Preparing predicts recall:

An event-related potential (ERP) study

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Statement of contribution

Experimental question:	Dr. Leun Otten & Tsee Leng Choy
Experimental design & programming:	Dr. Leun Otten & Tsee Leng Choy
Participant recruitment:	Tsee Leng Choy (with help from Maro Machizawa, Giulia Galli & Matthias Gruber)
Behavioural piloting:	Tsee Leng Choy
EEG & behavioural testing:	Tsee Leng Choy (trained by Giulia Galli)
EEG data pre-processing:	Tsee Leng Choy (trained by Maro Machizawa)
EEG and behavioural analysis:	Tsee Leng Choy & Dr. Leun Otten
Statistical analysis:	Tsee Leng Choy (with help from Matthias Gruber & Maro Machizawa) & Dr. Leun Otten
Thesis write-up:	Tsee Leng Choy (with advice from Dr. Leun Otten).

Abbreviations

ANOVA	Analysis of variance
Cf.	Compared with
cm	Centimetres
dB	Decibels
EEG	Electroencephalogram
e.g.	For example
EOG	Electro oculogram
ERPs	Event-related potentials
Et al.	And others
fMRI	Functional magnetic resonance imaging
Hz	Hertz
i.e.	That is
kΩ	Kilo Ohms
MEG	Magnetoencephalography
ms	Milliseconds
μV	Microvolts
PET	Positron emission tomography
s	seconds

Abstract

Contemporary findings have found neural activity preceding event onset to accurately predict its later recognition. This highlights the importance of pre-stimulus neural activity in memory formation, in contrast to previous research focusing on post-stimulus activity. The activity's functional significance is unknown, as it was unclear if the activity was an inherent brain state, or under conscious control. The current study examined the volitional control of pre-stimulus activity in recall prediction, using instructed mnemonics of rote and elaborative strategies. 24 healthy young adults memorized short lists of intermixed visual-auditory words, with a cue of corresponding modality preceding each word. A written free recall task followed each word list, with electroencephalogram (EEG) recorded from 33 electrode sites. Results showed pre-stimulus activity to have a negative frontal distribution as before, but being maximal fronto-centrally, and predicting recall in the elaborative strategy, specifically the auditory condition. This reflected the activity's susceptibility to strategy differences and modality, demonstrating it to be voluntarily controlled. Further examination postulates it to be a necessary preparatory mechanism for memory, with implications in aging and learning.

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Introduction

How do we remember, and why do we care? In an era of overloaded schedules, declarative memory (that is, (i.e.) memories that are consciously retrieved, comprising of semantic (facts) and episodic (events) memory) is predominantly and heavily utilized in our daily lives (Staresina & Davachi, 2006). Whether it is retrieving an old memory or forming new ones, doing so with the least possible effort and time increases efficiency, enabling one to keep abreast with today's fast paced world. Understanding memory formation and if it is controllable to some extent, is applicable to the masses though quality of life improvement. It benefits education, particularly those with learning deficits; patient cognitive rehabilitation and understanding memory loss. Our prolonged lifespan and increasing aging population makes the latter a pertinent problem.

A critical factor to remembering depends on how an event is encoded (i.e. processes mediating an experience and its memory formation (Rugg & Allan, 2002)) (Paller & Wagner, 2002). The present study examines how neural encoding activity occurring *before* presentation of an item, is able to predict its successful recall. Specifically, it investigates if this activity is under conscious control. If so, one can essentially prepare to remember better. An overview of previous studies on neural encoding correlates predicting recall is first addressed, concentrating current findings and gaps. This leads to the conception of the present study, its contribution to present research literature and its relevance.

1.1 Encoding literature overview – functional neuroimaging

Encoding is thought to consist of of two components – internalization of sensory inputs in memory and its integration (Paller & Wagner, 2002; Werkle-Bergner et al., 2006). Previous behavioural and neuropsychological studies have

indicated the importance of encoding in memory formation (among other factors), as successful recall depends on the close overlap of encoding and retrieval operations (Wagner, Koustaal & Schacter, 1999; Brown & Craik, 2000; Friedman & Johnson, 2000; Rugg & Wilding, 2000; Paller & Wagner, 2002; Rugg et al., 2008). Indeed, the transfer appropriate processing principle (Morris et al., 1977 & Roediger et al, 1989, cf. Rugg, 1995; Rugg et al., 2008) appropriately states that an item is more readily remembered if encoding and retrieval processes are similar (e.g. learning and taking an exam in an identical format). As encoding predates retrieval, studying encoding essentially allows prediction on subsequent item memorability (Werkle-Bergner et al., 2006).

Memory research has benefitted considerably from brain lesion studies, which has been invaluable in classifying different memory types (for example (e.g.). declarative versus non-declarative/unconscious memory) and their functional brain localization. However, it does not permit distinction of encoding neural correlates from retrieval, as lesions are non-reversible. Functional magnetic resonance (fMRI) and positron emission tomography (PET) studies have addressed this by allowing for separation and examination of encoding and retrieval neural correlates (Wagner et al., 1999) while testing healthy and patient populations. Both methods provide superior spatial but poor temporal resolution, as they reflect changes in blood flow (Rugg & Wilding, 2000). Still, functional neuroimaging has been instrumental in identifying neural substrates predicting subsequent memory performance. Encoding differences between remembered and forgotten words (known as the subsequent memory effect) (Wagner et al., 1999) is widely utilized in encoding research.

Functional neuroimaging studies on subsequent memory effects have demonstrated production of stronger memories with extensive recruitment of the prefrontal cortex and medial temporal lobes (Wagner et al., 1999). The former

reflects executive processes facilitating encoding, while the latter is susceptible to item characteristics and mediates integration (Werkle-Bergner et al., 2006). The activation extent of each structure is reliant on the nature of the task (Wagner et al., 1999; Otten & Donchin, 2000; Werkle-Bergner, 2006). Stronger subsequent memory effects are seen in extensively encoded items, and similarities in encoding and retrieval processes were also noted (Wagner et al., 1999), substantiating the transfer appropriate processing principle and related studies.

These findings also complement the levels of processing framework (Craik & Lockhart, 1972, cf. Rugg, 1995), another influential principle in memory literature. This principle postulates that an item is more memorable if processed at a higher level or depth (e.g. remembering a word based on its length is less memorable than remembering it based on its meaning). This implies semantic (i.e. meaningful context of a word or task) based decisions essentially receive increased encoding. However, functional neuroimaging studies were unable to address the nature of temporal interactions between brain regions during encoding, due to its limited temporal resolution (Werkle-Bergner et al., 2006).

1.2 ERPs and encoding

ERP encoding studies far preceded their functional neuroimaging counterparts, with possibly the earliest study conducted by Chapman et al. in 1978 (Wagner et al., 1999). Crucially, ERP findings are consistent with the aforementioned functional neuroimaging findings, validating the subsequent memory effect as a reliable phenomenon. As researchers sought to document the temporal interactions in encoding even more specifically, interest shifted rapidly to ERPs. This is due to the many merits ERPs has to offer and its high compatibility with memory research. But how are ERPs different from fMRI and PET?

ERPs are evoked responses in the EEG (i.e. recordings of random brain electrical activity) responding to a stimulus presented at a specific time. ERPs are extracted from the background EEG using repeated stimulus presentation at set time periods (epochs) over numerous trials. This increases ERP signal strength, while the random EEG decreases to zero. An ERP component is usually described in terms of its latency/timing and polarity (e.g. a P300 is a positive going wave occurring 300 milliseconds (ms) after stimulus onset) (Luck, 2005), allowing for comparisons across experiments for a particular task or effect.

ERPs provide a direct, online measure of brain activity - enabling detailed recording of a memory as it unfolds, with superior temporal resolution. Being independent of behavioural responses (brainwaves are elicited involuntarily) makes it a reliable, standardized measure of high validity (Rugg, 1995; Luck, 2005). Its non-invasive, painless and flexible settings enable memory to be studied naturally, as opposed to being confined in a chamber (fMRI) or being injected with radioactive isotopes (PET), which introduces anxiety to many participants.

A single ERP waveform can be measured in terms of amplitude, latency or scalp distribution, and stimulus can be presented in different modalities simultaneously, for example audition and vision (Luck, 2006). This permits a realistic, wide range of experimental stimuli and response evaluation; rendering it a highly appropriate measure as memory is multifaceted. Indeed, ERPs are widely used in memory research and instrumental in the development of several memory paradigms, the most crucial being the subsequent memory paradigm. Although originally developed for ERPs, this paradigm is widely used in functional neuroimaging in examining the subsequent memory effect due to its efficacy (Sanquist et al., 1980; Paller & Wagner, 2002).

1.3 Encoding literature overview - ERPs

The most established and commonly used method examining encoding is the subsequent memory paradigm, whereby neural activity is measured and correlated with subsequent recall (Sanquist et al., 1980; Paller & Wagner, 2002). This paradigm is illustrated in Figure 1.3.1. An experiment comprises of a study (encoding) and test (retrieval) phase. Neural responses are recorded when items are learned in the study phase, followed by the test phase, where memory is tested for the learned items. Neural activity for remembered and forgotten items are classified based on their recall in the test phase, allowing subsequent analysis and extraction of specific neural activity related to each item at the encoding phase (Paller & Wagner, 2002; Rugg, Otten & Henson, 2002).

The subsequent memory paradigm is important as it extracts pertinent neural activity crucial for encoding (i.e. by contrasting neural activity for remembered and forgotten items, known as the subsequent memory effect). This is pivotal considering other factors and operations can be simultaneously engaged during encoding (Wagner et al., 1999). Subsequent memory effects are assumed to reflect successful encoding as it provides a measure of encoding neural activity predictive of accurate recall (Paller & Wagner, 2002). By indicating processes during encoding which determines an item's memorability, subsequent memory effects establish a solid, concise link between encoding and neural function (Paller & Wagner, 2002). Sanquist et al., 1980 was credited with being the first ERP subsequent memory study (Rugg, 1995; Wagner et al., 1999) as Chapman et al., 1978 had encountered validity issues in experimental measurement (Wagner et al., 1999).
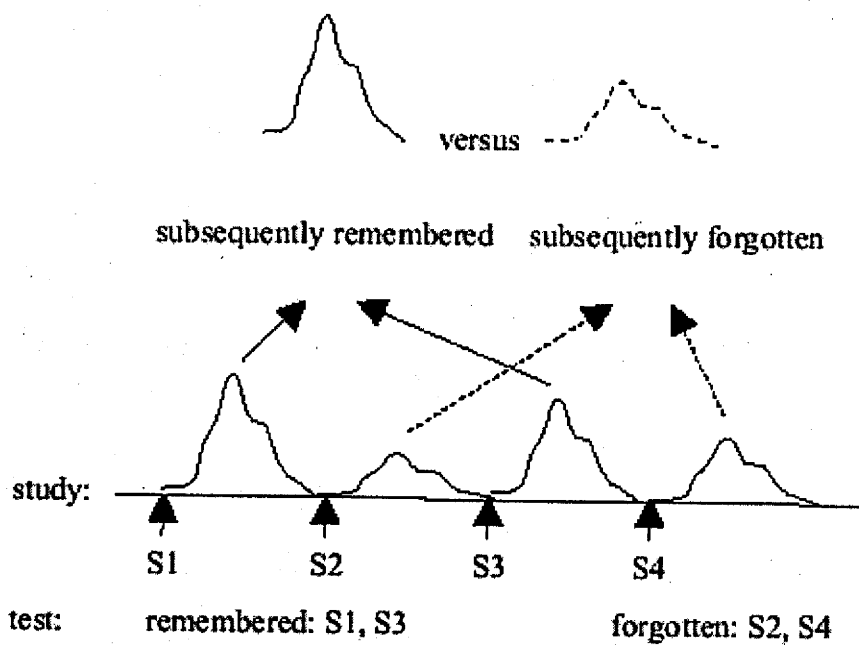
Figure 1.3.1. The subsequent memory paradigm. The experiment is split into a study (encoding) and test (retrieval) phase. Neural activity is recorded during the study phase when participants are presented with a series of items. Subsequently, memory is tested in the test phase. The neural activity elicited by each item in the study phase is distinguished according to if the items are remembered or forgotten in the test phase. The differences in neural activity between remembered and forgotten words (subsequent memory effect) represent the neural correlates of memory encoding (Taken from Rugg, Otten & Henson, 2002).

