 60.8 (16.9) |
| | | Rearranged | 32.8 (9.3) | 30.6 (11.1) |
| | | new | 17.0 (11.0) | 8.6 (9.1) |
| | Rearranged pairs | Intact | 23.0 (11.0) | 18.3 (10.4) |
| | | Rearranged | 50.0 (13.5) | 64.5 (15.1) |
| | | new | 27.0 (12.3) | 15.3 (13.3) |
| | New pairs | Intact | 3.5 (5.5) | 2.0 (3.1) |
| | | Rearranged | 17.7 (13.3) | 28.5 (13.9) |
| | | new | 78.7 (14.6) | 67.3 (15.3) |

### *ERPs*

#### *Prestimulus anticipatory activity*

As statistical analyses (see the next paragraph) revealed no significant memory effect, grand-average ERPs elicited by preparatory cues were formed for word cues and picture cues combining across associative hits and associative misses. Figure 16 illustrates the ERP waveforms at 9 representative electrode sites for the two types of material in younger and older adults respectively. In younger adults, waveforms elicited by word cues were more positive-going than those for picture cues. Between around 140-200 ms after cue onset, there was a positive peak that was more prominent for word cues. This was followed by a sustained positive-going effect for word cues that was larger over mid-frontal and central sites. In older adults, there was a positive peak that appeared to be larger for picture cues between around 200-270 ms after cue onset. From around 300 ms, waveforms elicited by word cues were more positive-going than those for picture cues. This effect was also sustained but focused over the anterior frontal sites.

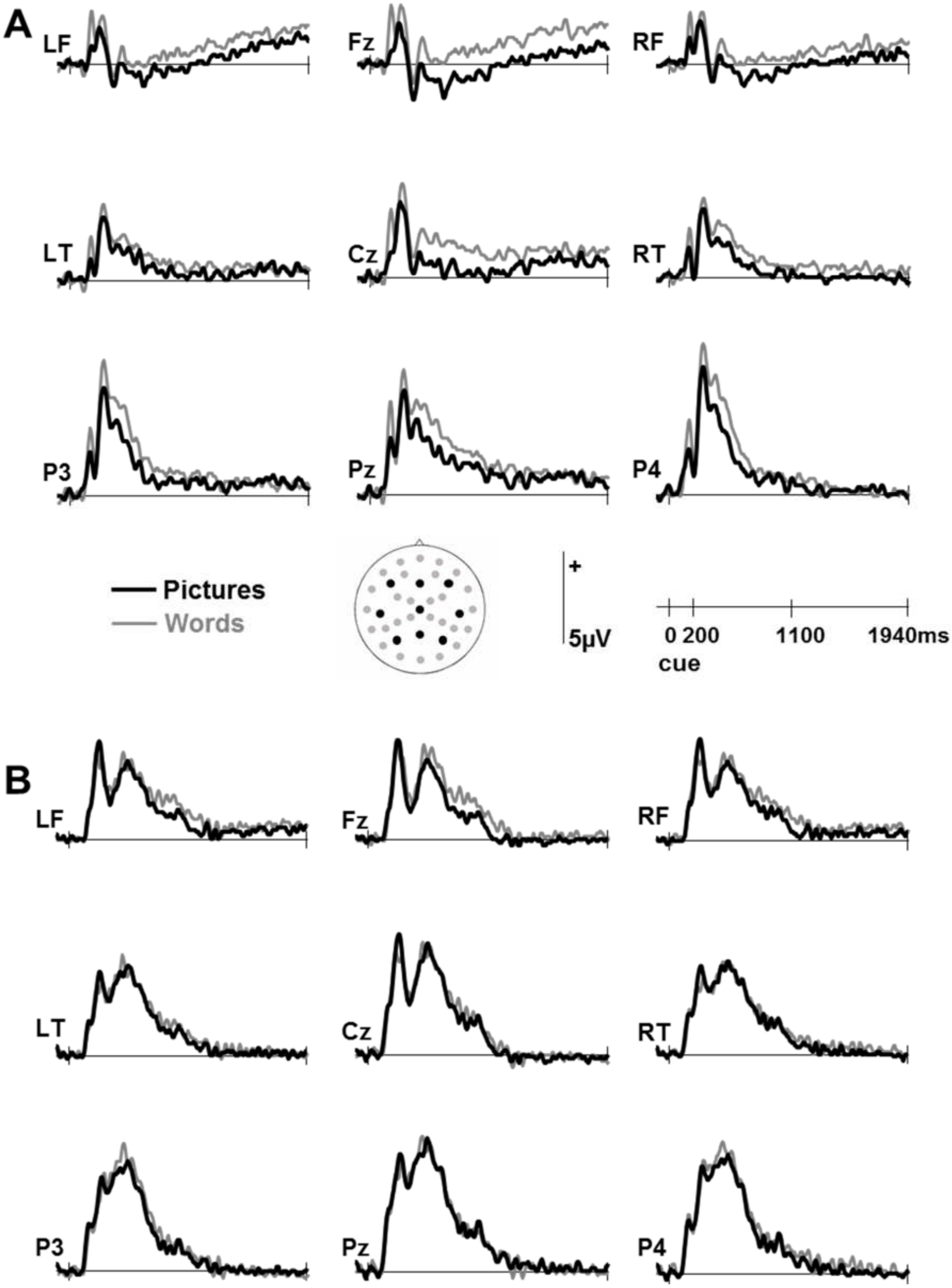


**Figure 16. Grand-average ERPs elicited by cues during encoding according to whether they preceded picture pairs or word pairs in (A) younger adults and (B) older adults. The insert shows the locations of the 9 representative electrode sites including frontal, centro-temporal, and parietal sites.**

Comparing across the groups, overall morphology of waveforms appeared to differ across age. Consistent with the first study, waveforms in younger adults were more negative-going around 300-700 ms post-stimulus compared to those in older adults, especially over the frontal sites. In older adults, there was a prominent P3-like component peaking at around 500 ms that was largest over posterior sites, which was not seen in younger adults. Although overall morphological differences across age cannot be easily interpreted (Rugg & Morcom, 2005), the larger N400-like component in younger adults might indicate that they engaged more semantic processing of the cues relative to older adults. In comparison, the larger P3-like component in older adults might reflect that they devoted more effort to ‘context updating’ (Donchin, 1981) following the encoding cues, i.e., setting up a neural context according to the cues, relative to their younger counterparts.

An initial mixed-model ANOVA incorporating the factor of interval revealed no significant effect of interest involving interval. Therefore, the 2 intervals were combined for further analyses. There was a memory × group interaction that was approaching significance ($F(1,46) = 3.99$, $p = .052$), reflecting that in older adults, the ERPs related to associative hits were more positive-going than those related to associative misses (1.68 μV and 1.29 μV respectively), whereas in younger adults this pattern was reversed (0.70 μV and 1.02 μV respectively). However, subsidiary within-subject ANOVAs revealed no significant effect involving memory in either group. In younger adults, there was a main effect of material ($F(1,23) = 7.49$, $p = .012$), reflecting that waveforms for word cues were more positive-going that those for picture cues (1.11 μV and 0.61 μV respectively), as well as a significant material × anteriority × site interaction ($F(2.3,52.1) = 3.46$, $p = .034$). This 3-way interaction was followed up with subsidiary ANOVAs conducted on data from anterior and posterior sites separately. A significant main effect of material was found over anterior sites ($F(1,23) = 6.74$, $p = .016$) and a condition × site interaction was found over posterior sites ($F(2.3,53.8) = 10.14$, $p < .001$), reflecting that the effect was reliable over frontal and central sites and faded away over posterior sites. No significant main effect of material was found in older adults ($F(1,23) = 0.54$, $p = .468$) although the direction of the difference was consistent to that in the young (1.60 µV for word cue and 1.36 µV for picture cue).

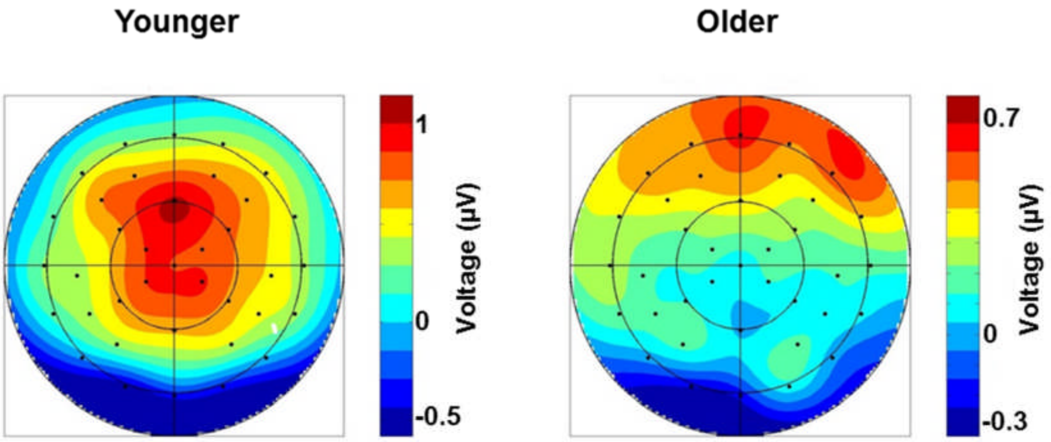


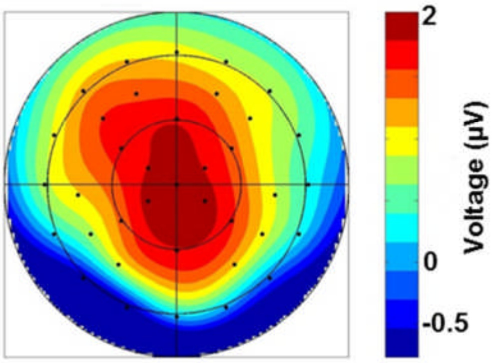
**Figure 17. Voltage spline maps for younger and older adults showing the scalp topographies of ERP material-specific prestimulus effects (word cue – picture cue) in the 200-1944 ms interval after cue onset. The maps are range scaled.**

As encoding RTs varied between materials, it is possible that prestimulus material-selective ERP effect reflects RT difference between materials. Correlation analyses were performed to assess the relationships between the ERP effect and RT difference ($RT_{word}$-$RT_{picture}$) in younger adults. The material-dependent ERP effect was quantified as the difference in mean amplitude between ERPs elicited by word cues and by picture cues (word – picture) across the 14 anterior sites at 200-1940 ms after cue onset. Pearson correlation coefficient tests revealed no significant correlation between the ERP effect and

RT difference (*r* = .29, *p* = .17), indicating that prestimulus material-selective ERP effect did not vary with RT difference.

Additional analyses were conducted to evaluate the early difference between the 2 types of cues in younger adults as reflected in the positive peak following word cues at 140-180 ms (Figure 18). Within-subject ANOVAs revealed that in younger adults, there was a main effect of material (*F*(1,23) = 11.28, *p* = .003), reflecting that waveforms for word cues were more positive-going that those for picture cues (1.94 µV and 1.13 µV respectively), and a material × anteriority × hemisphere interaction (*F*(1,23) = 9.87, *p* = .005). Subsidiary analyses revealed a significant main effect of material over anterior (*F*(1,23) = 12.21, *p* = .002) but not posterior (*F*(1,23) = 3.08, *p* = .093) sites, suggesting that the effect was reliable only over anterior sites.

**Figure 18. Voltage spline map for younger adults showing the scalp topographies of ERP material-specific prestimulus effect (word cue – picture cue) in the 140-180 ms interval after cue onset. The map is range scaled.**



*Subsequent associative memory effects*

Grand-average ERPs elicited by item pairs were formed for subsequent associative hits and associative misses across materials, as statistical analyses (see the next paragraph) revealed no significant effect involving material. Figure 19 illustrates the waveforms at 9 representative electrode sites in younger and older adults respectively.

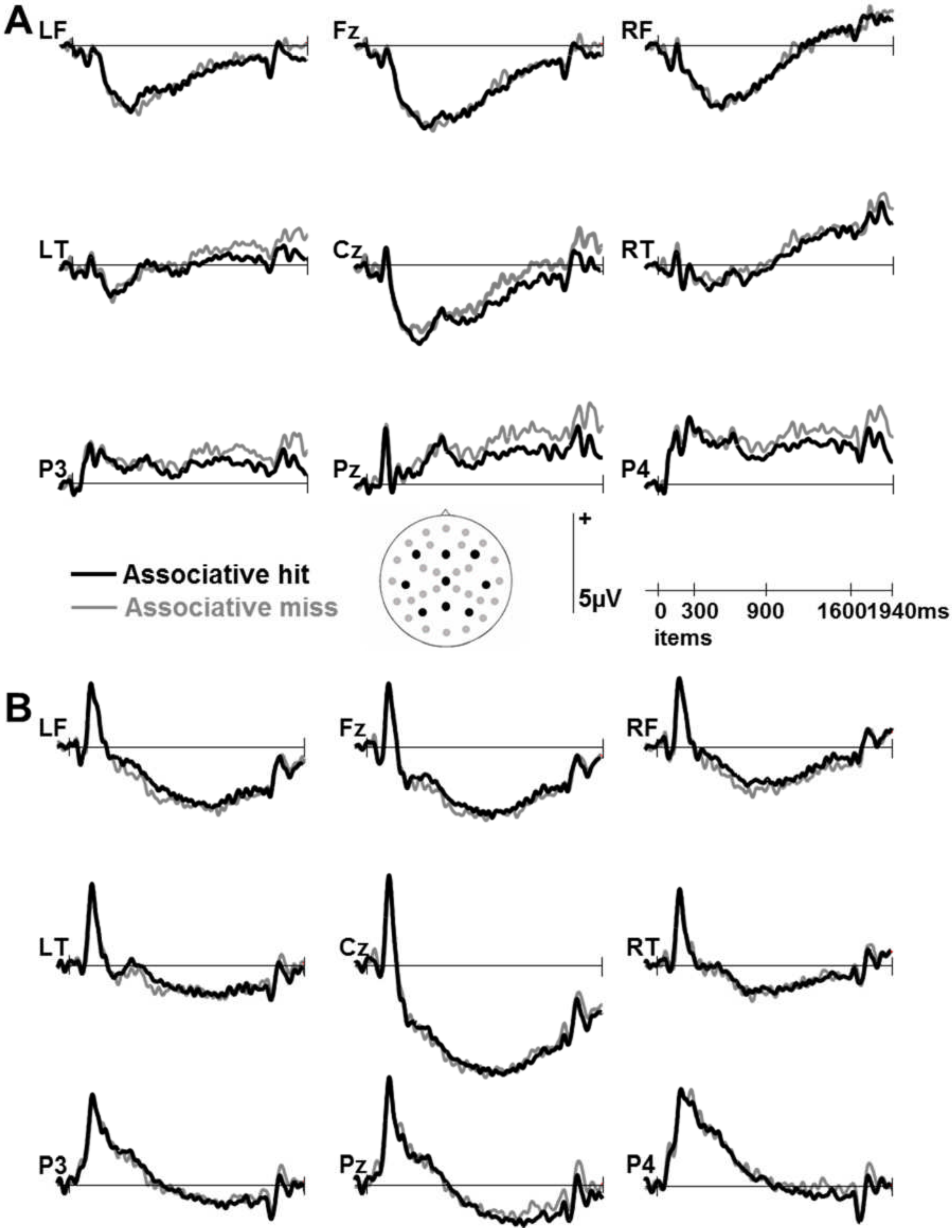


**Figure 19. Grand-average ERPs elicited by item pairs during encoding according to whether they were related to subsequent associative hits or associative misses in (A) younger adults and (B) older adults. The insert shows the locations of the 9 representative electrode sites including frontal, centro-temporal, and parietal sites.**

In younger adults, waveforms for associative hits and associative misses started to diverge at around 300-400 ms poststimulus. Waveforms for associative hits were more positive-going than those for associative misses over anterior frontal sites, and this pattern was reversed over middle and posterior sites. The positive frontal effect was sustained throughout the epoch, whereas the negative posterior effect increased in amplitude from around 900 ms. In older adults, the pattern of effects was similar to that in the young, albeit the size of the negative effect was smaller.

An initial mixed-model ANOVA incorporating the factor of interval revealed a significant memory × condition × interval interaction (*F*(1,46) = 5.91, *p* = .019), suggesting that subsequent associative memory effects were not the same across the 2 intervals. Subsidiary mixed-model ANOVAs were conducted for each interval separately. For the 300-900 ms interval, there was a significant memory × anteriority interaction (*F*(1,46) = 4.35, *p* = .043), reflecting that the subsequent associative memory effect (intact - rearranged) was negative-going over posterior sites (-0.12 µV) but positive-going over anterior sites (0.20 µV). For the 900-1600 ms interval, there was also a memory × anteriority interaction (*F*(1,46) = 9.96, *p* = .003), reflecting that the subsequent associative memory effect was negative-going over posterior sites (-0.41 µV) and positive-going over anterior sites (0.08 µV). These effects were not modulated by either group or condition factor.

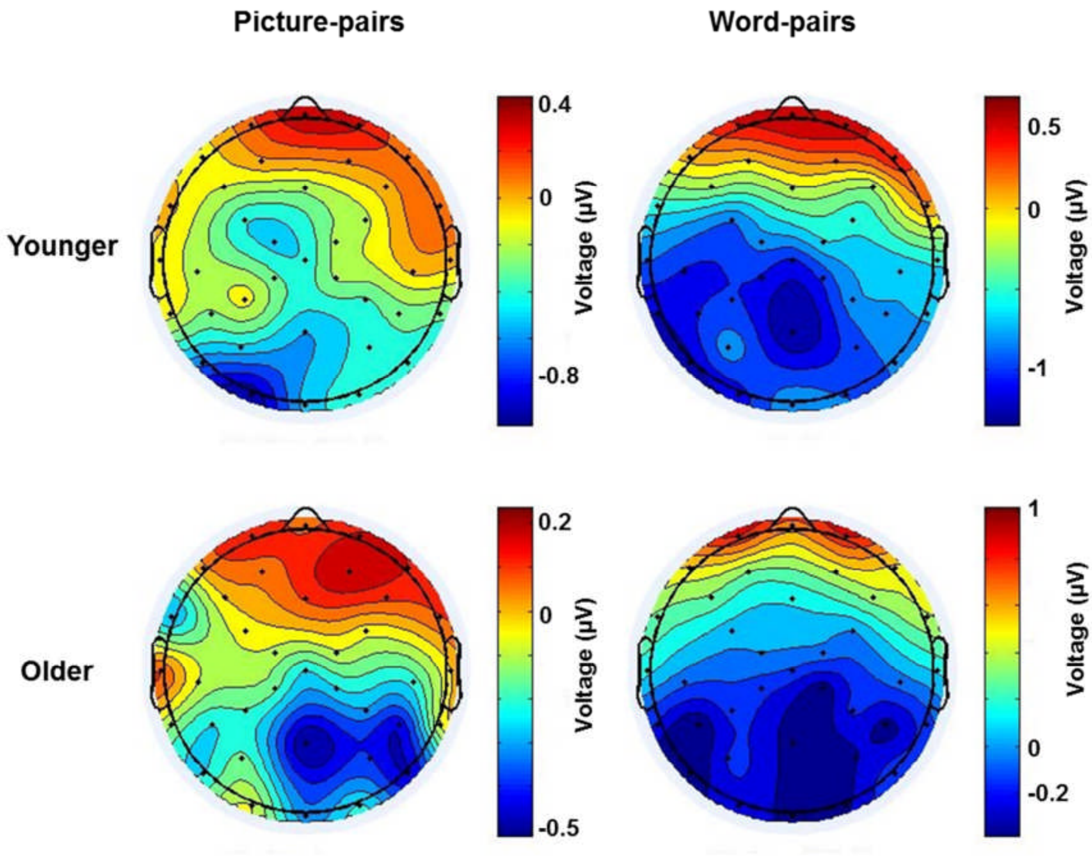


**Figure 20. Voltage spline maps for younger and older adults showing the scalp topographies of ERP subsequent associative memory effects (subsequent associative hits – subsequent associative misses) for pictures and words in the 900-1600 ms post-stimulus interval. The maps are range scaled.**

### *2.3.1.4 Discussion*

The present experiment addressed the question whether prestimulus neural activity, as indexed by ERP, predicts successful and unsuccessful associative memory when different types of encoding materials are intermixed. More importantly, the experiment considered the effect of age on prestimulus neural activity. Behaviourally, associative recognition accuracy was higher in younger adults relative to older adults. In line with previous findings, the age-related associative deficit is consistent across words and pictures (for meta-analyses see Old & Naveh-Benjamin, 2008). The present finding of better memory for word pairs than picture pairs, however, is inconsistent with previous research (e.g., Addante et al., 2015; Park & Rugg, 2011). Pictures are usually better remembered than words (i.e. the picture-superiority effect), because pictures provide much richer perceptual details that facilitate semantic elaboration to a greater extent (Yonelinas, 2002). It has been argued that superior memory for pictures may be mediated by more effective and automatic engagement of areas important for visual memory, including bilateral visual and medial temporal cortices (Grady, McIntosh, Rajah, & Craik, 1998). A possible explanation for the reverse of the picture-superiority effect in the present study is the difference in how pictures are presented. As explained in the Methods, grey scale pictures are used in the present study whereas previous studies usually presented colourful pictures. Also, pictures were smaller in size in the present study relative to those in previous studies. The use of small grey scale pictures minimizes eye-movements and perceptual difference between pictures and words, but also results in perceptual difficulties for pictures, which is consistent with participants' subjective report. Such picture-specific perceptual difficulties may be responsible for the reversed picture superiority effect.

Despite perceptual difficulty for pictures, both younger and older adults spent less time processing picture pairs than word pairs, as reflected in shorter encoding RTs for pictures, which is consistent with previous studies (Addante et al., 2015; Park & Rugg, 2011). As expected, older adults were slower to respond relative to younger adults, but the age difference did not vary with material.

### *Prestimulus brain activity*

ERP analyses revealed a difference in prestimulus brain activity elicited by picture cues and word cues in younger adults. There was a sustained positive-going effect for word cues compared with picture cues that was prominent over mid-frontal and central scalp sites, suggesting that younger adults recruit different neural mechanisms in anticipation of different study materials. As encoding RTs were shorter for pictures than words, it may be argued that the material-selective prestimulus effect simply reflects the level of attention. If this is true, the size of the effect should be expected to co-vary with RT difference between materials. However, no significant correlation was found between the ERP effect and RT difference, indicating that the effect is unlikely to represent a difference in attention per se. Nevertheless, the relationship between RTs and the ERP effect can be complicated as multiple neural processes are likely to be involved when the RTs are relatively long, as has already been discussed in the previous chapter. It is presently not clear whether the material-selective prestimulus effect may be influenced by levels of attention.

Material-selective prestimulus effects similar to those in the present study have been reported in an ERP study investigating retrieval orientation (Johnson & Rugg, 2006). When young adults were cued to retrieve either pictures or words, greater frontal positivity was found for words compared to pictures. A similar material-selective retrieval orientation effect has also been reported in a number of studies contrasting correctly rejected foils (e.g., Herron & Rugg, 2003; Hornberger et al., 2004; Morcom & Rugg, 2004). In a follow-up fMRI study, Hornberger et al. (2006) demonstrated that orienting towards pictures or words at retrieval differentially activates corresponding material-specific brain areas. Therefore, analogous to retrieval orientation, material-selective prestimulus activity at encoding may reflect the selective activation of neural networks specific to the processing of targeted class of material prior to the presentation of the study items. It may be questioned then why such prestimulus activity is not correlated with subsequent memory, which should be expected assuming that setting-up an appropriate encoding context facilitates memory encoding. However, the lack of correlation either between cue-related orientation and retrieval performance or between cue-related orientation and corresponding probe-related effects is not uncommon in the retrieval orientation research (*cf*. Bridger et al., 2009). It may be that the retrieval orientation and pre-probe retrieval-related effects tap into different kinds of anticipatory activity. Similarly, ‘encoding orientation’, as shown in the present study, may reflect different anticipatory mechanisms from those underlying PSMEs.

ERPs elicited by cues showed an early positive deflection peaking at around 160-170 ms that was larger for word cues than picture cues. The time course and scalp distribution of this component resembles the vertex positive potential (VPP) (Jeffreys, 1989), or its posterior negative counterpart the N170, which is a visually evoked early component to meaningful stimuli. The VPP/N170 is typically associated with visual processing of faces but also with non-facial objects for which participants have expertise, e.g., cars, birds, and fingerprints (see Rossion & Jacques, 2012 for a review). The N170 is not affected by either low-level visual features such as luminance and contrast (Rossion & Jacques, 2012), or by levels of attention (Eimer, 2000). The VPP/N170 is thought to index the first stage of identification and categorisation of visual objects. If the currently observed effect is driven by neural mechanisms underlying the VPP/N170, it is not clear why it is specific to word cues. One possibility is that participants prioritised the identification of word cues because of the perceptual difficulty specific to pictures. This prioritisation for words may also manifest in more positive-going ERPs elicited by word cues. If this was the case, however, it is difficult to explain why the material-specific anticipatory effect is not found in older adults who encountered greater perceptual difficulty than younger adults. Furthermore, such a material-selective effect should also be observed in post-stimulus processing, if it simply reflects perceptual difficulty.

In older adults, there was no significant difference in prestimulus brain activity between picture cues and word cues, indicating an age deficit in anticipatory brain activity. A similar age difference in material-selective effects has also been reported in a study investigating retrieval orientation (Morcom & Rugg, 2004). In that study, younger adults showed a positive-going effect when word retrieval was required as compared to when picture retrieval was required, similar to the present study. The effect was much smaller and shorter-lived in older adults. It may be argued that the lack of cue-related effects in older adults is because they failed to use the preparatory cues, or simply ignored them. However, a prominent P3-like component in ERPs was observed in older adults, indicating that they made good use of the cues to prepare for the upcoming stimuli. A likely interpretation is that older adults are less able than younger adults to vary anticipatory brain activity in response to different preparatory cues. It may reflect a malfunctioning of top-down control mechanisms that affect material-selective anticipatory processing.

Unlike the fMRI finding from Addante et al. (2015), the material-selective prestimulus effect does not affect subsequent memory. In Addante et al., associative PSMEs were found for pictures in bilateral fusiform and parietal cortex regions that are recruited for picture-selective processing. Furthermore, the present study also failed to show material-invariant prestimulus effects that were identified in Addante et al. The lack of PSMEs in the present study cannot be explained by the level of memory performance, as recognition accuracies for pictures are comparable across studies (*Pr*: 0.38 in younger adults in the present study and 0.40 in Addante et al.). A potentially critical difference is the length of the cue-item interval. The cue-item interval in Addante et al. study randomly varied between 2, 4, and 6 s, whereas in the present study it was 2 s which is much shorter than the average in Addante et al. Although 2 s or even shorter intervals have been used in previous research (e.g., Otten et al., 2006), a longer interval may be needed for the emergence of ERP PSMEs for inter-item associative encoding. Whether the length of cue-item interval affects the emergence of PSMEs has not been systematically investigated, but it is possible that a longer cue-item interval gives rise to greater probability of PSMEs, as participants have sufficient time to reconfigure task-set and to prepare for an encoding context/strategy accordingly. Further research is needed to test this hypothesis in relation to associative encoding.

### *Subsequent associative memory effects*

In both younger and older participants, statistically equivalent associative SMEs emerged across materials, manifested as a negative-going effect over posterior scalp sites with reversed polarity over anterior sites. The effects were much smaller in amplitude than those found in the first experiment. The small size of the present effects may be related to the associative recognition task, which may not be best suited to measure SMEs. Nevertheless, the effects were reliable in the later latency interval, which was consistent with the second study when paired items were presented simultaneously. The polarity and scalp distribution of these effects differ from typically observed SMEs that are positive-going with a frontal focus (Paller & Wagner, 2002; Rugg et al., 2002; Friedman & Johnson, 2000). Similar SMEs, i.e., a frontal positivity together with a posterior negativity, have been reported in a previous study (Otten et al., 2009) using a remember/know paradigm. However, there is insufficient evidence to determine whether these effects are specific to associative encoding.

Comparing the present study to the first study, an obvious difference is the encoding task. The present task was to decide which object of a pair fits into the other one, which requires participants to form clear visual images of the objects and to manipulate them. In contrast, the encoding task in the first study was to link an object to a location, which can be achieved not only by visual imagery but also by verbal strategies such as verbal reasoning or sentence making. Thus, different SMEs across the two studies may reflect different kinds of encoding processing, i.e., greater visual imagery in the present study. In support of this proposal, Gonsalves and Paller (2000) found an SME similar to that in the present study using an imagery encoding task. In that study, participants visualised objects when cued with the corresponding names at encoding. Half of the items were followed with a colour photograph of the object. During retrieval, participants were presented with the object names auditorily and judged whether each object was seen in photograph during encoding. The critical comparison for the SME was between correctly and incorrectly identified items that were not accompanied by photographs. It was found that ERPs over posterior sites were less positive-going for correctly identified items relative to incorrectly identified items. This effect may represent better source memory encoding of the visual images for correctly identified items, on the assumption that correct identifications are based on correct source attribution of the visual images. Therefore, the posterior negative-going associative SME in the present study may be related to visual imagery encoding processing. In addition, the presently observed SMEs were material-invariant, suggesting that fundamentally the same neural mechanisms were recruited for associative encoding of words and pictures. These mechanisms may represent a common associative encoding strategy, possibly visual imagery, which was used not only for pictures but also for words.

Regardless of whether the present SME reflects inter-item associative encoding or visual imagery encoding, an important finding is that there was no age difference in SMEs. This finding is in line with that in the first study, further strengthening the argument that older adults engage in fundamentally the same neural processes as younger adults for associative encoding. Previous studies have reported age differences in SMEs for both words (Friedman & Trott, 2000) and pictures (Cansino et al., 2010). The present studies indicate that for inter-item associative encoding, regardless of intentional or incidental encoding, the same neural networks are activated for both younger and older adults.

In conclusion, the findings of the present study suggest that when different types of study material are intermixed at encoding, younger adults are able to recruit material-specific neural mechanisms flexibly in response to preparatory cues, whereas older adults are impaired in this kind of anticipatory activity. The absence of associative PSME may be explained by the relatively short cue-item interval, which does not allow participants to set up an appropriate context for associative encoding. Alternatively, it may suggest that inter-item associations are not influenced by prestimulus brain activity. Further research is required to test these hypotheses. In line with the first study, younger and older adults show the same associative SMEs, which do not vary with study material. This finding adds to the evidence that there is no age deficit in post-stimulus brain activity for inter-item association, despite an age-related impairment in associative memory performance.

### 2.3.2 Retrieval

#### *2.3.2.1 Introduction*

In the first study, it was found that in older adults a negative-going pre-probe ERP effect can predict successful associative retrieval. In the second study, it was further revealed that the effect also emerges in younger adults, possibly as the result of poor memory due to impoverished encoding. Thus, this pre-probe associative retrieval effect is likely to be compensatory in nature, reflecting the recruitment of anticipatory control mechanisms that enhance the recovery of goal-related information upon encountering a retrieval probe. In those two studies, memory tests were in a “blocked” design, i.e., the same retrieval goal was maintained throughout the retrieval blocks. Under those conditions, presumably the same kinds of anticipatory activity were engaged for retrieval. An interesting question arises whether a similar pre-probe ERP effect will emerge when different retrieval goals are intermixed during retrieval. Under such conditions, it may be assumed that the engagement of pre-probe anticipatory activity would be more demanding on cognitive control.

To answer this question, clues can be taken from previous research on retrieval orientation. Retrieval orientation is a tonically maintained retrieval set, or retrieval strategy that influences probe processing to optimise the recovery of goal-related information (Herron & Wilding, 2006; Rugg & Wilding, 2000). The concept of retrieval orientation is similar to the interpretations for the pre-probe retrieval-related activity (Addante et al., 2011). Retrieval orientation can be investigated by contrasting brain activity elicited by correctly rejected new (unstudied) items (Rugg & Wilding, 2000) or neural activity elicited by pre-probe cues under different retrieval requirements. Variations in brain activity with different retrieval goals are taken as indications of retrieval orientation. When the retrieval of different kinds of episodic information varies unpredictably on a trial-by-trial basis, retrieval orientation effects have been found on switching trials, i.e., trials on which the current target is different from the previous trial, but not on stay trials, i.e., trials on which the current target is the same as the previous trial (Herron & Wilding, 2006; Johnson & Rugg, 2006). This has led to the proposal that pre-probe cue-elicited retrieval orientations reflect either an initial task set reconfiguration or a selective pre-activation of memory representations for the targeted information (Johnson & Rugg, 2006). Surprisingly, there is little evidence supporting that retrieval orientations, as measured by pre-probe cue-elicited activity, directly influence memory retrieval (*cf.* Bridger et al., 2009 for a positive correlation between retrieval orientation, as measured by contrasting correct rejections, and memory performance). It would be interesting to find out whether the same, or partly overlapping, neural networks give rise to retrieval orientations and the pre-probe associative retrieval effect.

Retrieval orientation has been investigated mostly in single-item retrieval. In an EEG study, Johnson and Rugg (2006) presented participants lists of words and pictures intermixed together at encoding. At retrieval, each retrieval probe was preceded by a preparatory cue signalling whether the upcoming item was a picture or a word. It was found that cue-elicited brain activity differed according to whether pictures or words were expected, in the form of positive ERPs that were greater for words than for pictures from around 500 ms following cue onset over lateral and anterior frontal scalp sites. Retrieval orientations have also been reported in response to other kinds of pre-probe cues, e.g., cues indicating whether spatial location or encoding operation is to be retrieved (e.g., Herron & Wilding, 2004; 2006). Across these studies, scalp distributions of the retrieval orientations are consistently found to be focused over frontal scalp sites.

Ranganath and colleagues conducted parallel EEG and fMRI studies to investigate the neural generators of retrieval orientations. In the initial EEG study (Ranganath & Paller, 1998), it was established that ERPs related to the retrieval of specific information (size change of objects) were more positive-going than those related to the retrieval of general information (old/new judgement irrespective of size change) at the left anterior frontal scalp sites. The same task procedures were used in the fMRI study (Ranganath, Johnson, & D'Esposito, 2000) and it was found that a region in the left anterior PFC was more active during the retrieval of specific information relative to the retrieval of general information. Thus, the frontal ERP retrieval orientations may reflect the engagement of PFC in control processes at retrieval to constrain and specify goal-related probe-processing. Even though no preparatory cue was used in these studies, it is possible that similar control processes operate upstream in response to preparatory cues.

