INVESTIGATION OF THE NEURAL CORRELATES OF RECOGNITION MEMORY USING MAGNETOENCEPHALOGRAPHY

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Neuroimaging literature has identified several regions involved in encoding and recognition processes. A review of the literature illustrated considerable variations in the precise location and mechanisms of these processes, and it was these variations that were investigated in the studies in this thesis. Magnetoencephalography (MEG) was used as the neuroimaging tool and a preliminary study identified Synthetic Aperture Magnetometry (SAM) and not a traditional dipole fitting technique, as an appropriate tool for identifying the multiple cortical regions involved in recognition memory.

It has been suggested that there is hemispheric asymmetry in encoding and recognition processes. There are two main hypotheses: the first suggesting that there is task-specificity, the second that this specificity is determined by stimulus modality. A series of experiments was completed with two main aims: first to produce consistent and complementary recognition memory data with MEG, and second to determine whether there exists any hemispheric asymmetry in recognition memory.

The results obtained from five experiments demonstrated activation of prefrontal and middle temporal structures, which were consistent with those reported in previous neuroimaging studies. It was suggested that this diverse activation may be explained by the involvement of a semantic network during recognition memory processes. In support of this, a subsequent study involving a semantic encoding task demonstrated that category-specific differences in cortical activation also existed in the recognition memory phase.

Controlling for the involvement of such semantic processes produced predominantly bilateral activation. It was suggested that the apparent hemispheric asymmetry findings reported in the literature may be due to the 'coarse' temporal analysis available with earlier imaging techniques, which over-simplified the networks reported by being unable to recognise the early complex processes associated with semantic processing which these MEG studies were able to identify. The importance of frequency-specific activations, specifically theta synchronisation and alpha desynchronisation, in memory processes was also investigated.

Synthetic Aperture Magnetometry; Encoding; Retrieval; Frequency Specific Activation; Semantic Network

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1 INTRODUCTION

1.1 Overview

Memory is a dynamic process involving primarily, three distinct stages; encoding, storage and retrieval. Within the literature, a distinction is highlighted between the processes involved in episodic memory (the capacity to recollect individual events) and those involved in semantic memory (information relating to knowledge and meaning). Although these are no longer believed to involve completely separate mechanisms, this thesis focuses on those involved in episodic memory. Furthermore, whilst episodic retrieval mechanisms have been explored using both tests of recognition and recall, it is the neural correlates of episodic recognition memory which are primarily investigated in this thesis.

This introductory chapter first provides an overview of some of the main psychological models that underpin research in recognition memory. This includes the traditional stage theories which form the basis for many of the more recent single and dual process models. The main findings from the lesion and neuroimaging literature are then presented and discussed.

Areas within the prefrontal cortex (PFC) and medial temporal lobes (MTL) have been a particular focus of investigation, with many studies suggesting roles for these regions in both encoding and recognition processes. One of the theories within the recognition memory literature that is discussed is the idea that there is hemispheric asymmetry, some authors suggesting an encoding / retrieval asymmetry, others a modality-specific asymmetry. Evidence is also provided that demonstrates that functional speciality may be frequency-specific, with particular focus placed on alpha and theta-frequency activations.

1.2 Models of Recognition Memory

Memory involves three distinct stages; encoding, storage and retrieval. These stages encompass the processes occurring during the initial presentation of the material, the storage of some information as a result of this encoding and finally the recovery or

extraction of stored information from within the memory system. Both the organisation (structure) of the memory system and the processes (activities) operating within are important considerations for theories of recognition memory. Although the various theoretical models may differ in their emphasis of these two aspects,

"One cannot have structure without process, or retrieval without previous encoding and storage" (Eysenck & Keane, 1995, p123).

Furthermore,

"Only that can be retrieved that has been stored, and... how it can be retrieved depends on how it was stored." (Tulving & Thomson, 1973, p359).