Sanquist et al. (1980) utilized an incidental encoding task (i.e. tasks where participants are unaware their memories would be subsequently tested), where word pairs were presented. Participants made 'similar/different' judgements if word pairs rhymed (phonological), were synonyms (semantic) or had matching upper/lower letter cases (orthographic), and received a surprise recognition test on the second word of each pair afterwards. Although word proportion eliciting 'similar/different' responses were unbalanced and only some of the responses could be used, this study was seminal in demonstrating subsequently remembered items evoking more positive-going ERPs than forgotten items. This finding has since been consistently replicated (Rugg, 1995; Wagner et al., 1999), although there are subtle differences across tasks.

ERP findings show subsequent memory effects to have a primarily sustained, maximal frontal topography (Rugg, 1995), particularly for intentional encoding tasks (i.e. tasks where participants are explicitly told to memorize, aware of an impending test) (Munte et al., 1988, cf. Wagner et al., 1999; Takashima et al., 2006). However, changes in distribution, polarity, magnitude and timing are reliant on task type, among others (Wagner et al., 1999; Otten & Donchin, 2000; Otten, Sveen & Quayle, 2007). Verbal tasks are consistently demonstrated to predict subsequent memory performance (Sanquist et al., 1980; Paller, Kutas & Mayes, 1987; Paller, McCarthy & Wood, 1988; Weyerts et al., 1997; Paller & Wagner, 2002), with semantic tasks showing a bigger difference due to greater processing (Wagner et al., 1999; Rugg, Otten & Henson, 2002).

Taken together, ERP and functional neuroimaging subsequent memory effect studies show the influence of brain region interactions on encoding, particularly the prefrontal and medial temporal cortex (Werkle-Bergner et al., 2006). This is exemplified by the influence of task type on the effects' characteristics, as

well as extent of brain region activation. Furthermore, these interactions are suggestive of different neural processes sustaining encoding (Otten et al., 2006a). Subsequent memory effects are particularly robust in semantic tasks, implying a role in semantic processing and indirectly, memorability by meaningful association (Otten, Sveen & Quayle, 2007).

Remaining outstanding was the issue of how remembered items are processed within encoding that consequently affects its successful retrieval. This was an issue insufficiently addressed in functional neuroimaging literature due to its lethargic temporal resolution. This question is relevant as it enables distinction of different encoding processes and brain region interactions (Otten et al., 2006a). ERPs seemed a tailored solution, but what could be done that has not already been done, almost 4 decades ago? All previous ERP studies have examined how neural activity *elicited* by the stimulus predicts subsequent free recall (i.e. unaided memory retrieval) or recognition (i.e. retrieval aided by presentation of new and old items (Lockhart, 2000)). Figure 1.3.2a shows a dissociation between remembered and forgotten items, apparent 1 second (s) after a word is presented (Otten et al., 2006a).

However, recent ERP studies (Otten et al., 2006a & b) have demonstrated neural activity *preceding* stimulus to also predict recognition (Figure 1.3.2b), and that pre and post-stimulus neural activity are dissociable (Otten et al., 2006a & b). This stirring observation is promising as it segregates processes within encoding, allowing detailed examination of its neural correlates, thus, addressing the gap in encoding literature. This leads us to the aim of the present study, which focuses on this pre-stimulus neural activity and recall prediction.
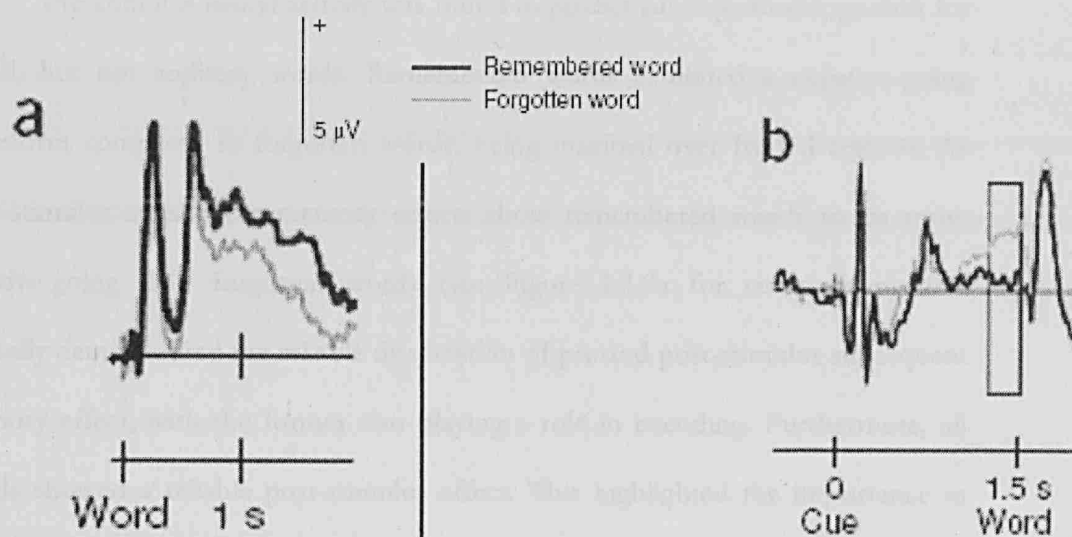
Figure 1.3.2(a). Dissociation of remembered and forgotten word ERPs, a second after word presentation (the subsequent memory effect). (b) Clear dissociation of remembered and forgotten word ERPs, 1.5s before word onset. This is a representative site of the group averaged ERPs (Site 50, equivalent to Fp1 in the 10/20 system (Taken from Otten et al, 2006a).

1.4 Pre-stimulus neural activity predicts recall – Otten et al., 2006a & b

As mentioned, Otten et al. 2006a & b have observed distinct pre-stimulus neural activity predicting recognition, in both visual and auditory modalities. In Otten et al., 2006a, Experiment 2, participants made semantic decisions in an incidental encoding task of intermixed visual and auditory words. A visual cue (i.e. an image of an eye and ear, for visual and auditory words respectively) indicated the upcoming word modality 1.5 s before each word onset, and memory was later assessed using a surprise recognition memory task.

Pre-stimulus neural activity was found to predict subsequent recognition for visual, but not auditory words. Remembered words exhibited a negative-going waveform compared to forgotten words, being maximal over frontal regions. As post-stimulus subsequent memory effects show remembered words to be more positive-going than forgotten words (see Figure 1.3.2a for comparison), this critically demonstrated the reliable dissociation of pre and post-stimulus subsequent memory effect, with the former also playing a role in encoding. Furthermore, all words showed a reliable post-stimulus effect. This highlighted the importance in considering neural activity *before* and after stimulus onset in memory formation (Otten et al., 2006a).

An unanswered question lingered as to why the pre-stimulus activity was exclusive to visual words. As all cues were visual, this was postulated to affect encoding for auditory words, as resources were needed to switch modalities upon encountering a visual cue, to processing an auditory word (Otten et al., 2006b). Otten et al., 2006b ascertained this by retaining similar experimental parameters, but standardizing corresponding cue and word modality. Separate visual (a red square) and auditory (auditory tone) cues now preceded visual and auditory words respectively, with encouraging results. The previously observed pre-stimulus

subsequent memory effect was now found for *both* visual and auditory words, similarly with maximal frontal topography. This reinforced the importance of neural activity preceding an event in memory formation (being present across modalities), implying a functional role in the establishment of a neural context during encoding that influences consolidation efficacy (Otten et al., 2006a & b).

Three key observations were noted. Firstly, this activity only affects encoding in a semantic task, indicating the presence of higher cognitive processes in memory formation. Secondly, it is unlikely to be a priming (i.e. observed improvement in recognition performance due to prior exposure (Tulving, 2000), in this case, the cues preceding each word) or purely attentional effect. Remembered words did not demonstrate shorter reaction times (Otten et al., 2006a & b) or larger P1/N1/P2 components (early attention related ERPs) (Mangun & Hillyard, 1995, cf. Otten et al., 2006b). Moreover, priming is indicated to be pre-semantic and modality specific (Rugg & Nieto-Vegas, 1999), which is clearly not the case here.

Lastly, the unpredictable, intermixed switch and sequence of auditory and visual words enabled constant renewal of this pre-stimulus activity, as opposed to maintaining a sustained activity state. The establishment of the pre-stimulus activity on a trial by trial basis facilitates individual encoding of each word, indicating an influence of experimental sequence on pre-stimulus activity. Additionally, the earlier occurrence of pre-stimulus activity in Otten et al., 2006b compared to Otten et al., 2006a (due to the cue-related change) substantiates the activity's sensitivity towards experimental parameters. This observation bodes well with post-stimulus subsequent memory effect research with regard to its susceptibility to experimental parameters, increasing pre-stimulus activity reliability.

An issue of interest concerned the exact functional significance of this pre-stimulus activity, which was still evasive. Was it an existing property of the brain, or

dictated by conscious control? The amenability of this pre-stimulus activity to experimental parameters suggests the latter was feasible (Meeter et al., 2004, cf. Otten et al., 2006b), and validating this may provide further insight on the activity's exact role in encoding. Capitalizing on the reliable influence of experimental manipulations, the present study's aim was refined to examining the voluntary control of this pre-stimulus activity on recall prediction.

1.5 Mnemonic instruction - Fabiani, Karis & Donchin 1990.

One of the oldest and most effective experimental manipulations affecting recall is the instructed use of different mnemonics or memory strategies (Eagle, 1967; Craik & Watkins, 1973; Weyerts et al., 1997; Brown & Craik, 2000; Rugg & Wilding, 2000; Davachi, Maril & Wagner, 2001; Speer, Jacoby & Braver, 2003; Tsukiura, Mochizuki-Kawai & Fujii, 2005; Cornejo et al., 2007). While there are many types (Eagle, 1967; Roberts, 1968; Camp, Markley & Kramer, 1983; Kondo et al., 2005), rote and elaborative strategies have proven to be the most common and frequently adopted types (Eagle, 1967).

The rote strategy involves silent word repetition in any manner; whilst the elaborative strategy requires word association with sentences, stories or images (Fabiani, Karis & Donchin, 1990). Generally, elaborative strategies produce better recall as it is more extensively encoded (Craik & Tulving, 1975, cf. Brown & Craik, 2000) due to its semantic based approach, as well as linkage to pre-existing knowledge (Brown & Craik, 2000; Otten & Donchin, 2000). This provides good contrast between strategies in terms of subsequent memory recall.

While the instructed use of these 2 strategies on recall prediction have been previously examined in both incidental and intentional paradigms (see Wagner et al., 1999 & Rugg, 1995 for reviews), Fabiani, Karis & Donchin's incidental study in

1990 proved to be the most similar in vein to the present study. Nonetheless, three differences are noteworthy. Firstly, their focus was on neural activity elicited *after* stimulus onset, not pre-stimulus neural activity. Secondly, they were examining isolates (i.e. a word made distinct from the rest by its size) and the Von Restorff effect (i.e. enhanced recall of isolates with respect to other words (Fabiani, Karis & Donchin, 1990)), not normal words. Finally, they were concerned with recall prediction of a specific ERP component (P300) between strategies, not so much the subsequent memory effect in general.

Participants studied short word lists, followed by a written free recall task. Strategy manipulation was effective, with enhanced recall for the elaborative strategy and the P300 predicting recall only in the rote strategy in a Von Restorff paradigm (Fabiani, Karis & Donchin, 1990). The first two findings were illustrated with the use of serial position curves (i.e. a curve generated during word free recall, with enhanced recall for the first and last few positions (primacy and recency effects) compared to the other positions (plateau portion) (Rushby, Barry & Johnstone, 2002)). The 2 strategies also produced distinct ERP waveforms, with the elaborative waveform noted to be slightly more negative-going.

These findings attest to the effectiveness of instructed mnemonic use in recall prediction, providing reliable, overt strategy differences for comparison. Thus, it seemed plausible to adopt instructed mnemonic use as the experimental manipulation for the current study in investigating the voluntary control of pre-stimulus activity.