The effect of age on such material-selective retrieval orientations has also been investigated (Morcom & Rugg, 2004). Older and younger adults studied words and pictures depicting objects in separate blocks, and were tested in an old/new recognition task with words as retrieval probes. Retrieval orientations to material types, as measured by contrasting ERPs elicited by correctly rejected new items, were found in both younger and older participants. The effect took the form of more positive-going ERPs for words than pictures, starting at around 300 ms after probe onset with a wide-spread scalp distribution. The effect was smaller and briefer in older adults relative to that in the young, although scalp distributions of the effects were statistically indistinguishable between the two age groups. Furthermore, the effect of age on retrieval orientation remained reliable when recognition performance was equated across groups by the manipulation of task difficulty. These findings suggest that older adults are less able to adapt their processing of retrieval probes according to different retrieval goals, even though the same neural mechanisms are recruited across age. It would be interesting to find out whether older adults are able to recruit such mechanisms for associative retrieval.

The aim of the present study was to investigate how pre-probe anticipatory brain activity varies with intermixed retrieval goals. It would also be interesting to see whether material-selective retrieval orientations emerge in an associative retrieval task in younger and older adults, and if so, how it may interact with the pre-probe associative retrieval effect as observed in the previous studies. Most importantly, it was to find out whether older adults are able to recruit the pre-probe retrieval effect when frequent switching between different retrieval goals is required. As described in the encoding section, in the present experiment participants learned picture pairs and word pairs in an incidental encoding task. Their memory was tested in an associative recognition test in which all studied pairs were presented as either intact or rearranged pairs, along with unstudied pairs. The critical contrast was between correctly identified intact pairs and intact pairs incorrectly classified as ‘rearranged’. Similar associative recognition tests have been widely used in associative memory research, but usually using only one type of material. Typical retrieval effects, including the left-parietal and the right-frontal ERP effects, have often been reported (e.g., Donaldson & Rugg, 1998). It was suggested that associative recognition involves largely overlapping, if not the same, neural activity as associative recall (Donaldson & Rugg, 1999).

#### *2.3.2.2 Methods*

Information about participants, stimuli, and experimental procedures has been reported in the previous chapter.

*ERP analyses*

Activity elicited by preparatory cues and retrieval probes was aligned separately to the onset of each event. Epochs of 2048 ms duration were extracted, starting from 100 ms before each event onset, and down-sampled to 125 Hz. For pre-probe activity, artifact rejections and ERP computation methods were the same as those in the first study. For post-probe activity, analyses were performed using the EEGLAB Toolbox (Delorme & Makeig, 2004) and the ERPLAB Toolbox (Lopex-Calderon & Luck, 2014) for Matlab. Methods for artifact rejections and ERP computation have been reported in the previous chapter.

*Pre-probe anticipatory activity*

Average ERPs were formed for cue-elicited activity related to subsequent associative hits and associative misses for words and pictures separately. In younger adults, the average numbers and ranges of artefact-free trials for associative hits and associative misses were respectively 38 (17-63) and 27 (15-48) for pictures and respectively 43 (22-67) and 24 (13-53) for words. In older adults, the average numbers and ranges of artefact-free trials for associative hits and associative misses were respectively 33 (16-59) and 32

(18-52) for pictures and respectively 37 (19-58) and 24 (16-40) for words. All participants had at least 16 artefact-free trials, except one younger participant had 15 associative miss trials for picture cues and another younger participant had 13 associative miss trials for word cues.

Mixed-model ANOVAs were performed including 24 electrodes as used in the previous studies. The 24 electrodes were subjected to ANOVAs with factors of anteriority (anterior/posterior), and site (12 positions), in addition to the experimental factors of group (older/younger), material (word/picture), and response (associative hit/subsequent miss). In line with previous studies, ERPs were quantified in 2 continuous time intervals: 200-1100 ms and 1100-1948 ms. An initial mixed-model ANOVA was conducted incorporating the factors of interval along with all other factors. Significant interactions including latency and memory would suggest that pre-probe activity varied across intervals, and therefore warrant separate ANOVAs for each latency. The effects of interest were those involving the factor of response and the factor of material. Significant interactions involving these factors were followed up with subsidiary within-subject ANOVAs to further elucidate those effects.

Similar to prestimulus ERPs at encoding, in younger adults there appeared to be a positive deflection that peaked at around 160-170 ms, larger following word cues than picture cues (Figure 21). Additional analyses were performed to evaluate this early material-specific difference. Mean amplitudes in younger adults were measured between 140–180 ms for picture cues and word cues separately irrespective of memory performance using all 37 electrode sites. A within-subject ANOVA was conducted including factors of material, hemisphere, location, and site.

In addition, previous studies are inconsistent in whether retrieval orientation effects emerge on stay and switch trials (e.g., Herron & Wilding, 2004; 2006). Whether the effects emerge when switching between retrieval goals is required, or when the same goal is maintained across trials may shed some light on the nature of the effects. Therefore, trials were sorted according to whether they are stay or switch, and average ERPs were formed for stay trials and switch trials across associative hits and associative misses, separately for words and pictures. In younger adults, the average numbers and ranges of artefact-free trials for stay and switch trials were respectively 32 (18-42) and 33 (21-42) for pictures and respectively 33 (22-41) and 34 (26-40) for words. In older adults, they were respectively 33 (21-47) and 32 (18-41) for pictures and respectively 30 (19-41) and 31 (24-38) for words. To determine whether pre-probe material-selective effects differ on stay and switch trials, mixed-model ANOVAs were performed incorporating factors of group, material, trial type (stay/switch), anteriority, and site for each interval during which significant material-selective anticipatory effects were found. Significant effects involving trial types were followed up with subsidiary ANOVAs conducted for stay and switch trials separately. In line with the previous studies, significant differences in topography were verified using ANOVAs conducted on scaled data, and the Greenhouse-Geisser correction for nonsphericity was used when appropriate for all analyses, as indicated by the adjusted degrees of freedom.

### *Post-probe associative retrieval-related activity*

Averaged ERPs were formed for item-elicited activity related to subsequent associative hits and associative misses for words and pictures separately. In younger adults, the average numbers and ranges of artefact-free trials for associative hits and associative misses were respectively 41 (22-65) and 29 (17-49) for pictures and respectively 48 (23-68) and 25 (16-54) for words. In older adults, the average numbers and ranges of artefact-free trials for associative hits and associative misses were respectively 35 (19-62) and 35 (14-53) for pictures and respectively 41 (14-59) and 27 (13-46) for words. Note that only one older participant contributed fewer than 16 artefact-free trials for associative misses for pictures and associative hits and misses for words due to excessive eye-movements.

In line with the previous study, statistical analyses were conducted including 28 electrodes partitioned into 4 quadrants. ERPs were quantified using 4 latency intervals: 300-500 ms, 500-800 ms, 800-1200 ms, 1200-1940 ms. Unlike the first study, these latency intervals were selected on the basis of data from younger adults, as ERP waveforms (Figure 23) showed that there was very little associative retrieval effect in older adults. Using younger adults, previous studies have found associative recognition effects in these intervals (e.g., Donaldson & Rugg, 1998; Tibon, Gronau, Scheuplein, Mecklinger, & Levy, 2014). To first determine whether associative recognition effects emerge in younger adults and whether the effects differ across the intervals, an initial within-subject ANOVA was conducted on data from younger adults incorporating the factors of interval (4 intervals), material (word/picture), response (associative hit/subsequent miss), hemisphere (left/right), anteriority (anterior/posterior), and site (7 positions). Significant interactions including latency and response would suggest that the effects varied across intervals, and mixed-model ANOVAs including the factors of group, material, response, hemisphere, anteriority, and site would be performed for each latency region to see whether the effects differ across age groups. The effects of interest were those involving the factor of response (i.e., associative recognition effects).

Significant interactions involving this factor were followed up with subsidiary ANOVAs to further elucidate the effects.

Analyses of scalp distribution were performed using the same method as reported in the first study. Significant differences between the topographies of different conditions were verified by ANOVAs conducted on the scaled data. The Greenhouse-Geisser correction for nonsphericity was used when appropriate.

### ***2.3.2.3 Results***

Behavioural results are reported in the previous chapter.

*ERPs*

*Pre-probe anticipatory activity*

As statistical analyses (see the next paragraph) revealed no significant memory effect, grand-average ERPs elicited by preparatory cues were formed for word cues and picture cues combining across associative hits and associative misses (see Appendix for ERPs separated for associative hits and associative misses). Figure 21 illustrates the ERP waveforms at 2 electrode sites representing the two materials in younger and older adults respectively. In younger adults, ERPs were more positive-going when words were the retrieval targets. Similar to prestimulus encoding ERPs, there was an early peak for word cues between around 140-200 ms after cue onset. This was followed by a sustained positivity over frontal scalp sites. In older adults, there was a sustained frontal positivity for word cues from around 200 ms, similar to that in the young. This effect changed polarity over posterior scalp sites.

An initial mixed-model ANOVA incorporating the factor of interval revealed a significant group × interval × response × material × anteriority × site

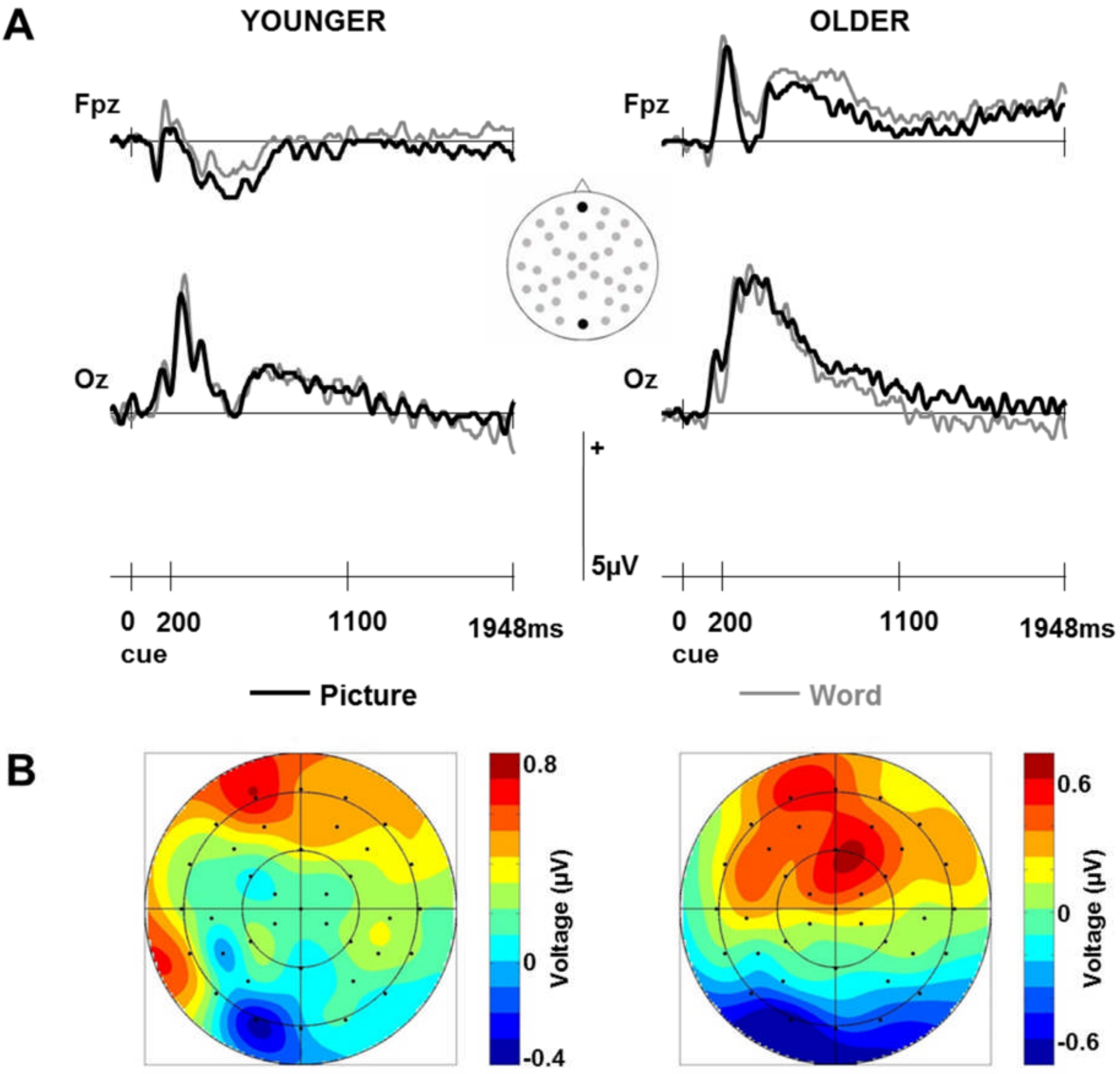


**Figure 21. Material-specific pre-probe brain activity. (A) Grand-average ERPs of the two groups elicited by retrieval cues signalling whether the upcoming item pairs were pictures or words. The insert indicates the locations of the 2 electrodes (site 35 and 43 from Montage 10; www.easycap.de/easycap/e/electrodes/13_M10.htm; equivalent to site Fpz and Oz of the 10-20 system). (B) Voltage spline maps for younger and older adults showing the distribution of the difference in cue-elicited activity between materials (word–picture) in the 200-1940 ms interval. The maps are range scaled.**

interaction (*F*(4.9,226.4) = 2.55, *p* = .029), which did not survive data scaling: *F*(4.9,227.6) = 1.94, *p* = .090), indicating no significant difference in pre-probe activity between the 2 intervals. Thus, the 2 intervals were combined for further analyses. For the 200-1948 ms interval, there was a significant material ×

anteriority interaction (*F*(1,46) = 6.46, *p* = .014), reflecting that ERPs elicited by word cues were more positive-going than those elicited by picture cues over anterior (0.50 µV) but not posterior sites (-0.01 µV). This material-related effect was not modulated by subsequent memory or age group.

Additional analyses were conducted to evaluate the early difference between the 2 types of cues in younger adults as reflected in the positive peak following word cues at 140-180 ms. Within-subject ANOVAs revealed no significant effect involving material (*F*s < 1.64, *p*s > .21).

As response bias also varied as a function of material type, it is possible that the pre-probe material-selective ERP effect reflects the setting and maintenance of more stringent response criteria for pictures. Therefore, correlation analyses were performed to assess the relationships between the ERP effect and Br for pictures in younger and older adults. The material-dependent ERP effect was quantified as the mean amplitude difference between ERPs elicited by word cues and by picture cues (word - picture) over the 12 anterior sites at 200-1940 ms after cue onset. Pearson correlation coefficient tests revealed no significant correlation between the ERP effect and Br for pictures in either younger (*r* = -.37, *p* = .073) or older (*r* = .11, *p* = .60) adults.

To compare stay and switch trials (Figure 22), mixed-model ANOVAs were conducted over the 200-1948 ms interval. There was a significant material × anteriority interaction (*F*(1,46) = 5.36, *p* = .025), reflecting that ERPs elicited by word cues were more positive-going than those elicited by picture cues over anterior sites (0.42 µV) but not posterior sites (-.08 µV). This material-related effect was not modulated by either trial type or group.

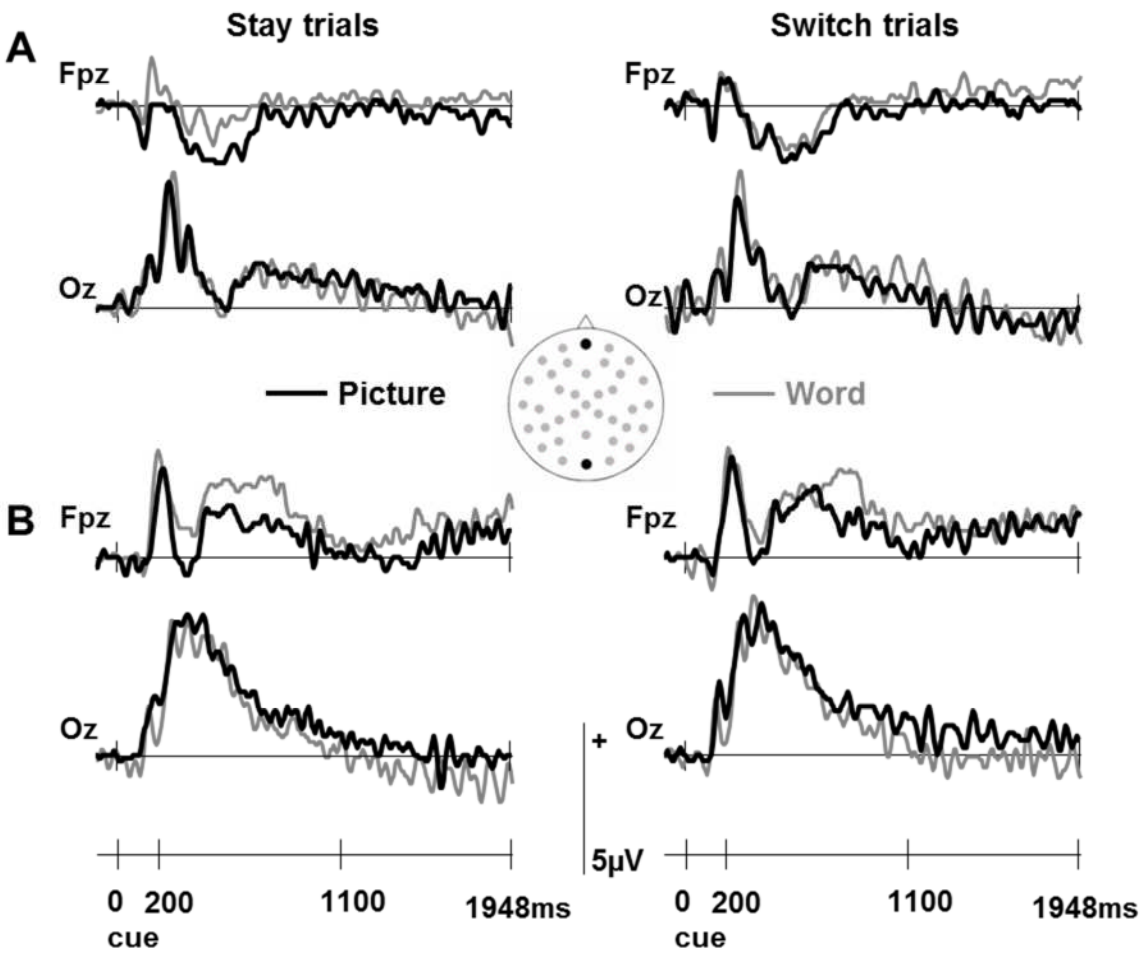


**Figure 22. Grand-average ERPs elicited by picture cues and word cues separated for stay and switch trials in (A) younger adults and (B) older adults. The insert indicates the locations of the 2 representative electrodes (site 35 and 43 from Montage 10; www.easycap.de/easycap/e/electrodes/13_M10.htm; equivalent to site Fpz and Oz of the 10-20 system).**

### *Post-probe associative retrieval effects*

Grand-average ERPs elicited by picture pairs and word pairs were formed for associative hits and associative misses separately for younger and older adults (Figure 23). In younger adults, for both pictures and words, waveforms for associative hits were more positive-going than those for associative misses, starting at around 300 ms for words and around 500 ms for pictures. These positive shifts were temporally sustained and spatially widespread, becoming more right-lateralised, especially over right frontal scalp sites from around 1200 ms after probe onset. The size of this right-lateralised positivity appears to be larger for words than pictures. For older adults, there was a small positive-going effect over frontal sites from around 400 ms after probe onset, more right-lateralised for words than pictures. There was also a sustained small negative-going effect over left-lateralised scalp sites, mostly for words.

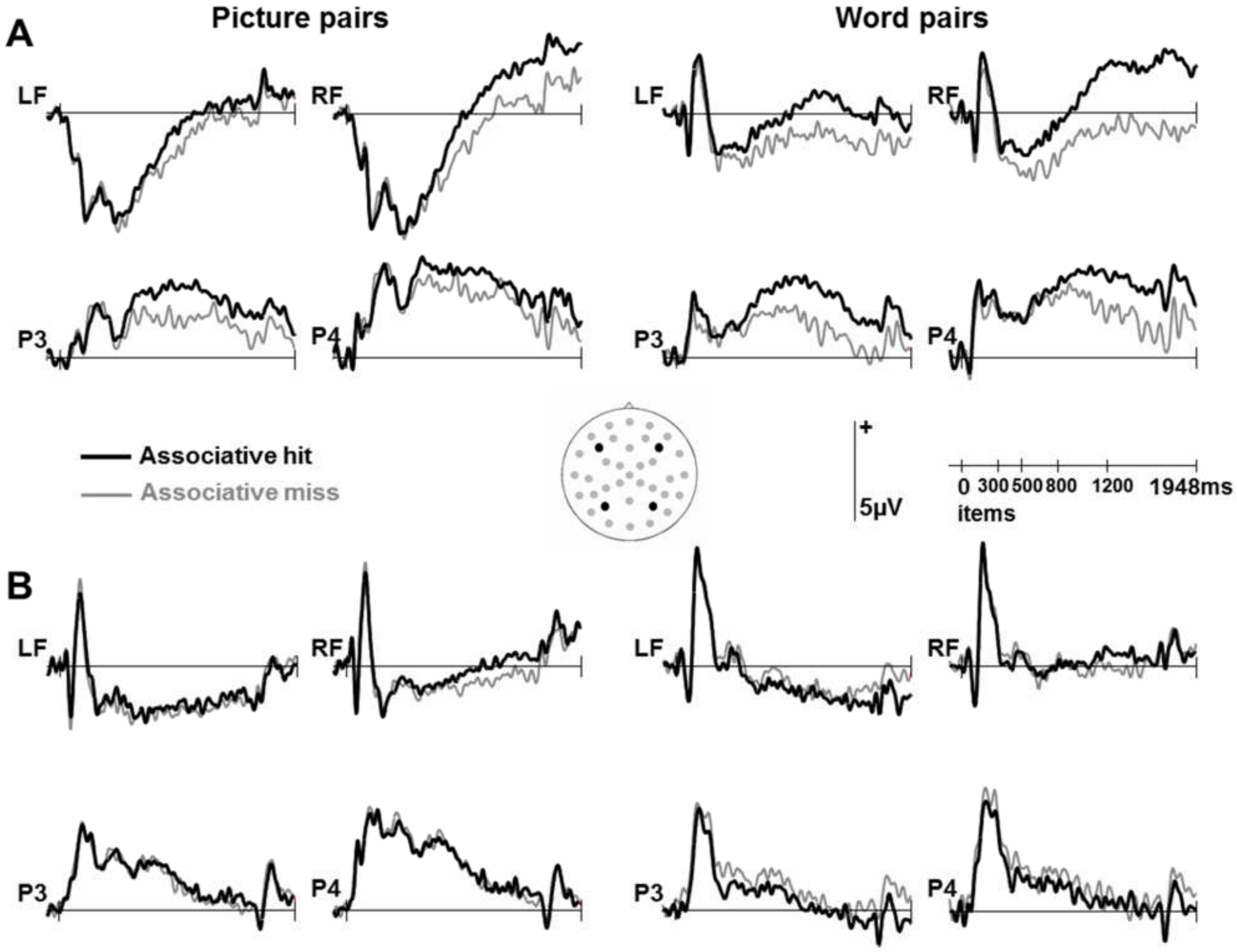


**Figure 23. Grand-average ERPs elicited by picture pairs and word pairs according to whether they were related to subsequent associative hits or associative misses in (A) younger adults and (B) older adults. The insert shows the locations of the 4 representative electrodes including (site 33, 22, 29, 26 from Montage 10; www.easycap.de/easycap/e/electrodes/13_M10.htm; equivalent to site LF, RF, P3, and P4 of the 10-20 system).**

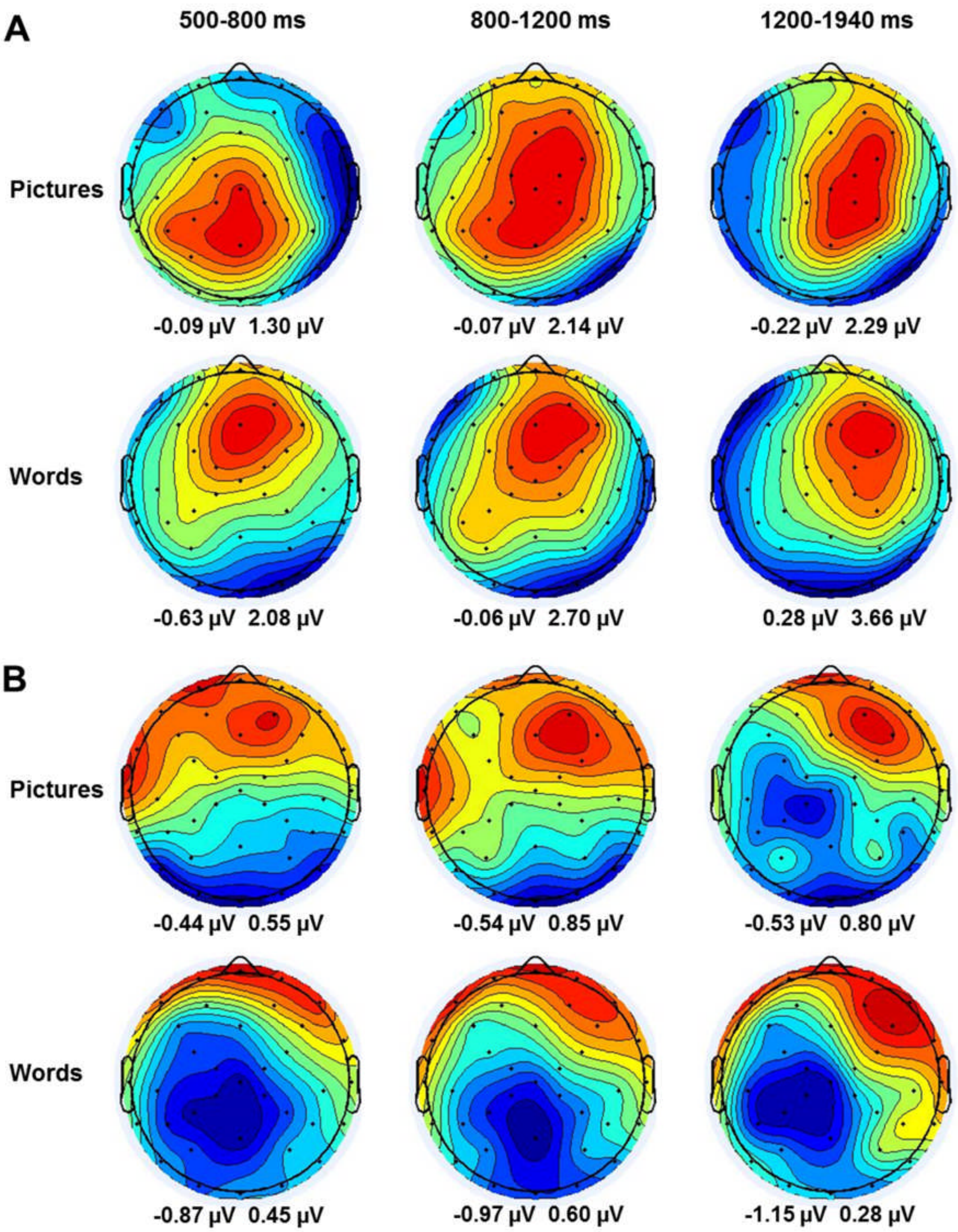


**Figure 24. Voltage spline maps for younger (A) and older (B) adults showing the distribution of associative retrieval effects (associative hits – associative misses) separately for pictures and words in each of the 3 intervals when the effects were reliable. The maps are range scaled with the minimum and maximum values shown.**

Initial within-subject ANOVAs conducted on data from younger adults including time intervals revealed that between the 1st and 2nd intervals, there was a significant response × interval interaction (F(1, 23) = 14.64, p = .001) and a response × interval × anteriority × hemisphere interaction (F(1, 23) = 6.67, p = .017) that did not survive after data scaling (F(1, 23) = 0.10, p = .759). Between the 2nd and the 3rd intervals, there were significant interactions of response × interval (F(1, 23) = 12.08, p = .002) and response × interval × anteriority × hemisphere (F(1, 23) = 8.67, p = .007; after data scaling: F(1, 23) = 8.09, p = .009). Between the 3rd and the 4th intervals, there was a significant interaction of response × interval × hemisphere (F(1, 23) = 32.96, p < .001; after data scaling: *F*(1, 23) = 24.46, *p* < .001). Subsequent mixed-model ANOVAs were conducted for each interval separately. Significant results are presented in Table 10.

**Table 10. Significant ANOVA results for the post-probe EPR associative retrieval effects.**

| Time Interval | Condition | Effect | df | F | p |
|---|---|---|---|---|---|
| 300-500 ms | Overall | RS × AP | 1, 46 | 6.75 | .013 |
| 500-800 ms | Overall | RS | 1, 46 | 4.15 | .048 |
| | | RS × GP | 1, 46 | 8.04 | .007 |
| | | RS × AP | 1, 46 | 4.40 | .042 |
| | | RS × AP × HM | 1, 46 | 5.59 | .022 |
| | Younger | RS | 1, 23 | 10.43 | .004 |
| | | RS × AP × HM | 1, 23 | 6.51 | .018 |
| 800-1200 ms | Overall | RS | 1, 46 | 14.99 | <.001 |
| | | RS × GP | 1, 46 | 13.51 | .001 |
| | | RS × AP* | 1, 46 | 4.11 | .049 |
| | | RS × AP × HM | 1, 46 | 15.71 | <.001 |
| | Younger | RS | 1, 23 | 24.27 | <.001 |
| | | RS × AP × HM | 1, 23 | 13.67 | .001 |
| | Older | RS × AP | 1, 23 | 6.43 | .019 |
| 1200-1940 ms | Overall | RS | 1, 46 | 7.65 | .008 |
| | | RS × GP | 1, 46 | 13.51 | .001 |
| | | RS × GP × CC | 1, 46 | 5.30 | .026 |
| | | RS × HM | 1, 46 | 17.86 | <.001 |
| | | RS × AP × HM | 1, 46 | 10.88 | .002 |
| | Younger | RS | 1, 23 | 19.89 | <.001 |
| | | RS × HM | 1, 23 | 13.36 | .001 |
| | | RS × AP × HM | 1, 23 | 10.32 | .004 |
| | Older | RS × HM | 1, 23 | 4.82 | .039 |

Note: no other effect of interest was significant (all F < 2.8, all p > .11)
RS = response; GP = group; HM = hemisphere; AP = anterior/posterior; CC = material

In the 500-800 ms interval, the main effect of response reflected that waveforms for associative hits were more positive-going than those for associative misses (0.29 µV). The response × group interaction reflected that the positive associative retrieval effect was shown in younger adults (0.70 µV) but not older adults (-0.12 µV).

In the 800-1200 ms interval, the main effect of response reflected a positive-going associative retrieval effect (0.72 µV), and the response × group interaction reflected that this positive associative memory effect was larger in younger adults (1.40 µV) than older adults (0.04 µV). In younger adults, subsidiary analyses following up the response × anteriority × hemisphere interaction revealed main effects of response over both anterior sites ($F(1, 23) = 23.25$, $p < .001$) and posterior sites ($F(1, 23) = 14.52$, $p = .001$), as well as a response × hemisphere interaction over posterior sites ($F(1, 23) = 5.33$, $p = .030$), reflecting a positive-going associative memory effect over frontal and left-posterior sites across materials. In the older group, the response × anteriority reflected that the associative memory effect was positive-going over anterior sites (0.29 µV) but negative-going over posterior sites (-0.21 µV). Subsidiary analyses revealed no significant associative memory effect over either anterior or posterior sites (Fs < .10, *p*s > .24).

In the 1200-1940 ms interval, the main effect of response reflected a positive-going associative retrieval effect (0.65 µV), and the response × group interaction reflected that this positive associative memory effect was evident in younger adults (1.46 µV) but not older adults (-0.16 µV). In younger adults, subsidiary within-subject ANOVAs revealed main effects of response over both anterior sites ($F(1, 23) = 21.65$, $p < .001$) and posterior sites ($F(1, 23) = 11.10$, *p*

= .003), as well as a response × hemisphere interaction over anterior sites (*F*(1, 23) = 26.79, *p* < .001), reflecting a positive-going associative memory effect over right-frontal and posterior sites across materials. In older adults, the response × hemisphere interaction reflected that associative memory effect was more negative-going over left-hemisphere (-0.31 µV) than right-hemisphere scalp sites (-0.01 µV). Subsidiary within-subject ANOVAs conducted on data from each hemisphere separately revealed a significant response × anteriority interaction over right-hemisphere scalp sites only (*F*(1, 23) = 4.58, *p* = .043), reflecting that the associative memory effect was positive-going over right-anterior sites (0.26 µV) but negative-going over right-posterior sites (-0.27 µV). Thus, in older adults there was a positive-going right-frontal effect and a negative-going effect over posterior and left-frontal sites.

#### *2.3.2.4 Discussion*

The present experiment aimed to investigate how pre-probe anticipatory brain activity varies with retrieval materials in associative memory across age. The results show that when target materials vary unpredictably on a trial-by-trial basis, material-selective retrieval orientations emerge for associative retrieval, and the effects are indistinguishable between younger and older adults. However, no pre-probe associative retrieval effect was observed in either age group.

Compared to the first study, the proportion of associative hits in the present study increased in older adults (0.35 in the first study, 0.50 for words and 0.43 for pictures in the present study) but not in younger adults (0.60 in the first study, 0.61 for words and 0.52 for pictures in the present study). The improvement in associative memory in older adults is consistent with the notion that older adults are less impaired in recognition tests relative to recall tests, possibly as a result of additional ‘environment support’, i.e., more informative retrieval probes in a recognition test (Craik & Rose, 2011).