To perform successfully on tasks of recognition memory, an individual must ensure that the to-be-remembered item has been successfully encoded and stored in memory. It is the common train of thought that recognition memory can occur in two different ways; either through familiarity or through the remembering of relevant contextual information (Gardiner & Java, 1993). This distinction between knowing and simply remembering has been addressed in a number of studies. The fact that you need to access memory stores when performing object recognition tasks, so that you are able to match what you see in front of you with stored representations, suggests that there should indeed be similarly activated regions in both encoding and recognition memory tasks.

Over the past twenty to thirty years, there has been a great debate within the episodic memory literature over the existence of single or dual processes in recognition memory. The idea that there are several separate components involved in episodic memory has been around for centuries (Yonelinas, 2001) and consequently, there has been much interest in developing models to account for these processes.

1.2.1 Early Memory Models

1.2.1.1 Traditional Stage Theories

Traditional models of memory can be described as being 'stage theories' as their fundamental structure is the existence of several memory storage systems (Gleitman, 1995), each of these accounting for different functions, depending on the specific model.

These models all promote a sequential pattern of information processing (Eysenck & Keane, 1995), a concept initially developed by Broadbent (1958) and his theory of attention, which is now incorporated into the majority of cognitive processing models. The existence of multiple storage systems is used in the majority of models to account for both recently encountered information, as well as for knowledge gathered previously (probably years before). To accommodate these two different types of memories, the early 'multi-store' memory models (e.g. Waugh & Norman, 1965; Atkinson & Shiffrin, 1968) introduced two memory stores, the short-term system (responsible for recently encountered material) and the long-term system (for material being stored for a long time, up to a lifetime) with experimental evidence indicating that a distinction between the two stores existed (Brown, 1958; Peterson & Peterson, 1959).

Further evidence for this distinction was provided through neuropsychological studies of patients with anterograde amnesia, such as the case of HM (Scoville & Milner, 1957). HM underwent a bilateral hippocampectomy to treat severe epilepsy. Following surgery, although his performance on tests of short-term memory function, such as digit span, was normal, his long-term memory was severely disrupted. This and similar evidence from other brain damaged individuals with anterograde amnesia provided substantial evidence for the system of memory processing described by the multi-store memory models. These studies of brain-damaged individuals and also of animals with cortical lesions generated the first information about the neural correlates of memory functioning and principally guided the research undertaken in the field of neuroimaging today, and as such are discussed further in section 1.2.3.

One of the most influential stage theories of memory was that of Atkinson & Shiffrin (1968), and is commonly used as the generic 'multi-store' model of memory (Figure 1.1). It incorporates an additional sensory store, which precedes the short- and long-term memory systems. The multi-store model describes the process of memory as information sequentially passing through each of these stores, it being processed along the way. Initially, material from the environment is received by one of the sensory stores, their existing different sensory stores for each of the modalities (i.e. visual, auditory etc.). Material is only maintained here for a very brief period of time, the exact length of time being dependent upon the specific sensory store involved. For example, there is evidence to suggest that visual information will decay from the visual (or iconic) store after only 0.5 seconds (Sperling, 1960), and from the auditory (echoic) store after 2 seconds (Treisman, 1964). However, through attentional processes, much information (before it decays) can be

transferred into the short-term memory store (STM). This store has been show to have a very limited capacity, Miller (1956) detailing it as having a span of "seven plus or minus two". Consequently, information is constantly displaced by new material and the store is very susceptible to distracting influences which can cause this displacement. The process of rehearsal is then used to transfer knowledge from STM to the long-term memory store (LTM). Whilst there is no accurate indication of the capacity of the long-term store, the fact that we are able to remember information from our childhood and that we continue to