1.6 Study aim and hypotheses

To our knowledge to date, we know of no study employing the use of instructed mnemonics investigating pre-stimulus activity on recall prediction, given

the novelty of this area. If strategy and recall differences are also reflected and modulated in pre-stimulus activity, it implies the volitional nature of the activity since it is susceptible to instructions. By confirming the voluntary control of this pre-stimulus activity and observing its neural correlates under these circumstances, its functional significance and precise role in recall prediction can be further ascertained.

Based on these key studies (Otten et al., 2006a & b; Fabiani, Karis & Donchin, 1990) and to summarize, the present study aims to investigate if pre-stimulus neural activity can be voluntarily controlled, via experimental mnemonic instructions. Participants will be instructed to memorize cued, random, intermixed sequences of visual and auditory word lists using rote & elaborative strategies, and tested using a written free recall task.

Cues allow a clear time window for visualization of the pre-stimulus activity before word onset. Intermixed visual and auditory words enables the activity to be renewed on a trial by trial basis, influencing encoding in each word and demonstrating the activity's sensitivity to experimental parameters. Different word modalities simultaneously checks for any pre-stimulus activity differences across modalities (Otten et al., 2006a &b) and prevents priming effects due to the unpredictable switch and sequence in modality (Rugg & Nieto-Vegas, 1999). Rote and elaborative strategies provide reliable recall and strategy contrast (Fabiani, Karis & Donchin, 1990), as the latter is more semantically based and thus more extensively encoded.

The intentional encoding paradigm is paired a written free recall task as an accurate retrieval measure. Free recall is compatible with the study's presentation of numerous but short word lists, ensuring sufficient words are remembered and forgotten for analysis using the subsequent memory paradigm. Using a recognition

task results in almost all words being remembered (given the short word lists and memory aid), making it necessary to include more word lists to obtain enough forgotten words and prolonging experimental time. Seeing if pre-stimulus activity is altered for intentional vs. previous incidental paradigms (Otten et al., 2006 a & b studies) also exemplifies the influence of instructions on the activity (Rugg & Wilding, 2000), as previous post-stimulus subsequent memory effect studies have indicated subtle topography and latency differences (Wagner et al., 1999). Additionally, free recall is more representative of how memory is retrieved in our daily lives (Staresina & Davachi, 2006).

The study's 2 hypotheses were generated after considering previous literature and findings from the 3 key studies (Otten et al., 2006a & b; Fabiani, Karis & Donchin, 1990). Firstly, there will be differences in pre-stimulus activity predicting recall for both rote and elaborative strategies. As each strategy entails distinct approaches, pre-stimulus differences should reflect encoding preparations given the activity's early occurrence and as strategy use was instructed.

Secondly, the elaborative strategy would produce better recall. Given that the elaborative strategy is more semantically based (through meaningful word associations), pre-stimulus subsequent memory effects are expected to be more pronounced, signifying more extensive encoding and resulting in higher recall.

The differences in pre-stimulus activity between strategies and modality would imply the activity is volitionally controlled, as it is susceptible to changes in instructions and experimental parameters. Being an intentional encoding study, the pre-stimulus activity may differ slightly in distribution, but should remain largely similar to that of previous studies due to the studies' similar natures (Otten et al., 2006a & b).

Materials and methods

The experimental parameters are largely based on Otten et al., 2006b and Fabiani,

Karis & Donchin, 1990; with stimuli materials identical to Otten et al., 2006b.

2.1 Participants

24 healthy, native English speaking, dextral adults (13 females, 11 males) participated in this University College London and University College London Hospital approved study. Ages ranged from 19-31 years (mean age 23 years), one was colour blind (as assessed by the Ishihara Colour Blindness Test) and none self-reported any visual, hearing, neurological, psychiatric or cognitive problems, or any prescriptive medication use interfering with cognition. The colour blindness test served to ensure sufficient perception of the visual cue (red square), but as attention to cue was not the primary focus in the study, it was not an exlusion criterion. Moreover, debriefing and analysis of the colour blind participant revealed satisfactory cue detection and similar ERP data with other participants.

Recruitment was done through word of mouth and the laboratory's participant database, with selection based on eligibility for the aforementioned criteria. Participants self-reported abstaining from drugs and alcohol 24 hours preceding the experiment and consisted of undergraduate and graduate students. All gave written informed consent and were paid at an hourly rate of £7.50.

2.2 Stimuli and materials

Stimuli consisted of 384 concrete nouns (length 3-12 letters, written frequency 0-500 occurrences per million) (Kucera & Francis, 1967; cf. Otten et al., 2006b) in both written and spoken forms. Written words were presented in white Helvetica font (size 24) against a black background (500ms duration, ~0.7°

vertically, 1-4.5° horizontally) and spoken words were delivered by a native British adult male voice (650ms mean duration, range 310-1130ms). Cues had 250ms duration, consisted of visual (small red square, 0.7° by 1°) and auditory (500 Hertz (Hz) pure tone) forms and appeared 1.5s before word onset. A central fixation point (a plus sign) remained continuously on screen, except when a word or cue was presented. The stimuli were programmed using Cogent 2000 (Wellcome Centre for Imaging Neuroscience, London) and presented using MATLAB (The Mathworks Inc., USA).

Stimuli were pseudo-randomly split into 4 sets of 96 words each (384 words - 192 visual, 192 auditory), ensuring comparable word length distribution across sets. These 4 sets were rotated across participants to create a new list for every participant, with restricted sequences for each word to appear equally in visual and auditory form for each position in the list; with equiprobability in rote and elaborative strategies. Each strategy consisted of 12 lists, with each list comprising 16 intermixed visual-auditory words. 2 sets of 16 words (16 visual, 16 auditory) were used for practice trials (one for each strategy) for every participant. Instructions were added to the start and end of each list, with short rest breaks in between.

2.3 Task procedures

Testing took place in the Cognitive Electrophysiology Group's Laboratory (Room B07) in the Institute of Cognitive Neuroscience. Participants were tested individually in a single session, which took approximately 3 hours. They were fitted with an elastic cap containing electrodes (see Section 2.6 for details) before the testing session.

Participants were instructed to remember a series of randomized, intermixed visual and auditory words, centrally presented via the computer monitor

and binaurally through headphones adjusted to a comfortable hearing level of 60 decibels (dB). Participants sat 100 centimetres (cm) away from the computer screen. Each word was presented one at a time, preceded by a cue indicating subsequent stimulus modality (e.g. a visual cue indicated an upcoming visual stimulus) in the study phase. This was followed by a 30 s distractor task, whereby participants were to count (out loud) backwards in threes from a random number between 81-99 shown on screen.

The distractor task was introduced as our behavioural pilot study revealed significant recency effects (i.e. enhanced recall for the final few word positions in the word list (Rushby, Barry & Johnstone, 2002)). This task is commonly adopted in free recall tasks to eliminate the effect (Paller, Kutas & Mayes, 1987; Paller, McCarthy & Wood, 1988; Fabiani, Karis & Donchin, 1990; Strange et al., 2002; Staresina & Davachi, 2006; Dickerson et al., 2007)

Immediately after the distractor task, participants were given one minute to write down words they remembered from the preceding list on a recall sheet held by a clipboard. Our behavioral pilot study and previous findings have indicated the one minute recall period to be sufficient for similarly numbered word lists (Fabiani, Karis & Donchin, 1990; Dickerson et al., 2007). Written words could be in any order and inclusion of unsure words was encouraged, but not random guessing. A microphone tap indicated that the recall sheet should be moved from the clipboard to the floor, so that a new sheet would be ready for the following list. At the end of the experiment, electrodes were removed and participants were debriefed.

2.4 Strategy instructions

Participants were required to remember words using 2 separate strategies/conditions, the order of which was counterbalanced across participants.

In the rote condition, they were to silently repeat the words in their heads. In the elaborative condition, they were to create word associations, stories or images. Utilization of the given strategy was emphasized, although it was recognized that the method may not be to their preference and word recall may be affected. Strategy instructions appeared at the start of every list as a reminder, and participants were required to indicate if they had used the assigned strategy at the bottom of every recall sheet to avoid tentative lapses in strategy use. Participant 29 was the only one who did not use the assigned strategy for 4 lists (3 elaborative and 1 rote), and these 4 lists were excluded from analysis. A practice list for each strategy preceded each condition. Each condition took about 45 minutes.

2.5 Study design

This was a 2 x 2 x 2 within subject, visual-auditory, intentional encoding ERP study. Independent variables were strategy (rote, elaborative), modality (visual, auditory) and subsequent memory performance (remembered, forgotten words). Figure 2.5 summarizes the experimental design.

EEG set up

↓

Testing phase :
Strategy order counterbalanced, either:
Rote practice, lists 1-12 & Elaborative practice, lists 1-12
OR
Elaborative practice, lists 1-12 & Rote practice, lists 1-12

↓

"Memorize words using rote/elaborative strategy.
A red square cues an upcoming visual word,
an auditory tone cues an auditory word."

↓

Debriefing

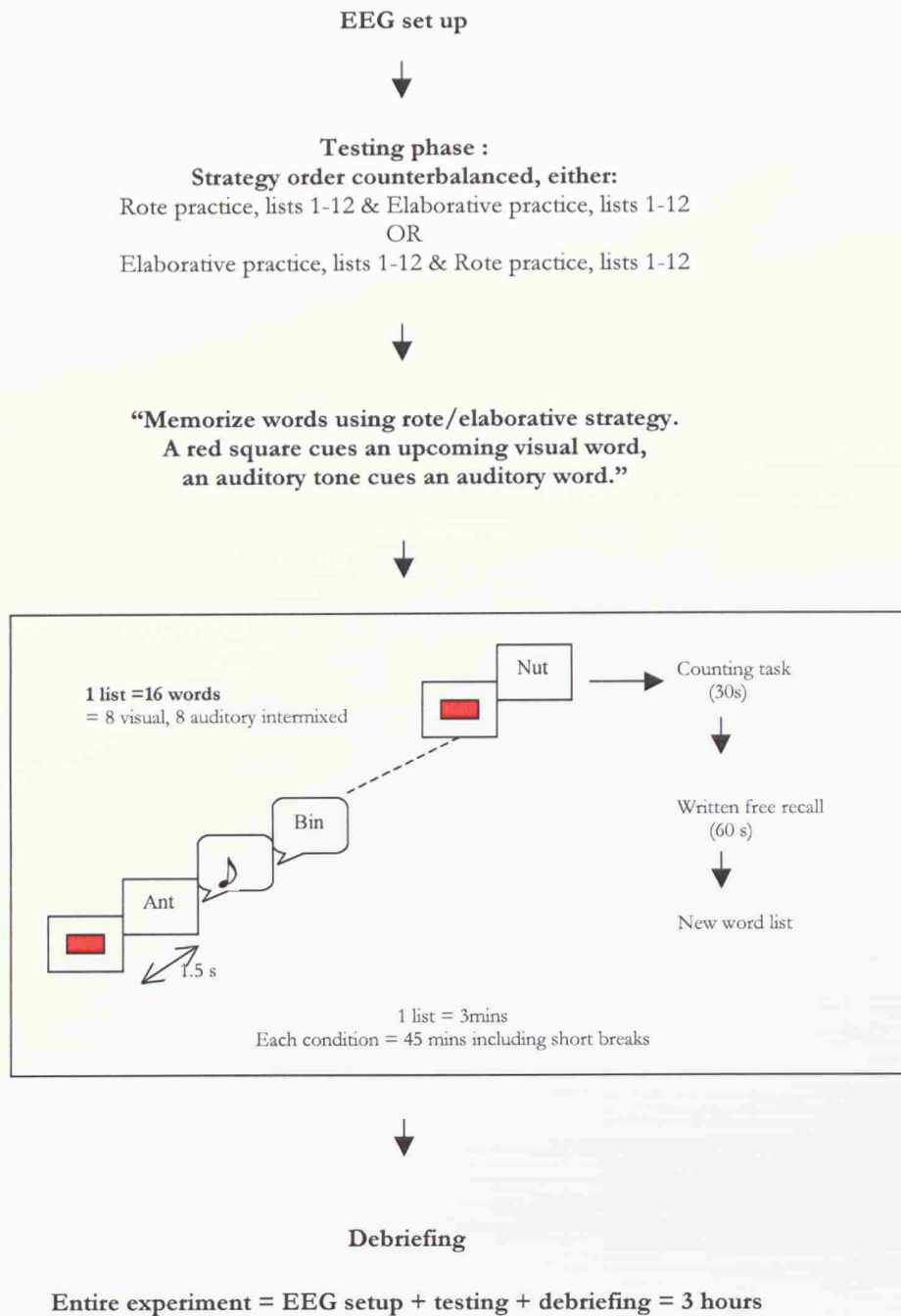**Entire experiment = EEG setup + testing + debriefing = 3 hours**

Figure 2.5. The present study's experimental design.