With the present associative recognition paradigm, it was thought that correct associative recognition decisions cannot be based upon familiarity of individual items, as all items consisting intact and rearranged pairs are old studied items. However, relative to younger adults, older adults made more ‘rearranged’ responses, including both associative misses and false alarms, i.e., falsely categorising rearranged pairs as ‘intact’ (21% for pictures and 22% for words in older adults; 14 % for pictures and 18% for words in younger adults). Such performance patterns suggest that older adults preferentially employed familiarity-based item retrieval over more effortful recollection processing. In contrast, younger adults spontaneously engage in recollection processing that involves the elaboration of recognition probes to reinstate encoding processing (Jacoby, Shimizu, Velanova, & Rhodes, 2005). Using an associative recognition task similar to the present study, Light and colleagues (2004) provided further support to such age-related changes in associative recognition. In that study, the strength of memory was manipulated by repeating some of the word pairs at encoding. It was found that strengthening word pairs reduced, or had no effect, on false alarms in younger adults, but increased FA in older adults. These findings indicate a shift from recollection-based to familiarity-based recognition processing in ageing. Such a shift in older adults may be due to associative deficits (Naveh-Benjamin, 2000) or the failure to engage in recollection-based retrieval strategies, i.e., recall-to-reject strategy (Light et al., 2004).

*Pre-probe anticipatory brain activity*

In the present study, a pre-probe material-selective ERP effect emerges in the associative retrieval task, in the form of more positive-going ERPs for word cues than for picture cues over frontal scalp sites. This effect is similar in both polarity and scalp distribution to those reported in previous studies for single item retrieval (Johnson & Rugg, 2006; Morcom & Rugg, 2004), which have been interpreted as the setting up and maintenance of retrieval sets for the recovery of goal-related information. The similarity between these retrieval orientations suggests that similar material-selective anticipatory neural mechanisms may be recruited for both item retrieval and associative retrieval.

As response biases also vary with material type, the possibility arises that retrieval orientation, i.e., the pre-probe material-selective ERP effect, is merely a side effect of response bias. For example, it may be that the ERP effect reflects the setting and maintenance of a more stringent response bias for pictures. However, as the ERP effect is uncorrelated with response bias, this interpretation seems unlikely. Similarly, the ERP effect is unlikely to reflect across-material RT differences as such RT differences occurred only in older adults but not in younger adults.

In the Johnson and Rugg (2006) study, preparatory cue-elicited retrieval orientations only emerged on switch trials but not stay trials. The authors interpreted the effects as representing either an initial task set reconfiguration or a selective pre-activation of memory representations for the targeted information when the target changes. In the present study, however, the pre-probe material-selective effects were indistinguishable between stay and switch trials, suggesting that effects cannot merely reflect an initial task set reconfiguration. Thus, the present effect may represent the pre-activation of material-selective memory representations, which is set up anew in response to each preparatory cue.

An interesting observation is that the present effect is similar in timing, polarity, and scalp distribution to the prestimulus material-selective effect for encoding. It is possible that the same anticipatory neural mechanisms are engaged at encoding and retrieval. Both of these activities may reflect the pre-activation of material-selective neural networks that optimise the processing of the upcoming stimuli. If so, however, it is surprising that the age difference is only observed at encoding and not retrieval. In a previous study (Morcom & Rugg, 2004), material-selective retrieval orientation was found to be significantly smaller and briefer in older adults compared to younger adults. This age-related difference is consistent with that observed at encoding in the present investigation. In contrast, the present pre-probe material-selective effect at retrieval is age-invariant. Thus, it appears that older adults are able to recruit such anticipatory neural mechanisms to a greater extent at retrieval than at encoding, and also to a greater extent for associative retrieval than for item retrieval. It is not clear how to reconcile the discrepancies across studies and across encoding and retrieval. It is possible that older adults are generally impaired in anticipatory processing, but they are able to recruit such neural mechanisms under certain conditions, such as during the retrieval of associative information. Such an interpretation implies a preference of older adults to prioritise associative retrieval over item retrieval, and retrieval over encoding. Further investigation is needed to test this hypothesis.

In the present study, there was no pre-probe associative retrieval effect as observed in the previous studies. This may be related to higher levels of associative memory performance, as compared to the occasions when pre-probe retrieval effects were found, i.e., in older adults in the first study and younger adults in the second study. If this is the case, it would support the hypothesis that pre-probe associative retrieval effects reflect compensatory mechanisms for poor memory. However, as experimental procedures were not identical across the studies, other possible explanations must be considered. One possibility is that frequent switching between retrieval goals hinders the employment of anticipatory retrieval-related activity. With consistent retrieval goals, participants are able to maintain the same cognitive operations across successive trials. In contrast, when retrieval materials vary unpredictably from trial to trial, participants have to process preparatory cues and prepare for the retrieval of different materials accordingly, both of which are resource demanding. As a consequence, switching between retrieval targets leads to a reduction of processing resources in the cue-probe interval. Reducing processing resource has been shown to negatively affect the engagement of anticipatory encoding-related brain activity (Galli & Otten, 2013). Similarly, pre-probe retrieval effects may also be affected by a reduction of processing resources when frequent switching of retrieval goals is needed. If this is the case, it may be expected that when the same retrieval goal is maintained across trials, i.e., stay trials, pre-probe retrieval effects will emerge. However, in the present study it is not possible to contrast associative hits and associative misses separately for stay trials and switch trials due to insufficient trial numbers. Also, even stay trials are not the same as a blocked design, as there is always a risk that the retrieval goal will change.

An alternative explanation is that merely pre-specifying material type is not enough to elicit anticipatory associative retrieval effects. In the previous study, the retrieval targets were words in a specific category, i.e., locations. It may be that the level of retrieval target specificity is crucial for the engagement of pre-probe retrieval-related activity. That is, retrieval can be enhanced by pre-probe neural activity only when specific target information is pre-specified. This hypothesis has not been systematically investigated, but some clues can be taken from a pilot study (not reported in this thesis) conducted in preparation for the second experiment. The experimental procedures in the pilot study were identical to those in the second experiment, except that each item pair in the pilot study consisted of two object words, one served as retrieval probe and the other one as target. These objects words depicted a wide variety of object categories, including living and non-living objects. In the pilot study there was no hint of any pre-probe associative effect as observed in the second experiment. As the only difference between the two studies is the retrieval target, this finding may suggest that pre-probe associative retrieval effects only emerge when the targets belong to a more specific category, i.e., locations, but not when they belong to a general category such as objects. Further research is needed to test this hypothesis as the pilot study is only preliminary with data from only five subjects.

It is presently not clear which factor, the level of associative memory, the frequent switching between retrieval goals, or the lack of specificity of the to-be-retrieved target information, hindered the emergence of the pre-probe associative retrieval effect. Nevertheless, the sensitivity of such effects to such factors strongly suggests that anticipatory retrieval-related activity is subjected to top-down control processes.

### *Post-probe associative recognition effects*

In younger adults, a spatially wide-spread positive-going associative retrieval effect was present from 500 ms after probe onset. Unlike in the previous two studies, there is no reliable associative retrieval effect in the 300-500 ms time window. Compared to the previous studies, a major difference in the present retrieval procedures is that item pairs, but not single items, were used as retrieval probes. Item pairs should take longer to process than single items, which may have delayed associative retrieval processing. The timing of the effects is also consistent with findings from other associative recognition studies (Bader, Mecklinger, Hoppstädter, & Meyer, 2010; Donaldson & Rugg, 1998; 1999; Tibon et al., 2014).  For semantically unrelated word and picture pairs, associative retrieval effects do not emerge until around 500-600 ms after probe onset using (Donaldson & Rugg, 1998; 1999; Tibon et al., 2014), unless the paired items are unitized (i.e., integrated into a new concept) at encoding (Bader et al., 2010). Thus, the lack of associative retrieval effect at 300-500 ms, often taken as an indication of familiarity, may be explained by the processing of two unrelated items presented simultaneously as retrieval probes.

Significant differences in scalp distribution between associative hits and associative misses emerged from around 800 ms. The left-parietal effect was evident in the 800-1200 ms interval, along with a bilateral frontal effect. Compared to the previous studies, effects in this latency interval appear to have a more anterior distribution. More anteriorly focused retrieval effects have often been reported when pictures are the targets of retrieval, relative to words (e.g., Galli & Otten, 2010; MacKenzie & Donaldson, 2009; Yick & Wilding, 2008). For example, MacKenzie and Donaldson (2009) reported a typical left-parietal effect at 500–700 ms post-probe for words but a different effect over anterior scalp sites for faces. Similarly, it was also reported that left-parietal old/new effects extended more anteriorly for objects and faces than those for words (Galli & Otten, 2010; Yick & Wilding, 2008). A more recent ERP study (Yick & Wilding, 2014) has extended this finding to show that while the left-parietal effect is a material-independent index of recollection, the anterior effect is associated with recollection of details of visual (facial) features. Taken together, these studies suggest that the effect over anterior sites may be associated with the recollection of perceptual details of pictures. In the present study, scalp distributions of the associative retrieval effects are similar across both pictures and words. As discussed earlier for the SMEs, similar processes across materials may be related to the use of visual imagery strategies in the present study. Using these strategies, word pairs are also encoded with rich visual details. According to the transfer-appropriate processing principles (Morris, Bransford, & Franks, 1977), the retrieval of these word pairs should involve a reinstatement of perceptual processes engaged during encoding.

From 1200 ms, there was a right-frontal effect that extends into posterior scalp regions. The associative retrieval effects found in the present study closely resemble those reported in Donaldson and Rugg (1999) using a similar associative recognition task for word pairs only. In that study, similar ERP effects were found for both recognition and recall of associative information, including a sustained left-parietal effect and a late right-frontal effect. The authors proposed that recognition and recall of associative information engage overlapping neural activity. Consistent with this proposal, the present study also revealed sustained positive-going effects in younger adults, including the left-parietal and the right-frontal effects, which are similar to those found in the previous studies. These findings suggest that younger adults are able to use associative recall strategies spontaneously for associative recognition.

In older adults, however, associative retrieval effects were much smaller in the present study relative to those in the first study. This may reflect the difference between associative recognition and associative recall in ageing. As discussed earlier, in an associative recognition task older adults may rely on more familiarity-based item processing than effortful recollection of associative information. As a consequence, neural activity related to associative hits does not vary a great deal from that related to associative misses.

Despite the smaller size, a frontal positivity and a posterior negativity emerged in the 800-1200 ms time window and later developed into a left-lateralised negativity and a right-frontal positivity. Visual inspection of the ERPs (Figure 23) suggests that there is also a hint of the left-lateralised negativity in an earlier time window, particularly in the retrieval of words. This finding indicates that older adults might have engaged neural activity underlying the left-lateralised negativity to a lesser extent in the recognition, relative to the recall of associative information. As discussed earlier in the Introduction chapter, the left-lateralised negativity in associative retrieval is likely to reflect a goal-directed search for the target information, probably via top-down executive control mechanisms. Thus, this finding suggests that older adults are less inclined to engage in controlled search processing in associative recognition, consistent with the behavioural findings.

In addition, a right-frontal effect emerged in the present study, which was not observed in the first study. The right-frontal effect is thought to reflect post-retrieval monitoring, the emergence of which depends on task demands for such post-retrieval verification or monitoring (Rugg et al., 2000). Thus, older adults may have recruited post-retrieval mechanisms in the service of correct associative recognition decisions, possibly because of the greater needs for such operations as a consequence of familiarity-based retrieval processing.

In conclusion, when target materials vary unpredictably across retrieval trials, both younger and older adults engage in pre-probe material-selective retrieval orientations in associative retrieval. Unlike that during encoding, no age deficit was observed in such material-selective anticipatory activity during retrieval. There may be a number of explanations for the lack of pre-probe associative retrieval effect in the present study, but it is clear that anticipatory retrieval-related activity is subjected to top-down control processes. For post-probe associative retrieval, different neural mechanisms are recruited by younger and older adults. In younger adults, associative recognition memory shares much of the recollective processes engaged in associative recall, indicating the spontaneous use of associative recollective strategies. In contrast, older adults may have relied more upon familiarity-based processing in associative recognition relative to associative recall.

# Chapter 3: Time-frequency analyses

## 3.1 Experiment 1: Does anticipatory memory-related activity vary with age?

### 3.1.1 Introduction: Review of theta and alpha activity in episodic memory processing

Oscillatory brain activity is a hallmark of neuronal network function, and it has a fundamental role in cognitive processing (Varela, Lachaux, Rodriguez, & Martinerie, 2001; Buzsáki, Anastassiou & Koch, 2012). Electrophysiological characteristics of normal ageing, particularly during cognitive processing, have not been extensively investigated. Resting state EEG has been found to change in ageing, with a pronounced decrease in alpha (8-12 Hz) amplitude and increases in theta (4-8 Hz) and delta (2–4 Hz) activity (see Klimesch, 1999; Rossini, Rossi, Babiloni, & Polich, 2007 for reviews). A resting eye-closed EEG study using a large sample of healthy adults (N = 215, 18–85 years) also showed an age-related amplitude decrement of alpha in parietal, occipital, and temporal scalp regions, but a decrease of occipital delta oscillations with age (Babiloni et al., 2006). Thus, it is generally agreed that alpha activity decreases with age but the pattern of theta modulations is less clear.

Slow frequency oscillations are thought to be important for content-specific representation during perception and episodic memory (Watrous, Fell, Ekstrom, & Axmacher, 2015). Neural oscillations in alpha and theta frequencies are most often associated with memory performance (Klimesch, 1999). In particular, theta oscillations are thought to be crucial for episodic memory formation and retrieval. It provides a mechanism for binding individual memory representations into coherent episodes and the reinstatement of memory representations during later retrieval, as well as top-down control mechanisms to modulate these encoding and retrieval processes (Nyhus & Curran, 2010). Alpha is traditionally related to brain state, with alpha decrease indicating an active brain state (Klimesch, 1997). In memory, alpha activity has been related to semantic processing (Klimesch, 1999) and WM rehearsal (Meeuwissen, Takashima, Fernandez, & Jensen, 2011). To better understand the functional roles of theta and alpha oscillations in relation to episodic encoding and retrieval, relevant previous studies will be reviewed in the following section.

#### ***3.1.1.1 Theta and alpha activity in episodic encoding***

Previous research has shown that theta oscillations increase whereas alpha and beta oscillations decrease in amplitude with cognitive effort (see Sauseng & Klimesch, 2008 for reviews). In memory encoding, a number of scalp EEG studies have reported SMEs in alpha and theta frequency bands (see Hanslmayr & Staudigl, 2014; Klimesch, 1997, 1999 for reviews). Theta SMEs often manifested as power increases during encoding for items that are subsequently recollected (see Hsieh & Ranganath, 2013; Klimesch, 1999; Nyhus & Curran, 2010 for reviews). Convergent evidence from an iEEG study also found that theta power increases in the right temporal and frontal cortex during encoding predict successful free recall (Sederberg et al., 2003). As described in the Introduction chapter, studies have shown that theta power increases may reflect item-context binding that facilitate episodic memory (Staudigl & Hanslmayr, 2013; Summerfield & Mangels, 2005).

Alpha and theta activity may reflect different kinds of encoding processing. Alpha oscillations are often related to semantic memory because alpha desynchronisations consistently occur with the presentation of semantically related items (e.g., Klimesch, 1997, 1999; Klimesch, Freunberger, Sauseng, & Gruber, 2008; Klimesch et al., 2004; Vogt, Klimesch, & Doppelmayr, 1998). Important evidence for functional dissociation between theta and alpha frequencies is also present. For example, when semantic (living/non-living) encoding and non-semantic (alphabetical) encoding are contrasted (Hanslmayr, Spitzer & Bäuml, 2009), theta power increases were specific to successful non-semantic encoding, whereas alpha power decreases were mostly found in semantic encoding, albeit also in non-semantic encoding but at a different time interval. Similar patterns of alpha/theta dissociation were also reported by Klimesch (1999), with theta power increased only in episodic encoding, whereas the largest alpha effect was found in semantic encoding. Thus, it was suggested that theta increase reflects stronger item-context binding, and alpha decrease reflects semantic processing that occurs earlier in semantic encoding (500-1000 ms) than non-semantic encoding (1000-1500 ms) (Hanslmayr et al., 2009). However, an inherent confound in such semantic vs. non-semantic (shallow) encoding comparisons is that semantic encoding is more effective than non-semantic encoding, as reflected in significantly better retrieval performance. A later study (Fellner, Bäuml, & Hanslmayr, 2013) contrasted semantic encoding to a more efficient encoding strategy (survival relevancy judgements), and showed that alpha/beta power decreases specifically predicted successful encoding in semantic but not survival conditions. These findings suggest that the alpha decreases are unlikely to reflect the efficiency of encoding, but are indeed more specific to semantic processing. Although survival judgements also require semantic processing, they mostly rely on other kinds of processing that manifested as increased long range synchronization in alpha and beta oscillations, which are thought to indicate increased communication between distant cortical regions.

Further support for the functional dissociation of theta and alpha/beta activity in memory encoding came from a simultaneous EEG-fMRI study (Hanslmayr et al., 2011). Using a free recall test for words learned during encoding, the authors found a theta increase and a beta (adjacent to alpha) decrease (alpha decrease was also found but was not significant) that predicted subsequent recall. In fMRI, stronger BOLD signals in the left inferior prefrontal cortex and the right parahippocampal gyrus predicted subsequent recall. Consistent with the fMRI results, EEG source localisation indicated that the beta SME and the theta SME could be localised to the left inferior frontal gyrus (IFG) and MTL regions respectively. In addition, beta power decrease was significantly correlated with BOLD signal increase in the left IFG on a trial-by-trial basis, particularly in trials in which items were successfully recalled. As left IFG activation is often related to semantic processing (e.g., Gabrieli, Poldrack, & Desmond, 1998; Otten & Rugg, 2001), the authors argued that alpha/beta SMEs reflect semantic processing at encoding. The lack of significant correlation between the theta SME and BOLD signal in the MTL may be due to the use of single word learning that is not best suited to activate the MTL, especially the hippocampus, which is more strongly activated for associative memory (Kim, 2011).

It may be inferred from the abovementioned studies that alpha decreases and theta increases are oscillatory features of memory formation. However, alpha power increases have also been associated with successful memory encoding in an MEG (Meeuwissen et al., 2011) and an EEG (Khader et al.,

2010) study. Both of these studies used a WM task and investigated whether alpha power during a rehearsal period predicted later LTM retrieval. During WM rehearsal, alpha power usually increases with WM load (Klimesch et al., 1999), possibly reflecting a de-activation of task irrelevant neural regions (Jensen, Gelfand, Kounios, & Lisman, 2002; Meeuwissen et al., 2011). Alpha increase SMEs may reflect the same processes underling WM retention, such as inhibiting task-irrelevant activity. Thus, alpha increases and decreases may reflect different encoding strategies, with alpha increases reflecting WM maintenance and alpha decreases reflecting semantic processing that both facilitate memory formation (see Hanslmayr & Staudigl, 2013 for a discussion).

In the same vein, theta power decreases have also been associated with successful episodic memory encoding in scalp EEG (Long, Burke, & Kahana, 2014), iEEG (Burke et al., 2013; Lega, Jacobs, & Kahana, 2012; Sederberg et al., 2007), and MEG (Guderian et al., 2009) studies. Such task-related decreases in low-frequency power are thought to reflect a decrease in synchronized local neural activity (Singer, 1993). Based on findings that low-frequency power decreases correlate with BOLD signal increases (Kilner, Mattout, Henson, & Friston, 2005), it has been proposed that theta decreases during successful memory encoding may reflect the transition of cortical activity to an active state (Burke et al., 2013). However, it is difficult to explain why some studies found theta power increases whereas other studies found theta decreases during episodic encoding. It is also difficult to compare these studies because of large variations across studies in task procedures, recording scalp/brain regions, latency intervals, and frequencies analysed. Nevertheless, some hypotheses have been made to explain different directions of theta SMEs. For example, Düzel and colleagues (2010) proposed that poststimulus theta amplitude is influenced by preparatory neuronal tuning before stimulus onset, such that poststimulus theta SMEs tend to correlate negatively with prestimulus theta SMEs (Fell et al., 2011; Guderian et al., 2009). Related to this, it was proposed that poststimulus theta power decreases may reflect the shutting down of prestimulus preparatory theta activity (Fell et al., 2011). However, post-stimulus theta decreases do not always occur immediately after stimulus onset (Guderian et al., 2009), and it could be sustained throughout a long poststimulus time window (Sederberg et al., 2007), both of which argue against Fell et al.'s (2011) hypothesis.

Another possibility is that the direction of theta SMEs may be determined by the dominant frequencies in the theta range, i.e., high or low theta. Lega et al. (2012) measured the 3 Hz “slow-theta” and the 8 Hz “fast-theta” oscillations, which are at the edges of the traditional 4–8 Hz theta range, in the hippocampus of neurosurgical patients during episodic memory encoding. It was found that the slow-theta activity increased with successful memory encoding, whereas the fast theta decreased with successful encoding. The authors proposed that there are two distinct hippocampal theta oscillations in episodic memory encoding, with the slow-theta being the human analogue to the memory-related theta oscillations observed in rats. No clear interpretation for high-theta oscillation was offered by the authors. Watrous and colleagues (2013) proposed that while 1–4 Hz oscillations in the delta range are linked to spatial memory, 7–10 Hz oscillations are linked to temporal memory, suggesting that high- and low-theta bands support different mechanisms and memory operations. This interpretation, however, does not explain why high- and low-theta encoding effects should take different directions. Another possibility is that high-theta is at least partly driven by oscillations in the adjacent alpha band, particularly low-alpha oscillations (8-10 Hz). As discussed above, alpha power decreases are usually associated with semantic encoding, and low-alpha has also been related to attentional processing (Klimesch, 1997). Thus, extending Lega et al.'s hypothesis, theta increases and decreases may reflect different encoding strategies and processes, with theta increases driven by low-theta oscillations reflecting mnemonic processing and theta decreases driven by high-theta oscillations possibly reflecting semantic or attentional processing. Although very few previous studies measured low-theta and high-theta in separation, visual inspection of time-frequency graphs from some studies appears to support this hypothesis (e.g., Long et al., 2014). Also, an analogous dissociation of low-theta and high-theta has been found during memory retrieval (Pastötter & Bäuml, 2014).

Taken together, increases and decreases in theta and alpha power may reflect different cognitive processes underlying memory encoding. Decreases in theta and alpha power might reflect semantic elaboration for item-specific information. Increases in theta power are thought to reflect item-context binding (Hanslmayr et al., 2009; Staudigl & Hanslmayr, 2013), whereas alpha increases may reflect inhibitory processing similar to that seen during WM maintenance.

#### *3.1.1.2 Theta and alpha activity in episodic retrieval*

In terms of retrieval, theta power modulation has been linked to item recognition, with enhanced theta power during correct recognition of studied items relative to correct rejection of new items (Düzel, Neufang, & Heinze, 2005; Klimesch, Doppelmayr, Schwaiger, Winkler, & Gruber, 2000; Osipova et al., 2006), and item recollection, with higher theta power for recollected than familiar items (Klimesch et al., 2001). As already described in the Introduction chapter, theta power increases during episodic retrieval are thought to reflect the reinstatement of contextual memory traces through projections from the hippocampus (e.g., Jafarpour et al., 2014; Nyhus & Curran, 2010). In addition, theta increase over the frontal scalp sites has been related to top-down control processing during retrieval, such as post-retrieval monitoring (Gruber et al., 2008; Guderian & Düzel, 2005; Khader & Rösler, 2011).

Top-down control during retrieval may also involve the inhibition of interference, as selectively retrieving some information can be interfered by the activation of other information also related to the probe. Theta oscillations have been shown to play an important role in resolving such interference during selective retrieval (Hanslmayr, Staudigl, Aslan, & Bäuml, 2010; Staudigl, Hanslmayr, & Bäuml, 2010). For example, using a retrieval-induced forgetting paradigm, Staudigl et al. (2010) found enhanced theta power for high compared to low levels of interference during retrieval, and the interference-specific theta power increase predicted later forgetting of items (i.e., items closely related to selectively-retrieved ones) that were not retrieved. These findings were interpreted that theta power increases reflect the inhibition of competing associations to resolve interference during selective retrieval. This interpretation is in close agreement with a computational model (Norman, Newman, & Perotte, 2005) proposing an inhibitory role of theta oscillations such that competitor memories are suppressed while targets are selectively strengthened. This model is based on neurophysiological findings that long-term potentiation and long-term depression occur at different phases of theta oscillations (e.g., Huerta & Lisman, 1996), which explains the role of theta activity in gating information during selective retrieval, and similarly during WM maintenance (Jensen & Tesche, 2002; Sauseng, Griesmayr, Freunberger, & Klimesch, 2010).

Compared to theta, alpha oscillations have not often been reported in relation to LTM retrieval. Using an STM task, Klimesch and colleagues (1999) found a pronounced upper alpha (10.2-12.2 Hz) power decrease during retrieval that was largest over the occipital sites, which was thought to be related to the reactivation of sensory representations during retrieval (Klimesch, Schack, & Sauseng, 2005). Later studies investigating LTM retrieval also reported alpha old/new effects over posterior scalp sites, with stronger alpha power decrease related to recognition hits relative to correct rejections (e.g., Zion-Golumbic, Kutas, & Bentin, 2010). For example, Burgess and Gruzelier (2000) found power decrease retrieval effects in upper alpha/lower beta frequencies (~10-13 Hz) in a continuous recognition task for words and faces. Interestingly, the topography of these effects varied with the type of materials, with effects over left parietal sensors for words and effects over right parietal sensors for faces. These findings again support the proposal that alpha/beta power decreases are associated with the reactivation of memory representations of old items. In a study directly testing this idea, Khader and Rösler (2011) manipulated the type and amount of to-be-retrieved information (objects and their spatial locations), and demonstrated that alpha/beta power decreases varied as a function of the amount and the type of retrieved information. Larger amounts of retrieved information induced stronger alpha/beta power decreases, which also differed significantly in topography between the types of retrieved information. The retrieval of spatial locations elicited effects over parietal sites, whereas the retrieval of objects elicited more widespread effects over frontal, parietal, and left-temporal sites. Interestingly, theta power varied only with the amount of retrieved information but not with material type, suggesting that theta power may reflect higher order control processing during memory retrieval (Hanslmayr et al., 2012).

In addition to alpha/beta decreases, alpha/beta increases also serve important roles in memory retrieval. Using a visual half-field manipulation in an episodic memory task, Waldhauser and colleagues (2012) found alpha/beta power decreases over the hemisphere where the target information was stored, replicating the findings in Khader and Rösler (2011), and alpha/beta increases over the hemisphere where the competitor information was stored. The amount of alpha/beta power decrease also predicted successful inhibition of competitor information during retrieval. Alpha power increase is thought to reflect a role in gating irrelevant information from the visual stream (Bonnefond & Jensen, 2012).Therefore, alpha/beta increases during memory retrieval may reflect the inhibition of competing memories, which serves an active role in facilitating successful recovery of target information. In this study, frontal theta power increased during competitive retrieval relative to non-competitive retrieval, but did not show lateralisation effects as in alpha/beta oscillations. These findings again suggest that theta power reflects higher order control processing during retrieval.

Taken together, theta power increases have often been related to memory retrieval, possibly playing important roles in neural reinstatement of contextual representations and top-down control, e.g., inhibition and post-retrieval monitoring and evaluation. In terms of alpha oscillations, the present evidence, although based on a limited number of studies, suggests that alpha power decreases index the reactivation of the sensory features of memory traces, whereas alpha power increases reflect interference inhibition during retrieval. Thus, both theta and alpha power increases may be involved in inhibitory processing, which is consistent with the proposals that theta/alpha increases represent an inactive state of cortical neural assemblies (Lisman & Jensen, 2013) and that desynchronisation in brain oscillations increases the degree of information processing (Hanslmayr et al., 2012). Although both theta increases and alpha decreases have been related to reinstatement of memory representations, they are unlikely to reflect the same retrieval processes. Theta increase occurs in an earlier time window (250-700 ms post-probe in Jafarpour et al., 2014), whereas alpha decreases occur in later time windows (~600-1800 ms in Waldhauser et al., 2012; 3500-4000 ms in Khader & Rösler, 2011). Such time differences suggest that while theta increases may reflect the recovery of episodic information, alpha decreases are likely to support the reactivation of memory traces for post-retrieval evaluations.

#### *3.1.1.3 Anticipatory memory-related activity*

As discussed in the Introduction chapter, previous studies have demonstrated that theta activity preceding an event can influence memory encoding (Fell et al., 2011; Fellner et al., 2013; Gruber et al., 2013; Guderian et al., 2009) and retrieval (Addante et al., 2011). Such theta PSMEs are thought to be related to hippocampal activation and activity in other cortical regions, especially the PFC, that are closely connected to the hippocampus (Hsieh & Ranganath, 2013). This proposal is supported by findings from scalp EEG (Gruber et al., 2013) and MEG (Guderian et al., 2009) studies that theta PSMEs are observed over frontal, especially left frontal, scalp sites/sensors.

Because stimulus-elicited hippocampal theta activity has been found to be important for memory encoding (Guderian & Düzel, 2005; Osipova et al., 2006), it may be hypothesised that theta PSMEs reflect the pre-activation of memory-related neural networks. However, previous findings suggest that the pre- and post-stimulus theta SMEs are dissociable (Fell et al., 2011; Fellner et al., 2013; Gruber et al., 2013; Guderian et al., 2009), and the same theta PSMEs emerge regardless of whether the encoding task was semantic or non-semantic (Fellner et al., 2013; Guderian et al, 2009), both of which argue against this hypothesis. Furthermore, these findings suggest that theta PSMEs are independent of cognitive factors that also influence memory encoding, such as LOP. Another possible interpretation is that theta PSMEs may reflect the activation of a mnemonic context in preparation for the upcoming stimulus. A mnemonic context may consist of any associative source information such as the timing and the position of the stimulus presentation, in which the subsequently presented stimulus can be embedded. This hypothesis is consistent with previous findings in the sense that theta PSMEs are associated with episodic encoding success that requires the item-context binding (Fell et al., 2011; Fellner et al., 2013; Gruber et al., 2013; Guderian et al., 2009). Nevertheless, further research is needed to test this hypothesis with memory tasks specifically designed to tap into item-context binding.

With respect to anticipatory brain activity during retrieval, enhanced theta power before the presentation of retrieval probes has also been associated with successful retrieval of source information. Addante et al. (2011) recorded scalp EEG while participants performed an incidental source memory task for visually-presented words, with two different encoding tasks (pleasantness and animacy judgments) serving as source during retrieval. At retrieval, participants gave an item-recognition judgement followed by a source-recognition judgment, both on a 5-point confidence scale to reduce the possibility that the effects were contaminated by guesses. It was found that theta power increase just before probe onset over mid-frontal scalp sites was positively correlated with participants’ ability to retrieve source information, and also positively correlated with a post-probe parietal theta retrieval effect. Therefore, this pre-probe theta effect was interpreted in terms of retrieval control processing such as ‘retrieval orientation’ or ‘retrieval mode’.

In contrast to theta activity, very few studies have reported anticipatory memory-related alpha activity. In an iEEG study, Fell et al. (2011) found a prestimulus hippocampal/rhinal alpha enhancement before successful memory encoding, and this increase was immediately preceded by a theta power increase. As the alpha and theta PSMEs were positively correlated, it was thought that alpha increases were initiated by theta increases. Based on findings from the WM domain that alpha activity plays a role in inhibitory control of task irrelevant information (Jokisch & Jensen, 2007), Fell and colleagues argued that the MTL alpha enhancement before successful memory encoding might reflect inhibitory top-down control processes. Considering the continuous recognition paradigm used in Fell et al. (2011), it may be assumed that prestimulus alpha increases reflect the inhibition of brain activity related to the processing of items in the preceding trials. As prestimulus memory-related alpha and theta increases correlated with early poststimulus alpha and theta memory-related decreases, prestimulus oscillatory activity was thought to reflect the preparation for poststimulus memory-related processing. Thus, in addition to prestimulus theta activity that may reflect the preactivation of contextual information, prestimulus alpha activity may also be important for memory formation.

#### *3.1.1.4 Ageing*

The effects of ageing on brain oscillations related to cognitive processes are largely unknown. In relation to memory processing, a number of WM studies investigating age-related oscillatory effects have produced conflicting results. In a study using visual-spatial delayed match-to-sample tasks (Babiloni et al., 2004), oscillatory brain activity was contrasted between a memory condition, in which participants had to memorized a cue during a delay period of a few seconds, and a non-memory condition, in which the cue remained available during the entire delay period. During the delay period, theta and alpha power reductions were associated with later correct responses in both younger and older adults, with alpha power reduction stronger during memory than non-memory task. Power decreases in both alpha and theta frequencies were greater in young than in older adults at frontal and posterior sites, most pronounced over frontal sites. In contrast, McEvoy, Pellouchoud, Smith, & Gevins (2001) observed a different pattern of age differences in alpha and theta oscillations. When contrasting easy and difficult versions of a visual-spatial WM task, it was found that as task difficulty increased, only the young participants showed a theta power increase over frontal-midline sites and an alpha power decrease over parietal sites, whereas the older adults showed alpha power reductions over both frontal and parietal regions. Age-related reduction in frontal-midline theta has also been reported by Kardos and colleagues (2014) contrasting high and low levels of visual-spatial WM load. Younger adults showed greater enhanced frontal theta activity relative to older adults during the retention period. This frontal-midline theta effect was sensitive to both the levels of memory load and memory performance in younger adults but not older adults. Despite the differences in age-related oscillatory activity patterns across the studies, these results suggest that normal ageing is associated with alterations in the fronto-parietal networks that are associated with age-related decline in WM maintenance.

Studies investigating auditory WM have also reported age-related differences in alpha and theta oscillations. Karrasch, Laine, Rapinoja, and Krause (2004) found greater reduction of alpha power in younger relative to older adults during both encoding and retrieval phases in an auditory WM task. In contrast, theta power was more enhanced for younger than older adults at both encoding and retrieval. The statistically significant differences between the age groups were more marked during retrieval than during encoding. A similar age difference in theta activity was also reported by Cummins and Finnigan (2007), with theta power greater for young than older adults during both retention and recognition intervals. In both studies, older and younger adults had equal memory performance, suggesting that these effects are not due to performance differences.