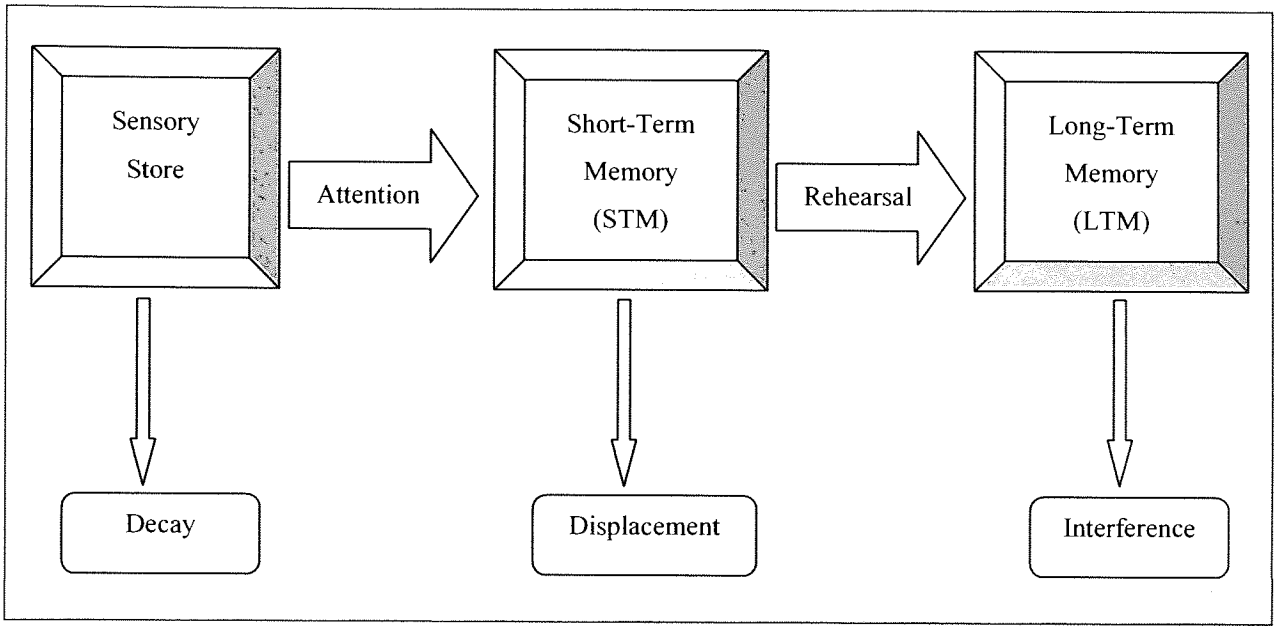


Figure 1.1 The Multi-Store Model of Memory (adapted from Atkinson & Shiffrin, 1968)

acquire new information throughout our lives, does suggest that it may have an infinite capacity. However, there are processes such as interference, which can lead to information being lost from this store.

The multi-store model is considered to be one of the most important models in the memory literature as it provided the initial structure from which many models are now derived. However, its inability to account for a number of psychological findings has necessitated that other models need to be developed. For example, the sequential structure of the multi-store model suggests that impairment of the STM (through brain damage, for example) would result in impaired LTM too. There is some evidence that this indeed may be the case, for example, Korsakoff amnesiac's can perform at normal levels on tasks associated with STM, but experience problems with LTM tasks. However, there is also conflicting evidence from the neuropsychological literature which demonstrates that performance on LTM tasks is good, despite poor results on tasks of STM (see for example, the case of patient KF, Shallice & Warrington, 1970).

1.2.1.2 *Working Memory Model*

Evidence such as that reported above, lead to heavy critique of the sequential multi-store models and as a consequence Baddeley and Hitch (1974) developed a model which adopted the concept of a working memory system as a replacement to a STM system. Essentially, it comprises three systems, the phonological loop, visuo-spatial sketch pad and the central executive. Information from the environment is handled by the two 'slave' systems, auditory and verbal information monitored by the phonological loop, and the visuo-spatial sketch pad concerned with visual input. The central executive is considered to be the attentional component, responsible for the entire system.