2.6 EEG acquisition & analysis

A commercial elastic cap containing a subset of 33 scalp sites (sintered silver/silver chloride electrodes) was used for EEG recording (EasyCap, EasyCap GmbH, Germany), using an equidistant electrode montage (Montage 10, www.easycap.de/easycap/e/electrodes/13_M10.htm). Electro-oculogram activity (EOG) was recorded from electrodes placed at the outer canthi of both eyes (horizontal EOG) and above and below the left eye (vertical EOG). Site 8 (Fz equivalent in the 10-20 system) and an electrode anterior to Fz served as the online reference and ground respectively. Impedances were kept below 5 kilo Ohms (kΩ). Signals were amplified and band-pass filtered between 0.01 and 35 Hz (Contact Precision amplifier; 3 dB roll-off) and digitized at 500Hz (12-bit resolution).

Data were digitally filtered between 0.05 and 20Hz (96dB roll-off, zero phase shift filter) to eliminate low and high frequency noise, and re-referenced algebraically to the linked mastoids. Events of interest in the study phase were extracted in 2460ms epochs from the continuous EEG record, where separate cue and word elicited activity ERPs were created. Both cue and word related ERPs were referred to a 100ms period before onset, and resampled at 125Hz and 100Hz respectively, as epochs spanning events of interest differed for both due to a technical limitation. ERP waveforms were generated for each electrode site, strategy and stimulus modality by averaging epochs separately for remembered and forgotten words during the study period.

Blink artefacts contaminating ERP waveforms were removed using a standard regression technique (Rugg et al., 1997), and trials with horizontal, non-blink vertical movements, EEG drifts (~50 microvolts (μV)) and analog to digital saturation were excluded off line from the averaging process. ERPs were based on a minimum of 15 artefact-free trials. ERP waveforms were quantified by calculating

mean amplitudes across selected intervals. Statistical analyses was conducted using repeated measures of analyses of variance (ANOVA), with the Greenhouse-Geisser correction to account for violations of sphericity (Keselman & Rogan, 1980, cf. Otten et al., 2006b).

2.7 Behavioural analysis

The written free recall lists were manually scored. Recalled items were defined as "words showing clear evidence of retrieval without additional cues, although their representations are not perfect" (c.f. Otten & Donchin, 2000, page 647). Phonologically (e.g. hair/hare), orthographically (e.g. clock/cloak) and semantically (e.g. bunny/rabbit) similar words were considered remembered, they accounted for 2% of total words recalled overall. Additionally, recalled words from previous lists (rather than the immediately preceding list) were also categorized as remembered if they occurred within the next 5 lists. 0.2% of words were recalled in this category.

The total percentage of remembered words was computed for each position in the word list, word modality and assigned strategy for every participant. These files were then matched to the participant's corresponding EEG to analyze the neural activity for remembered and forgotten items according to the subsequent memory paradigm. Serial position curves were also computed from these files to examine the effects of word position, strategy and stimulus modality on recall. To reiterate, the serial position curve is a curve generated during free recall, with enhanced recall for the first and last few word positions (primacy and recency effects respectively) (Rushby, Barry & Johnstone, 2002; Azizian & Polich, 2008). Repeated measures ANOVAs and Greenhouse Geisser correction for violation of sphericity were employed for statistical corroboration.

Results

3.1 Free recall data

The serial position curves in Figure 3.1 display recalled word percentages (across 12 lists) for rote and elaborative strategies, divided into visual and auditory modalities. These data are summarized in Table 3.1.

Collectively, these data show visible recall differences between strategies, but not modality. Thus, visual words were not remembered better than auditory words or vice versa, but recall rates differed depending on strategy. Overall, participants recalled 34% and 68% of the words in the rote and elaborative strategies. Primacy effects for both strategies are evident in Figure 3.1, with enhanced recall for the first few word positions. Conversely, recency effects were absent for both strategies.

A repeated measure (2 strategies x 2 modalities x 16 positions) ANOVA revealed significant main effects of strategy and position ($F_{1,23}$ = 5.32, p < 0.001 and $F_{7,161.4}$ = 3.15, p < 0.001) and an interaction between the two ($F_{9.2,210.6}$ = 2.16, p = 0.008). This indicated the presence of the primacy effect in both strategies. To localize this effect and facilitate statistical analyses, the 16 word positions were divided into 4 blocks of 4 positions and analysed in a 2 factor (2 strategies x 4 blocks) ANOVA.

Significant main effects of strategy and blocks ($F_{1,23}$ = 299.1, p < 0.001 and $F_{2.1,47.6}$ = 33.03, p < 0.001) and an interaction between the two ($F_{2.6,59.2}$ = 3.97, p = 0.016) prompted further division of the 1st block of 4 positions into 2 blocks of 2 positions and separate analysis in a 2 factor (2 strategies x 2 blocks) ANOVA. Significant main effects of strategy and the 1st block of 2 positions ($F_{1,23}$ = 12.08, p < 0.001 and $F_{1,23}$ = 6.32, p < 0.001) with an interaction between the two localized the primacy effect for both strategies ($F_{1,23}$ = 5.20, p = 0.032), demonstrating the

first 2 words in each strategy was processed differently from other word positions. This issue will be further addressed in the discussion.

In sum, recall was higher for the elaborative strategy, and not affected by modality.

Serial position curves: free recall
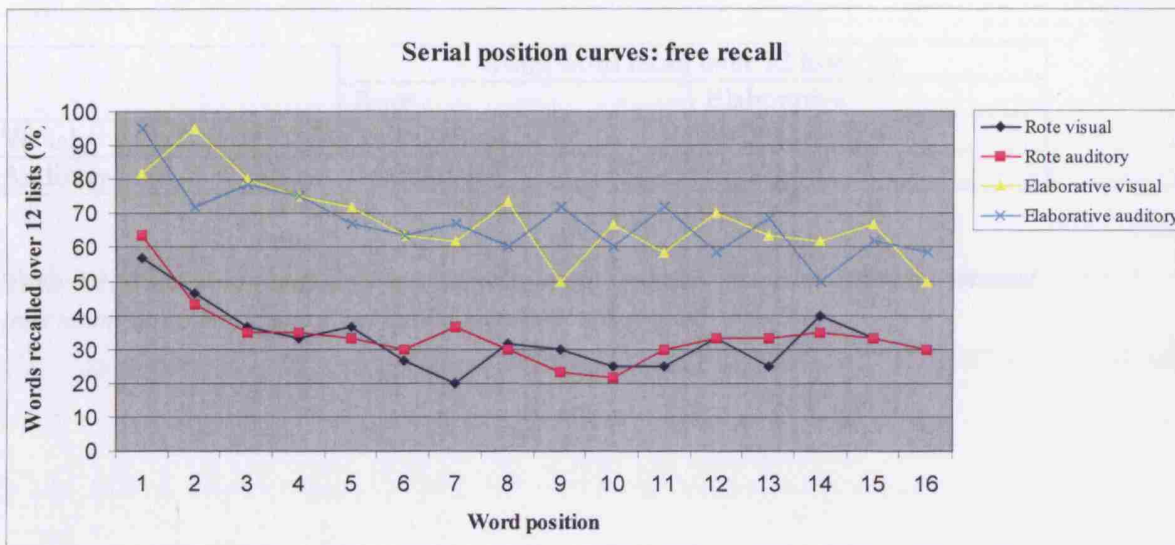
Figure 3.1. *Serial position curves for free recall. Words recalled for 12 lists are shown for both strategies (rote, elaborative) and modality (visual, auditory). A recall difference between strategy is visible, but not modality. Primacy effects (enhanced recall for first few word positions) are apparent in both strategies, but not recency effects (enhanced recall for last few word positions).*

	Total word recall over 12 lists (%)	
	Rote	Elaborative
Visual	33.1 (7.4)	68.0 (11.3)
Auditory	34.2 (10.0)	67.3 (11.2)

Table 3.1. Total words recalled for rote and elaborative strategies (standard deviations obtained from means across participants), subdivided into visual and auditory stimuli.

3.2 EEG data

In line with the study's focus on pre-stimulus activity, only cue-elicited ERP waveforms (i.e. neural activity between cue onset and word onset) preceding visual and auditory words in both strategies are discussed. EEG data are separated into overall strategy differences and subsequent memory effects and presented first, later ensued by their statistical analyses.

3.2.1 Overall strategy differences

To ensure trial contributions for both strategies were representative and not outliers (i.e. values deviating substantially from data distribution), individual participant averages were weighted and collapsed across modality and subsequent memory performance. Figure 3.2.1.1 displays the group average of both strategies for all sites, intended to bring out strategy differences. A clear, sustained difference is noted between strategies. The elaborative waveforms are more negative-going and maximal over fronto-central regions, beginning approximately 200 ms after cue onset.

To verify if there were modality differences between strategies, visual and auditory waveforms for both strategies were collapsed across subsequent memory effects and compared. Figure 3.2.1.2a & b depicts visual and auditory group averages respectively for both strategies for all sites. While they obviously differ in morphology (being of separate modalities (Ruchkin et al., 1997)), the differences expressed between strategies seem identical. The elaborative waveforms are more negative-going and maximal over fronto-central regions, with a sustained difference of approximately 1000ms.