Taken together, the above mentioned studies consistently show age-related reduction of oscillatory effects in WM processing, including the effects of alpha power decrease and theta power increase. Alpha decreases have been related to the reactivation of the sensory features of memory traces (Waldhauser et al., 2012) and general attentional demands (Klimesch, 1997). Thus, healthy ageing may be associated with declines in attention to a task or the ability to maintain memory representations in WM. Theta increases, especially over fronto-midline scalp sites, are mostly greater in younger relative to older adults, which may or may not be accompanied by age-related performance differences. One exception is Babiloni et al. (2004), in which theta power decrease, but not increase, was found during WM retention, and the decrease was greater for younger than older adults. Such a discrepancy may be due to differences in WM tasks across studies. In Babiloni et al. (2004), participants were presented with two vertical bars and had to decide which one is longer after a retention interval. The memory load in this task was much lower than those used in other studies mentioned above. Theta power increases over frontal scalp sites are thought to reflect control processes such as active maintenance of information in WM and sustained, internally-driven attention that vary with increasing WM demands (Klimesch et al., 2008; Sauseng et al., 2010). Therefore, it may be that when only one bit of information has to be retained (Babiloni et al., 2004), such control processing is not engaged, at least not to the same extent as in other studies. Instead, other distinct cognitive processes, as indexed by theta decreases, might be activated.

It is currently unclear how these findings in WM can be translated to LTM. As it is thought that theta oscillations represent the involvement of parahippocampal–cortical circuits, and alpha oscillations represent the involvement of ‘‘executive’’ thalamo–cortical circuits (Babiloni et al., 2004), age-related changes in alpha and theta oscillations may also affect LTM processing. One study (Sebastian, Reales, & Ballesteros, 2011) has provided some clues using a haptic continuous recognition memory task, in which real objects were presented as stimuli. Younger and older adults showed comparable recognition accuracy and an ERP old/new effect at 550–750 ms after stimulus onset. In the same time window, a reliable old/new effect in theta activity was also found in both younger and older adults, with increased theta power for correctly classified old items than new items. Furthermore, older adults exhibited greater alpha/beta power reduction than younger adults, sustained from around 400 ms poststimulus. This effect was thought to reflect the recruitment of additional neural mechanisms, such as executive functions, to enhance memory performance. It is surprising that no age difference was found in theta activity, given that theta oscillations serve important roles in both WM maintenance and LTM processes (Düzel et al., 2010). This may be due to the continuous recognition paradigm used in Sebastian et al. (2011) that is not best suited to elicit theta effects that are often associated with recollection. Also, these findings may only be generalised to haptic memory that is relatively preserved in healthy ageing (Ballesteros & Reales, 2004).The question remains whether oscillatory memory-related brain activity is affected by ageing, particularly in theta and alpha bands.

#### *3.1.1.5 Research aim*

The aim of the present study was to investigate the effect of age on oscillatory neural correlates of successful encoding and retrieval of associative information, with an emphasis on prestimulus memory-related activity. EEG data from the first experiment were subjected to time-frequency analyses to extract theta and alpha power. In line with ERP analyses, the critical contrast was between associative hits and associative misses to isolate brain activity related to the encoding and retrieval of associative information. As previous research on anticipatory memory-related oscillatory activity, especially in relation to ageing, is very limited, the present study is mostly exploratory. Nevertheless, based on Guderian et al. (2009) and Addante et al. (2011), it was expected that younger adults might show anticipatory theta power increases for successful associative memory during both encoding and retrieval.

### 3.1.2 Methods

Information about participants, procedures, and EEG acquisition can be found in the ERP chapter.

#### *Time-frequency analyses*

The EEGLAB toolbox (Delorme & Makeig, 2004) was used for the oscillatory analyses and pre-processing. Continuous EEG was high-pass filtered at 0.5 Hz to remove slow drifts. Encoding epochs ranged from 600 ms before the neutral warning stimulus until 6200 ms thereafter. This epoch length covered the 2000 ms pre-source, 2000 ms pre-binding, and 1600 ms binding intervals. An extra 600 ms was also included after the intervals of interest to avoid edge effects in the analyses. Retrieval epochs ranged from 600 ms before the neutral warning stimulus until 4200 ms thereafter. This epoch length covered the 2000 ms pre-probe and 1600 ms post-probe intervals. Blinks and other artefacts such as eye-movements and muscle-related activity were removed by independent components analysis (ICA) (Delorme & Makeig, 2004). To optimize ICA decomposition, epochs were baseline-corrected using the mean signal in the 600 ms period before cue onset. For the same reason, trials in which EEG activity exceeded more than 3 standard deviations from the mean on one electrode or 5 standard deviations across all electrodes were excluded from the analyses. After the ICA rejection, any trials containing residual artefacts were manually rejected from the analyses. The data were then re-referenced to average mastoids.

Time-frequency analyses were conducted using Morlet wavelets (Percival & Walden, 1993) with 4 cycles and a sliding time window that moved in steps of 20 ms. The computation was done from 4 to 12 Hz with centre frequencies spaced 1 Hz apart. No baseline correction in the frequency domain was needed here as the main interest was in differences in oscillatory power between trial types (Gruber et al., 2012). For each subject, EEG data for relevant trials were binned according to associative memory performance, with the critical contrast being associative hits and associative misses. The mean numbers of artefact-free associative hits and forgotten trials at encoding were 79 and 38 for the younger group and 45 and 59 for the older group respectively, and at retrieval were 78 and 40 for the younger group and 46 and 61 for the older group. In total, the same 24 older and 24 younger participants as in ERP analyses entered into time-frequency analyses. All of them had at least 16 artefact-free trials in either condition.

For the statistical analyses, the data were collapsed into 200 ms time bins. For each bin, mean theta power (4-8 Hz) and alpha power (9-12 Hz) were calculated for each electrode, participant, and trial. Permutation tests were performed in each time window to reveal electrode sites with significant SMEs, i.e., theta and alpha power differences between associative hits and associative misses, for each scalp site and each time bin. To investigate the effect of age on oscillatory correlates of associative encoding, the initial analyses focused on the interaction between group and associative SMEs. Time-frequency clusters where between-group differences in SMEs were significant were then followed up with permutation tests within each group. If no significant interaction was found, further tests were performed across the two groups to see whether there was a main effect of memory.

The principles of permutation tests have been introduced in the Introduction chapter. The procedures, adopted from Gruber & Otten (2010), are as follows: First, two-tailed *t* tests were run on the data from each electrode site on the two critical conditions to derive a *t* value. In the case of between-group comparison, e.g., the difference in SME between younger and older adults, independent-samples *t* tests were run on the SMEs (associative hits – associative misses) between the two groups. Second, data from trials of each condition were pooled across subjects and randomly divided into two pseudo-conditions, which were compared to derive a pseudo *t* value. For between-group comparisons, power differences between the two critical conditions were pooled across groups and randomly divided into two pseudo-conditions, which were compared to derive a pseudo between-group *t* value. The second step was repeated 1000 times and used to obtain a distribution of 1000 pseudo *t* values. Finally, the 25th and 975th values of the pseudo *t* values (corresponding with an alpha level of 0.05) were used as the critical *t* values for significance testing. This procedure was conducted for all 37 scalp electrodes and would therefore be expected to lead to a Type 1 error on 1.85 electrodes (37*0.05) per time bin. Effects were therefore only considered if they spanned across two neighbouring electrodes. To further reduce the chance of Type 1 errors, only effects that spanned across at least two consecutive time bins were interpreted.

Previous research has demonstrated that oscillatory frequencies vary greatly between good and bad memory performers (Klimesch, 1999). Behavioural data in the present study also showed large inter-individual variations in memory performance across older adults (Chapter 2.1.1). Thus, the effects observed in the older group might not be uniform across all older adults. To shed more light on the nature of the associative memory-related effects found in older adults, further analyses were conducted to determine whether the effects were specific to better or poorer older performers. To this end, older individuals were divided into subgroups of better-performers and poorer-performers via a median split based on the percentage of associative hits. Means and SDs of percentage associative hits were 51.5 (12.2) for better-performers (*N* = 12) and 27.9 (7.2) for poorer-performers (*N* = 12).

### 3.1.3 Results

Behavioural analyses are reported in the ERP chapter.

#### ***Time-frequency analyses at encoding***

Initial between-group analyses revealed that associative encoding-related theta activity was significantly different between younger and older adults between 400-1000 ms after the neutral warning cue onset, 800-1200 ms after the location word onset, and 1000-1400 ms after the object word onset. Follow-up analyses in each group indicated that at 400-800 ms after cue onset, in younger but not older adults there was an increase in theta power over left-frontal scalp sites that predicting later successful associative retrieval. At 800-1200 ms after the location word onset, a theta PSME was found over the right-hemisphere scalp sites in younger adults, with reduced theta power predicting successful associative encoding. At 1000-1400 ms after the object word onset, a theta SME was found over anterior frontal and right posterior sites in older adults only, with reduced theta during successful associative encoding. Significant SMEs for the two groups are presented in Figure 25.

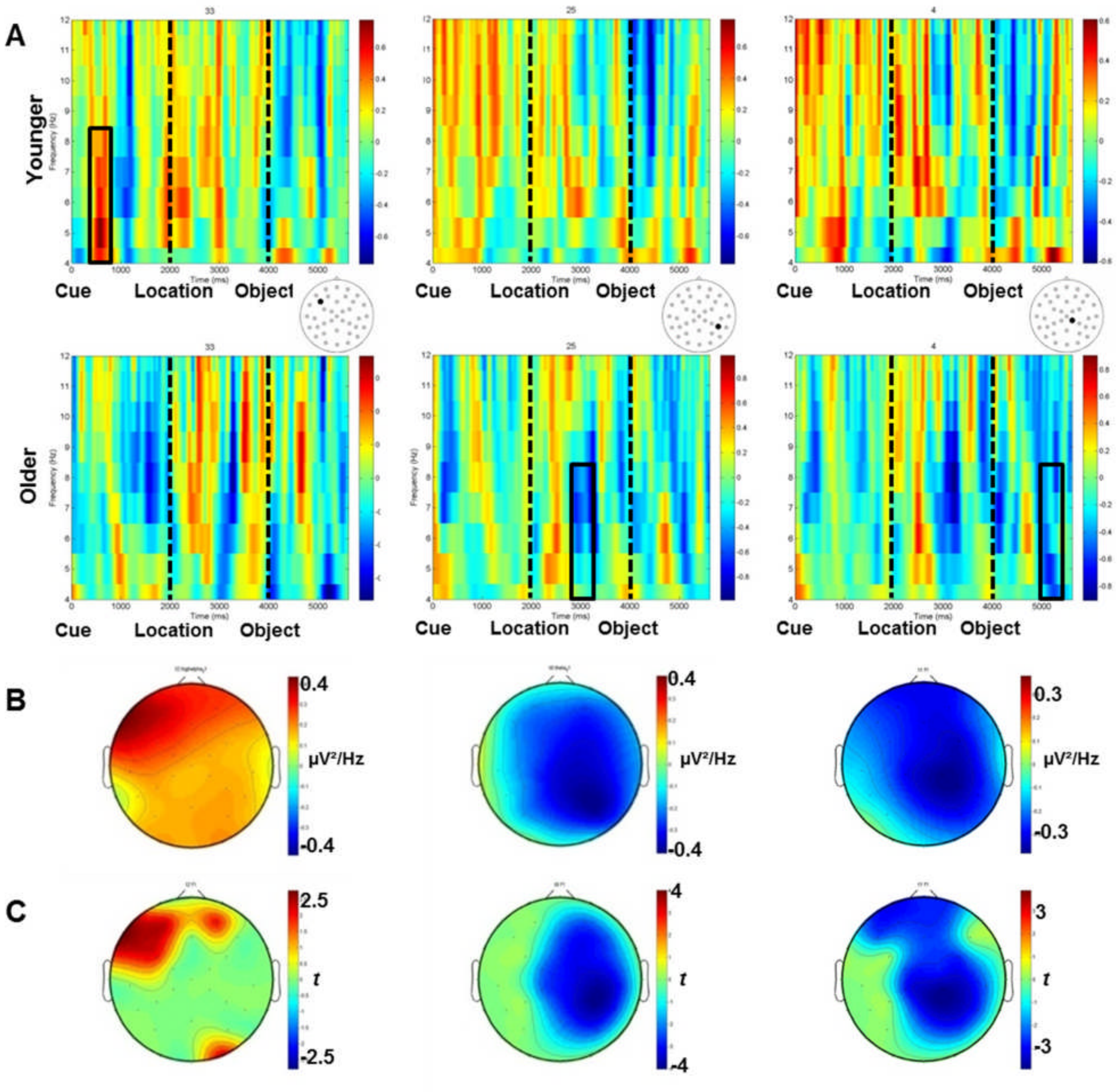


**Figure 25. Associative encoding-related theta activity.**

**A)** Time-frequency representations of the associative encoding-related theta effect (associative hits – associative misses) at 3 electrodes, as indicated by the inserts. The two graphs on the left show that the PSME during the pre-location interval was found in younger adults (lower), showing a left-frontal electrode (site 33 from Montage 10) that was part of the left-frontal electrode cluster where the effect was significant. The box drawn on the graph indicates the time (400-800 ms after cue onset) on the x-axis and the frequency range (4-8 Hz) on the y-axis of the effect. The two graphs in the middle show that the effect during the pre-object interval was found in older adults (upper), showing a right-parietal site (site 25 from Montage 10). The box indicates the time (800-1200 ms after location onset) of the effect. The two graphs on the right show the effect found during binding in older adults, showing a right-parietal site (site 4 from Montage 10). The box indicates the time (1000-1400 ms after object onset) of the effect. **B)** Scalp maps represent differences in theta power (associative hits – associative misses) corresponding to the effects as indicated in A. **C)** Scalp representations of the sites at which the associative encoding-related theta effect was statistically significant. The colour represents the corresponding t-values.

In alpha oscillations, the initial between-group analyses revealed a significant difference at 800-1400 ms after the location word onset. Follow-up within-group analyses indicated that in younger but not older adults, there was a significant PSME over bilateral occipital sites, with alpha power increase predicting subsequent associative retrieval success (Figure 26).

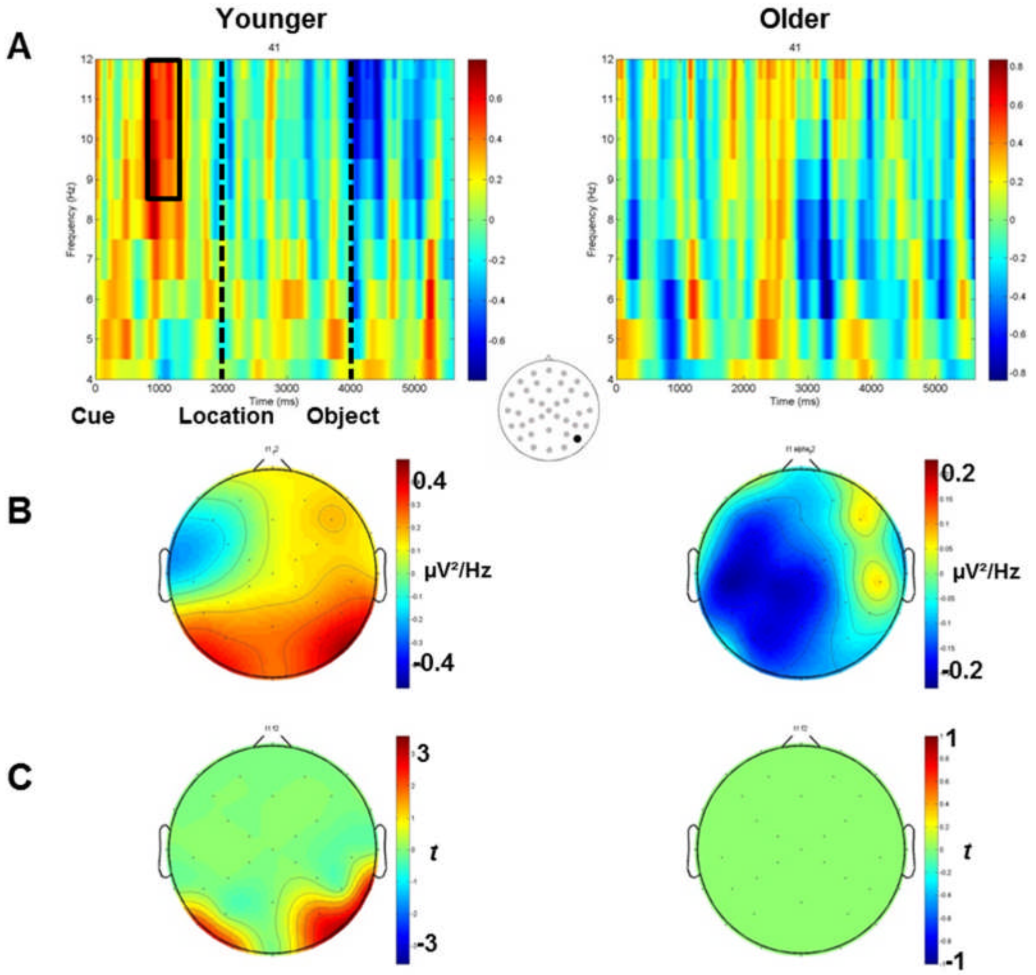


**Figure 26. Associative encoding-related alpha activity.**
**A)** Time-frequency representations of the associative encoding-related alpha effect (associative hits – associative misses) for younger and older adults at a right-posterior electrode (site 41 from Montage 10). A significant alpha PSME was found over the posterior electrodes in younger but not older adults during the pre-location interval. The box drawn on the graph indicates the time (800-1400 ms after cue onset) on the x-axis and the frequency range (9-12 Hz) on the y-axis of the effect. **B)** Scalp maps represent differences in alpha power (associative hits – associative misses) at the 800-1400 ms interval after cue onset for younger and older adults. **C)** Statistical maps show the scalp sites where the effect was significant . The colour represents the corresponding t-values.

Permutation tests were conducted separately for better- and poorer-performing older adults to determine whether significant effects found in older adults, i.e., theta decreases in the pre-binding and binding intervals, could be observed in each subgroup. The results indicated that the theta decrease PSME at 800-1200 ms after location word onset was specific to better-performing older adults, whereas the theta decrease SME at 1000-1400 ms after object word onset was reliable in both better- and poorer-performers (Figure 27).

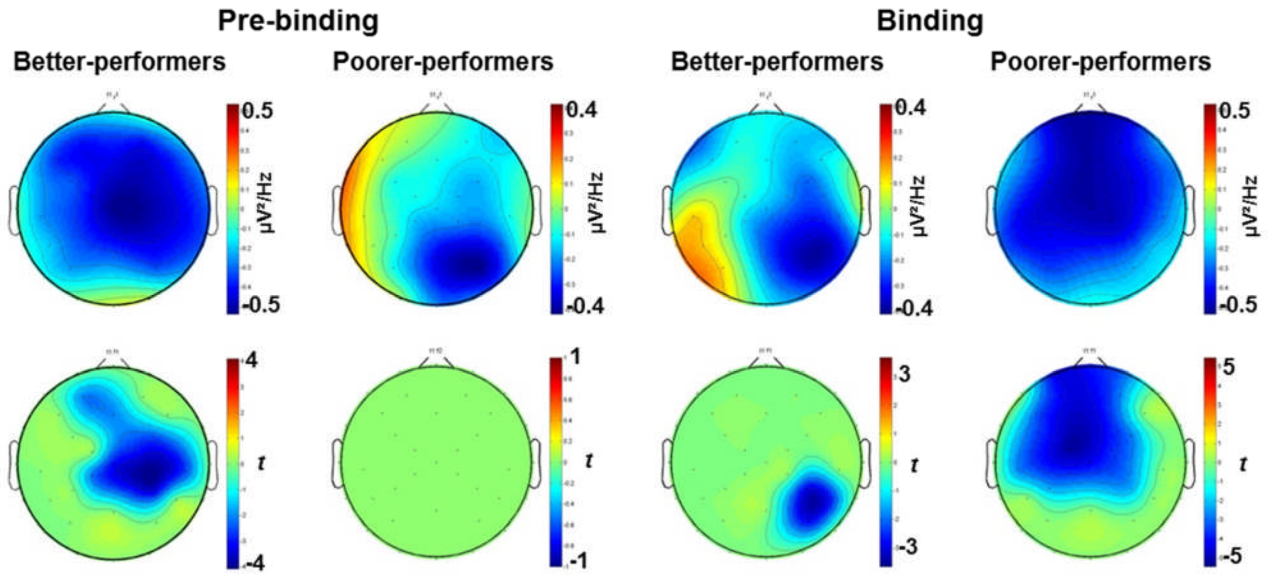


**Figure 27. Theta associative encoding-related effects in older adults separated for better- and poorer-performers.**
**Upper row:** scalp maps represent theta power differences (associative hits – associative misses) during the pre-object interval at 800-1400 ms after location word onset (left) and during the binding interval at 1000-1400 ms after object word onset (right).
**Lower row:** statistical maps show the scalp sites where the effect was significant.

During the pre-source interval, in younger adults the associative prestimulus subsequent memory-related theta increase (400-800 after cue onset) and alpha increase (800-1400 ms after cue onset) occurred in consecutive latency intervals. It is thus possible that alpha increases over occipital sites were initiated by theta increases over left-frontal sites. A Pearson correlation coefficient test was conducted to evaluate this possibility. Theta and alpha PSMEs were measured as mean theta and alpha power differences between associative hits and associative misses over a left-frontal electrode cluster (Figure 25) and a right-posterior cluster (Figure 26) respectively. The result revealed no significant correlation (*r* = -.10, *p* = .64), suggesting that the magnitude of alpha increases was not determined by the magnitude of theta increases.

In older adults, the theta decrease PSME during the pre-binding interval and the theta decrease SME during the binding interval appeared to be similar in scalp distributions. A Pearson correlation test was conducted to see whether the magnitudes of two effects were correlated across older individuals. As described above, the effects were measured as theta power differences between associative hits and associative misses over the representative electrode sites as shown in Figure 28. The result revealed a significant positive correlation (*r* =.60, *p* = .002), suggesting that the theta SME during binding could be driven by the theta PSME before binding.

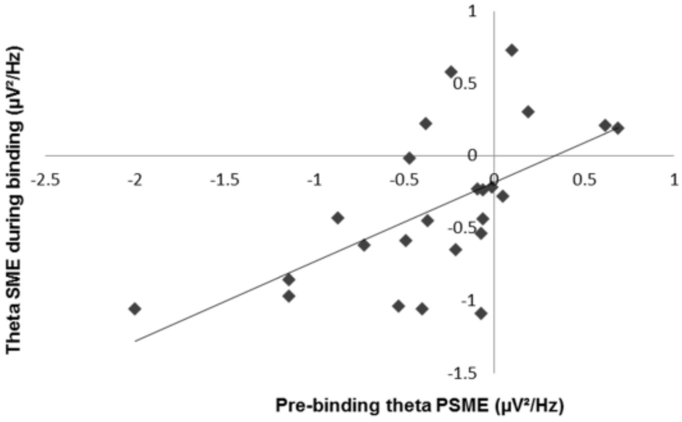


**Figure 28. Scatterplot showing the relationship between theta PSME in the pre-binding interval (800-1200 ms after location onset measured at a representative right-parietal electrode, site 25 from Montage 10) and theta SME in the binding interval (1000-1400 ms after object onset measured at a representative right-central electrode, site 4 from Montage 10).**

### ***Time-frequency analyses at retrieval***

Initial between-group analyses revealed that associative retrieval-related theta activity was significantly different between younger and older adults at 400-800 ms after probe onset. Follow-up analyses in each group revealed an increase in theta power in younger but not older adults during this time interval. This effect focused over left-temporal scalp sites. Across the groups, there were main effects of associative retrieval, including significant alpha decrease effects at 600-1600 ms and theta decrease effects at 1200-1600 ms after probe onset. No significant effect was found during the pre-probe interval in either theta or alpha band. Figure 29 shows the significant theta effects and Figure 30 shows the significant alpha effects as described above.

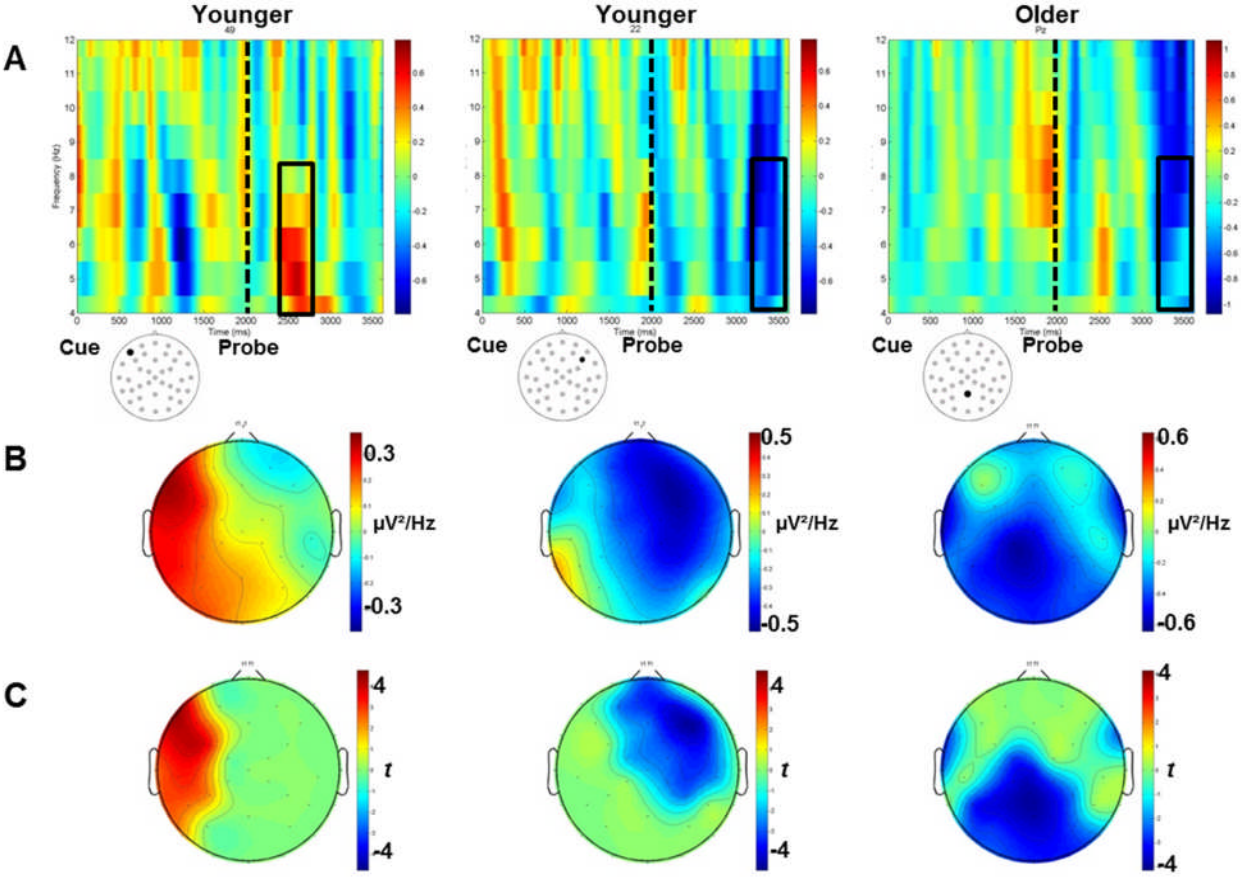


**Figure 29. Associative retrieval-related theta activity.**
**A)** Time-frequency representations of associative retrieval-related theta effect (associative hits – associative misses) over 3 electrodes as indicated by the inserts. The graph on the left shows the effect in younger adults at 400-800 ms after probe onset (as indicated by the box drawn on the graph) at a left-temporal electrode (site 49 from Montage 10). The graph in the middle shows the effect in younger adults at 1200-1600 ms after probe onset at a right-frontal electrode (site 22 from Montage 10). The graph on the right shows the effect at 1200-1600 ms in older adults at a posterior electrode (site 14 from Montage 10). **B)** Scalp maps represent differences in theta power (associative hits – associative misses) corresponding to the effects as indicated in A. **C)** Scalp representations of the sites at which associative retrieval related theta effects were statistically significant. The colour represents the corresponding t-values.

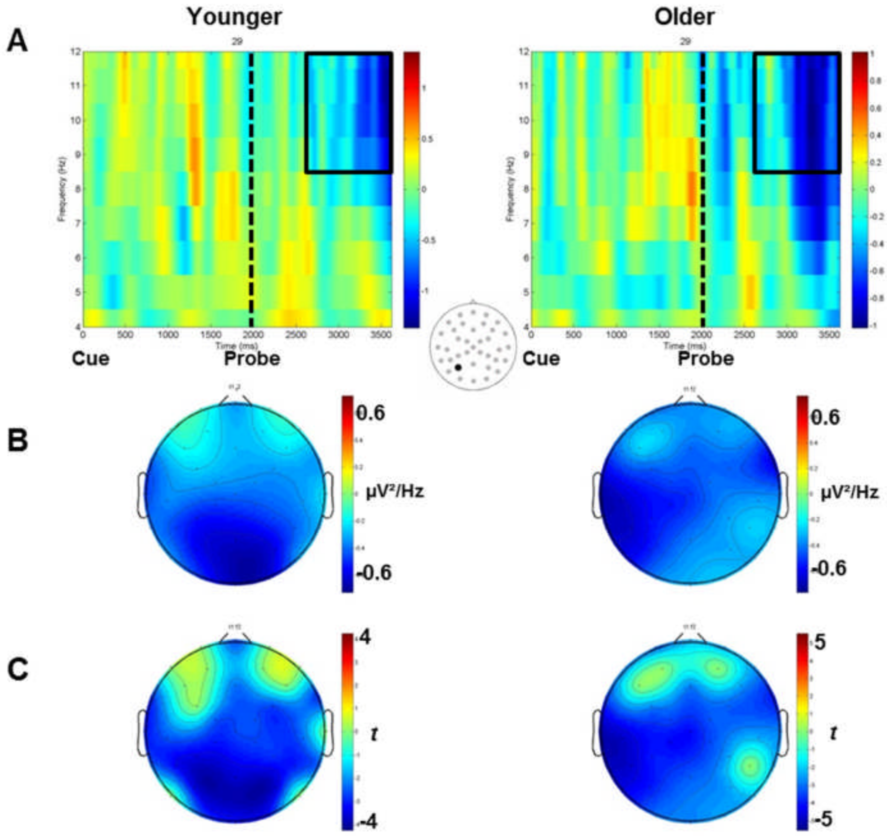


**Figure 30. Associative retrieval-related alpha activity.**
**A)** Time-frequency representations of the associative retrieval-related alpha effect (associative hits – associative misses) for younger and older adults over a left-parietal electrode (site 29 from Montage 10). Significant alpha decrease was found in both younger and older adults at 600-1600 ms after probe onset that was part of the left-parietal cluster where the effect was evident in both groups. **B)** Scalp maps represent differences in alpha power (associative hits – associative misses) at the 600-1600 ms interval in younger and older adults. **C)** Statistical maps show the scalp sites where the effect was significant.

As the time windows of theta and alpha decreases after probe onset largely overlapped, with alpha decreases preceding theta decreases, the possibility arose that theta decreases were driven by alpha decreases. A Pearson correlation test was conducted to evaluate whether the two effects correlated across subjects. Theta and alpha PSMEs were measured as mean theta and alpha power differences between associative hits and associative misses over the electrode clusters where the effects were significant as shown in Figure 29 and Figure 30. The results showed a significant correlation between alpha and theta decreases in older adults (*r* = .51, *p* = .011), suggesting that the magnitude of theta decreases was determined by the magnitude of alpha increases. The correlation was in the same direction in younger adults, although was not significant in that case (*r* = .39, *p* = .061).

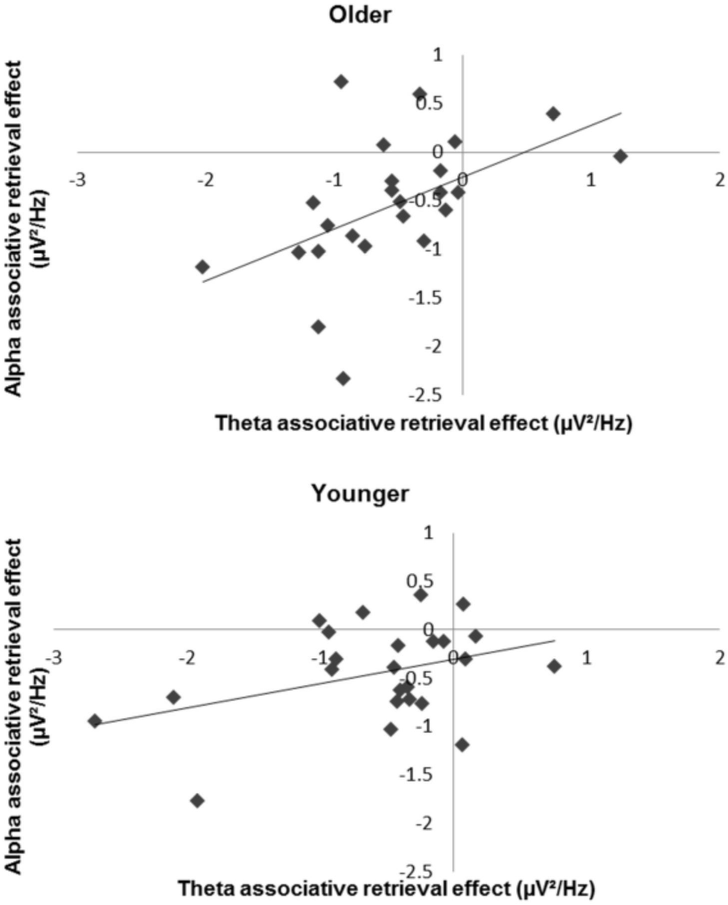


**Figure 31. Scatterplots showing the relationship between theta associative retrieval effect (1200-1600 ms after probe onset) and alpha associative retrieval effect (600-1600 ms after probe onset). Theta effects were measured at a representative right-frontal electrode for older adults (site 22 from Montage 10) and at electrode Pz for younger adults (site 14 from Montage 10). Alpha effects were measured at a left-parietal electrode (site 29 from Montage 10).**

### 3.1.4 Discussion

The primary interest of this study was the influence of age on associative memory-related anticipatory activity. At encoding, theta and alpha power increases during the pre-location interval in younger adults predicted subsequent associative encoding success. In older adults, a decrease in theta power during the pre-object interval predicted successful associative encoding. Associative SME during the binding interval emerged only in older adults, with theta decrease predicting subsequent associative hits. At retrieval, there is no pre-probe associative retrieval effect found in either group, which is in stark contrast with the ERP finding of a prominent pre-probe effect in older adults. Post-probe associative retrieval effects are similar across the groups, manifest as a sustained broadband power decrease which starts in alpha frequencies from around 600 ms after probe onset and spreads to theta frequencies from around 1200 ms. The only between-group difference was the theta power increase that was only found in younger adults at 400-800 ms poststimulus. A summary of these findings are shown in Table 11.