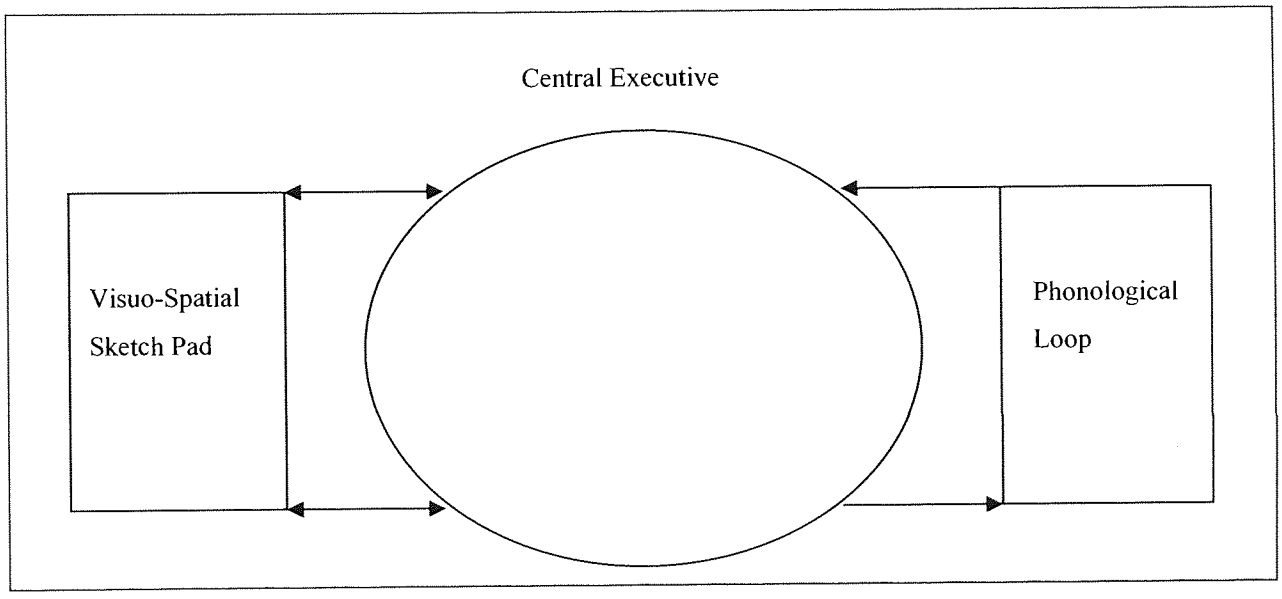


Figure 1.2 Working Memory Model (adapted from Baddeley & Hitch, 1974)

The phonological or articulatory loop loosely resembles the short-term memory store from the original multi-store memory models and it comprises two sub-components. Initially, there is a store that holds the memory trace. This has a time limit of about two seconds, which is only surpassed through the use of the second sub-component, a process of sub-vocal articulatory rehearsal. Evidence for the existence of the phonological loop and its sub-components are diverse. The necessity for a phonological component within a memory model, has been demonstrated numerous times, experiments such as those utilising acoustic and semantic paradigms (e.g. Baddeley, 1966; Kintsch & Buschke, 1969) just a small part of the literature showing this. Similarly, the word length effect (e.g. Baddeley, Thompson & Buchanan, 1975) in which fewer long-length words, compared to short-length words, can be remembered in any given time span, has been used as evidence for the sub-vocal rehearsal component of the phonological loop. Although the specific, and

recently evolutionary, function of the phonological loop is constantly altering in light of increased research, its existence as a necessary component of memory is still maintained.

The visuo-spatial sketch pad is responsible for the storage of visual information. It is reported to involve visual (Logie, 1986) and spatial coding (Baddeley, Grant, Wight & Thomson, 1973) processes, these findings refuting the role of verbal coding strategies within this process. Furthermore, the visual and spatial components of memory are believed to utilise separate processes, numerous neuropsychological studies providing evidence to support this (see for example, Della Sala, Baddeley, Papagno, & Spinnler, 1995).