Figure 3.2.1.1. Group averages for all sites comparing strategies, collapsed over modality and subsequent memory effects. Note the clear, sustained difference between strategies. The difference is maximal over fronto-central regions, beginning approximately 200 ms after cue onset, with the elaborative waveforms being more negative-going. This implies both strategies to be inherently different.
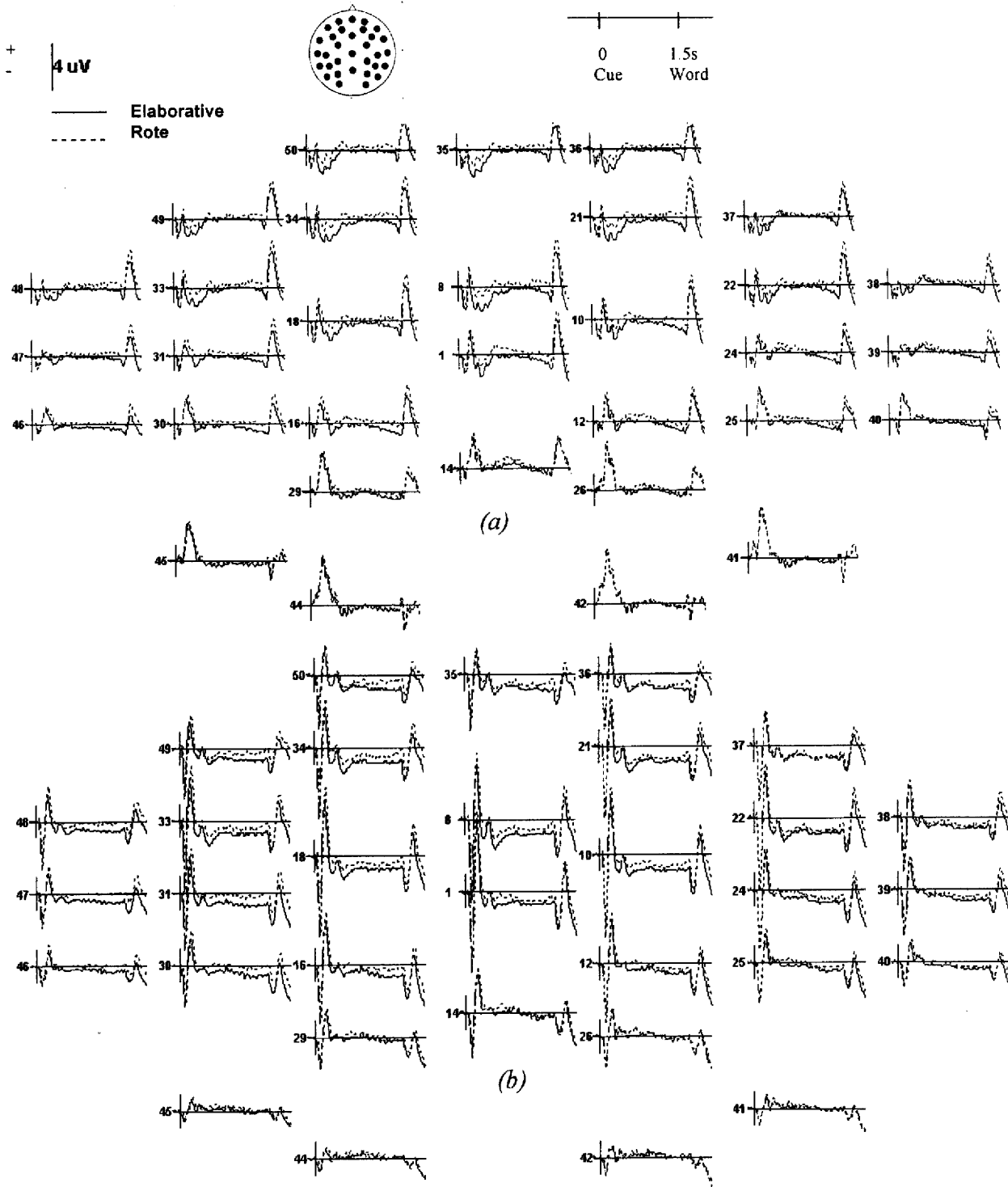
Figure 3.2.1.2. Group averages for all sites comparing strategies, collapsed over subsequent memory effects for (a) visual and (b) auditory conditions. While differing in morphology (being of separate modalities), the differences expressed between strategies seem similarly sustained. The elaborative waveforms are more negative-going, maximal over fronto-central regions with a sustained difference of approximately 1000ms. This implies no modality differences in terms of overall recall performance.
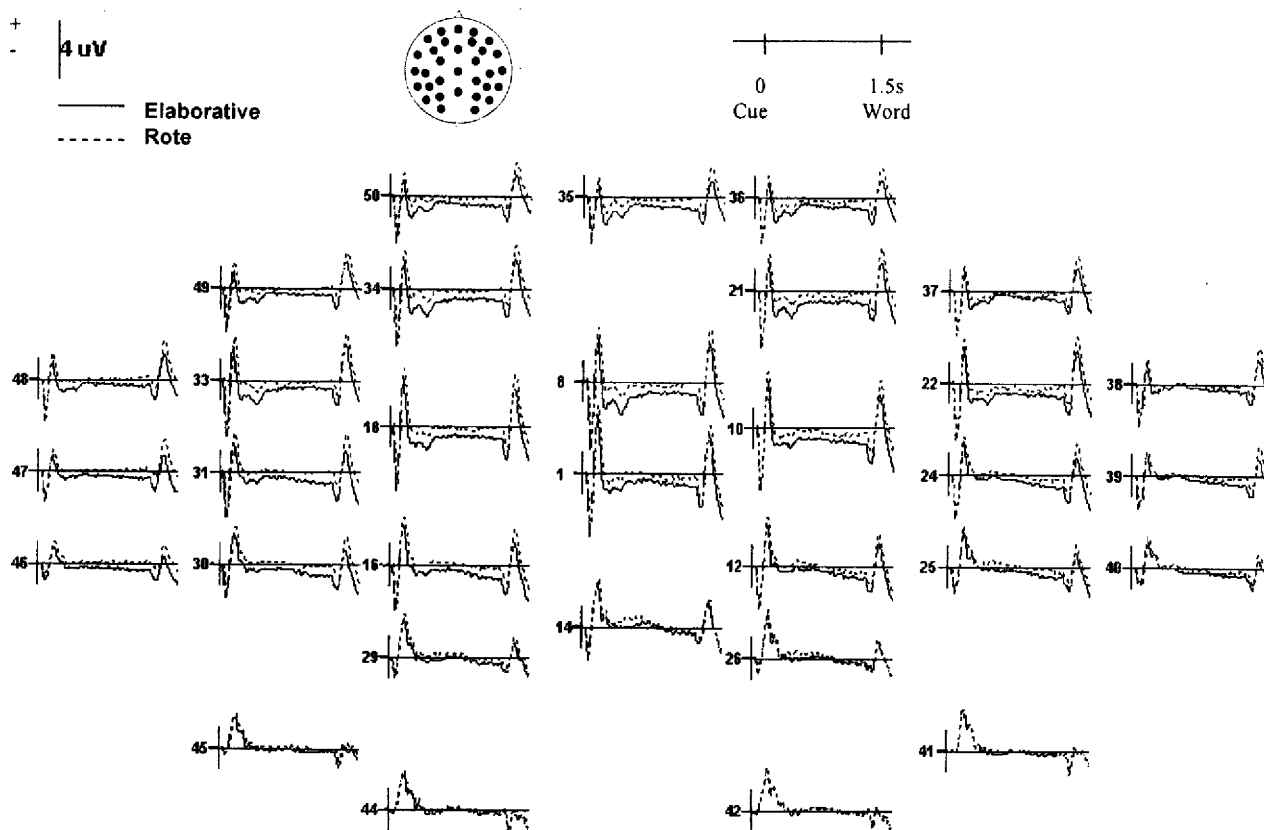
3.2.2 Subsequent memory effects

Remembered and forgotten words in the written free recall task was correlated to corresponding neural activity using the subsequent memory paradigm. The group averaged cue-elicited ERP waveforms are organized by strategy, modality and subsequent memory performance. For simplicity, the group averages are showcased by a representative electrode site (i.e. where effects were most robust) in the following figures.

To examine subsequent memory effects (i.e. difference between remembered and forgotten words) remembered and forgotten word waveforms were overlaid for each modality within each strategy, displayed in Figure 3.2.2.3. Subsequent memory effects can be seen in the elaborative auditory (Figure 3.2.2.3b) and rote visual (Figure 3.2.2.4c) conditions, but not in the elaborative visual (Figure 3.2.2.3a) and rote auditory (Figure 3.2.2.4d) conditions.

The observed subsequent memory effect in the elaborative auditory and rote visual conditions is consistent with Otten et al., 2006b in that it is negative-going for remembered words, appearing approximately 500ms after cue onset and fading just prior to word onset. It, however, differed in being maximal over central regions, with no polarity reversal at the posterior sites. Figure 3.2.2.4 portrays the subsequent memory effect for all sites for the elaborative auditory (a) and rote visual (b) conditions respectively.
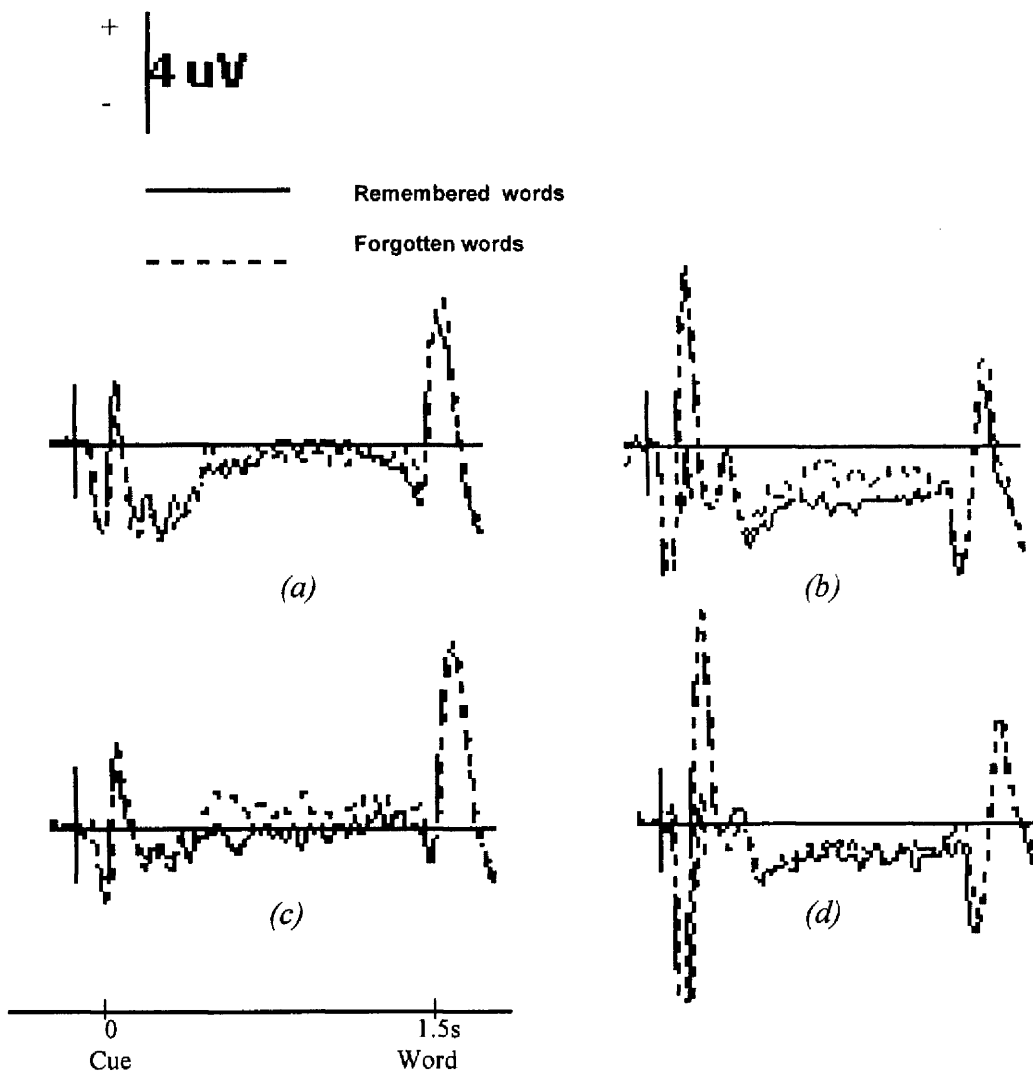
Figure 3.2.2.3. A representative electrode site (Site 8, equivalent to Cz in the 10/20 system) of the group averages for remembered and forgotten words in both strategies. The conditions are (a) elaborative visual (b) elaborative auditory (c) rote visual (d) rote auditory. A difference between remembered and forgotten words (subsequent memory effect) can be seen in the elaborative auditory (b) and rote visual (c) conditions, but not in the elaborative visual (a) and rote auditory (d) conditions. This difference is negative-going for remembered words, appears approximately 500ms after cue onset, is maximal over fronto-central regions and fades just prior to word onset. This implies modality differences in terms of preparation within the strategies.