**Table 11. Summary of significant associative memory effects in younger and older adults.**

| | | Younger | | Older | | Both | |
|---|---|---|---|---|---|---|---|
| Phase | Interval | Theta | Alpha | Theta | Alpha | Theta | Alpha |
| Encoding | Pre-location | Increase 400-800 ms left-frontal | Increase 800-1400 ms bilateral occipital | | | | |
| | Pre-object | | | Decrease 800-1200 ms right-hemisphere | | | |
| | Post-object | | | Decrease 1000-1400 ms anterior-frontal and right-posterior | | | |
| Retrieval | Post-probe | Increase 400-800 ms left-temporal<br>Decrease 1200-1600 ms right-frontal | Decrease 600-1600 ms widespread larger over posterior | Decrease 1200-1600 ms centro-parietal | Decrease 600-1600 ms widespread larger over left temporal-parietal | Decrease 1200-1600 ms | Decrease 600-1600 ms |

### *Pre-location associative encoding-related activity*

Consistent with previous findings (e.g., Gruber et al., 2013; Guderian et al., 2009), the present study showed that in younger adults, enhanced theta power before an event predicts later recollection of that event. Using an associative memory paradigm that emphasised the association between items and minimised the probability of "lucky guesses" at retrieval, the present study further demonstrated that prestimulus theta power increases facilitate subsequent memory for associative information. The theta PSME in the present study is observed over left-frontal scalp sites at 400-800 ms after neutral warning cue onset. Timing and scalp distributions of such theta PSMEs may vary across studies. In terms of timing, the theta PSME in Gruber et al. (2013) was between 1000 and 1600 ms after reward cue onset, whereas the effect in Guderian et al. (2009) was shortly (starting at -200 ms) before stimulus onset. The precise timing of the effect is probably determined by the timing of prestimulus cues, which were given 2 s before stimulus onset in Gruber et al. and the present study, and 0.5 s before stimulus onset in Guderian et al. Furthermore, it may also be influenced by the amount of information contained in the cue. In Gruber et al., the cue indicated the level of monetary reward, whereas in Guderian et al. and the present study, the cues contained no information other than warning about the upcoming of a stimulus. Therefore, it is likely that theta PSMEs reflect an anticipatory preparation for encoding initiated by prestimulus cues. If the cue contains more information, it will take longer to be processed.

In terms of scalp distributions, the present left-frontal theta PSME closely resembles that found in another scalp-recorded EEG study (Gruber et al., 2013). In an MEG study (Guderian et al., 2009), the effect was found over bilateral frontal sensors. Theta oscillations are thought to be important for associative memory functioning involving the hippocampus (Hasselmo & Eichenbaum, 2005), and theta SMEs have been recorded directly in the hippocampus (Fell et al., 2011) and the frontal cortex (Sederberg, 2003) in EEG studies. Scalp-recorded theta PSMEs are unlikely to reflect hippocampal activity directly, but rather represent activity in cortical regions that link closely to the hippocampus via theta oscillations, such as the PFC (Sirota et al., 2008). Theta activity is often associated with executive functions (Sauseng et al., 2010), and prefrontal theta is thought to index central executive functions in dynamic networking of the PFC and task-related posterior brain regions (Mizuhara & Yamaguchi, 2007). Thus, in episodic memory encoding, prefrontal theta may also play the role of top-down control to the hippocampus in a unified PFC-hippocampal network that is important for item-context binding, and therefore increase the chance of later successful retrieval. This proposal is consistent with Gruber et al. (2013) in that the theta PSME emerged only when prestimulus cues signalled high reward but not low reward, indicating that prestimulus theta increases during episodic memory formation are under voluntary control, possibly serve to prime the PFC-hippocampal network for effective encoding of item-context associations. Similar left-frontal scalp distributions of the theta PSMEs between Gruber et al. and the present study suggests that the present effect may also reflect a motivational anticipatory control processing that facilitates associative encoding.

In the present study, the prestimulus theta power increase was not found in older adults. Left-frontal activation has been associated with effective memory encoding in many neuroimaging studies, usually during intentional encoding, and also during accidental encoding when semantic processing was required (Buckner, Kelley & Peterson, 1999). These findings suggest that left-frontal activation may be related to the utilisation of semantic (deep) encoding strategies. Furthermore, left-frontal activation during encoding is reduced in ageing and in divided attention conditions (Anderson et al., 2000), suggesting that such strategic control is subject to the availability of processing resources. In the present study, the absence of the theta power increase effect in older adults may reflect the failure to engage prestimulus anticipatory mechanisms due to diminished processing resources.

A novel finding is that alpha PSME emerged in younger adults at 800-1400 ms after cue onset, with alpha power increased related to subsequent successful associative encoding. One previous iEEG study (Fell et al., 2011) reported a positive alpha PSME in hippocampal/rhinal regions. Based on findings that alpha power increases with increasing WM load (Sauseng et al., 2005) and its role in inhibiting interference (Jensen et al., 2002), Fell and colleagues argued that the MTL alpha enhancement before successful memory encoding might reflect inhibitory control processing. Similar interpretations have also been proposed for alpha power increases during memory encoding (Khader et al., 2010; Meeuwissen et al., 2011) and retrieval (Waldhauser et al., 2012). The scalp distribution of the present alpha PSME, focusing over occipital scalp sites, is consistent with that found in Waldhauser et al., which was thought to reflect the inhibition of visual features of competing memories. Also, alpha oscillations are thought to play a role in top-down control of visual attention (Sauseng et al., 2010), with increased alpha power related to preventing information uptake. Thus, although the present alpha PSME cannot be directly related to hippocampal/rhinal alpha PSME, it may also reflect an inhibitory control processing, possibly for task-irrelevant visual information.

Similar to the present study, Fell et al. (2011) found that the alpha PSME was preceded by a positive theta PSME. Dissimilar to the present study, however, the alpha PSME was positively correlated with the theta PSME in Fell et al. (2011). In Fell et al., the correlations were between theta and alpha PSMEs in close proximity, e.g., hippocampal theta and hippocampal alpha PSMEs. In contrast, in the present study the theta PSME is over left-frontal scalp sites and the alpha PSME is over occipital sites. Thus, although hippocampa/rhinal alpha increases may be initiated by theta increases in the same regions, the present theta and alpha PSMEs may reflect independent activity in different cortical regions. Nevertheless, it is interesting that prestimulus alpha increases are immediately preceded by theta increases across scalp EEG and iEEG studies. It may reflect a preactivation of the PFC-hippocampal network accompanied by an inhibition of task-irrelevant activity for effective associative memory encoding.

### ***Pre-binding associative encoding-related activity***

During the pre-binding interval, the only associative PSME emerged in older adults at 800-1200 ms after location word onset, with widespread theta decreases over right-hemisphere scalp sites predicting successful associative encoding. Theta decrease SMEs have been previously reported in a number of studies (Burke et al., 2013; Guderian et al., 2009; Lega et al., 2012; Long et al., 2014; Sederberg et al., 2007), but only in poststimulus intervals. In the present study, older adults also showed a poststimulus theta decrease SME during the binding interval. A correlation analysis indicated that the pre-binding and binding theta effects were positively correlated, suggesting that the theta SME during binding may be driven by the effect before binding. In contrast, previous studies usually find negative correlations between prestimulus theta increases and poststimulus theta decreases (Guderian et al., 2009; Fell et al., 2011). Thus, the present findings argue against the proposal that poststimulus theta power decreases merely reflect the shutting down of prestimulus preparatory theta activity (Fell et al., 2011).

Poststimulus encoding-related theta decreases are thought to be driven mainly by high-theta oscillations (Lega et al., 2012), possibly reflecting neural activity in the adjacent alpha range that smears into the theta range (Lisman & Jensen, 2013). This is particularly likely for older adults, as alpha frequency decreases linearly with age from 10.89 Hz in 20-year-old adults to 8.24 Hz in 70-year-older adults (Klimesch, 1999). Nevertheless, this idea can explain the pre-binding theta decrease only if parallel pre-binding SME could also be found in alpha oscillations, especially in low-alpha frequencies. To verify this idea, theta and alpha frequency bands were subdivided into low-theta (4-6 Hz), high-theta (7-8 Hz), low-alpha (9-10 Hz), and high-alpha (11-12 Hz) to test whether this effect could be observed in each sub-band. The results indicated that the pre-binding theta decrease effect was reliable only in high-theta but not any other sub-bands. Thus, although the present pre-binding theta decrease in older adults is mainly driven by high-theta activity (Figure 27), it is unlikely to reflect a ‘bleed-in’ from alpha oscillations.

Increases in theta power are thought to reflect item-context binding that facilitate episodic memory (Staudigl & Hanslmayr, 2013; Summerfield & Mangels 2005). In Staudigl and Hanslmayr’s (2013) study, theta power increase during encoding was associated with later successful retrieval only when contextual features between encoding and retrieval matched. In contrast, the opposite effect was found in the context-mismatch condition, with theta power increase associated with subsequently forgotten items. From these findings, it was concluded that theta increases during encoding reflect item-context binding. Enhanced item-context binding, as indexed by enhanced theta, benefits subsequent retrieval when items are presented with the original context at retrieval, and impairs retrieval when encoding-retrieval contexts mismatch. The present findings that theta decreases during the pre-binding and binding intervals predicted successful retrieval of associative information seem to contradict this hypothesis. However, the timing and scalp distributions of the effects between the two studies are different, with the effect in Staudigl and Hanslmayr's study emerging much earlier (100-700 ms post-stimulus) over left-frontal and bilateral posterial scalp sites, suggesting that they may reflect fundamentally different neural mechanisms. More importantly, the present effects emerge only in older but not younger adults, giving rise to the possibility that the present effects, particularly the pre-binding theta decrease, reflect compensatory mechanisms recruited in older adults to enhance associative memory encoding. This hypothesis is supported by the finding that the pre-binding theta effect is only reliable in better- but not poorer-performing older adults.

Theta/alpha decreases are thought to reflect the transition of cortical activity to an active state (Burke et al., 2013), based on the correlation between low-frequency power decreases and BOLD signal increases (Kilner et al., 2005). Thus, similar to alpha oscillations, theta decreases and increases may represent the engagement and disengagement of neocortical neural assemblies respectively, which is different from hippocampal theta activity (Lisman & Jensen, 2013). Indeed, the activity pattern of cortical theta is much less clear than that in the hippocampus. Findings fromm iEEG studies are inconsistent with some recording sites that show positive theta SMEs whereas many others show the opposite effect (e.g., Sederberg et al., 2003, 2007). As observed by Sederberg et al. (2007), when the dominant effect across a large number of electrodes and subjects is considered, negative SMEs in lower frequencies (including theta and alpha) tend to emerge. In addition, Hanslmayr and colleagues (2012) have applied the information theory to brain oscillations, and demonstrated that oscillatory power decreases are positively correlated with the richness of information represented in the brain. Thus, similar to alpha decreases, theta decrease SMEs may reflect information-rich processing, possibly the elaborative encoding of study items. In the present study, older adults might have relied upon such elaborative encoding to compensate for the ‘associative deficit in ageing’ (Naveh-Benjamin, 2000). For example, the pre-binding theta decrease may reflect an elaborative encoding of the location words that serves to lay down a richer context for the upcoming object words to be embedded in. Thus, different from positive theta PSMEs, negative theta PSMEs may be interpreted as a semantic preparation for the binding across individual items.

Taken together, the present findings suggest that ageing affects anticipatory associative encoding-related brain activity as reflected in theta and alpha oscillations. Anticipatory mechanisms in younger adults are recruited at an early stage before the presentation of either location or object information, possibly reflecting top-down control processing, i.e., a preactivation of the PFC-hippocampal neural network for associative encoding and an inhibition of task irrelevant information. In older adults, anticipatory encoding-related effects do not emerge until the locations words are presented, possibly reflecting a semantic elaboration of the locations in preparation for the objects to be bound to their locations. Therefore, there may be a strategic difference between younger and older adults in associative encoding. For older adults, engaging semantic preparatory mechanisms just before binding may compensate for their deficits in executive control mechanisms that are recruited by younger adults to facilitate associative encoding.

### ***Retrieval***

Consistent with previous studies (e.g., Gruber et al., 2008; Guderian & Düzel, 2005), a positive theta retrieval effect emerged in younger adults. In particular, the timing and scalp distribution of the present effect closely resemble that found in Jafapour et al. (2014). Using MVPA in MEG recordings, Jafapour et al. demonstrated that the theta effect is associated with the reactivation of episodic memory traces. Interestingly, the timing of this effect overlaps with that of the classic ERP left-parietal retrieval effect, which is thought to reflect the recovery of episodic information (e.g., Wilding, 2000). Similarly, other studies (Klimesch et al., 2000; Sebastion et al., 2011) also found the temporal overlap between theta old/new effects and ERP old/new effects at around 550-750 ms after probe onset, strongly suggesting that both effects reflect similar neural mechanisms. Thus, the present theta increase effect is likely to index neural reinstatement of associative information. In line with previous findings of an age difference in the left-parietal ERP effect (e.g., Dulas & Duarte, 2013; Swick et al., 2006), the absence of the theta effect in older adults in the present study indicates that older adults are impaired in the recovery of associative episodic information.

Similar widespread alpha power decreases from around 600 ms after probe onset were found in both age groups. Alpha decreases during retrieval have been reported in several previous studies (e.g., Khader & Rösler, 2011; Zion-Golumbic et al., 2010). It has been argued that while theta increases are hippocampally generated and index the recovery of episodic information, alpha decreases are cortically generated (Burgess & Gruzelier, 2000) and index the activation of sensory features of memory traces (Khader & Rösler, 2011). Alpha decrease effects vary in topography between types of retrieved information (Khader & Rösler, 2011). For example, the retrieval of spatial locations elicited effects over posterior sites, whereas the retrieval of objects elicited more widespread effects over frontal, parietal, and left-temporal sites (Khader & Rösler, 2011). Thus, the present widespread alpha decreases may reflect the engagement of widely distributed cortical regions to facilitate the retrieval of rich, complex information for inter-item associations.

Compared to the early, relatively brief theta increase effect that related to memory replay, the later sustained alpha decreases are more consistent with the role of post-retrieval monitoring and evaluation. For source retrieval in particular, it is important that recovered memory representations are subjected to goal-directed evaluation, usually manifest as a sustained effect such as the right-frontal ERP effect (e.g., Wilding & Rugg, 1996). An alpha decrease retrieval effect of similar timing and scalp distribution has been reported in a previous study (Sebastion et al., 2011). In that study, sustained alpha power decreases were greater in older compared to younger adults during retrieval. As memory performance was equivalent across age, greater alpha decreases were interpreted as additional neural resources engaged by older adults as a compensatory mechanism to boost memory retrieval. In the present study, alpha retrieval effects were indistinguishable between age groups, and memory performance was poorer in older than younger adults. The discrepancy across the two studies is possibly related to the nature of the memory tasks. In Sebastion et al.’s study, a haptic memory task was used, which is known to be relatively preserved in old age. In contrast, the present associative memory task is known to be difficult for older adults. Thus, across the two studies, it is demonstrated that neural processes underlying the alpha decrease retrieval effect are unimpaired in ageing. Under certain circumstances, they may be recruited to a greater extent by older adults as a compensatory mechanism to boost memory retrieval.

A novel finding in the present study is the late theta decrease retrieval effect. Previous studies have consistently reported theta increases for correct recognition (e.g., Düzel et al., 2005; Klimesch et al., 2000), item recollection (Klimesch et al., 2001), and source retrieval (Gruber et al., 2008; Guderian & Düzel, 2005). These theta increase effects are usually found in time windows earlier than the present effect, suggesting that they may reflect distinct retrieval processing. In the present study, the theta effect was preceded by the alpha effect, and together they form a sustained broadband power decrease associative retrieval effect. Also, there was a positive correlation between alpha and theta effects, indicating that theta decreases may be driven by alpha decreases. It is therefore possible that theta and alpha decreases reflect similar neural processes, for example a resource demanding, elaborative post-retrieval evaluation. More importantly, both age groups are able to recruit these processes to the same extent to support associative retrieval.

An interesting point to note is that neural correlates of associative retrieval and the pattern of age-related differences revealed in time-frequency analyses are in stark contrast with those in ERP analyses. In time-frequency analyses, no significant pre-probe associative retrieval effect was found in either age group, and post-probe effects were similar across age except the theta increase effect specific to younger adults. In contrast, ERP analyses revealed a prominent pre-probe negative-going associative retrieval effect in older adults, and distinct post-probe retrieval effects across age. Different patterns of oscillatory and ERP results were also found at encoding, with PSMEs only revealed in oscillatory analyses whereas SMEs were found in both oscillatory and ERP analyses. Although there may be some overlap between oscillatory and ERP findings, e.g., theta increases and the left-parietal ERP retrieval effect, fundamentally different neural processes are revealed by oscillatory and ERP analyses. This may be related to the inherent differences between the two analysis methods, with ERSPs more sensitive than ERPs in non-phase-locked event-related EEG. Further discussion on different findings related to the two analysis methods can be found in the overall discussion.

## 3.2 Experiment 2: Are age differences in anticipatory memory-related activity related to poor memory?

### 3.2.1 Introduction

As previously discussed, the aim of the second experiment was to further investigate age-related differences in associative memory effects found in the first experiment. In the second experiment, a concurrent auditory digit monitoring task was administered in a group of healthy young adults to reduce their cognitive resources for associative memory encoding. This manipulation was to mimic age-related associative memory deficits in younger adults, and to see whether previously observed age-specific associative memory effects would emerge. The rationale was that if those effects also occur in younger adults when their associative memory was impaired, it would suggest that the effects reflect neural mechanisms recruited as a result of memory deficits in ageing. Finding such links between poor associative memory and age-related oscillatory memory effects would shed more light on the nature of memory deficits in ageing. It needs to be pointed out that the design of the second experiment was tailored to test the pre-probe ERP retrieval effect found in older adults. Thus, pre-stimulus oscillatory encoding effects could not be tested because of the auditory secondary task administered during encoding.

In the first study, anticipatory associative memory effects differed between younger and older adults, with theta and alpha power increase PSMEs found in younger adults whereas theta decrease PSME found in older adults. Furthermore, these anticipatory mechanisms were recruited at an early stage by younger adults, before the presentation of any to-be-encoded information. In contrast, older adults did not recruit anticipatory mechanisms until after the presentation of the location words. Thus, it was thought that the PSMEs in the two age groups are related to different preparatory strategies. The effects in younger adults may reflect executive control processing that involves a preactivation of the PFC-hippocampal neural network for associative encoding and an inhibition of task irrelevant information. In contrast, the effect in older adults may reflect a semantic elaboration of the locations in preparation for the objects to be bound to their locations. For older adults, engaging such a semantic preparation just before binding may compensate for the impairments in executive control mechanisms. Similarly, a theta decrease SME emerged only in older adults after the presentation of both location and object words, possibly also playing a compensatory role in ageing.

As discussed in the ERP chapter, by mimicking age-related memory impairments in younger adults, the present study can also provide more insights into the nature and purpose of these ‘compensatory’ activities. According to the STAC model (Reuter-Lorenz & Park, 2010), compensatory recruitment of additional brain mechanisms is an adaptive response, which can occur across the life span when new or demanding tasks have to be tackled. Thus, if age-related differences in associative memory effects can be replicated in younger adults when the level of memory difficulty is manipulated, it would suggest that neural activity underlying those ‘compensatory’ effects are engaged in response to poor memory regardless of age. In contrast, if no such effect is found even when memory levels in younger adults are equated to those in adults, it would suggest that poor memory is insufficient to initiate the compensatory mechanisms, which are possibly associated with other age-related impairments.

As already explained in the ERP chapter, the associative memory paradigm was similar to that used in the first study, except that the pre-stimulus encoding interval was much shorter (500 ms) and the location-object pairs were presented simultaneously to accommodate a sufficient number of trials needed for the present design. The focus of the present study was retrieval-related brain activity, during both pre- and post-probe intervals. Post-stimulus encoding-related activity was also analysed to see how this may differ between full attention (single-task) and divided attention (dual-task) conditions. Prestimulus activity was not analysed for reasons already explained in the previous chapter. Again, the critical contrast was between associative hits and associative misses.

### 3.2.2 Methods

Information about participants, procedures, and EEG acquisition can be found in the ERP chapter.

#### ***Time-frequency analyses***

Methods for data analyses and artefact rejection were identical to those used in the first study. Encoding epochs ranged from 600 ms before the cue until 3200 ms thereafter. This epoch length covered the 500 ms prestimulus and 2100 ms poststimulus intervals, with an extra 600 ms after the intervals to avoid edge effects. Retrieval epochs were from 600 ms before the cue until 4400 ms post-cue, covering the 2000 ms pre-probe and 1800 ms post-probe intervals. The mean numbers of artefact-free associative hit and associative miss trials at encoding were respectively 62 and 31 in the single-task condition and respectively 37 and 48 in the dual-task condition, and at retrieval were respectively 61 and 29 in the single-task condition and respectively 36 and 46 in the dual-task condition. The same 25 participants as in ERP analyses entered into the analyses. All of them had at least 16 artefact-free trials in either condition.

The critical contrasts were between associative hits and associative misses, i.e., associative memory effects. Initial statistical analyses focused on the interaction between associative memory effect and condition (single-task/dual-task). Time-frequency clusters where significant interactions emerged were followed up with permutation tests within each condition. If no significant interaction was found, further tests were performed across the two conditions to see whether there was a main effect of memory.

### 3.2.3 Results

Behavioural results are reported in the encoding section in the ERP chapter.

#### *Time-frequency analyses*

At encoding, initial analyses revealed a significant difference in associative theta SME between conditions at 1200-1600 ms after word pair onset. Follow-up analyses within each condition revealed a theta SME in the dual-task but not single-task condition, with theta power decreases over a cluster of fronto-parietal scalp sites predicting later successful associative retrieval (Figure 32). No significant interaction was found in alpha oscillations during encoding.

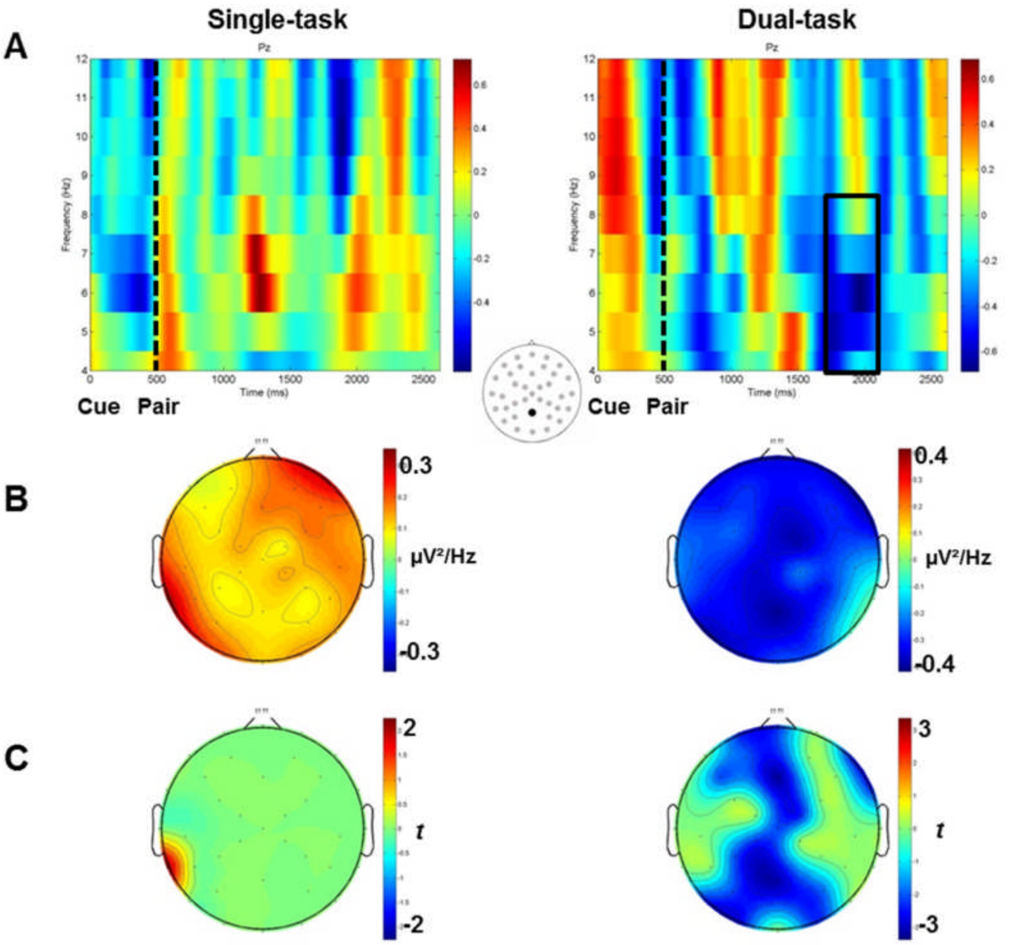


**Figure 32. Associative encoding-related theta activity.**
**A)** Time-frequency representations of associative encoding-related effects (oscillatory power difference between subsequent associative hits and associative misses) in single-task and dual-task conditions at electrode Pz (site 14 from Montage 10, as indicated by the insert) representing the fronto-parietal cluster where the effect was reliable. Significant theta decreases were found in the dual-task but not single-task condition at 1200-1600 ms after word pair onset (as indicated by the boxes drawn on the graphs). **B)** Scalp maps represent differences in theta power in the 1200-1600 ms interval. **C)** Statistical maps show the scalp sites where the effect was significant.

At retrieval, initial analyses revealed that in theta oscillations, there were significant differences in associative retrieval between conditions in 1400-1600 ms after cue onset and at 1000-1400 ms after probe onset. Follow-up analyses within each condition revealed a theta increase in the single-task but not dual-task condition in the pre-probe interval. This effect was reliable over a cluster of mid-frontal and bilateral posterior sites. At the post-probe interval, a theta decrease was found in the dual-task but not single-task condition over right-frontal scalp sites. In addition, across-condition analyses revealed a significant theta decrease between 1400-1800 ms after probe onset in both conditions, consistent with findings from the first study. This effect was largest over right-frontal scalp sites (Figure 33).

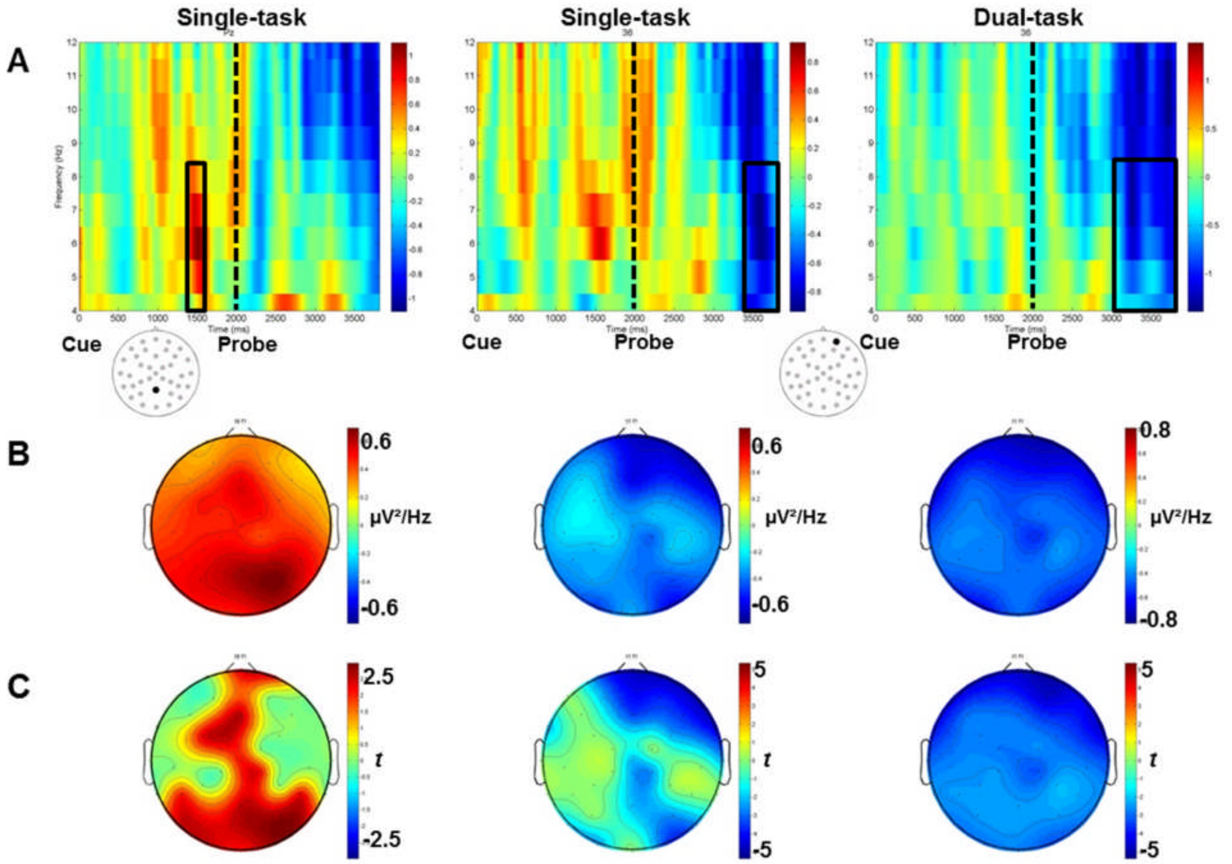


**Figure 33. Associative retrieval-related theta activity.**
**A)** Time-frequency representations of associative retrieval-related effects (oscillatory power difference between associative hits and associative misses) in single-task and dual-task conditions. The graph on the left shows the pre-probe effect in the single-task condition at 1400-1600 ms after cue onset (as indicated by the box drawn on the graph) at electrode Pz (site 14 from Montage 10, as indicated by the insert) representing the fronto-posterial cluster where the effect was significant. The graph in the middle shows the post-probe effect in the single-task condition at 1400-1800 ms after probe onset at a right-frontal electrode (site 36 from Montage 10) where the effect was largest. The graph on the right shows the post-probe effect in the dual-task condition at 1000-1800 ms after probe onset at the same right-frontal electrode. **B)** Scalp maps represent differences in theta power (associative hits – associative misses) corresponding to the effects as indicated in A. **C)** Statistical maps show the scalp sites where the effect was significant.

In alpha oscillations, initial analyses revealed significant differences in associative retrieval between conditions at 1200-1600 ms after cue onset and at 0-600 ms after probe onset. Follow-up analyses within each condition revealed that in the pre-probe interval, there was an alpha increase in the single-task condition with a maximum over left-frontal scalp sites, and an alpha decrease in the dual-task condition focusing over left temporo-parietal scalp sites. Figure 34 shows the significant pre-probe alpha effects as described above.

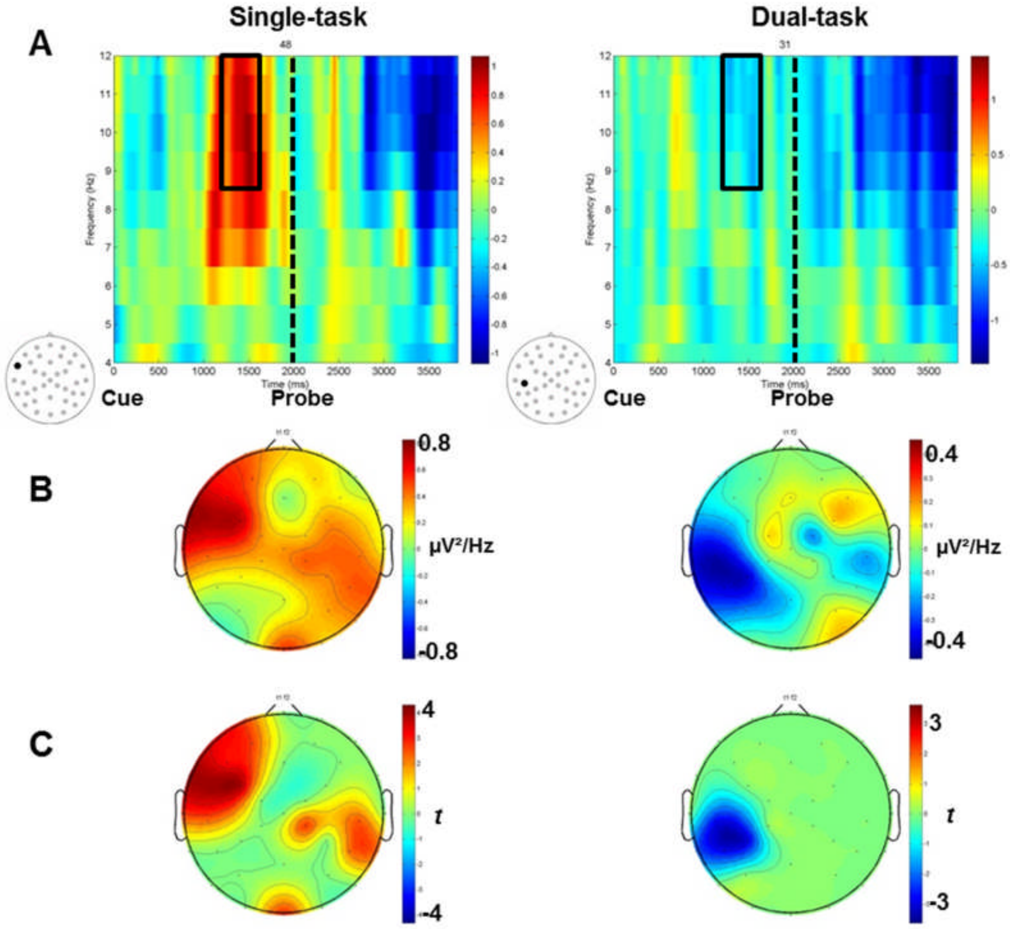


**Figure 34. Pre-probe associative retrieval-related alpha activity.**
**A)** Time-frequency representations of pre-probe associative retrieval-related alpha effect for single-task and dual-task conditions. Significant alpha decrease were found in both conditions at 1200-1600 ms after cue onset (as indicated by the boxes drawn on the graphs), shown at a left-frontal electrode (site 48 from Montage 10, as indicated by the insert) for the single-task condition and a left-temporal site (site 31 from Montage 10) for the dual-task condition. **B)** Scalp maps represent differences in alpha power (associative hits – associative misses) at the 1200-1600 ms interval in the two conditions. **C)** Statistical maps show the scalp sites where the effect was significant.