The central executive is proposed to be the attentional component of the working memory model, responsible for all executive processes. However, the diversity and complexity of these executive processes has failed to produce a sufficient description of the central executive. Whilst anatomically, it is believed to utilise the frontal lobes (Baddeley, 1986), neuropsychological assessments of patients with damaged frontal lobe regions are needed to distinguish between these numerous executive functions. Furthermore, the structure and distribution of all executive functions is still unclear. Baddeley (2000) highlights this, suggesting that whilst there may exist a hierarchical structure dominated by a specific function, it may also be that all executive functions are equally distributed. Perhaps, this is where functional neuroimaging can be of use, providing some answers to the many unanswered questions.

1.2.1.3 Levels of Processing Model

One of the simple assumptions of the Atkinson-Shiffrin multi-store model was that an item was more likely to be transferred to the long-term memory store if it was maintained within the short-term memory for a long period of time. This approach however, is too simplified and Craik and Lockhart (1972) provided substantial evidence that an important factor in long-term memory was the nature of the encoded material and as such developed their Levels of Processing model of memory.

This approach suggests that memory cannot be defined by three or indeed any specific number of stores, but instead varies along a potentially infinite number of levels depending on the depth of encoding of the information. The strength of a memory trace does not depend on the type of store within which it is located (STM or LTM) but on how

much attention is paid to the information at the time of encoding. Specifically, deep, meaningful kinds of information processing, such as semantic encoding, leads to more permanent retention than shallow, sensory kinds of processing, such as visual or phonological encoding.

The theory however does not attempt to explain why deep processing is more effective than shallow processing. It is also difficult to tell which level of processing is being used by a person as there is no independent measure of processing depth. Nevertheless, Gabrieli, Brewer, Desmond and Glover, (1997) indicated through functional magnetic resonance imaging (fMRI) that different brain regions may be involved in different kinds of processing. They reported greater activation in the left inferior prefrontal cortex for semantic rather than perceptual processing.

1.2.2 Theoretical Models of Recognition and Recall

Both the multi-store model of memory and the working memory model provided qualitative and theoretical reasoning for the existence of separate memory components. Many of the more recent memory models have used these earlier models as a basis, developing them in order to comprehensively account for a range of tasks and data. Many of these theoretical models of recognition memory highlight a distinction between recognition and recall.

Theoretical models of recognition memory can basically be separated into two categories, single-process and dual-process models. The basic assumption maintained in the majority of single-process models is that there is one single element, that of familiarity, upon which recognition judgements are made. Similarly, the dual process models of recognition memory also include this concept of familiarity, but promote, in addition, a second process that utilises extra material encoded at the time of initial exposure.

1.2.2.1 Single Process Models

The simplicity of the single process models, in which there is only one single memory component, is still very appealing and as such many single process models of recognition memory have been developed, incorporating assumptions about storage and representation of memories. Within the division that is single process models, the most

popular are a number of global memory models. These include Search of Associative Memory Model, composite vector models such as the Composite Holographic Associative Recall Model (CHARM) and the Theory of Distributed Associative Memory (TODAM) and finally MINERVA. There are also some new generation global memory models which have been developed to account for the some of the data that the older models could not sufficiently explain. It is necessary to discuss some of these popular single process models, before considering the now favoured dual process models. The term 'global memory models' is used when referring to these models, primarily because of their general assumption that a test item will interact with most, if not all, of the relevant stored memories (Ratcliff & McKoon, 2000), and also because of their ability in being used to explain a large amount of experimental data generated from diverse tasks and changeable paradigms.

1.2.2.1.1 Search of Associative Memory Model

The Search of Associative Memory (SAM) model is a mathematical model developed using the principle of encoding specificity. It is an associative network model of memory where nodes connect according to their relatedness. It was originally developed to account for many of the results from free recall experiments (Raajimakers & Shiffrin, 1981) and was later modified by Gillund and Shiffrin (1984) to also accommodate data from studies of recognition memory. The basic principle within this model is that the information which is stored in memory is the strength of associations between encoded cues to memory, i.e. test items, and items already stored within memory, assumed to be images (Ratcliff & McKoon, 2000). The strengths of these associations are increased during the encoding process during the time a to-be-remembered item is in a buffer. During retrieval, this model assumes that the test item matches an image within memory and that a familiarity score is produced, enabling a decision to be made about whether indeed the item was part of the encoded material.