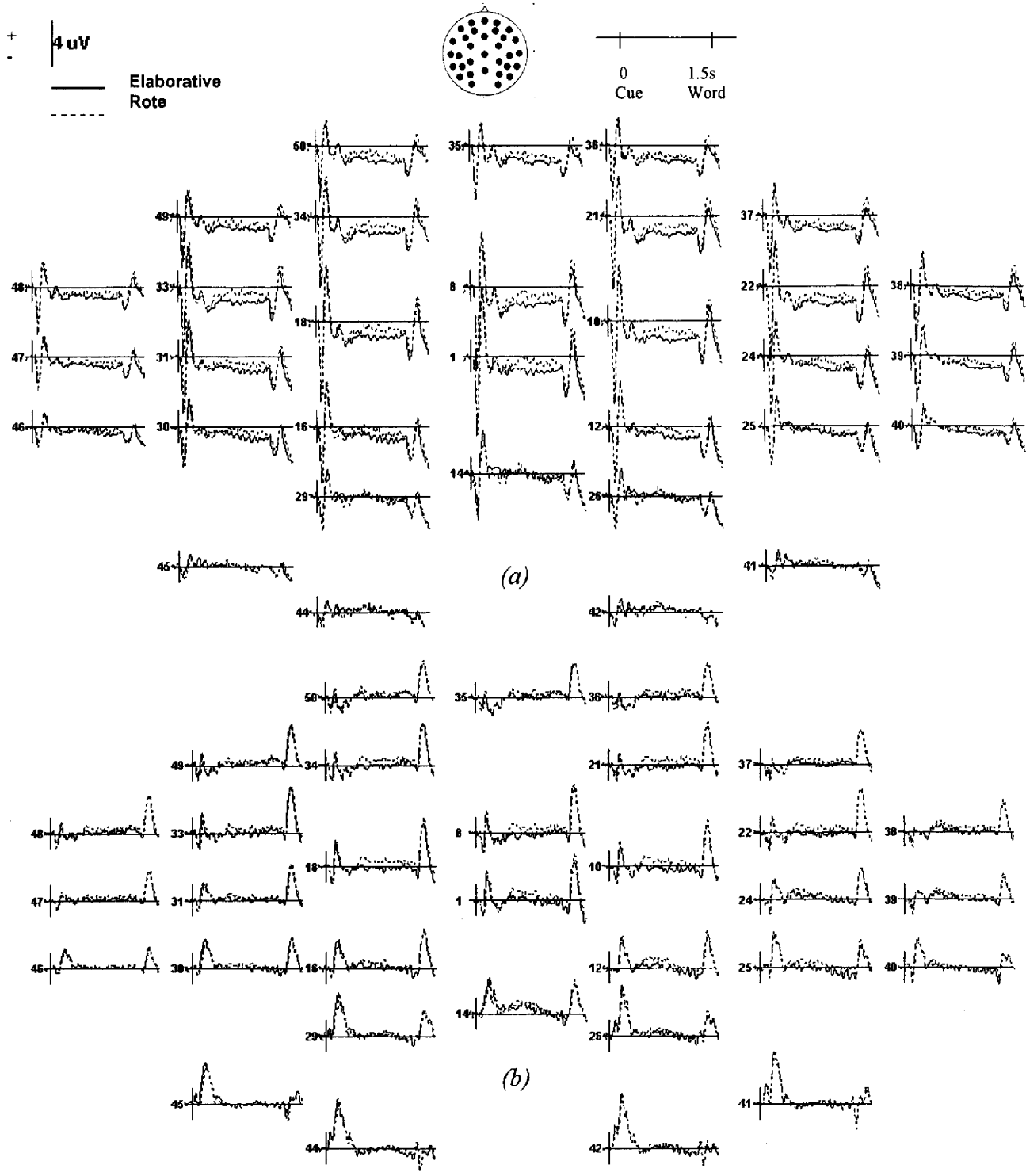*Figure 3.2.2.4. The subsequent memory effect for (a) elaborative auditory and (b) rote visual conditions for all electrode sites.*

3.2.3. EEG statistical analyses

Quantification of these pre-stimulus differences was done through calculation of mean amplitudes for all electrodes sites (excluding the mastoids and EOG channels) for the 500-1500ms interval after cue onset (when effects were maximal). This approach was guided by visual inspection of the ERP waveforms and previous pre-stimulus studies (Otten et al., 2006a & b). The analyses are organized to coincide with the previous subsections, so statistics for the overall strategy differences will lead those for the subsequent memory effects.

To characterize overall strategy differences, a 2 factor (2 strategies x 32 electrode sites) ANOVA was applied, revealing significant main effects of strategy and site ($F_{1,23}$ = 20.07, p <0.001 and $F_{2.4,55.8}$ = 8.56, p <0.001) for both strategies. This confirms inherent strategy differences between rote and elaborative. As site main effects are not crucial, they will not be discussed for all subsequent sections.

Two separate 2 factor (2 strategies x 32 sites) ANOVAs examining modality differences between strategies were performed for visual and auditory modalities. Significant main effects of strategy ($F_{1,23}$ = 15.43, p = 0.001 and $F_{1,23}$ = 10.53, p = 0.004) were noted for visual and auditory modalities, indicating no modality differences in overall recall performance.

Representation of subsequent memory effects was first done with a 4 factor (2 strategies x 2 modalities x 2 subsequent memory performance x 32 sites) ANOVA, which revealed main effects of strategy, modality and subsequent memory performance ($F_{1,23}$ = 14.76, p = 0.001; $F_{1,23}$ = 19.63, p <0.001 and $F_{1,23}$ = 10.70, p = 0.003), with only an interaction between modality and site ($F_{3.7,84.9}$ = 17.59, p <0.001). The 4 way interaction between strategy, modality, subsequent memory performance and site only approached significance ($F_{4.7,108.7}$ = 2.05, p = 0.081). The big subsequent memory performance main effect ($F_{1,23}$ = 10.70, p =

0.003) and the absence of any interaction involving it indicates a strong presence of subsequent memory effects collapsed across all conditions. Give separate modalities activate different scalp sites, the interaction between modality and site is expected.

To ascertain if there were modality differences in subsequent memory effects (pre-hypothesis based on Otten et al., 2006a &b, where none were found) as well as the present study's focus on strategy differences, separate 2 factor (2 subsequent memory performance x 32 sites) ANOVAs examining subsequent memory effects within modalities in elaborative and rote strategies was performed. A main effect of subsequent memory performance was localized in the elaborative auditory condition ($F_{1,23} = 4.31$, p $= 0.05$). The apparent visual difference in the rote visual condition only approached significance ($F_{1,23} = 3.58$, p $= 0.07$). This implies that while encoding preparations occur in the elaborative strategy, only the auditory condition predicts recall. In contrast, preparation and recall for rote was not statistically supported.

Figure 3.2.2.5 illustrates the topographical distribution of the subsequent memory effect in the elaborative auditory condition with a voltage spline map. This pre-stimulus subsequent memory effect has a negative, fronto-central maximal distribution.

In sum, while modality does not influence overall recall performance, it affects *preparation* for recall *within* the two strategies. Only pre-stimulus activity in the elaborative strategy predicted subsequent recall, specifically the auditory condition. This distinguishes strategy differences in pre-stimulus activity.
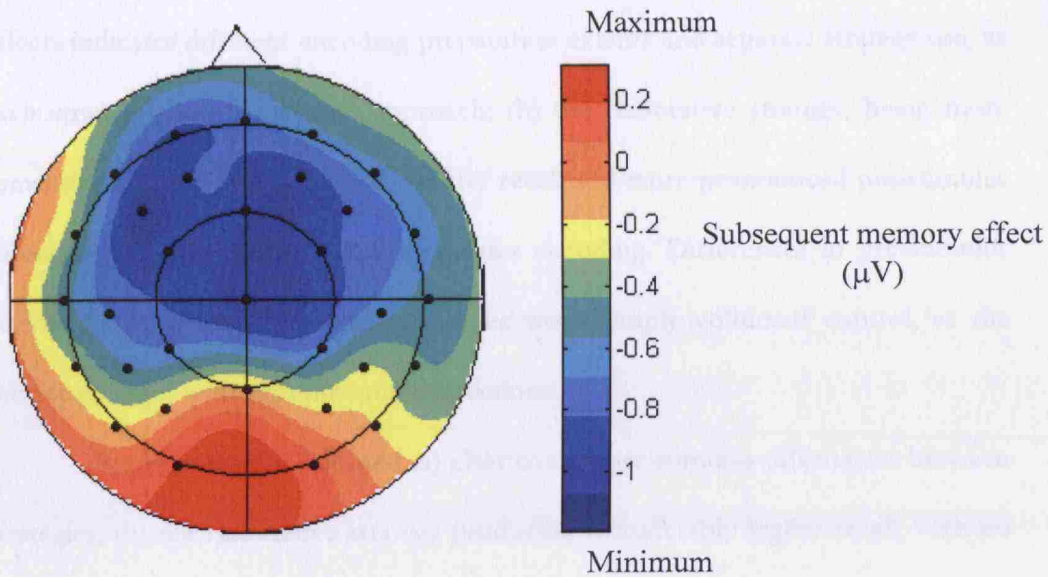
Figure 3.2.2.5. Voltage spline map showing the topographical distribution of the subsequent memory effect (difference between remembered and forgotten words) in the elaborative auditory condition, for the 500-1500ms interval before word onset. This pre-stimulus subsequent memory effect has a negative, fronto-central maximal distribution.

Discussion

The present study examined if pre-stimulus neural activity can be voluntarily controlled via experimental instructions of rote and elaborative strategies, employing a visual-auditory intentional encoding ERP paradigm. The hypotheses were that (a) between strategy differences in pre-stimulus subsequent memory effects indicates different encoding preparation extents and separate strategy use, as each strategy entails a distinct approach; (b) the elaborative strategy, being more semantically based, would produce better recall and more pronounced pre-stimulus subsequent memory effects due to greater encoding. Differences in pre-stimulus activity between strategies and modalities would imply volitional control, as the activity changes with experimental instructions.

The main results indicated (a) clear overall pre-stimulus differences between strategies; (b) the elaborative strategy producing considerably higher recall, with no modality differences in overall recall performance; and (c) differences in pre-stimulus subsequent memory effects between strategies and modality differences within strategies. While the elaborative strategy demonstrated encoding preparation, only the auditory condition specifically predicted recall. This demonstrates the pre-stimulus activity's susceptibility to instructions and modality, implicating voluntary control. Findings will be discussed, followed by study implications, limitations/future directions and conclusion.

4.1 Findings: support for previous studies

The present study supports previous studies (Otten et al., 2006a & b) on the importance of pre-stimulus activity in productive memory formation, through the display of pre-stimulus subsequent memory effects. The present effect is also negative-going, starting 500ms after cue onset, fading prior to word onset and

occurring in semantically based tasks, consistent with Otten et al., 2006b. Encoding processes are therefore not limited to activity after, but also activity prior to stimulus onset. The activity's early occurrence is highly suggestive of it being some form of encoding preparation, to be further elaborated subsequently.

Overall recall performance (illustrated in the serial position curves in Figure 3.1) and clear, consistent ERP differences between strategies (Figure 3.2.1.1 & 3.2.1.2) supports previous behavioural (Eagle, 1967; Camp, Markley & Kramer, 1983) and post-stimulus ERP studies (Fabiani, Karis & Donchin, 1990; Cornejo et al., 2007) on inherent strategy differences and effective implementation of instructed mnemonic use. Strategy differences are supplemented with differing recall rates, with participants recalling double the number of words in the elaborative (68%) compared to the rote (34%) strategy, as expected. Stimulus modality did not affect overall recall performance, (i.e. visual or auditory words were not remembered any differently), consistent with Otten et al., (2006b). Higher recall in the elaborative condition could thus be attributed primarily to strategy use.

Meaningful associations and connections are made in the elaborative strategy, in contrast to mere repetition in the rote strategy. This results in increased encoding and also facilitates retrieval due to an increased number of cues, in line with the levels of processing theory (Craik & Lockhart, 1972, cf. Rugg, 1995). Indeed, it supports the notion that strategy type, not sheer rehearsal amount and time, leads to better recall (Craik & Watkins, 1973; Greene, 1987; Bower, 2000). This is validated by participants reporting extra recall time would not have changed their amount of recall during debriefing.

Recency effects were absent for both strategies, demonstrating inclusion of the distractor task to be effective (see Figure 3.1). As recency effects reflect maintenance of freshly encoded items in short term memory, it is abolished when a

distractor task is introduced (Green, 1986 and Glanzer & Cunitz, 1966; cf. Azizian & Polich, 2008; Strange et al., 2002). This enabled the inclusion of the last few word positions for analysis, increasing statistical power. It also safeguards against comparison of two different memory processes (short and long term memory), which might jeopardize results validity, although both share common neural substrates (Speer, Jacoby & Braver, 2003).

4.2 Findings: new ground

This is the first time pre-stimulus subsequent memory effects between strategies have been demonstrated. As overall pre-stimulus differences encompass other factors (e.g. inherent strategy differences) besides encoding, locating pre-stimulus subsequent memory effects pinpoints how encoding processes can differ even before presentation of an event or item. Given the different strategy approaches and the early dissociation, this difference is likely indicative of some form of preparation (as mentioned earlier), suggesting one can adopt suitable measures to learn or remember more effectively. This discloses the activity's spontaneous nature and corroborates encoding being dependent on both state (i.e. one's state of mind) and item (i.e. task) related neural correlates (Otten, Henson & Rugg, 2002).

The presence of a pre-stimulus subsequent memory effect in an intentional encoding paradigm is also novel, given the previous studies used incidental encoding paradigms (Otten et al., 2006a & b). This establishes this pre-stimulus effect to be a robust and generalizable finding. Moreover, the present effect showed a maximal fronto-central distribution, diverging from the frontal distribution seen for post-stimulus subsequent memory effects in intentional encoding paradigms (Munte et al., 1988, cf. Wagner et al., 1999; Takashima et al., 2006). This feature

further distincts pre and post-stimulus subsequent memory effects, besides the conspicuous observation of the latter being positive-going and the former negative-going for remembered items (see Figure 1.3.2).