In the post-probe interval, there was a widespread alpha decrease between 0-600 ms after probe onset. Across-condition analyses found a widespread alpha decrease between 600-1800 ms after probe onset. This effect was reliable in either condition. Figure 35 shows the significant post-probe alpha effects.

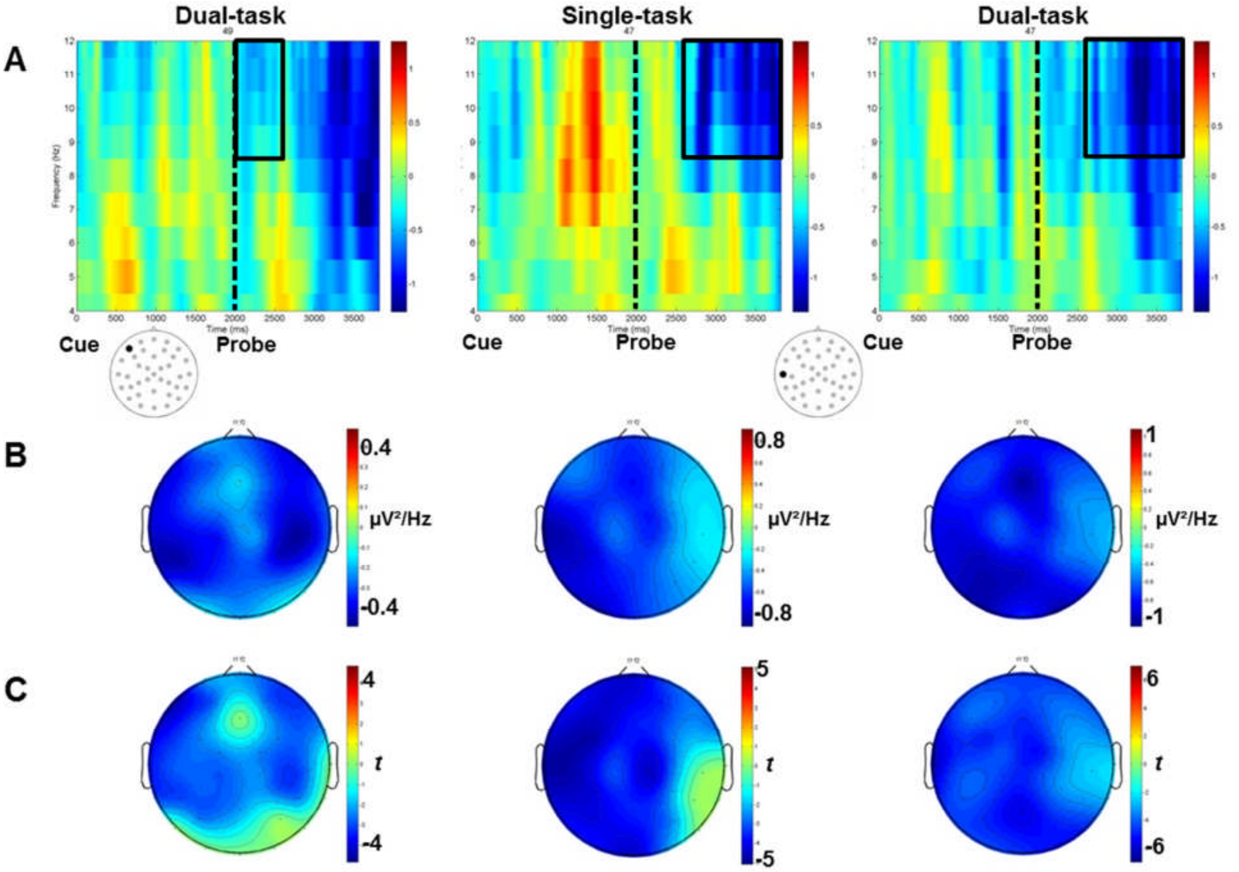


**Figure 35. Post-probe associative retrieval-related alpha activity.**
**A)** Time-frequency representations of post-probe associative retrieval-related alpha effect. The graph on the left shows the early effect at 0-600 ms after probe onset (as indicated by the box drawn on the graph) in the dual-task condition at a left-frontal electrode (site 49 from Montage 10, as indicated by the insert) that was part of a widespread fronto-parietal area where the effect was significant. The graph in the middle shows the effect in the single-task condition at 600-1800 ms after probe onset at a left-temporal electrode (site 47 from Montage 10) that was part of a widespread electrode cluster where the effect was significant. The graph on the right shows the effect in the dual-task condition at the same latency interval and electrode. **B)** Scalp maps represent differences in alpha power (associative hits – associative misses) corresponding to the effects as indicated in A. **C)** Statistical maps show the scalp sites where the effect was significant.

### 3.2.4 Discussion

The present study was designed to investigate whether associative memory effects previously observed in older adults would also emerge in younger adults when their memory is impaired by a concurrent task at encoding. The results show that when processing resources are limited at encoding, younger adults displayed a theta decrease SME similar to that observed in older adults in the first study. At retrieval, distinct pre-probe associative retrieval effects were found in the two conditions. An alpha increase effect and a theta increase effect were found in the single-task condition, whereas an alpha decrease effect was found in the dual-task condition. Moreover, no post-probe theta increase effect as previously observed in younger adults occurred in either condition in the present study. However, sustained broadband power decrease effects similar to those found in the first study were observed across single-task and dual-task conditions. Both theta and alpha effects were stronger and started earlier in the dual-task than single-task condition. A summary of all significant effects found in the present study is shown in Table 12.

**Table 12. A summary of significant associative memory effects in the present study.**

| | Encoding | | Retrieval | | | |
|---|---|---|---|---|---|---|
| | Post-stimulus | | Pre-probe | | Post-probe | |
| Condition | Theta | Alpha | Theta | Alpha | Theta | Alpha |
| Single-task | | | Increase<br>1400-1600 ms<br>frontal and posterior | Increase<br>1200-1600 ms<br>left-frontal | Decrease<br>1400-1800 ms<br>right-frontal | Decrease<br>600-1800 ms<br>widespread |
| Dual-task | Decrease<br>1200-1600 ms<br>frontal and parietal | | | Decrease<br>1200-1600 ms<br>left temporo-parietal | Decreases<br>1000-1800 ms<br>right-frontal | Decrease<br>0-1800 ms<br>widespread |
| Both | | | | | Decrease<br>1400-1800 ms | Decrease<br>600-1800 ms |

*Post-stimulus associative encoding effect*

A theta decrease SME emerged in the dual-task condition, with timing and scalp distribution similar to the SME observed in older adults in the first study. The similarities suggest that the two SMEs may reflect the same underlying neural mechanisms, possibly playing a compensatory role in response to poor memory. In the present study, cognitive resources were limited by a concurrent auditory task in the dual-task condition. Under such conditions, additional neural mechanisms are needed to support associative encoding. Theta decrease SMEs have been reported in a number of studies (e.g., Burke et al., 2013; Guderian et al., 2009). Unlike hippocampal theta, scalp-recorded theta power decreases are thought to reflect an active state of cortical activity (Burke et al., 2013). Analogous to alpha, theta decreases may represent the engagement of neocortical neural assemblies (Lisman & Jensen, 2013). Thus, theta decrease SME may represent the engagement of additional neural activity for items that are successfully encoded. As previously discussed, theta decreases are possibly related to information-rich processing, such as semantic elaboration of study items. Across the two studies, the presence of similar theta decrease SMEs suggests that neural mechanisms underlying these effects are recruited in response to reduced processing resources. Also, older adults' associative encoding deficits are caused, at least partly, by a reduction of cognitive resources in ageing, consistent with the diminished processing resources theory of ageing (Craik, 2006; Craik & Byrd, 1982).

### ***Pre-probe associative retrieval effects***

Distinct pre-probe associative retrieval effects were found in the two conditions, with alpha and theta increases in the single-task condition and alpha decreases in the dual-task condition. The presence of pre-probe effects in the present experiment is in contrast with the absence of any pre-probe effect in the first experiment in either age group. Comparing across the two experiments, an interesting observation is that the pre-probe effects in the single-task condition share some similarities with the prestimulus encoding-related effects in younger adults in the first experiment. Both anticipatory encoding- and retrieval-related effects manifest as power increases in theta and alpha frequencies, involving initially left-frontal scalp sites and then posterior sites. In parallel, the pre-probe effect in the dual-task condition can be compared to the PSME previously found in older adults, both shown as power decreases, albeit in alpha band for younger adults in the present study but in high-theta band for older adults in the first experiment. As previously discussed, the properties of scalp-recorded theta may not be fundamentally different from those of alpha oscillations (Lisman & Jensen, 2013). It is therefore possible that pre-probe alpha/high-theta power decreases represent the same underlying neural mechanisms, possibly an activation of additional neocortical neural assemblies when memory is impaired. Thus, these results suggest that parallel anticipatory mechanisms can be recruited at encoding and retrieval to enhance associative memory. The similarities in anticipatory memory-related activity across the two experiments, between the single-task condition and younger adults and between the dual-task condition and older adults, again support the hypothesis that age-related differences in anticipatory activity are related to poor memory and diminished processing resources at encoding (Craik, 2006).

As previously discussed, left-frontal activation during encoding may be related to strategic control processing such as the utilisation of semantic (deep) encoding strategies (Buckner et al., 1999), which are subject to the availability of processing resources (Anderson et al., 2000). It has been shown that left-frontal activation is reduced in ageing and divided attention conditions during encoding (Anderson et al., 2000). In addition, both theta and alpha oscillations have been related to executive control processing, with theta oscillations representing the involvement of hippocampal–cortical circuits, and alpha oscillations representing the involvement of ‘‘executive’’ thalamo–cortical circuits (Babiloni et al., 2004). In terms of memory-related anticipation, theta increases are thought to prime the PFC-hippocampal network for effective processing of item-context associations (Gruber et al., 2013), and alpha increases are thought to reflect an inhibitory control processing (Fell et al., 2011; Meeuwissen et al., 2011; Waldhauser et al., 2012). Based on this evidence, it may be assumed that anticipatory theta and alpha power increases reflect the dynamics of executive control systems that serve to enhance effective episodic memory encoding and retrieval. The present findings of anticipatory theta and alpha power increase effects in the single-task condition, as well as in younger but not older adults in the previous study, point to age-related impairments in these executive control mechanisms during associative memory processing.

It has to be noted that there are also differences between anticipatory encoding-related activity in younger adults in the first study and anticipatory retrieval-related activity in the single-task condition. The PSMEs started with left-frontal theta increases that were followed by posterior alpha increases. In contrast, pre-probe retrieval effects started with left-frontal alpha increases followed by frontal and posterior theta increases. Such differences suggest that maybe cortical theta and alpha oscillations are not fundamentally different from each other, as pointed out by Lisman and Jensen (2013). Alternatively, the differences may indicate that distinct neural mechanisms underlying theta and alpha increases are recruited dynamically in preparation for associative encoding and retrieval. There is currently not enough knowledge to determine which interpretation is more likely. In any case, there may be large overlap between the two kinds of anticipatory activity.

Across the two studies, the pre-probe theta/alpha decrease in the dual-task condition and in older adults suggest that different anticipatory neural mechanisms are recruited when memory is impaired either in ageing or divided attention conditions. In the first study, the theta decrease PSME was thought to reflect an elaborative encoding of the location words that serves to lay down a rich context for the upcoming object words to be embedded in. Although alpha decreases are traditionally associated with semantic processing (e.g., Klimesch, 1996, 1999), this interpretation cannot be applied to the pre-probe alpha decrease in the present study. Scalp distributions of these effects are different, with the PSME spreading over right-hemisphere scalp sites whereas the present pre-probe effect focuses over a cluster of left temporo-parietal sites. It is therefore likely that the two anticipatory effects reflect different underlying neural mechanisms. The scalp distribution of the present pre-probe effect resembles those of post-probe theta retrieval effects, which have been related to the reinstatement of memory traces that are important for episodic retrieval (e.g., Jafarpour et al., 2014). Although it is currently not clear what the underlying neural mechanisms may be, the present pre-probe theta decrease may reflect certain anticipatory neural processing related to episodic retrieval, possible a preactivation of episodic memory traces. More importantly, such anticipatory retrieval-related activity may play a compensatory role when memory is impaired.

An obvious question arises why there was no pre-probe associative retrieval-related effect in the first study, neither in younger or older adults. A possible explanation lies in the difference in memory performance across studies. As discussed in the ERP chapter, although the proportions of associative hits were comparable between the single-task condition and younger adults in the first study, overall recognition accuracy (Pr) was lower in the present study. It may be that pre-probe anticipatory mechanisms are engaged by younger adults only when they are needed, e.g., when memory is poor. In the first study, there is no need for younger adults to recruit anticipatory mechanisms when the retrieval is relatively easy. In contrast, a prominent ERP anticipatory retrieval effect emerged in older adults in the first study, suggesting that they did recruit anticipatory mechanisms, albeit not in theta or alpha oscillations. This again demonstrates that ERP and time-frequency analyses are complimentary techniques that can reveal distinct brain activity.

### ***Post-probe associative retrieval effects***

Consistent with the first study, the present study reveals sustained post-probe broadband power decreases across conditions. These effects start with widespread alpha decreases which are followed by theta decreases larger over right-frontal scalp sites. In the dual-task condition, both theta and alpha effects start much earlier than those in the single-task condition. Particularly, alpha decreases start as soon as probe onset in the dual-task condition, suggesting that the effect may begin even before the probe onset. Comparing across studies, the onset of the alpha decrease effect in the single-task condition is identical to that in the first study. As memory is relatively impaired in the dual-task than single-task condition, it may be assumed that the broadband power decrease, particularly alpha decrease, reflects neural mechanisms at retrieval that can be recruited early in compensation for poor memory. Based on the effect timing, in the first study the late onset (> 600ms post-probe), sustained alpha decreases are likely to reflect post-retrieval monitoring and evaluation processes that are important for associative retrieval. In the present study, however, the alpha decrease effect starts very early in the dual-task condition. A more comprehensive interpretation is that alpha decreases reflect a kind of top-down control processing that serves to facilitate associative retrieval. This interpretation is also consistent with findings from a previous study (Sebastian et al., 2011) that older adults exhibit greater sustained alpha power decreases than younger adults during retrieval when memory performance is matched across age. The authors proposed that the alpha decrease reflects the recruitment of additional neural mechanisms, such as executive functions, to enhance memory performance. Therefore, alpha decreases at retrieval may serve as a compensatory mechanism when memory is impaired.

However, it may be questioned why older adults in the first study did not show greater, or earlier, alpha decreases relative to younger adults. A likely explanation is that the engagement of such compensatory control activity is resource demanding, and therefore can only be successfully engaged by older adults to enhance retrieval under certain circumstances. For example, Sebastian et al. (2011) used a haptic continuous recognition task with real objects, which taps into the kind of memory that is relatively preserved in ageing (Ballesteros & Reales, 2004). In contrast, associative memory tasks tap into the kind of memory with which older adults are most impaired. It is therefore likely that older adults are able to recruit compensatory mechanisms for the former but not the latter task.

An interesting observation is that across conditions, as well as in younger adults in the first study, post-probe theta effects are largest over right-frontal scalp sites. Both timing and scalp distributions of these effects resemble those of the ERP right-frontal retrieval effects. Such parallel occurrences of theta/delta and ERP retrieval effects have also been demonstrated in previous studies, albeit in different time windows (e.g., ~400-650 ms in Klimesch et al., 2000). Co-occurrences of oscillatory and ERP effects give rise to the possibility that they may reflect the same underlying retrieval-related activity. Klimesch and colleagues (2000) also proposed that ERP old/new effects are generated by very slow frequencies that are below the delta band. Nevertheless, in the present study the theta effect started much later in the single-task than dual-task condition, whereas such a between-condition difference did not emerge in ERP analyses. Further evidence is needed to determine whether ERP effects are generated by very slow oscillations, which may also influence theta activity.

Unlike in the first study, no theta increase associative retrieval effect emerged in the present study in either condition. Post-probe theta increase effects are thought to reflect neural reinstatement of episodic memory traces (e.g., Jafarpour et al., 2014). The absence of this effect in the present study suggests that participants could not rely on these mechanisms, but rather those underlying the sustained broadband power decrease effects to recover associative information. This may be explained by the difference in memory performance across studies. As discussed in the ERP chapter, although the proportions of associative hits were comparable between single-task condition and younger adults in the first study, overall recognition Pr is lower in the present study. It can therefore be assumed that when memory is poor, participants have to rely on executive control processes, as reflected by sustained broadband power decreases, to recover associative information. The same argument can also be made to explain the absence of a pre-probe associative retrieval-related effect in the first study. It is possible that pre-probe anticipatory activity is engaged by younger adults when their memory is poor, whereas older adults are unable to engage such activity due to age-related impairment in anticipatory processing.

Taken together, the present study revealed that anticipatory associative memory effects in the single-task condition are similar to those found in younger adults in the first study, whereas the anticipatory effect in the dual-task condition resembles that previously found in older adults. Similarly, previously observed post-stimulus theta SME in older adults was also replicated in the dual-task condition, indicating a compensatory role of such activity in ageing. Consistent with ERP analyses, the present findings show that age-related differences in anticipatory associative memory effects found in the first study can be replicated in younger adults when their memory is impaired by a reduction of processing resources at encoding. These findings support the diminished processing resources theory of ageing (Craik, 2006). They also indicate that compensatory associative memory effects in older adults are adaptive responses to poor memory that can be brought online by younger adults, consistent with the STAC model of compensation (Reuter-Lorenz & Park, 2010).

## 3.3 Experiment 3: Age differences in anticipatory memory-related activity when target materials are intermixed

### 3.3.1 Encoding

#### *3.3.1.1 Introduction*

In the first study, anticipatory associative encoding-related activity differed between younger and older adults, with enhanced prestimulus theta and alpha power related to successful associative encoding in younger adults and reduced theta power related to successful associative encoding in older adults. It was thought that PSMEs in the two age groups reflect different preparatory strategies. The effects in younger adults emerged after neutral warning cue onset, possibly reflecting executive control mechanisms that involve a pre-activation of the PFC-hippocampal neural network for associative encoding and inhibition of task-irrelevant information. In contrast, the effect in older adults did not emerge until after the presentation of location words, possibly reflecting a semantic elaboration of the locations to enable the objects to be more tightly bound with the locations.

These age-related differences in anticipatory brain activity indicate a difference in mnemonic strategy across age. Younger adults seem to recruit executive control mechanisms in a proactive manner before encountering any to-be-encoded information. In contrast, older adults may rely more on semantic preparation based on part of the information that is presented. Thus, ageing could lead to a shift from a proactive (i.e., mediated by cues) to a reactive (i.e., mediated by stimuli) shift in cognitive control strategy, as proposed in the early-to-late shift in ageing (ELSA) model (Dew et al., 2012). The present study aimed to further investigate the relationship between anticipatory encoding-related activity and executive control in ageing by increasing the cognitive control requirements in the task.

As already discussed in the ERP chapter, previous studies investigating PSMEs (e.g. Galli et al., 2011, 2012, 2013; Otten et al., 2006, 2009) usually use at least two different types of encoding tasks or stimuli that are intermixed to form the study lists. When different kinds of encoding stimuli are intermixed, studies usually find material-invariant PSMEs, that is, PSMEs common to both classes of material (e.g. intermixed visually and auditorily presented words: (Otten et al., 2009; Park & Rugg, 2010). This kind of PSME has been interpreted in terms of general semantic preparation across modalities, which can be engaged in a flexible manner to facilitate memory formation.

A recent fMRI study using an item-item associative memory task (Addante et al., 2015) contrasted prestimulus encoding-related brain activity for word–word and picture–picture pairs. It was revealed that similar to single item encoding, inter-item associations are also influenced by prestimulus neural activity. Material-invariant PSMEs were found in several cortical regions, including bilateral prefrontal and parietal cortex, insula, posterior cingulate cortex, and the hippocampus. These regions overlap with the distributed cortical network that is thought to support cognitive control functions, such as the adoption and maintenance of task sets in service of behavioural goals (e.g., Cole et al., 2013). Accordingly, the material-invariant PSMEs were thought to reflect differential engagement of these control processes in response to pre-stimulus preparatory cues.

In addition, a material-selective PSME was found for picture pairs only, in bilateral fusiform cortex and intraparietal sulcus. These regions overlap with cortical regions selectively activated by pictures (Addante et al., 2015). This finding supports the proposal that memory encoding can benefit from "pre-activation" of material-selective cortical regions (Adcock et al., 2006; Otten et al., 2006; Park & Rugg, 2010). This is in line with findings from attention studies (see Driver & Frith, 2000 for a review) that a pre-stimulus attentional cue can lead to pre-stimulus activation of domain-selective cortical regions. Thus, the findings from Addante et al. (2015) indicate that memory encoding may benefit from a pre-activation of material-selective cortical regions.

The aim of the present study was to investigate whether associative PSMEs emerge when frequent switches between different classes of study materials are required in an associative recognition paradigm. It was assumed that the engagement of anticipatory activity under such conditions would be more demanding and rely to a greater extent on executive control. The question of interest was whether older adults engage prestimulus encoding-related activity under such conditions and, if so, how this differs from how younger adults approach the task. If material-invariant PSMEs emerge under such conditions, it would suggest that anticipatory activity reflects a trial-by-trial task set configuration. In comparison, material-selective PSMEs more likely reflect a pre-activation of material-specific cortical regions. Based on previous findings that older adults are impaired in the ability to utilise cue information to benefit task performance (Paxton et al., 2006), and show pre-activation of material-selective brain regions in expectation of study material (Bollinger et al., 2011), it was expected that age differences in PSMEs would emerge in the present study.

As described in the ERP chapter, an associative memory paradigm was employed using picture-picture pairs and word-word pairs that were randomly intermixed in an incidental study task. Each pair was preceded by a cue that indicated which type of stimulus material would be presented next. Memory for the study pairs was tested with an associative recognition test, during which studied items were presented either as intact or rearranged pairs, along with pairs of new items. The critical contrast was between intact pairs that were correctly identified as “intact” (associative hits) and intact pairs that were incorrectly judged as “rearranged” (associative misses). Using this contrast, associative memory was isolated without being confounded by the strength of item memory.

#### ***3.3.1.2 Methods***

Information about participants, stimuli, experimental procedures, and EEG acquisition has been reported in the ERP chapter. Methods for EEG pre-processing and artefact rejection were identical to those used in the first study.

*Time-frequency analyses*

EEG epochs ranged from 600 ms before cue onset until 4400 ms thereafter. This epoch length covered the 2000 ms pre-stimulus and 1800 ms post-stimulus intervals, with an extra 600 ms after the intervals to avoid edge effects. For encoding, the mean numbers of artefact-free associative hit and associative miss trials were respectively 39 and 26 for pictures and 46 and 22 for words in younger adults, and 33 and 33 for pictures and 38 and 25 for words in older adults. The same 24 younger and 24 older participants used in the ERP analyses were entered into the oscillatory analyses. All participants had at least 16 artefact-free trials except for one younger and one older participant who respectively contributed 13 and 14 associative miss encoding trials for words.

Associative SMEs were computed by subtracting activity elicited during associative miss trials from activity elicited during associative hit trials. The initial statistical analyses focused on the interaction between associative SMEs and age, separately for pictures and words. Time-frequency clusters where significant interactions emerged were followed up with permutation tests within each age group to see whether SMEs were reliable for each age group. Latency intervals that did not show significant memory by age interactions were subjected to analyses to assess main effects of memory irrespective of age. In addition, when significant PSMEs or SMEs emerged for both words and pictures, further analyses were performed to see whether the effects were material-invariant or material-specific. As done previously, effects were only considered if they spanned across at least two neighbouring electrodes and two consecutive time bins to reduce the chance of Type 1 errors.

### *3.3.1.3 Results*

Behavioural results can be found in the ERP chapter.

*Time-frequency analyses*

In the theta range, the analyses revealed a significant interaction between associative SME and age at 800-1200 ms after cue onset for words. Follow-up analyses within each group revealed a pre-stimulus theta increase in younger but not older adults over a cluster of electrode sites spanning from mid-frontal to posterior regions. For pictures, there were significant interactions between 400-800 ms after cue onset and 200-600 ms after probe onset. Follow-up analyses within each group revealed a pre-stimulus theta increase in younger but not older adults over a widespread electrode cluster with right-frontal and left-parietal maxima, and a post-stimulus theta increase also in younger adults over left-frontal and right temporo-parietal sites. Figure 36 shows the significant associative encoding-related theta effects described above.

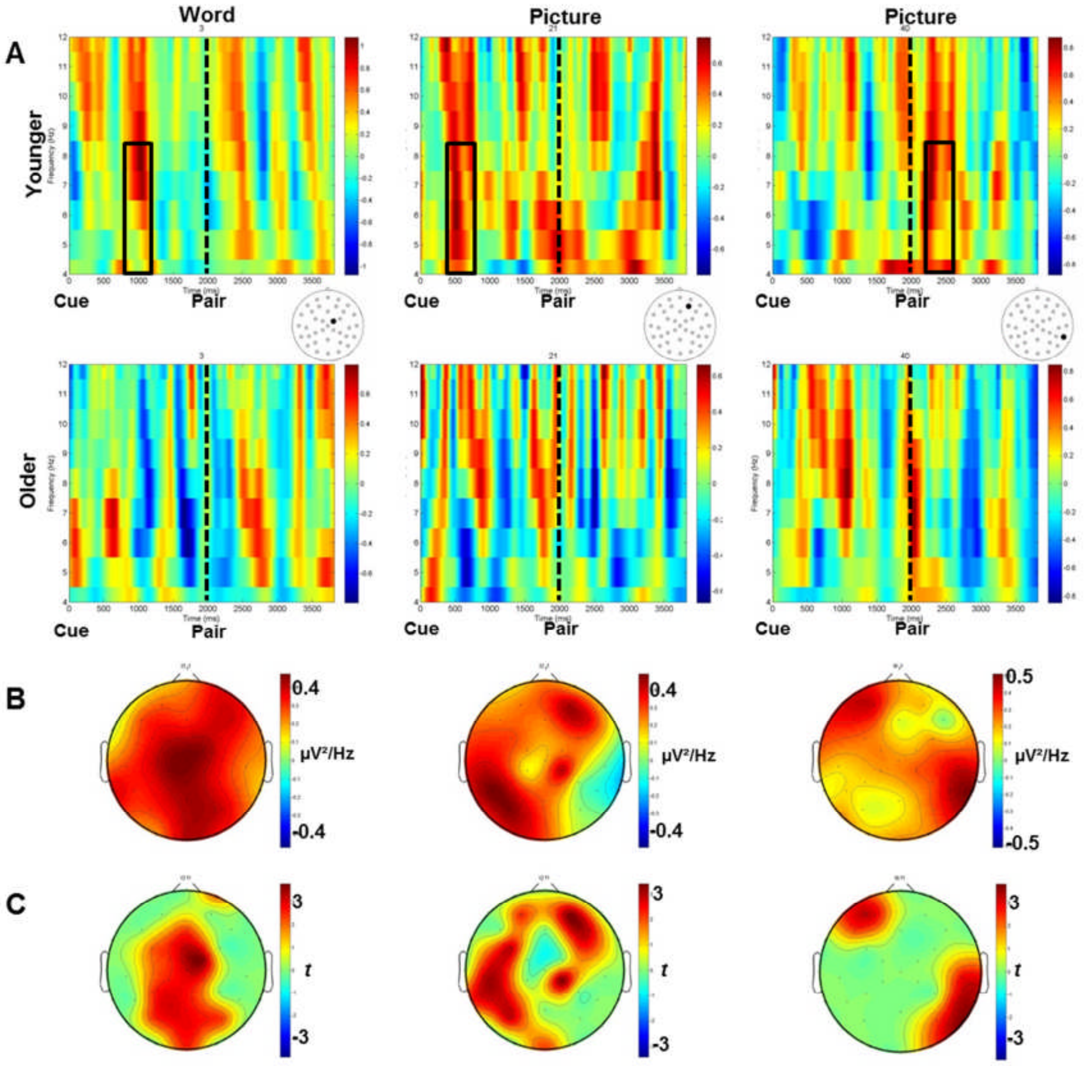


**Figure 36. Associative encoding-related theta activity.**
**A)** Time-frequency representations of associative encoding-related theta subsequent memory effects (power difference between associative hits and associative misses) for picture and word pairs in younger and older adults at 3 electrode sites as indicated by the inserted head models. The graph on the left presents the PSME for words between 800-1200 ms after cue onset (indicated by the box drawn on the graph) that was found in younger (upper) but not older (lower) adults, showing a central electrode (site 3 from Montage 10) that was part of the left-frontal electrode cluster where the effect was significant. The graph in the middle presents the PSMEs for pictures between 400-800 ms after cue onset, showing a right-frontal site (site 21 from Montage 10). The graph on the right presents the post-stimulus SME for pictures in younger adults between 200-600 ms after stimulus onset, showing a right-parietal site (site 40 from Montage 10). **B)** Scalp maps represent differences in theta power (associative hits – associative misses) corresponding to the effects indicated in A. **C)** Statistical maps showing the scalp sites where the effect was significant.

In the alpha range, the analyses revealed a significant interaction between associative SME and age between 800-1200 ms after cue onset for words. Follow-up analyses within each group revealed a prestimulus alpha increase in younger but not older adults, focused over left-parietal scalp sites. For pictures, there were significant interactions between 600-1000 ms and 1400-1800 ms after cue onset. Follow-up analyses revealed a prestimulus theta increase between 600-1000 ms in younger but not older adults over a cluster of parietal scalp sites with a left-hemisphere asymmetry. No reliable PSMEs were found in the 1400-1800 ms interval in either group, although the difference between groups was in the same direction as in the 600-1000 ms interval. Figure 37 shows the significant associative encoding-related theta effects as described above.

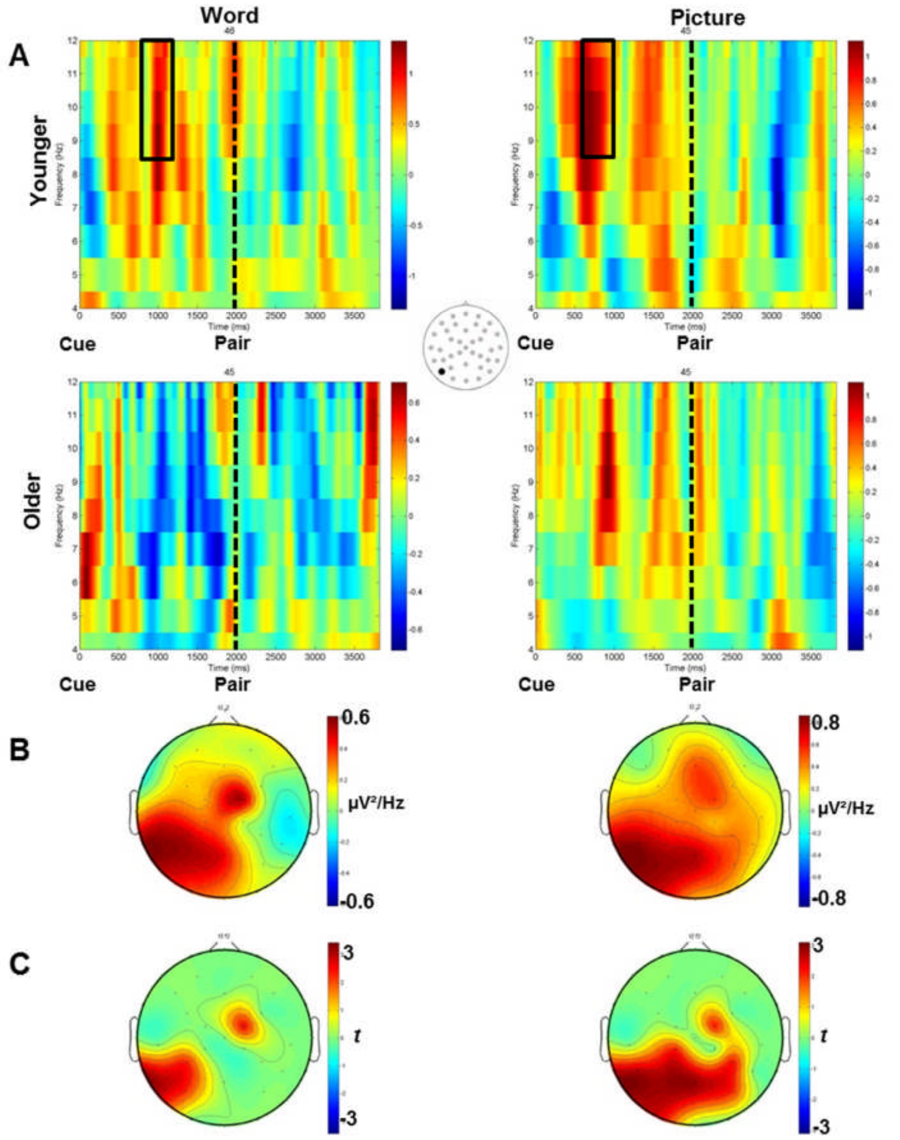


**Figure 37. Associative encoding-related alpha activity.**
**A)** Time-frequency representations of associative encoding-related alpha activity (power difference between associative hits and associative misses) for picture and word pairs in younger and older adults at a left-parietal electrode (site 45 from Montage 10, as indicated by the insert) that was part of the left-parietal cluster where effects were significant. The graph on the left presents the PSME in the word condition between 800-1200 ms after cue onset (indicated by the box drawn on the graph). The graph on the right shows the PSME in the picture condition between 600-1000 ms after cue onset. Both effects were found in younger (upper) but not older (lower) adults. **B)** Scalp maps representing differences in theta power (associative hits – associative misses) corresponding to the effects indicated in A. **C)** Statistical maps showing the scalp sites where the effects were significant.