The appeal of this cue-dependent model is that its basis mirrors the accepted assumption that retrieval processes during memory tasks are cue-dependent (Tulving, 1974). Consequently, the important component of this model is how well the study and test cues match and thus the production of a familiarity value used in subsequent yes / no recognition tasks.

Although one of the basic assumptions of SAM is that an individual should be able to, if required, perform some sort of memory search task during the recognition process, for the purpose of developing the model, it is assumed that no individual actually performs this search. For a simple 'yes' / 'no' recognition test SAM assumes that the participant searches their memory with two cues, the test item and a context cue. The LTM store is assumed to contain permanent interconnected 'images' that contain information. These include contextual and temporal detail associated with the encoding of an item, specific information about a particular item which may help in identifying it, and also information which is used in creating links between items. In SAM, therefore, the result of probing memory with the contextual cue and test item is that images and interconnections within the LTM store will be activated. The amount of activation that occurs produces the value of familiarity, which is used in the decision process. The activation of more than just the stored image of the test item is why this model and others are referred to as global models. The generated familiarity value is compared to a criterion value set by the individual. If the familiarity is greater than the criterion value then the participant believes that the item is a previously encountered stimulus and responds 'yes'. Conversely, if it is lower the participant responds 'no'.

As demonstrated by the numerous simulation experiments performed by Gillund and Shiffrin (1984), as a model for recognition memory SAM works. It is simple and can be applied to a number of different episodic memory paradigms and data. It does not, however, incorporate a component to account for the memory search process, which the authors themselves acknowledge is assumed to play a significant role in the recognition memory process. It may, therefore, not be the most appropriate model of recognition memory, but it is acknowledged to be the most successful model in accounting for free-recall data (Ratcliff & McKoon, 2000).

1.2.2.1.2 Composite Vector Models

CHARM

The Composite Holographic Associative Recall Model (CHARM) (Metcalfe, 1985) is a model of cued recall. CHARM is based around the level of processing framework (Craik & Lockhart, 1972) with items being characterised as patterns of features. Each feature within an item has either a unique positive or negative value (i.e. no two features

will have the same value), with the sum of all the item's features being zero. It has been suggested that these could be considered as neural units (Estes, 1979) and as the numerical values of the features are represented in vector format (as for TODAM), they could be assumed to represent neural firing frequency, zero being a background / baseline firing rate. Similarly, in cognitive terms, the representation of an item will be a unique configuration, or vector, of its features, all items having different patterns.

This idea means that the independent features values within unrelated items will be statistically independent. For related items, however, there will be some overlap of some (but not all) feature values. If items are unrelated no feature has the same value whilst if items are related the amount of similarity between them is calculated.

When an association is made between two items, the end convolution or product matrix produces a new matrix, which is unique to the association but does not correspond to either of the items. Therefore a new memory trace has been created and for purposes of retrieval processes this memory trace needs to be deconvolved to get back to the original items. Each convolution is added together so that a composite memory trace incorporating all encoded items is created. At retrieval, the cue / test item is correlated with the composite trace created during encoding. Due to the nature of the composite trace, the retrieved item is not 100% identical to that encoded; rather it is retrieved containing some noise from the convolution process and from the other encoded items. For recognition, however there is also an element of auto-association in which not only are two items associated with each other but that each item is also associated with itself. These auto-associations are therefore also included in the composite trace. At recognition, the cue is correlated with the trace and if it retrieves itself (the auto-association) then positive recognition occurs, if not the participant responds 'no' or 'new'.

TODAM

The Theory of Distributed Associative Memory (TODAM) (Murdock, 1983) is a "theory for the storage and retrieval of item and associative information" (Murdock, 1982, p609). Its basic principle is that items or events are stored as vectors in a common memory vector. Information about a particular item is obtained by adding the vector of the item to that of the memory vector. Associative information can also be accounted for in the TODAM model; the vectors of two items are first combined, the result then added to the

memory vector. The vectors for the separate items and for the associative information are also multiplied by forgetting and weighting parameters, which can have values between 0 and 1. The outcome of this model is that following the presentation of an encoded list of items, there is no single vector for each list item, but rather a composite memory vector, or trace, which enables an individual to accurately respond in the recognition process.