The finding of modality differences *within* strategies in the analyses of subsequent memory effects was unexpected. Considering the different strategy approaches, one would expect clear preparation differences between them. More preparation was presumed for the elaborative condition, as semantic associations understandably required more effort (i.e. associating random words into a story requires linkage to past and existing knowledge) than mere repetition. In spite of this, statistical analyses showed a noticeable subsequent memory effect in only the elaborative auditory condition (see Figure 3.2.2.3). This initial puzzle was reconciled once the nature of each strategy and its compatibility within the respective stimulus modality was taken into account (Greene, 1987).

Participant debriefing revealed utilization of sentence/story association and visualization in the elaborative strategy, involving heavy use of mental imagery. Visual words are much easier to incorporate into a mental picture or story (Gonsalves & Paller, 2000 c.f. Paller & Wagner, 2002), as they are both processed in the same modality. In contrast, auditory words require more preparation, as the initial switch in modality is necessary (i.e. hearing the word 'nut', then imagining it) before integration in an existing mental picture or story (i.e. linking nut with other visualized words). Thus, visual words require less preparation, unlike its auditory counterpart. Participants also reported to be predominantly visual learners during debriefing, supplementing this finding. This observation is quite similar to Otten et al., 2006a, where a visual cue foregoing an auditory word prevented detection of subsequent memory effects in the auditory condition, due to the cue-word modality incongruence (Otten et al., 2006b).

Considering the effect in the present study was larger approaching word onset, further analyses was conducted for the 1000-1500ms window in the cue-word interval with a repeated measure (2 strategy x 2 modality x 2 subsequent memory performance x 32 sites) ANOVA. All 4 main effects were significant (see Appendix A), but more importantly, a significant interaction between strategy, modality, subsequent memory performance and site was noted ($F_{4.9,112.1} = 2.74$, p = 0.024). This suggests the present pre-stimulus subsequent memory effect being specific to the elaborative auditory condition, as the effect differs for each condition. Thus, between-strategy differences could very well be attributed to modality differences within strategies.

Taken together, the fact that this pre-stimulus subsequent memory effect is susceptible to different strategies and parameters is indicative of it being under volitional control (Otten et al., 2006b). While the present effect differed from previous studies (Otten et al., 2006a & b) in scalp distribution (being more fronto-central) with no polarity reversal in the posterior sites, this may not be conclusive as the interaction between subsequent memory performance and site was close to significance ($F_{4.9,112.6} = 1.94$, p = 0.096). Thus, it is plausible that the pre-stimulus effects seen in all three studies are similar.

While modality differences within strategies were noted in the present study, interactions between modality with strategy or subsequent memory performance were absent. This suggests the present study's pre-stimulus differences may be attributed to changes in experimental parameters, rather than being a different phenomenon altogether (involving more blatant changes, e.g. effect being positive-going). If so, the implications are promising.

4.3 Implications

The present study extends previous pre-stimulus studies (Otten et al., 2006a & b) on the importance of pre-stimulus activity in encoding and subsequent prediction of successful recall, by establishing the activity to be voluntarily controlled. This brings us a step closer to revealing the functional significance of this activity, which is still unknown.

A role that is becoming increasingly likely is the preparatory establishment of a neural framework or context. While general in that it occurs regardless of input modality (Otten et al., 2006b), it appears specific to one's approach to an upcoming task and its factors (e.g. pre-stimulus modality differences within strategies). As neural connections are made to different brain structures depending on different task parameters and adopted mindsets, among others (Speer, Jacoby & Braver, 2003; Otten, Henson & Rugg, 2002), the voluntary control of this activity becomes a necessity, as demonstrated by the present study (e.g. pre-stimulus between strategy differences). This supports past research of multiple, task specific encoding systems (Otten & Rugg, 2001; Tsukuira, Mochizuki-Kawai, Fujii, 2007; Rugg et al., 2008) and that different responses to identical stimuli can be attributed to pre-stimulus activity (Britz, Landis & Michel, 2008).

Memory deficits in the elderly are also thought to be attributed to reduced encoding abilities (Craik & Byrd, 1982, cf. Grady et al., 1999). A PET study revealed activation of multiple encoding networks in young participants, whilst the elderly only showed one while performing the same task, corresponding to poorer recall (Grady et al., 1999). Replication of the present study with elderly participants would be pivotal in endorsing the postulated preparatory role of the pre-stimulus activity more definitively, as no study has yet examined pre-stimulus activity in the elderly

or patient population. If encoding deficits are indeed associated with memory decline, this would provide new avenues for dementia treatment and research.

Tulving's concept of a 'retrieval mode' (Rugg & Wilding, 2000; Rugg et al., 2008) and the transfer appropriate processing principle also adds credence to the neural context preparation role. To reiterate, the transfer-appropriate processing principle basically states that the likelihood of recall is dependent on the similarity or overlap between encoding and retrieval processes (Morris et al., 1977; cf. Rugg et al., 2008). Tulving reasoned for the existence of some control mechanism, as an entire experience is not relived each time something is remembered. Only when a specific cognitive state (i.e. retrieval mode) is employed would encoding events be processed as retrieval cues (Tulving, 1983, cf. Rugg et al., 2008; Rugg & Wilding, 2008). Thus, preparation of a neural context may not only establish encoding connections, but also specify retrieval cues, as several cues may be retained from a particular experience (Brown & Craik, 2000). This has promising implications for students with learning abilities, or even cognitive rehabilitation patients (Miotto et al., 2006), as most people are unaware of optimal learning strategies (Brown & Craik, 2000).

The observation of pre-stimulus activity and its predictive influence in varied areas like bistable perception (Britz, Landis & Michel, 2008), attention (Driver & Frith, 2000) vision (Hanslmayr et al., 2007; van Dijk et al., 2008) and problem solving or insight (Kounios et al., 2006) with methodologies including EEG oscillations, microstates and fMRI, may suggest non-exclusivity to memory and generalizability to cognition as a whole. Nonetheless, it is also possible that the observed pre-stimulus activity in these studies may not be identical across experiments. Despite this, if the activity encompasses cognition as a whole, it could

point to a conceivable function as an evolved, predictive brain mechanism. Still, this possibility would definitely need to be bored out with more studies.

Otten et al., 2006a crucially pointed out the poor temporal resolution in fMRI and PET may actually present a mixture of pre and post-stimulus subsequent memory effects in previous subsequent memory studies. If this can be reconciled, findings from these studies may provide useful clues for comparison, due to the possible mix of pre and post-stimulus effects. While the present study's pre-stimulus effect shows a maximal fronto-central distribution, its exact localization is speculative due to the poor spatial resolution in ERPs. Future studies should certainly localize these effects more explicitly in suitably designed studies.

Although the present implications are undoubtedly encouraging, some findings warrant further contemplation and corroboration. These are addressed in the following section.

4.4 Limitations and future directions

A reason contributing to the elusivity of this pre-stimulus activity's functional significance (aside from its novelty) is due to the inability to pinpoint its precise location in the brain, as ERP localization is poor. Identification of neural generators of ERPs involve making a number of assumptions (i.e. the inverse problem), which are questionable (Rugg, 1995). By localizing neural generators of the effect, region contributions and interactions in encoding can be determined. As fMRI has excellent spatial but poor temporal resolution, future studies should consider combining both methods, yielding more definitive results. Indeed, EEG-fMRI studies are becoming more common as findings are compatible (Wagner et al., 1999, Friedman & Johnson, 2000; Paller & Wagner, 2002). MEG is also promising (offering superior temporal resolution but much better localization than

ERPs), although there are only three studies on subsequent memory to date (Walla et al., 2003; Osipova et al., 2006; Takashima et al., 2006).

Nevertheless, careful consideration of experimental paradigms is needed with these joint techniques. For example, concurrent MEG-fMRI recordings would not be feasible, as each requires the head to be encased in a specific chamber (Wagner et al., 1999). Employing the present study's constant, quick, cue-word intervals is problematic in fMRI (even with trial by trial glimpses in event-related fMRI) as blood responses have limited resolution in seconds (Wagner et al., 1999). Therefore, it may be more fruitful to have simultaneous EEG-MEG recordings for further investigation of this pre-stimulus activity. By concurrently localizing and correlating the activity's timing and activation, more definitive brain regions and functions can be confirmed. Having established concrete regions, finer grained localization can be conducted with fMRI without much need for synchronized, rigid temporal requirements.

As remarked earlier, pre-stimulus activity in other cognitive areas have been investigated with EEG oscillations (Hanslmayr et al., 2007; Van Dijk et al., 2008). Visual inspection of the present study's ERP waveforms for remembered words in visual and auditory rote conditions revealed possible time-locked oscillations, particularly in the posterior sites. It may prove worthwhile to analyse the present results using EEG oscillations, as the functional relevance of oscillations are being rediscovered (see Sauseng & Klimesch, 2008 for a review). Oscillations like alpha, gamma and theta in particular are consistently documented in memory (Wagner, 2001; Osipova et al., 2006; Bauml et al., 2008; Sauseng & Klimesch, 2008).

Post-stimulus subsequent effects have even been documented in olfaction with oscillations (Walla et al., 2003). Smell is acknowledged to have a powerful effect on memory, even more than vision and audition, due to the olfactory bulb's

proximity to memory regions (Reineke, 2008). It would be compelling to investigate pre-stimulus activity in olfaction using ERPs. Not only would it extend pre-stimulus activity findings across modalities other than vision and audition, but memory in the olfaction is still relatively understudied. Moreover, olfaction is intricately linked with emotion, also known to have a potent effect on memory (Reineke, 2008).

Significant primacy effects were found for both strategies in this study. As primacy items are rehearsed more, it enhances long term memory (Azizian & Polich, 2002; Strange et al., 2002). As parahippocampal and anterior hippocampal regions in the medial temporal lobe are found to predict subsequent memory only for initial word positions (Strange et al., 2002), contribution from these regions in the present study is not unrealistic. Although the primacy effect is thought to reflect the strong link between encoding and recall (Azizian & Polich, 2008), future studies may want to minimize this effect. This can be done by increasing list lengths or stimulus presentation rates (Azizian & Polich, 2008), or omitting analyses for the first and last two word positions (Paller, McCarthy & Wood, 1988). This was not done in the present study in the interest of time, as it would have decreased the number of remembered/forgotten words and required testing of more participants.

Besides word positions, word-elicited neural activity was recorded and analysed, but not presented due to time constraints. Juxtaposing both cue and word-elicited neural activity would be useful in investigating their link (both processes are dissociable (Otten et al., 2006a & b)) as well as present a more complete picture of pre and post stimulus subsequent memory effects in terms of encoding and retrieval. Examining how the brain reacts before and after stimulus presentation in stages would be beneficial. These intermediate periods are often overlooked (Paller & Wagner, 2002) and may yield information on different stages in encoding and how each stimulus is processed.

Investigating encoding differences in stimulus type may also be illuminating. Studies have shown pictures to be more readily remembered than words, as pictures instinctively activate numerous real world associations (e.g. seeing a picture of a beach may bring back memories of Hawaii), facilitating widespread encoding (Palvio, 1971; Craik & Tulving, 1974; Nelson, 1979, cf. Grady et al., 1999). Contrasting verbal and pictorial differences may yield explicit details on how each are encoded, as they have different properties. These different properties are most apparent when investigating age-related changes.

As remarked earlier, repeating this study with elderly participants is vital in determining age-related differences in encoding processes, as pre-stimulus activity has never been studied in the elderly population. Additionally, elderly participants were no different from younger participants in remembering pictures, in contrast to words (Grady et al., 1999). Investigating these age-related differences would be useful in deciphering which aspect of encoding is sensitive to aging and clarify encoding properties of stimulus types.

If stimulus types, timing and position are worth contemplation, what about participant differences? Indeed, a proliferating area in encoding is the consideration of individual differences. Although individual averages were visually inspected to ensure representative group averages in the present study, exploring some of the findings at an individual level could be helpful, particularly if group effects are inconsistent. Studies have shown individual encoding differences for various aspects like processing speed (Rypma & D'Esposito, 1999), effort (Heun et al., 2000), problem solving (Kounious et al., 2007), strategy use (Shelton & Gabrieli, 2004; Kondo et al., 2005; Kirchoff & Buckner, 2006) and free recall (Dickerson et al., 2007).