As significant theta and alpha PSMEs emerged in younger adults for pictures and words when each was considered separately, further analyses were performed to investigate whether the effects were the same across materials. Permutation analyses did not reveal significant differences between words and pictures in the theta PSMEs during 400-800 ms and 800-1200 ms intervals. Similarly, no significant differences emerged as a function of stimulus material for the alpha PSME during 600-1000 ms and 800-1200 ms  Thus, the data point to equivalent encoding-related effects for words and pictures, suggesting that the effects are material-independent.

#### ***3.3.1.4 Discussion***

The present experiment intended to investigate the effect of age on prestimulus encoding-related oscillatory activity when different types of encoding material are intermixed in an associative recognition task. Under such conditions, it would be important to recruit cognitive control mechanisms, such as task-set reconfiguration, in anticipation of upcoming stimuli. Consistent with the first study, PSMEs were found in younger adults, with enhanced theta power over frontal and parietal sites and alpha increases over posterior sites predictive of successful later retrieval of associative information. These effects were similar across materials, except that the effects for pictures emerged in earlier time windows than those for words. Following picture cues, theta increases were observed from 400 to 800 ms over right-frontal and left-parietal sites and alpha increases from 600-1000 ms over posterior sites. Following word cues, theta increases were observed from 800 to 1200 ms over midline frontal and parietal sites and alpha increases in the same interval over left posterior sites. In stark contrast, older adults did not show any significant PSMEs. For post-stimulus activity, again only younger adults showed an SME for picture pairs, manifesting as theta increases over left-frontal and right temporo-parietal scalp sites from 200 to 600 ms after stimulus onset.

### *Prestimulus brain activity*

The PSMEs in younger adults closely resemble those in the first study, consisting of theta and alpha power increases over frontal and posterior scalp sites. As previously discussed, fronto-posterior theta increases may index executive functions in a dynamic network of the PFC and task-related posterior brain regions (Mizuhara & Yamaguchi, 2007). Frontal theta may serve to prime the PFC-hippocampal network for effective encoding of item-context associations. In contrast, alpha enhancements before successful memory encoding are thought to reflect inhibitory control processing for task-irrelevant information (Fell et al., 2011; Meeuwissen et al., 2011). Together, prestimulus theta and alpha increases may reflect the dynamics of a preactivation of the PFC-hippocampal and PFC-posterior networks and the inhibition of task-irrelevant information, serving to facilitate effective associative memory encoding.

The anticipatory control processes may be common to both classes of material given that no differences between the encoding of word pairs and picture pairs were observed. Similarly, Addante et al. (2015) reported material-invariant PSMEs identified in bilateral prefrontal, parietal cortex, hippocampus, as well as insula and posterior cingulate cortex. The overlap between these regions and those comprising neural networks supporting cognitive control functions, such as the adoption and maintenance of task sets in service of behavioural goals (e.g., Cole et al., 2013), supports the above interpretations for the oscillatory PSMEs observed in the present experiment. Thus, the existent evidence across studies supports the hypothesis that the encoding of inter-item associations, as well as single items, is influenced by prestimulus neural activity possibly related to executive control mechanisms, such as trial-by-trial task set reconfiguration according to different encoding goals. The absence of material-selective effects argues against the hypothesis that PSMEs represent a pre-activation of material-selective brain regions in expectation of studying a certain class of material (Bollinger et al., 2011).

In the present study, PSMEs for pictures emerged in earlier time windows relative to effects for words. The timing of PSMEs is thought to be influenced by the information load of the cues and the length of the cue-stimulus interval, as discussed in the first study. However, these two factors do not vary across materials in the present study. One possibility is that picture cues elicit faster anticipatory responses, which may be related to the perceptual difficulty of pictures. That is, participants may prepare early for an upcoming stimulus that is more difficult to process. This is an interesting contrast to the early positive peak in ERPs at around 160-170 ms that was larger for word cues than picture cues. It seems that anticipatory processes are engaged for both word pairs and picture pairs, but that these processes can be reflected in ERPs or oscillatory activity. An interesting direction for future studies is to discern under what circumstances anticipatory processes give rise to changes in ERPs or oscillations, and what the functional role is of each.

An important finding in the present study is that no PSMEs emerged in older adults, unlike the first study. In the first study, an associative PSME emerged in older adults during the pre-binding interval, after location word onset, with theta decreases over right-lateralised scalp sites predicting successful associative encoding. This effect was thought to reflect an elaborative encoding of the location words that enhances subsequent binding between locations and objects. Together, the present findings suggest that older adults are able to engage in anticipatory brain activity to enhance binding, but only when the cues contain some of the to-be-encoded information. Such advance information may either facilitate the binding process itself, or allow for an early processing of the information that needs to be bound. Unlike younger adults, older adults may not be able to recruit executive control mechanisms to facilitate encoding in the absence of knowledge about at least some aspects of the to-be-encoded information. This is consistent with the findings in Paxton et al. (2006) that older adults are unable to take advantage of the cue information to benefit performance, an effect related to reduced activation of lateral PFC which, in turn, has been associated with goal maintenance (Paxton et al., 2008). Such findings support the ELSA model, which proposes that ageing is related to a shift from a proactive (i.e., mediated by cues) to a reactive (i.e., mediated by stimuli) cognitive control strategy. Consistent with similar age-related impairments in associative memory performance across pictures and words, the absence of PSMEs in older adults indicate an age-related impairment in anticipatory encoding-related neural activity regardless of encoding material.

### *Subsequent associative memory effects*

In younger adults, enhanced theta power over left frontal and right temporo-parietal scalp sites during the encoding of picture pairs was associated with subsequent recognition success. Previous studies using subsequent memory paradigms have often reported greater theta power for subsequently remembered than forgotten items (Hanslmayr et al., 2009; Osipova et al., 2006; Sederberg et al., 2003). Theta oscillations are thought to be important for binding and ordering individual episodic components (Nyhus & Curran, 2010). The present finding that theta increases for subsequent successful recovery of associative information is consistent with this proposal. Furthermore, the characteristics of the present theta SME are consistent with findings from previous studies. For example, Osipova et al. (2006) found greater right temporal–parietal theta power for subsequently recognised than not recognised pictures, and the effect emerged in a time window similar to that in the present study (300 to 1000 ms after stimulus onset). Similar findings have also been reported when faces are used (Mölle et al., 2002). In that study, greater theta power over right parietal scalp areas was found for subsequently recalled than not recalled faces, whereas greater theta power over left frontal and temporal scalp sites was found for subsequently recalled than not recalled words. Thus, the present theta SME for picture-picture associations may represent the activation of neural networks for picture processing, similar to those during the encoding of single pictures. Pictures are thought to provide much richer perceptual details that facilitate semantic elaboration (Yonelinas, 2002). Pictures have been shown to elicit effective and automatic engagement of brain regions important for visual memory, including bilateral visual and medial temporal cortices (Grady et al., 1998). Thus, the picture-selective theta SME may reflect the activation of those brain regions that are responsible for the processing of rich perceptual details.

It is not clear why parallel associative SMEs did not emerge for words in the present study. The absence of a material-specific oscillatory SME for word pairs in younger adults is consistent across all three experiments in this thesis, except for the divided attention condition in the second study. This is in contrast with ERP analyses that consistently found SMEs for word pair associations. ERP analyses in the present study also revealed equivalent SMEs for words and pictures, and these ERP effects differ from the picture-selective theta SME in both timing and scalp distribution. Taken together, the picture-selective theta

SME in the present study may represent the engagement of additional neural processes in younger adults for the encoding of picture pairs, besides those giving rise to material-invariant SMEs in ERPs. Such additional neural processes may be related to poorer memory performance for pictures than words (as reported in the ERP chapter). That is, additional material-selective neural mechanisms, as reflected in theta increases, may be needed for successful encoding when the task is demanding.

It is currently not clear what the underlying neural mechanisms are for the picture-selective SME, but an important finding is that older adults did not show such an effect. This is in contrast with ERP findings of comparable associative SMEs across age for both pictures and words. Thus, it appears that older adults are able to engage material-invariant encoding-related neural activity, as reflected in ERPs, but unable to recruit additional material-selective mechanisms in response to greater demands for picture encoding, as reflected in theta oscillations. This impairment may be an indication of strategic inflexibility in ageing.

Older adults in the present study also did not show compensatory encoding-related activity, as they did in the first study. In the first study, a theta decrease SME was found in older but not younger adults. A similar effect was also found in younger adults in the second study when processing resources were reduced by a concurrent task. Thus, the theta decrease SME in older adults was thought to reflect the recruitment of compensatory mechanisms in response to diminished processing resources during encoding. The absence of such an effect in older adults in the present study may be explained by the experimental manipulation. Frequent switching between different classes of encoding material is resource demanding. It is possible that older adults are unable to recruit compensatory mechanisms due to reduced processing resources.

In conclusion, the present findings point to an age deficit in anticipatory encoding-related brain activity, which may reflect a malfunction of top-down control mechanisms. Younger adults seem able to recruit anticipatory mechanisms for associative encoding even when switching between different classes of encoding material. These material-invariant anticipatory effects likely reflect executive control mechanisms such as task-set reconfiguration. In contrast, older adults may not be able to recruit such anticipatory mechanisms to benefit encoding. In terms of post-stimulus activity, older adults seem also impaired in the ability to engage additional material-selective processes in response to task demands, which may be an indication of strategic inflexibility in ageing. In addition, older adults in the present study did not engage compensatory mechanisms as observed in the first study, possibly due to reduced processing resources. Overall, older adults appear to be impaired in anticipatory processes and strategic flexibility, both of which are related to executive functions.

### 3.3.2 Retrieval

#### *3.3.2.1 Introduction*

As discussed in the ERP chapter, the aim of Experiment 3 was to investigate whether the associative retrieval effects found in the previous experiments would also emerge when different retrieval goals are intermixed. It was assumed that the engagement of pre-probe anticipatory activity under such conditions would be more reliant on cognitive control.

In the single-task condition in Experiment 2, as well as for younger adults in the first study, consistent anticipatory associative memory effects were observed, in the form of theta and alpha power increases over frontal and posterior scalp sites. Theta increases are generally thought to represent the involvement of hippocampal–cortical circuits that may serve to prime the PFC-hippocampal network for effective processing of item-context associations (Gruber et al., 2013). In contrast, alpha increases are thought to represent the involvement of thalamo–cortical circuits (Babiloni et al., 2004) and have been related to inhibitory control processing (Meeuwissen et al., 2011; Waldhauser et al., 2012). Across the two initial studies in this thesis, anticipatory theta and alpha increases varied in the order in which they occurred and in scalp distributions over a cluster of fronto-posterior scalp sites, indicating that they may represent the activation of a dynamic cognitive control system that facilitates effective episodic memory processing. The absence of anticipatory theta and alpha power increases in the single-task condition and in older adults indicates that these executive control mechanisms may be vulnerable to the effect of ageing and diminishing attentional resources.

In addition, decreases in anticipatory memory-related theta activity were found in the dual-task condition of Experiment 2 and for older adults in Experiment 1. This activity was thought to reflect anticipatory mechanisms that are recruited when memory is impaired, either in ageing or divided attention conditions. The functional role of this effect is not clear, but it might be related to the reinstatement of episodic memory traces based on the similarity in scalp distributions between this effect and typical post-probe theta retrieval effects (e.g., Jafarpour et al., 2014),

The aim of the present study was to investigate how pre-probe anticipatory brain activity varies with intermixed retrieval goals in an associative recognition paradigm. The question was whether older adults are able to engage pre-probe retrieval-related activity under such conditions and, if so, how it may differ from younger adults. It was expected that younger adults would show pre-probe associative retrieval effects, possibly in the form of theta and alpha power increases. It was more difficult to predict whether older adults would be able to engage pre-probe retrieval-related activity. Older adults might fail to engage such activity due to great demands on cognitive control because of having to switch between different retrieval goals. Alternatively, older adults might be able to engage some kind of anticipatory activity for retrieval as it is usually thought that older adults are less impaired in recognition relative to recall tests (Craik & Rose, 2012).

### *3.3.2.2 Methods*

*Time-frequency analyses*

EEG epochs ranged from 600 ms before cue onset until 4400 ms thereafter. This epoch length covered the 2000 ms pre-probe and 1800 ms post-probe intervals, with an extra 600 ms after the intervals to avoid edge effects. For retrieval, the mean numbers of artefact-free associative hit and associative miss trials in younger adults were respectively 38 and 27 for pictures and 45 and 23 for words. In older adults, these were respectively 32 and 33 in for pictures and 38 and 25 for words. The same 24 younger and 24 older participants as in the ERP analyses entered into the present analyses. All participants had at least 16 artefact-free trials except for one younger participant who contributed 13 associative miss retrieval trials for words. The methods for statistical analyses were identical to those used for the encoding data.

#### ***3.3.2.3 Results***

*Pre-probe anticipatory activity*

For words, the analyses revealed that in theta oscillations, there was a significant interaction between response and age between 1400 and1800 ms after cue onset. Follow-up analyses within each group revealed a pre-probe theta increase in younger, but not older, adults over a cluster of frontal scalp sites with a right-hemisphere asymmetry. Analyses across groups revealed a main effect of response during 1000-1400 ms after cue onset, with significant theta increases found in both groups. Figure 38 shows the significant pre-probe theta associative retrieval effects described above.

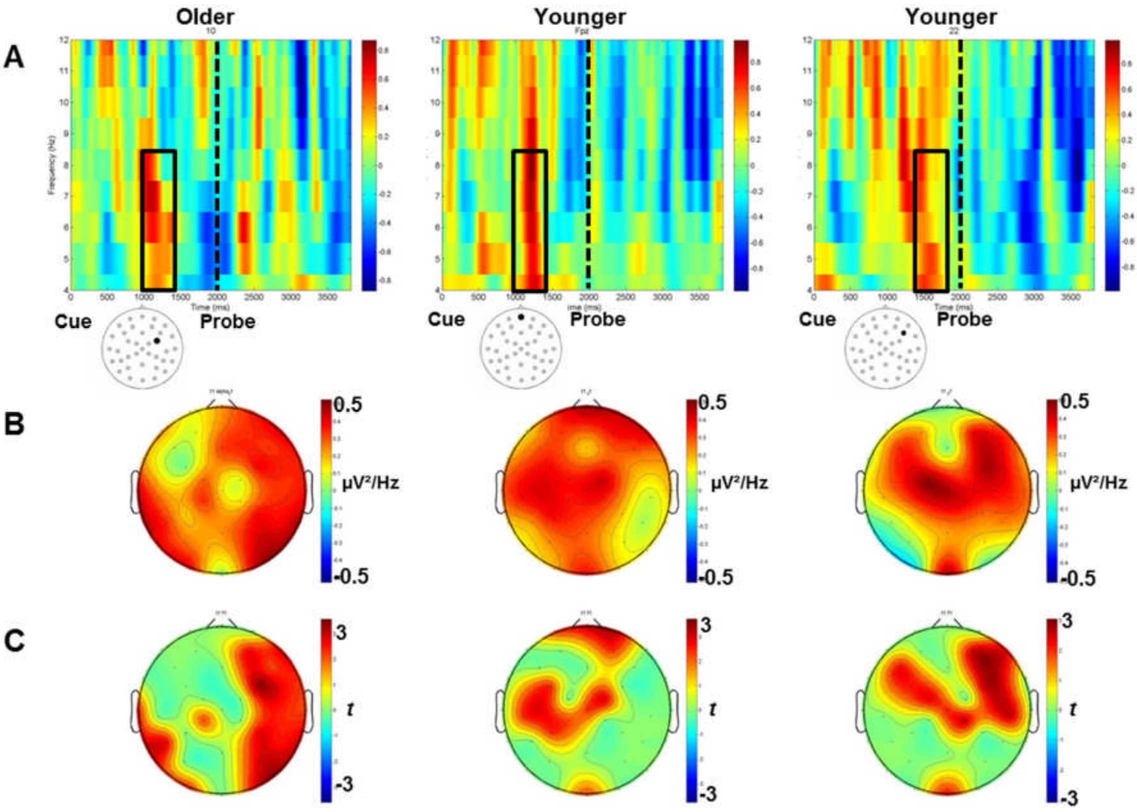


**Figure 38. Pre-probe associative retrieval effects for word pairs.**
**A)** Time-frequency representations of associative retrieval-related effects (oscillatory power differences between associative hits and associative misses) for words at 3 electrodes as indicated by the inserted head models. The graph on the left shows the pre-probe effect in older adults during 1000-1400 ms after cue onset (as indicated by the box drawn on the graph) at a right-frontal electrode (site 10 from Montage 10) representing the right-hemisphere cluster where the effect was significant. The graph in the middle shows the effect in younger adults in the same interval at FPz (site 35 from Montage 10) where the effect was largest. The graph on the right shows the effect in younger adults from 1400 to 1800 ms at a right-frontal electrode (site 22 from Montage 10). At this interval no significant effect was found in older adults. **B)** Scalp maps representing differences in theta power (associative hits – associative misses) corresponding to the effects indicated in A. **C)** Statistical maps showing the scalp sites where the effect was significant.

For pictures, there was a significant response by age interaction in theta oscillations in the 1400-1800 ms interval. Subsidiary within-group analyses revealed a pre-probe theta decrease in younger adults over bilateral frontal scalp sites, and a theta increase in older adults over left temporo-parietal sites. In alpha oscillations, a significant interaction between response and age was found between 1400 and 2000 ms after cue onset. Subsidiary within-group analyses revealed a pre-probe alpha decrease over bilateral anterior-frontal sites in younger, but not older, adults. Figure 39 shows the pre-probe retrieval effects for pictures.

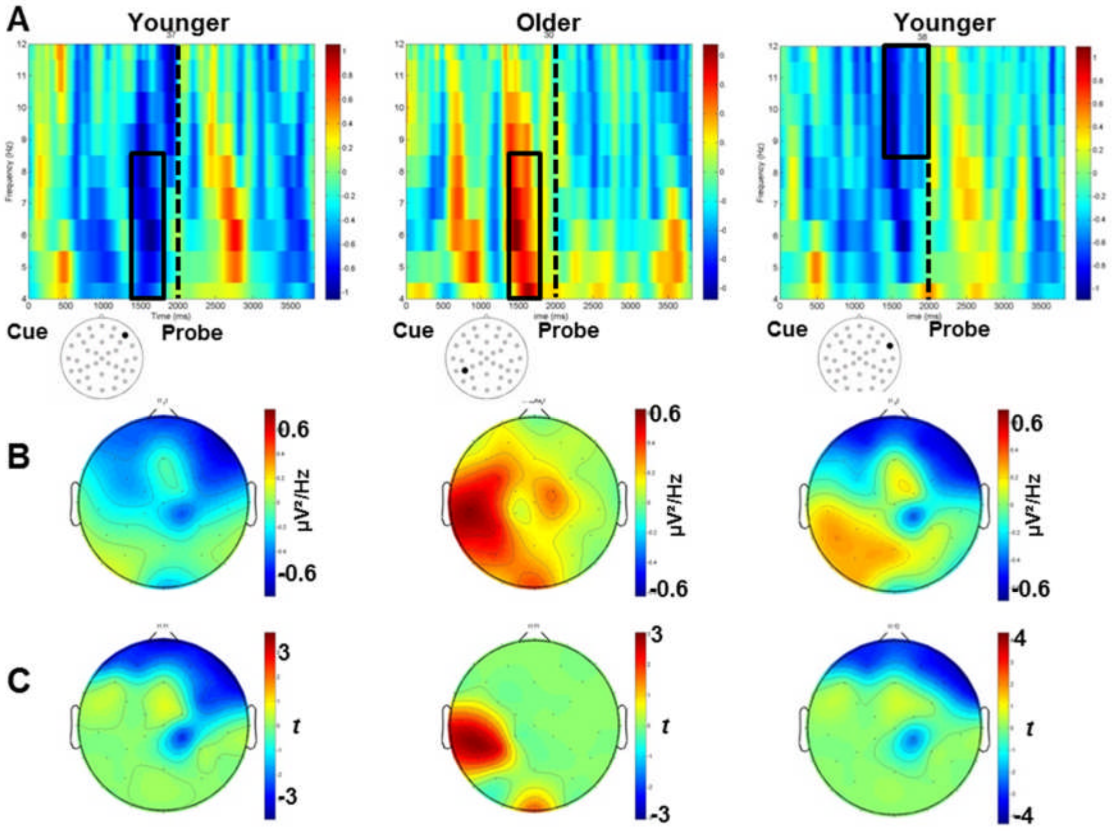


**Figure 39. Pre-probe associative retrieval effects for picture pairs.**
**A)** Time-frequency representations of associative retrieval-related effects for pictures at 3 electrodes as indicated by the inserts. The two graphs on the left show the pre-probe theta effects in younger and older adults during 1400-1800 ms after cue onset (as indicated by the boxes drawn on the graphs) at a right-frontal electrode (site 37 from Montage 10) and a left-parietal electrode (site 30 from Montage 10) respectively. The graph on the right shows the pre-probe alpha effect in younger adults during 1400-2000 ms after cue onset at a right-frontal electrode (site 38 from Montage 10). **B)** Scalp maps representing differences in theta power (associative hits – associative misses) corresponding to the effects indicated in A. **C)** Statistical maps showing the scalp sites where the effects were significant.

As significant pre-probe theta decreases emerged for both pictures and words in older adults, further analyses were performed to investigate whether these effects were identical across materials. Permutation tests revealed that there was no significant difference as a function of stimulus material between the effect during 1000-1400 ms and 1400-1800 ms. In younger adults, pre-probe theta effects also emerged for both materials albeit in opposite directions. As expected, these effects were significantly different from each other.

*Post-probe associative retrieval effects*

For words, the analyses revealed that in theta oscillations, there was a significant response by age interaction between 400 and1000 ms after probe onset. Subsidiary within-group analyses revealed significant theta decreases in younger adults over a cluster of right-frontal sites, and significant theta increases in older adults mainly over left temporo-parietal sites. Analyses across groups revealed a main effect of response for the 1000-1800 ms interval, manifested as significant theta decreases in both groups. Figure 40 shows the significant post-probe theta associative retrieval effects described above.

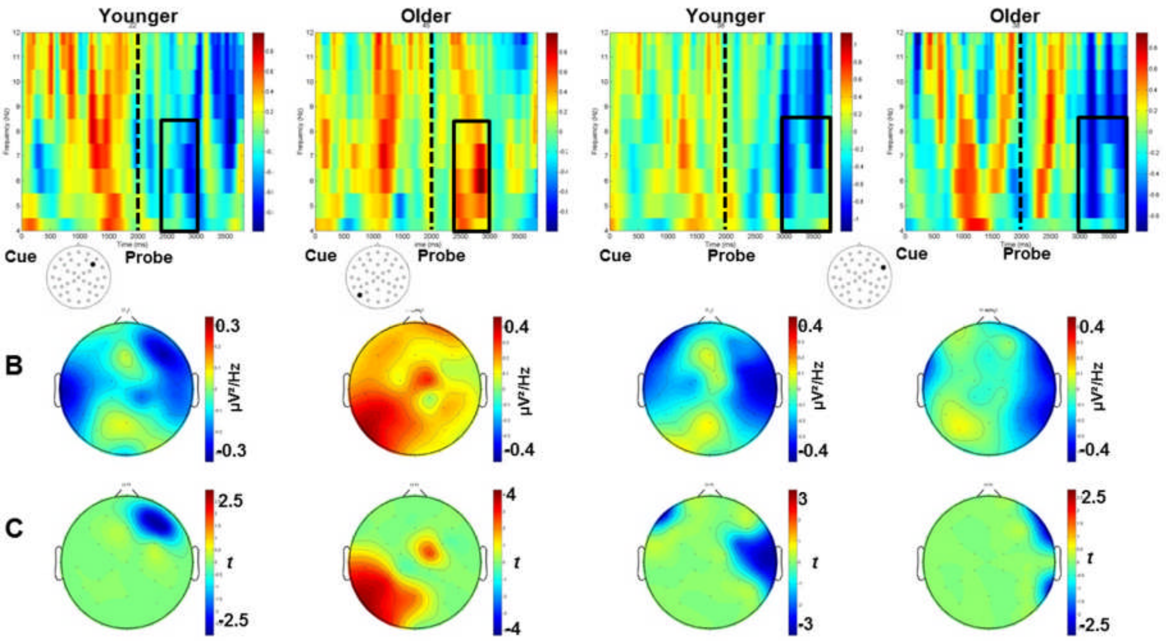


**Figure 40. Theta post-probe associative retrieval effects for word pairs.**
**A)** Time-frequency representations of associative retrieval-related effects for words at 3 electrodes as indicated by the inserts. The two graphs on the left show the effects in younger and older adults from 400 to 1000 ms after probe onset (as indicated by the boxes drawn on the graphs) at a right-frontal electrode (site 22 from Montage 10) and a left-parietal electrode (site 45 from Montage 10) respectively. The graphs on the right show the effects in younger and older adults during 1000-1800 ms after probe onset at a right fronto-temporal electrode (site 38 from Montage 10) where both effects are reliable. **B)** Scalp maps representing differences in theta power (associative hits – associative misses) corresponding to the effects indicated in A. **C)** Statistical maps showing the scalp sites where the effects were significant.

In alpha oscillations, there was also a response by age interaction between 400 and1000 ms. Subsidiary within-group analyses revealed significant alpha decreases in younger but not older adults over left-temporal scalp sites. A main effect of response was found during 1000-1800 ms interval, manifested as significant alpha decreases in both groups. Figure 41 shows the significant post-probe alpha effects described above.

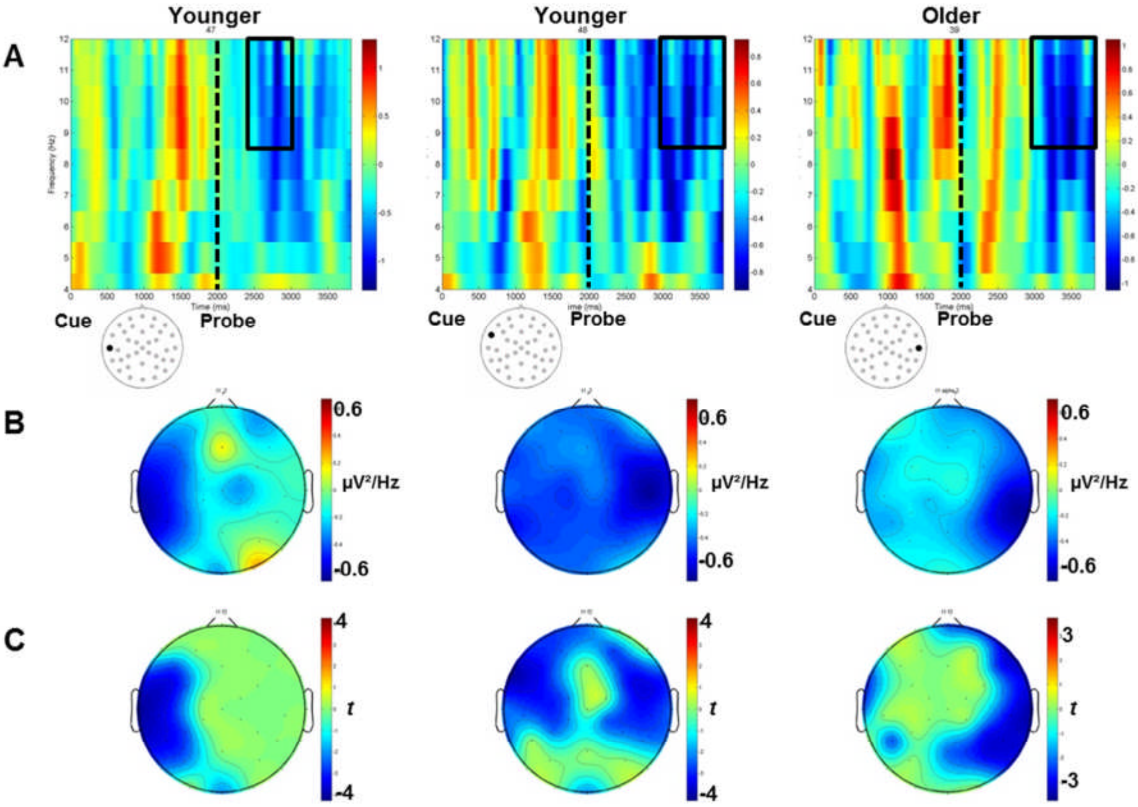


**Figure 41. Alpha post-probe associative retrieval effects for word pairs.**
**A)** Time-frequency representations of associative retrieval-related effects for words. The graph on the left shows the effect in younger adults during 400-1000 ms after probe onset (as indicated by the box drawn on the graph) at a left-temporal electrode (site 47 from Montage 10) representing the right-temporal cluster where the effect was significant. The graph in the middle shows the effect in younger adults from 1000 to 1800 ms at a left-frontal electrode (site 48 from Montage 10). The graph on the right shows the effect in older adults in the 1000-1800 ms interval at a right-temporal electrode (site 39 from Montage 10). **B)** Scalp maps representing differences in alpha power (associative hits – associative misses) corresponding to the effects indicated in A. **C)** Statistical maps showing the scalp sites where the effects were significant.

For pictures, there was a significant response by age interaction in the 1200-1800 ms post-probe interval in theta oscillations. Subsidiary within-group analyses revealed a theta decrease in younger adults over bilateral frontal scalp sites, and a theta increase in older adults focused over left frontal sites. In alpha oscillations, there was no significant interaction, only a main effect of response between 800 and 1800 ms after cue onset. Widespread alpha decreases were reliable in both groups. Figure 42 shows the post-probe retrieval effects for pictures.

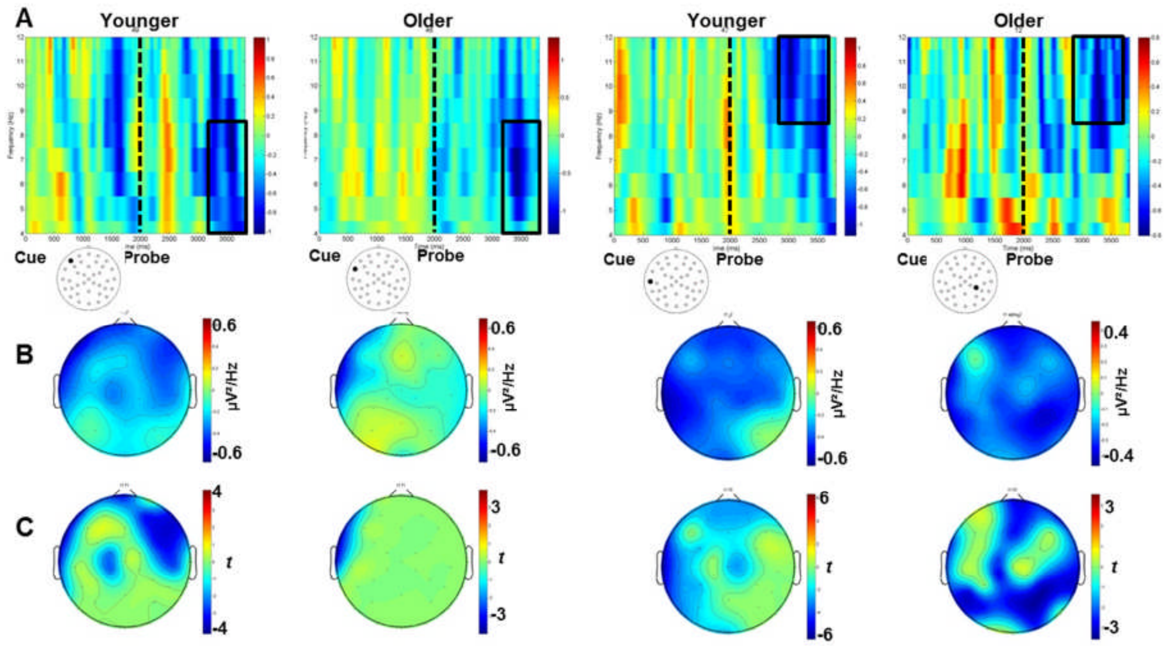


**Figure 42. Post-probe associative retrieval effects for picture pairs.**
**A)** Time-frequency representations of associative retrieval-related effects for pictures. The two graphs on the left show the theta effects in younger and older adults during 1200-1800 ms after probe onset at a left frontal electrode (site 49 from Montage 10) and a left fronto-temporal electrode (site 48 from Montage 10) respectively. The graph in the middle shows the post-probe effect in younger adults during 800-1800 ms at a left-temporal electrode (site 47 from Montage 10) and a right-parietal electrode (site 12 from Montage 10). **B)** Scalp maps representing differences in theta power (associative hits – associative misses) corresponding to the effects as indicated in A. **C)** Statistical maps showing the scalp sites where the effect was significant.

Further analyses across materials revealed that, for younger adults, there was no significant difference between either post-probe theta decreases (400-1800 ms for words and 1200-1800 ms for pictures) or post-probe alpha decreases (400-1800 ms for words and 800-1800 ms for pictures). For older adults, there was no significant difference between post-probe alpha decreases across materials (1000-1800 ms for words and 800-1800 ms for pictures), but the theta increase during 400-1000 ms for words and the theta decrease during 1200-1800 ms for pictures did differ significantly.

#### *3.3.2.4 Discussion*

The present experiment aimed to investigate pre-probe associative retrieval-related brain activity when different retrieval goals are intermixed in an associative recognition test. In stark contrast to ERP findings, the present results showed significant pre-probe associative retrieval effects in both groups. In younger adults, there was a theta power increase between 1000-1800 ms after word cue onset for associative hits relative to associative misses. For pictures, there was a theta decrease between 1400-1800 ms and an alpha decrease between 1400-2000 ms after picture cue onset. In older adults, theta power increased between 1000-1400 ms after word cue onset and between 1400-1800 ms after picture cue onset for associative hits. For probe-elicited activity, sustained broadband power decreases were found in younger and older adults for both pictures and words. Across the groups, there were theta and alpha power decreases between 1000-1800 ms after word pair onset and between 800-1800 ms after picture pair onset. In addition to these main effects, there were also effects that were specific to each group. In particular, there was a power increase in the theta range only for older adults after word pair onset. The results are summarized in Table 13.

**Table 13. A summary of significant associative retrieval effects in oscillatory activity in Experiment 3.**

| | | Pre-probe | | Post-probe | |
|---|---|---|---|---|---|
| Condition | | Theta | Alpha | Theta | Alpha |
| Words | Younger | **Increase** 1000-1800 ms<br>Mostly frontal | | **Decrease** 400-1800 ms<br>Right frontal<br>Right temporal | **Decrease** 400-1800 ms<br>Bilateral frontal<br>Bilateral temporo-parietal |
| | Older | **Increase** 1000-1400 ms<br>Right-frontal<br>Bilateral temporo-parietal | | **Increase** 400-1000 ms<br>Left parietal<br>**Decrease** 1000-1800 ms<br>Right fronto-temporal | **Decrease** 1000-1800 ms<br>Right frontal<br>Right temporo-parietal |
| | Both | **Increase** 1000-1400 ms | | **Decrease** 1000-1800 ms | **Decrease** 1000-1800 ms |
| Pictures | Younger | **Decrease** 1400-1800 ms<br>Bilateral prefrontal | **Decrease** 1400-2000 ms<br>Bilateral prefrontal | **Decreases** 1200-1800 ms<br>Left frontal, left temporal right frontal | **Decrease** 800-1800 ms<br>Left hemisphere widespread |
| | Older | **Increase** 1400-1800 ms<br>Left temporal | | **Decrease** 1200-1800 ms<br>Left-frontal | **Decrease** 800-1800 ms<br>Widespread |
| | Both | | | | **Decrease** 800-1800 ms |

*Pre-probe associative retrieval effects*

Following word cue onset, both younger and older adults showed pre-probe theta power increases for associative hits relative to associative misses, consistent with the findings in the previous study. The effect emerged at around 1000 ms after word cue onset in both groups, but was more prolonged in younger adults than older adults. Following picture cue onset, however, distinct pre-probe retrieval effects were found in the two groups. Older adults showed a theta increase that was statistically indistinguishable from the effect found for word cues. In contrast, younger adults showed a broadband power decrease that was completely different from the effect for word cues in terms of direction and scalp distribution.

As previously discussed, theta oscillations have been related to executive control processing, representing the involvement of hippocampal–cortical circuits (Babiloni et al., 2004). In terms of memory-related anticipation, theta increases are thought to prime the PFC-hippocampal network for effective processing of item-context associations (Gruber et al., 2013). The present finding of a pre-probe theta increase for word pairs in younger and older adults suggests that these retrieval control mechanisms may have been recruited by both groups to facilitate associative retrieval for word pairs. Furthermore, the similar pre-probe theta increase following picture cues in older adults suggests that the same anticipatory mechanism was recruited for the retrieval of picture pairs in this age group.

Similar to the effects in the present study, pre-probe theta decreases were found in the previous study in the dual-task condition. These decreases were thought to reflect anticipatory neural processes related to episodic retrieval, such as a preactivation of memory traces. However, the scalp distributions of the two effects are different, with the pre-probe effect in the previous study maximal over a cluster of left temporo-parietal sites and the present effect maximal over mid- and right-prefrontal sites. It is therefore likely that the two effects reflect different underlying neural mechanisms. Frontal brain activation in memory processing has often been related to strategic control mechanisms such as the utilisation of deep (semantic) encoding strategies (Buckner et al., 1999). The anterior scalp distribution of the present broadband power decrease suggests that it may be related to such strategic control processing, although the inverse problem prevents an inference that the observed activity on the scalp comes from frontal brain regions. As alpha activity has often been related to the processing of visual information (Bonnefond & Jensen, 2012), it may be that the decrease in alpha activity before probe onset reflects the preparation for the processing of picture pairs that are rich in visual information. Alternatively, considering the perceptual difficulty of the pictures used in the present experiment, it may be that the pre-probe theta/alpha power decreases reflect heightened attention in anticipation of processing picture pairs. This interpretation is consistent with the proposal that theta/alpha decreases represent an active state of cortical neural assemblies (Lisman & Jensen, 2013). However, it would be difficult to explain why the same effect did not emerge during encoding.

Taken together, the present findings suggest that when target materials vary unpredictably on a trial-by-trial basis, younger adults differentially recruit material-selective anticipatory mechanisms that facilitate associative retrieval. Older adults, however, recruit similar anticipatory mechanisms to support associative retrieval of words and pictures.

### *Post-probe associative retrieval effects*

Following the presentation of item pairs, both younger and older adults showed sustained broadband power decreases, consistent with findings from the previous study. For the retrieval of word pairs, this broadband power decrease started early in younger adults from around 400 ms after probe onset. In older adults, however, such broadband power decreases only emerged at around 1000 ms after word pair onset, preceded by a theta power increase between 400-1000 ms over left temporo-parietal scalp sites. This early theta increase was specific to older adults, and specific to successful retrieval of word pairs but not picture pairs. This theta effect is similar in timing and scalp distribution to the post-probe theta increase found in younger adults in the first study, and to the typical theta retrieval effects that are thought to reflect the neural reinstatement of episodic memory traces (Jafapour et al., 2014; Nyhus & Curran, 2010). As previously discussed, the timing and scalp distribution of the effect also resemble the classic ERP left-parietal retrieval effect which is thought to reflect the recovery of episodic information (e.g., Wilding, 2000). Thus, the present post-probe theta increase in older adults may be related to the reactivation of memory traces, which contributes to successful associative retrieval.

However, no such theta increase was found in older adults in the first experiment. Comparing across the two experiments, it may be suggested that in older adults, neural reinstatement of memory traces contributes to associative recognition but not associative recall. In an associative recall test, only one item is presented as the retrieval probe. In associative recognition, however, both items are presented and are therefore more likely to trigger memory trace reactivation. According to the frontal ageing hypothesis (West, 1996), cognitive deficits in ageing are caused by a decrease in frontally-based control mechanism. Thus, when ‘top-down’ control is impaired, older adults are likely to benefit from more ‘bottom-up’ information (Craik & Rose, 2012).

It is interesting that a post-probe theta increase was not found in younger adults in the present study. Instead, there was a broadband power decrease in younger adults in the same 400-1000 ms time window, and this effect persisted until the end of the post-probe epoch. Compared with the previous experiments, this effect is more in line with the post-probe retrieval effect in the second experiment than that in younger adults in the first experiment. In the second experiment, there was also an early-onset broadband power decrease alongside the absence of a theta increase. This pattern of retrieval effects was thought to be related to decreased memory performance, and the broadband power decrease was thought to reflect retrieval control that was engaged when memory was relatively poor. If this is the case, the present findings of a broadband power decrease in younger adults and a theta increase in older adults (followed by theta/alpha decreases) suggest that younger and older adults might have adopted different retrieval strategies for the retrieval of word pairs. It may be that younger adults mostly relied on neural mechanisms underlying the sustained broadband power decrease, such as controlled search or other kinds of cognitive control processing as previously discussed. In contrast, older adults may initially rely on neural mechanisms underlying the typical theta retrieval effect (i.e. memory trace reactivation) before recruiting post-retrieval control mechanisms (e.g., post-retrieval monitoring), as reflected in the late-onset theta/alpha power decrease. These findings may indicate that while older adults adopted retrieval strategies that are typical for episodic retrieval, younger adults adopted controlled retrieval strategies to enhance retrieval. Such age differences may be related to how younger and older adults approach the associative recognition task. Previous studies using the same paradigms usually found that, relative to older adults, younger adults are more likely to engage in elaborative retrieval strategies such as ‘recall-to-reject’ to differentiate between intact pairs and rearranged pairs (e.g., Light et al., 2004). To adopt such elaborative strategies is resource demanding, especially when there is a need to switch between different retrieval goals as in the present experiment. Possibly as a result, younger adults adopted additional control mechanisms as reflected in the early-onset broadband power decrease.

For the retrieval of picture pairs, younger and older adults showed similar sustained broadband power decreases. In both groups, the effect started with an alpha decrease from around 800 ms, which was followed by a theta power decrease from around 1200 ms. These effects were statistically indistinguishable from those for word pairs, only emerging in later time windows. The late onset of the effects may be related to the perceptual difficulty of the pictures, as previously discussed. An interesting point to note is the between-group difference in the scalp distribution of the theta effects, with the effect in younger adults found over bilateral frontal scalp sites whereas the effect in older adults was limited to left frontal sites. In the previous experiment, post-probe theta decreases were largest over right-frontal scalp sites. The theta effect resembles the ERP right-frontal retrieval effect in both timing and scalp distribution, indicating that they may reflect the same underlying retrieval-related activity. In the present study, the post-probe theta decrease was more reliable in younger adults, especially for the retrieval of picture pairs when the decrease was evident over right-frontal scalp sites in younger adults only. This is consistent with ERP findings in the earlier studies in this thesis that only younger adults showed reliable right-frontal effects. However, it may be too simplistic to claim that the theta decrease and right-frontal ERP effect are just different representations of the same retrieval activity. There are a number of differences between the two effects in the present experiment. For example, the theta decrease started from around 400 ms for the retrieval of word pairs, whereas the right-frontal ERP effect did not emerge until around 1200 ms after word pair onset. Further research is clearly needed to better understand the neural mechanisms of oscillatory and ERP activity, and how they may be related to memory processing.

In conclusion, when target materials vary unpredictably across trials, both younger and older adults showed pre-probe associative retrieval effects. These finding are in contrast with the absence of pre-probe associative retrieval effect in ERP analyses, as well with the lack of anticipatory encoding effect in older adults in oscillatory analyses. Even though both younger and adults were able to recruit pre-probe anticipatory mechanisms to facilitate associative retrieval, different patterns of effects were found across age groups. Whereas older adults engaged similar anticipatory retrieval-related activity for both words and pictures, younger adults engaged distinct anticipatory activity for each stimulus class. This suggests that relative to older adults, younger adults are more likely to recruit material-specific anticipatory mechanisms in a flexible manner to facilitate associative retrieval. For post-probe associative retrieval, the pattern of effects suggests that younger and older adults recruited similar retrieval mechanisms. There are also across-group differences indicating an age difference in the spontaneous use of elaborative strategies.

# Chapter 4: General discussion

The overarching research question in the present thesis was whether memory deficits in older age can be related to changes in anticipatory neural and cognitive processes. In this chapter, the main findings from the three experiments will be summarised in relation to the specific research questions raised in each. The chapter will then consider possible implications from the findings and discuss future research directions.

## 4.1 Summary of the findings

### 4.1.1 Does pre-stimulus associative encoding-related activity vary with age?

Age differences in pre-stimulus encoding-related activity were consistently found in the first and third experiments using a cued recall task and an associative recognition task respectively. In the first experiment, the experimental paradigm was designed to examine anticipatory activity for item-source binding in two separate stages. The first was the pre-source stage (i.e., after a neutral warning cue) intended to capture general anticipatory processes before the presentation of any to-be-encoded information. The second was the pre-binding stage (i.e., after encountering the source and before encountering the item) intended to capture anticipatory processes engaged by the encoding of partial information in preparation for the upcoming binding process. Using this paradigm, it was found that healthy younger adults elicit theta and alpha power increases after neutral cue onset, both of which predicted subsequent associative recall success. The theta PSME was found over left-frontal scalp sites, closely followed by the alpha PSME over occipital sites. Based on similar findings from previous studies (Fell et al., 2011; Gruber et al., 2013; Guderian et al., 2009), it was thought that the left-frontal theta increase reflects a pre-activation of the PFC-hippocampal network and the posterior alpha increase an inhibition of task-irrelevant visual information. These two kinds of anticipatory control processes may operate together to facilitate effective associative memory encoding.

In contrast, older adults showed a theta power decrease during the pre-binding interval, i.e., after the presentation of a source, which also predicted subsequent successful associative recall. This effect was in the high theta range (6-8 Hz), and was accompanied by a theta power decrease with a similar scalp distribution during binding, i.e., after the presentation of an item. The pre-binding theta decrease was thought to reflect a semantic elaboration of the source (i.e., location word) that serves to lay down a rich context that the upcoming item (i.e., object word) could be embedded in. This kind of semantic preparation might be activated to compensate for impaired executive control mechanisms in the pre-source stage. The pattern of these age differences in pre-stimulus encoding-related activity points to a strategic difference between younger and older adults in associative encoding. While younger adults engage in early, proactive processing, older adults rely on late, reactive processing for successful associative encoding. This is in agreement with the ELSA model (Dew et al., 2011) or a proactive-to-reactive shift hypothesis of ageing (Paxton et al., 2006, 2008).

In the third experiment, participants were asked to learn word-word pairs and picture-picture pairs that were intermixed in an associative recognition paradigm. In this experiment, there was no temporal separation in the prestimulus interval, i.e., the two items in each pair were presented simultaneously. Also different from the first experiment, the cues indicated whether the upcoming stimuli would be pictures or words. During the cue-stimulus interval, younger adults again showed theta and alpha power increases over frontal and posterior scalp sites, similar to those found in younger adults in the first study. These theta and alpha PSMEs were similar across pictures and words, reflecting material-invariant anticipatory activity that may be related to executive control mechanisms, such as trial-by-trial task-set reconfiguration according to different encoding goals. Older adults did not show any PSME, possibly indicating an inability to recruit such anticipatory executive control mechanisms. Previous studies have also demonstrated that older adults do not take advantage of instructional cues to benefit subsequent performance in a number of tasks, including attentional orienting (Zanto et al., 2011), executive control (Paxton et al., 2006; 2008), and WM and LTM (Bollinger et al., 2011). Findings from these studies point to a general anticipation deficit in ageing. In addition, in the third experiment older adults did not show a pre-stimulus theta decrease as found in the first experiment. This suggests that they are able to engage anticipatory activity to enhance associative encoding, but only when the cues contain some of the to-be-encoded information. Unlike younger adults, older adults seemingly cannot recruit executive control mechanisms to facilitate encoding using instructional cues alone.

Across the first and third experiments, it may be suggested that older adults are impaired in the ability to proactively recruit executive control mechanisms to facilitate associative encoding before encountering to-be-encoded information. As a consequence, they may rely on additional semantic elaboration on to-be-encoded information in a reactive manner.

### 4.1.2 Does pre-probe associative retrieval-related activity vary with age?

In the first experiment, a pre-probe associative retrieval-related ERP effect was found mostly in older adults. The waveforms that led to successful associative retrieval were more negative-going than those that led to recognition without associative retrieval. The effect was spatially widespread and largest over prefrontal scalp sites, similar in polarity and scalp distribution to the PSMEs reported by Otten and colleagues (Otten et al., 2006, 2010). Such PSMEs have been associated with semantic processing of the stimuli, and were interpreted as goal-directed mobilisation of semantic processing resources in anticipation of upcoming stimuli. Based on those studies, the pre-probe ERP retrieval effect was related to the adoption of cognitive control mechanisms that favour semantic processing of a retrieval probe to facilitate the recovery of associative information. Because the effect was reliable only in older adults, these mechanisms were thought to be recruited by older adults in compensation for relatively poor memory.

However, the magnitude of this pre-probe retrieval effect increased with the degree of memory impairment across older participants. Such a negative correlation is difficult to reconcile with the compensation interpretation. Nevertheless, as argued by de Chastelaine and colleagues (2011), this contradiction might be resolved with the ‘partial compensation’ hypothesis. Negative correlations between increased PFC activation and poor memory performance have also been found in fMRI studies during both encoding (e.g., de Chastelaine et al., 2011) and retrieval (Persson et al., 2011). It was proposed that the additional PFC activation is an adaptive mechanism that compensates for the failure of neural systems that should be responsible for the ongoing task, but the additional activation in itself contributes little to memory performance. Therefore, a larger PFC activation in older individuals (or, as in the present case, larger activity over frontal scalp sites) may indicate a larger impairment in the neural system that supports associative memory.

In the third experiment, there was no ERP pre-probe retrieval effect in either younger or older adults. The absence of the effect is likely related to the intermixed design used in the third experiment. When retrieval targets (i.e. words and pictures) vary unpredictably from trial to trial, participants have to process the instructional cues and prepare for the retrieval of different materials accordingly, both of which are resource demanding. The reduction of processing resources has been shown to negatively affect the engagement of anticipatory encoding-related brain activity (Galli & Otten, 2013). In a similar vein, pre-probe retrieval-related activity may be hindered by a reduction of processing resources when frequent switching between retrieval targets is required.

Evidence of anticipatory processes during retrieval was found, however, in the time-frequency analyses. Both younger and older adults showed oscillatory pre-probe associative retrieval effects in the third experiment that were not found in the first experiment. In older adults, the effect was material-invariant, manifesting as theta power increases associated with successful associative recognition. In younger adults, the effects were material-selective, with a theta power increase for word cues and a broadband theta/alpha decrease for picture cues. In line with the first experiment, the theta increase was thought to be related to the pre-activation of the PFC-hippocampal network for effective processing of item-context associations (Gruber et al., 2013). The frontal broadband power decrease might represent strategic control mechanisms related to the preparation for picture processing. These findings suggest that when target materials vary on a trial-by-trial basis, younger adults recruit material-selective anticipatory mechanisms flexibly in response to instructional cues. Older adults, however, recruit the same material-invariant anticipatory mechanisms to support associative retrieval of words and pictures. These findings point to an age-related change in the flexibility of adopting task-specific retrieval strategies. This again supports the general expectation deficit hypothesis of ageing (Zanto et al., 2011).

Across the two experiments, it may be concluded that even though older adults may be impaired in the flexible use of retrieval strategies in a goal-directed manner, they are able to recruit pre-probe anticipatory mechanisms to facilitate associative retrieval. When the same retrieval goal can be maintained across trials, older adults may employ retrieval-related anticipation to a larger extent relative to younger adults. In older adults, particularly poor-performing individuals, the probability that a probe will lead to recollection of associative information is influenced by pre-probe brain activity. The individual differences suggest that additional neural mechanisms might be recruited by poor performers in compensation for the impairment in neural systems that should be responsible for associative retrieval.

### 4.1.3 Are age differences in anticipatory memory-related activity related to poor memory?

The question of a possible relationship between anticipatory brain activity and overall memory performance was addressed in the second experiment using a divided attention task to reduce available processing resources for memory encoding in a group of healthy young adults. This manipulation was successful in reducing associative memory performance in those young adults. The pattern of results generally supports the idea that age differences in anticipatory memory-related activity are related to differences in memory performance.  At retrieval, young adults in the single-task condition showed oscillatory pre-probe retrieval effects that closely resemble the PSMEs found in younger adults in the first study, comprising theta and alpha power increases initially over left-frontal and then posterior sites. These anticipatory theta and alpha increases may reflect the dynamics of a pre-activation of the PFC-hippocampal and PFC-posterior networks, serving to facilitate effective associative memory encoding. These pre-probe retrieval effects also share similarities with those found in younger adults in the third experiment for the retrieval of word pairs, i.e., pre-probe theta increases over frontal scalp sites. This suggests that the anticipatory neural mechanisms underlying these effects were consistently recruited by younger adults across associative recall and associative recognition tasks.

In parallel, the pre-probe effect in the dual-task condition could be compared to the PSME previously found in older adults, both shown as power decreases, albeit in the alpha band for younger adults in the third experiment and in the high-theta band for older adults in the first study. As alpha frequency decreases linearly with age (Klimesch, 1999), it is possible that the pre-probe alpha decrease in younger adults and high-theta decrease in older adults represent the same underlying neural mechanisms, such as an activation of additional neural networks when memory is impaired. Thus, the oscillatory findings suggest that general anticipatory mechanisms can be recruited at encoding and retrieval to enhance associative memory. Anticipatory memory-related activities seem similar between the dual-task condition and older adults in the first study, as well as between the single-task condition and younger adults in the first study.

In the ERP analyses, young adults in the dual-task condition showed as expected a pre-probe ERP associative retrieval effect that was similar in polarity, timing, and scalp distribution to the effect found in older adults in the first experiment. The similarity between the two effects suggests that the pre-probe anticipatory mechanisms can be recruited by both older and younger adults to support associative retrieval. An unexpected finding was that the effect also occurred in the single-task condition, even though the level of associative retrieval was significantly higher in the single-task condition than the dual-task condition. This finding is inconsistent with the hypothesis that the pre-probe ERP effect is related to the level of memory performance. However, as recognition accuracy (Pr) was significantly lower in the single-task condition relative to younger adults in the first experiment, the difference in pre-probe neural activity between experiments may be explained by a difference in overall memory strength.

Taken together, the findings from the second experiment in both ERP and oscillations support the idea that age differences in anticipatory activity are related to poor memory.

## 4.2 Implications and future directions

### 4.2.1 Is ageing special?

As described in the Introduction chapter, numerous structural and functional changes in the ageing brain have been reported. A number of theories have been proposed to account for age-related changes in cognitive functions. It is currently still not clear what underlying neural mechanisms are responsible for memory functions in ageing. Do older adults recruit fundamentally different neural mechanisms for memory processing, or are the same neural mechanisms adapted to decreasing memory abilities?

Across the experiments in this thesis, a number of age differences in anticipatory memory-related activity were found. As discussed above, these differences are likely to stem from decreased memory performance (although causality cannot be implied given the available data). These findings are in line with the STAC, suggesting that additional brain activity found in older adults may reflect normal, adaptive neural processes that can also be engaged by younger adults when faced with increasing task demands (Reuter-Lorenz & Park, 2010). In terms of stimulus-elicited activity, there was very little difference between younger and older adults in terms of SMEs. Thus, older adults seem to fundamentally engage the same neural processes as younger adults for associative encoding, at least when ERPs are concerned. Even though age differences in ERP SMEs have been reported in a small number of studies (e.g., Cansino et al., 2010; Friedman & Trott, 2000), the findings are inconsistent in terms of whether older adults show smaller or larger SMEs. The present findings suggest that, at least when the explicit use of associative encoding strategies is required, older adults are able to recruit the same neural mechanisms for associative encoding regardless of whether the encoding is intentional or incidental.

However, there are also a number of age differences in memory-related activity that cannot be explained by different levels of memory performance. For example, the post-probe negative-going associative retrieval effect found in older adults in the first study was not replicated in younger adults when memory was impaired in the second experiment. Furthermore, older adults may be less able to recruit compensatory activity than younger adults to enhance memory performance. For example, in younger adults, the post-probe alpha power decrease emerged early in the second experiment when memory was impaired. Alpha decreases during retrieval are thought to reflect the recruitment of additional neural mechanisms, such as executive functions, when greater effort is required. Under certain circumstances, older adults seem able to engage such activity to a greater extent than younger adults, for example in a haptic continuous recognition task that is relatively preserved in ageing (Sebastian et al., 2011). Therefore, older adults may be limited in the ability to engage additional neural activity, possible due to diminished processing resources.

Some age differences in memory processing may be related to a difference in the use of strategies. As discussed above, age differences in oscillatory PSMEs in the first study may reflect a proactive to reactive shift in memory strategy. Younger adults are more flexible in the adoption of retrieval strategies in a goal-directed manner, as demonstrated by the material-selective pre-probe retrieval effect in the third experiment when different retrieval targets were intermixed. Furthermore, younger adults seem more likely to use elaborative memory strategies spontaneously. For example, younger adults showed similar post-probe ERP retrieval effects across associative recall (Experiments 1 & 2) and associative recognition (Experiment 3), whereas older adults showed very little post-probe associative retrieval activity, possibly reflecting controlled search, in the third experiment.

Taken together, although there is insufficient evidence to suggest that neural mechanisms for memory processing are fundamentally different across ages, older adults may recruit different mechanisms due to strategic inflexibility and spontaneity in ageing. This is consistent with the ‘frontal ageing hypothesis’ (West, 1996) suggesting that cognitive ageing is mostly reflected in executive control deficits, which can be linked to structural and functional changes in the frontal lobes. Although executive control is a broad concept including multiple cognitive functions, it is best suited to capture the wide range of age differences in memory and cognition.

Future research may target cognitive control processes such as anticipatory memory-related activity to improve memory functioning in older adults. For example, the pre-probe negative-going ERP retrieval effect, as found in the present experiments, is likely to reflect a compensatory strategy that can be adopted purposefully to enhance associative retrieval. However, the functional role of this effect is still not clear, in terms of whether it serves to enhance memory or simply as an indication of the degree of memory impairment. If it is indeed compensatory activity, it would be important to know what it is compensating for, and the necessary and sufficient conditions for it to emerge. It would also be important to understand the neural mechanisms underlying this effect. To this end, neuroimaging methods such as fMRI would be useful to elucidate the potential neural generators of this effect, and transcranial magnetic stimulation (TMS) may be used to further investigate the functional significance and necessity of the cortical regions that might be involved.

Further research should also seek ways to improve strategic flexibility and spontaneity in ageing. There has been an increasing number of studies investigating the effect of cognitive training in older adults, but with limited success (Ballesteros, Kraft, Santana, & Tziraki, 2015). To enhance memory performance, it may be fruitful to train older adults to use more elaborative strategies and to use them in a proactive manner. The present findings indicate that in terms of anticipatory memory-related activity, older adults are more impaired for encoding than retrieval. Future research should attempt to better understand PSMEs, and whether older adults can be trained to engage such activity spontaneously to improve memory.

### 4.2.2 Memory processing – theta and alpha activity

Across the three experiments, a number of anticipatory associative memory-related effects were found in the time-frequency analyses. These effects were consistent across experiments, and sensitive to the effect of ageing. The findings indicate that anticipatory theta and alpha power increases may reflect the dynamics of different executive control systems that serve to enhance effective episodic encoding and retrieval. These findings are novel as very few previous studies have investigated the effect of age in the time-frequency approach. Future studies are clearly needed to further investigate oscillatory brain activity to shed more light on memory and cognitive changes in ageing, especially anticipatory memory-related activity.

An important implication of the present findings is the importance of theta and alpha power increases in memory processing. Across the three experiments, prominent broadband theta/alpha power decreases occurred consistently during associative retrieval across age. There have been very few previous studies reporting power decreases, especially in theta oscillations. This could be due to a bias towards theta increases in memory, as early memory research using the oscillatory approach were mostly conducted using rats. Theta is the most dominant frequency in a rat's brain, and theta power increases have often been observed during memory processing (Lisman & Jensen, 2013). Theta oscillations are also prominent in the human hippocampus, which is important for memory.  As a consequence, attention has been mostly paid to theta power increases in oscillatory memory research. However, as Lisman and Jensen (2013) pointed out, cortical theta in humans may not serve the same function as hippocampal theta. The present findings suggest that theta and alpha power decreases may serve important functions in associative retrieval, such as controlled search and post-retrieval monitoring. There have been some interesting suggestions on the significance and potential mechanisms for oscillatory power decreases using the notion of information richness (Hanslmayr et al., 2012), but more evidence is clearly needed.

### 4.2.3 ERPs and oscillations

In the present experiments, the ERP findings of neural correlates of associative memory and the associated pattern of age differences are in stark contrast with the oscillatory findings. For example, in the first experiment, there was no significant oscillatory pre-probe associative retrieval effect in either age group, and post-probe broadband theta/alpha decreases were similar across age. In contrast, the ERP analyses revealed a prominent pre-probe negative-going associative retrieval effect in older adults as well as distinct post-probe ERP retrieval effects in each group. Different patterns of oscillatory and ERP results were also found at encoding, with PSMEs only emerging in oscillatory analyses whereas SMEs emerged in both oscillatory and ERP analyses. These differences suggest that ERPs and oscillatory activity capture distinct aspects of memory-related processes, or different processes.

However, similarities between ERP and oscillatory activity were also observed. As previously discussed, post-probe theta retrieval effects were largest over right-frontal scalp sites. Both the timing and scalp distributions of these effects resemble those of the ERP right-frontal retrieval effects. Such parallel occurrences of theta/delta and ERP retrieval effects have also been reported in previous studies. For example, ERP old/new effects between around 400-650 ms after probe onset have been linked to activity in slow frequencies such as the theta and delta bands (Klimesch et al., 2000). Similarly, it has been suggested that the CNV may reflect phase resetting of very low frequency cortical oscillations below, and including, delta band activity (Lakatos et al., 2008). The existing evidence is scarce, and further research is needed to determine whether ERP effects are generated by very slow oscillations.

Taken together, although there may be some overlap between oscillatory and ERP activity, the present findings suggest that fundamentally different neural processes are likely to be captured by oscillatory and ERP analyses. This may be related to the inherent differences between the two analysis methods, with ERSPs more sensitive than ERPs in non-phase-locked event-related EEG. Further research is clearly needed to better understand the neural mechanisms of oscillatory and ERP activity, and how they may be related to memory processing.

## 4.3 Final conclusion

In conclusion, this thesis contributes to existing knowledge on the neural mechanisms of ageing in relation to memory processing. It demonstrates that healthy ageing is related to impairments in anticipatory memory-related neural activity, which can be partly explained by decreased memory ability in ageing. Memory deficits in ageing are also related to impairments in cognitive control mechanisms. Overall, healthy older adults seem impaired in anticipatory neural mechanisms in addition to strategic flexibility and spontaneity, both of which can be related to deficits in executive functions.

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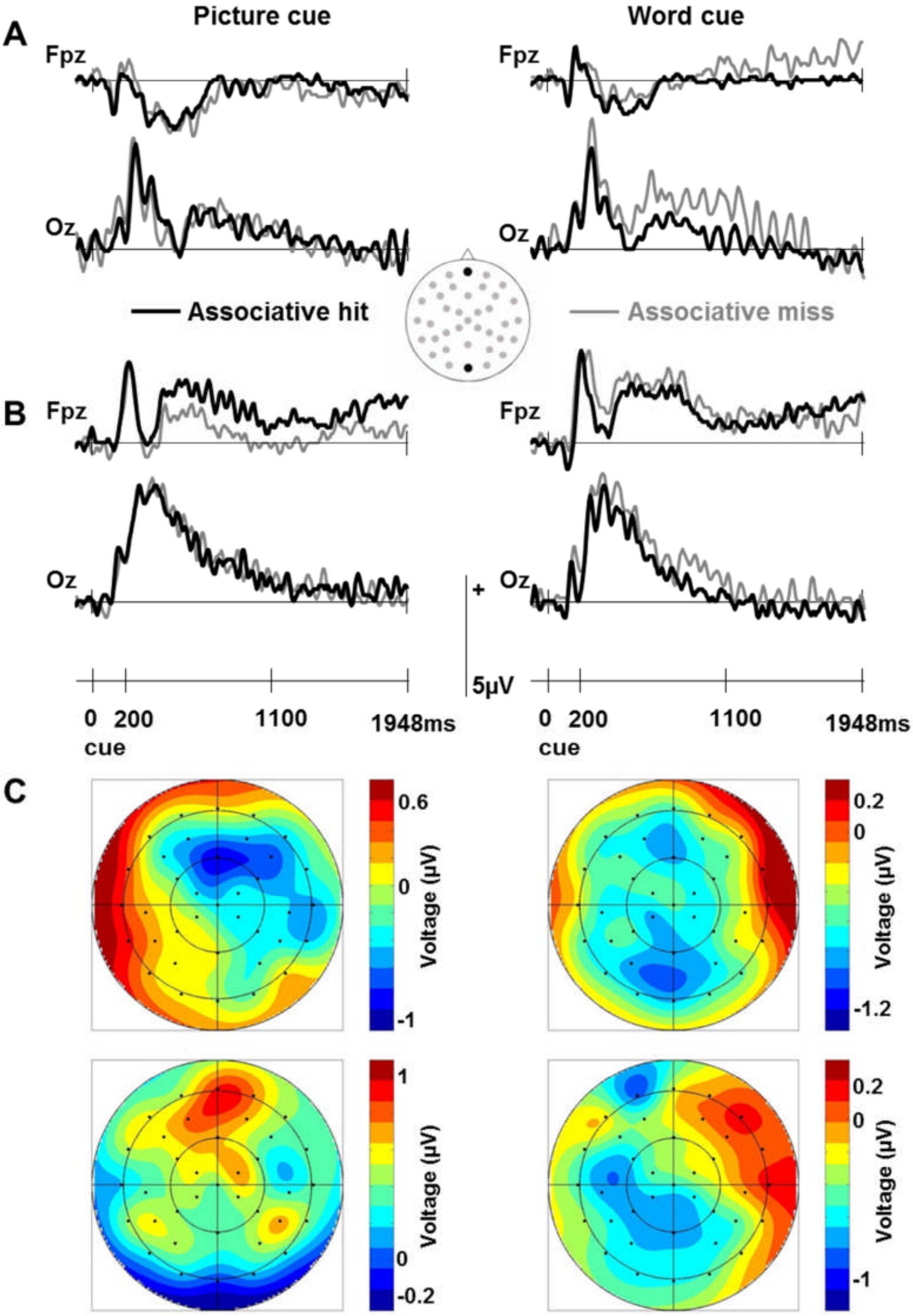
# Appendix



**Experiment 3. Grand-average ERPs elicited by picture cues and word cues in (A) younger adults and (B) older adults, according to whether they were related to associative hits or associative misses. The insert indicates the locations of the 2 representative electrodes (site 35 and 43 from Montage 10; www.easycap.de/easycap/e/electrodes/13_M10.htm; equivalent to site Fpz and Oz of the 10-20 system). (B) Voltage spline maps for younger (upper) and older (lower) adults showing the distribution of pre-probe associative retrieval-related activity (associative hits – associative misses) separately for picture cues and word cues in the 200-1940 ms interval. The maps are range scaled.**