Individual difference can be pertinent to the present study as individual preferences or comfort levels may affect strategy efficiency (Roberts, 1968; Shelton & Gabrieli, 2004; Kounious et al., 2007; Cornejo et al., 2007). For example, participants who were trained but did not master a particular strategy fared worse than those with no training (Camp, Markley & Kramer, 1983). An effective strategy is useless if one does not use or favour it. Debriefing revealed the present study's participants to prefer the elaborative strategy (due to regular usage and efficacy), and rote to be more difficult of the two (due to ineffectiveness and being unaccustomed to it). While highly unlikely to a determining factor (as rote recall generally increased with time, with participants reporting to get better with practice), the lower recall in rote could also be caused by incongruence in participant preferences. Future studies should definitely consider looking at individual data in addition to the group data to avoid any confounds due to individual differences.

In sum, these study limitations do not restrict the relevance of its findings, but rather, propagates more questions and directions for pre-stimulus activity in encoding, expanding areas of potential research in methodology, aging and learning. Indeed, pre-stimulus research is rapidly progressing.

4.5 Conclusion

This study has evidenced the volitional control of pre-stimulus neural activity in recall prediction via mnemonic instructions. The activity is found to predict recall in the elaborative strategy, specifically the auditory condition; reflecting modality and strategy differences. Its susceptibility to these factors demonstrates it to be voluntarily controlled, and postulates it to be a necessary preparatory mechanism not only for memory formation, but possibly cognition.

This has implications for memory encoding in terms of its direction, methodologies, memory deficits in aging and learning. To quote Louis Pasteur, "chance favours only the prepared mind" (Kauffman, 1998).

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Appendix A:

Statistical analysis

in the 1000-1500ms cue-word interval

Repeated measures (2 strategy x 2 modality x 2 subsequent memory performance x

32 sites) ANOVA for the 1000-1500ms cue-word interval

Source	$df1$	$df2$	F	P
Strategy	1	23	6.152	0.021*
Modality	1	23	17.777	<0.001*
Subsequent memory performance	1	23	8.860	0.007*
Site	3.1	71.2	6.090	0.001*
Strategy x modality	1	23	0.312	0.580
Strategy x subsequent memory performance	1	23	0.072	0.791
Strategy x site	3.1	70.3	1.715	0.172
Modality x site	3.9	90.5	13.220	<0.001*
Subsequent memory performance x site	3.3	75.5	0.899	0.451
Strategy x modality x subsequent memory performance	1	23	1.232	0.279
Strategy x modality x site	3.8	87.8	0.662	0.612
Strategy x subsequent memory performance x site	4.0	92.5	0.345	0.847
Modality x subsequent memory performance x site	3.6	83	0.229	0.906
Strategy x modality x subsequent memory performance x site	4.9	112.1	2.74	0.024**

Significant, $p < 0.05$
*** Note: 4-way interaction between strategy, modality, subsequent memory performance and site.*

Appendix B:

Stimuli lists

Stimuli lists: Practice lists

1: Rote visual
2: Rote Auditory
3: Elaborative visual
4: Elaborative auditory

2	marbles.wav	3	chopping-board
1	banknote	3	christmas-tree
2	trafficlights.wav	4	lemon.wav
1	camel	3	barbecue
1	mobile-phone	4	cards.wav
1	frying-pan	4	pen-knife.wav
2	chessboard.wav	3	fire-engine
1	sword	3	lobster
1	floppy-disk	3	ovenglove
2	apple.wav	4	lightbulb.wav
1	garden-hose	4	cassette-tape.wav
2	chick.wav	4	cd.wav
2	moped.wav	4	crocodile.wav
2	hairbrush.wav	3	army-tank
1	pig	4	barrel.wav
2	broccoli.wav	3	seahorse
9	93	9	85

Stimuli lists: Set 1

pen	Racquet
clogs	anchor
shark	Pushchair
crucifix	clown
toilet	fan
shorts	duck
rug	Croissant
thermos	handle
torch	Magazine
sandals	battery
axe	horse
rhinoceros	Ballerina
lighter	Strawberry
microwave	Caravan
hammer	Avocado
suitcase	Screwdriver
ring	plug
tissues	hat
fireplace	lamb
swan	Wineglass
jug	tank
folder	helmet
scales	Crossbow
kite	feet
television	flag
balloon	saw
cross	chair
snail	hoover
toothbrush	Phonebox
fox	door
belt	Hamster
wreath	toaster
present	ladder
carrots	bath
pipe	thread
dart	hose
nailclippers	tent
pillow	lorry
typewriter	pelican
tricycle	eye
guitar	Mountain
microscope	glove
tennisracket	wool
teddybear	Doughnut
drum	whistle
pyramid	Swimsuit
corkscrew	mirror
knife	Icecream

Stimuli lists: Set 2

sailboat	Monkey
jumper	Bulldozer
plunger	Postbox
car	cow
fridge	Hamburger
chicken	owl
octopus	Dolphin
plate	heron
cake	skirt
crane	missile
seal	Peacock
rocket	kettle
pliers	bin
drill	leek
beer	Stadium
wheelchair	Penguin
coin	shirt
daisy	onion
earrings	dragon
pot	Dinosaur
bacon	banana
cooker	screw
prawn	gorilla
comb	sheep
pigeon	Spanner
polar-bear	Goldfish
bucket	Gravyboat
table	jetski
spoon	Golfball
snowman	shoe
sandwich	Pinecone
safe	Coffeemaker
loudspeaker	sink
muffin	doll
paperclip	Escalator
key	pencil
crown	printer
thermometer	Dummy
wetsuit	Peppermill
aeroplane	bag
biscuit	clock
mixer	Paintroller
hand	bowtie
deer	lantern
padlock	Trainers
cushion	Sweetcorn
coathanger	Scissors
fence	curtain

Stimuli lists: Set 3

elephant	garage
flippers	goggles
mattress	tortoise
egg	whisk
eagle	rose
syringe	zebra
parrot	briefcase
life-jacket	raspberry
candle	skittles
gravestone	radio
skateboard	crayons
domino	Stethoscope
socks	flowerpot
scorpion	spade
helicopter	motorbike
toast	tiger
dustpan	bus
ant	planet
teapot	bride
frog	pool
rabbit	Cauliflower
ambulance	Lightswitch
glass	feather
wrench	asparagus
keyboard	pills
tweezers	peg
sieve	calculator
mask	peppers
earphones	iceskates
dog	holly
kangaroo	cheese
lizard	coffin
stiletto	hotdog
bear	sunglasses
highchair	pear
tomato	carpet
necklace	grater
church	yoyo
suit	sledge
iron	jacket
cot	peaches
dice	peanut
camera	scarf
pumpkin	shield
bell	skull
graph	globe
handcuffs	sofa
cigar	bottle

Stimuli lists: Set 4

cloak	slide
nutcracker	Lighthouse
piano	Coconut
jeans	sponge
tractor	Seashell
firehydrant	wheel
speaker	grass
wardrobe	shell
snake	razor
ashtray	rat
beetle	Pineapple
donkey	tree
joystick	sun
cat	tower
bench	bat
trumpet	tap
dress	badger
harp	stamp
thimble	baby
switch	tin
alarmclock	stapler
fairy	nose
fork	Squirrel
rolling-pin	desk
flowers	ear
spider	orange
palette	panda
cannon	mug
horseshoe	Wheelbarrow
compass	seagull
stool	bed
book	Mushroom
pizza	Slippers
football	Chocolates
lawnmower	Cherries
newspaper	ostrich
basket	Mousetrap
kiwi	Grenade
telephone	garlic
hinge	bicycle
hair	Butterfly
funnel	button
giraffe	heater
buddha	Accordion
boots	cactus
lamp	bee
volcano	Tambourine
broom	Binoculars

Appendix C:

Experimental instructions

R122 Instruction sheet – Elaborative

This task requires you to memorize words. The words will be presented one at a time, every few seconds. Some of the words will appear on the monitor in front of you, while others will be presented via headphones. Before a word is presented, you will either see a small red square or hear a brief tone. This is a cue that tells you whether the upcoming word will be seen or heard. If you see the red square, you know that the next word will be presented on the monitor. If you hear a tone, you know that the next word will be spoken via headphones. You are encouraged to use these cues to prepare for the upcoming word. The words will appear in the middle of the screen. There will be a small plus sign throughout the task to help you direct your eyes to where the words will appear.

We want you to try to memorize the words in a specific way. Initially, we want you to memorize the words by connecting them in some way, by associating them with each other. For example, you could create a story out of the words, or you could create images and combine those. It is really important that you try to memorize the words this way, even though you may feel that you do not remember many words this way. That is absolutely fine.

You will be given 16 words at a time to memorize. Half of these will be visual and half auditory. We will give you a clipboard with pieces of paper. At the end of each list of 16 words, a number will appear on the screen. You are required to count backwards from that number in threes out loud for 30 seconds (e.g. if the number is 100, 97, 94, 91 etc). Then, pick up the pen and write down whichever words you remember from the list, in any order that you want. You will be given a minute to do this, which should give you enough time. When you are done, indicate whether you were able to memorize the words by associating them meaningfully. There is a question at the bottom of each sheet that we want you to answer. Circle 'yes' if you were able to associate them, and circle 'no' if you were not. Then take the piece of paper off the clipboard and let it fall to the floor. This way the next sheet will be ready for the next list.

We will start with a practice list to familiarize you with the task. There will be intermittent breaks between blocks, but you can request for a short break anytime. During the actual experiment, there will be 12 lists of 16 words each. When you are ready, I will start the practice list. At the end of 16 words, you will see "Count backwards in threes starting with x (number)". After completing the counting task, you will see "Write down words you remember". At that point, start writing words on the clipboard.

Please remember to:
- Avoid horizontal eye movements and to fixate your eyes on the cross throughout the experiment. This will distort the EEG recording. You can blink normally.
- Relax and sit in a comfortable position to avoid too much movement.
- USE the instructed strategy to memorize words. The focus is ensuring the strategies are actually used when instructed, not so much on the number of words remembered.

R122 Instruction sheet – Rote

We are now going to do the same task, but we want you to try and memorize the words in a different way. This time, we want you to memorize the words by silently repeating them in your head (e.g. purple, purple, purple). Be sure not to repeat the words out loud or move your mouth – only repeat them in your head.

Everything else remains the same. Again, you will get lists of 16 words each. After each list and the counting task, we want you to write down whichever words you recall from the preceding list, in any order. Circle 'yes' or 'no' at the bottom of each sheet to indicate whether you were able to memorize the words in the list by silently repeating them. Then let the sheet fall to the ground.

Any questions?

Again, we will start with a practice list to allow you to switch memorization strategies. Are you ready for the practice?

Please remember to:

- Avoid horizontal eye movements and to fixate your eyes on the cross throughout the experiment. This will distort the EEG recording. You can blink normally.

- Relax and sit in a comfortable position to avoid too much movement.

- USE the instructed strategy to memorize words. The focus is ensuring the strategies are actually used when instructed, not so much on the number of words remembered.

Appendix D:

Written free recall and debriefing sheets

R122 Free-recall sheet

Participant #   **Rote**

<u>Please write down the words you remember from the list in ANY order. If you are uncertain about a word, write it down, but avoid random guessing.</u>

Did you memorize the words by silently repeating them?

(Please circle answer)

Yes   **No**

R122 Free-recall sheet

Participant #   **Elaborative**

Please write down the words you remember from the list in ANY order. If you are uncertain about a word, write it down, but avoid random guessing.

Did you use memorize the words by associating them?

(Please circle answer)

Yes   No

R122 Debriefing sheet

Participant

- How did you find the memorization, counting and free recall tasks?

- Was it easy to adopt each strategy?

- Did you find any difficulty switching strategies? If so, which one and why?

- Which strategy was more useful to you and why?

- Did you use the cues to get ready? Why/why not?

- Did you find the cues useful? Why/why not?

- How do you usually remember things?

- Are you more of a visual or auditory learner/person?

- Did you encounter any other difficulties performing the task?

- Do you think you would have memorized more words if more time was given during the free recall?

- Would you have any suggestions on how performance can be improved?

- Do you have any further questions?