Unlike encoding which is a combining (convolution) process, recognition is a correlation process. The vector for each test item is compared with the composite memory vector created during encoding using a method in which corresponding attributes are multiplied together and then the sum of these attributes obtained. As with the other global memory models, the outcome of this is a value that can be compared to a criterion value and a recognition judgement made.

The original TODAM model, however, was unable to account for the observed experimental dissociation that increasing retention intervals decreases the accuracy of item recognition, but does not affect associative recognition. Consequently, in the revised TODAM2 model (Murdock, 1997) additional parameters for context and for the probable use of mediators to aid remembering of associative information, (e.g., word pair ring – ladder presented and have mediator of rung because it rhymes with ring and there are rungs on ladders) were also incorporated.

1.2.2.1.3 MINERVA2

MINERVA2 was developed as a model for memory after SAM and TODAM had already been proposed for a few years. Like TODAM it incorporates the idea that items are vectors, but differs in the assumption that these vectors have elements +1, 0 or –1. Consequently, during encoding, each stored item is assumed to have its own unique vector. The model's assumptions for recognition are the same as that for the other global memory models; a value of familiarity is generated by comparing the test item with information stored in memory and this value is then used in the recognition decision process. Specifically, the vector of the test item is compared to each vector in the memory store, the product of which generates an 'activation' value, referring to the degree of match between test and stored items. As with SAM, if this value is greater than a criterion value, then the participant produces a 'yes' or 'old' response, if it less then the response is 'no' or 'new'.

1.2.2.1.4 Evaluation of Global Memory Models

At the time of their development it was presumed that what all these global memory models have in common is the fact that their parameters and assumptions can be slightly modified to accommodate a number of different scenario and data (Slamecka, 1991). Further investigation, however, suggested that these models were more rigid than first believed and consequently a number of situations arose which the global memory models could not accommodate. Specifically, two examples, the mirror effect and the list strength effect, arose which could be not be accommodated by the models despite modifying attempts.

The mirror effect is concerned with the assumption made by the global memory models that the output or 'familiarity' value increases as the strength of the stored items increases. Consequently, increasing this strength should increase the probability that the item will be recognised as 'old' or familiar (i.e. been in the encoded material), irrespective of whether it was actually an encoded item. If we consider low-frequency items, however, this is not the case. It has been demonstrated that if a low-frequency item was present in the encoded material, it is more likely to be recognised as old (than average or high frequency items). Also, if it was absent it more likely to be identified as 'new' (Glanzer & Adams, 1985; Glanzer, Adams, Iverson & Kim, 1993). The possible solution of incorporating a frequency decision judgement at the start of the recognition / retrieval process, which would alter the subsequent criterion value for 'old' versus 'new' judgements, has been disregarded as unsatisfactory (Ratcliff & McKoon, 2000). Data is available which demonstrates that irrespective of whether high and low frequency words are presented in separate lists or combined together, there is no difference in response time. Furthermore, participants appear to find it difficult to actually determine those words that are high frequency and those that are low. Also, if this were the solution to the problem, task difficulty would inevitably increase with increasing numbers of items with different frequencies.

In a similar way, the list strength effect is also a phenomenon that cannot be satisfactorily explained by the global memory models. This effect describes the way in which as the strength of an item increase, so does the variability in the strength values. Take for example an experiment where performance on a list when different items are studied for different lengths of time, is compared to performance on a list in which all items are studied for the same length of time. All of the global memory models would

predict that there would be lower accuracy for short studied items in the mixed list compared to when they were in the pure list. This is because of the change in familiarity value. In reality, however, for recognition memory experiments, this effect is never seen (Murnane & Shiffrin, 1991; Ratcliff, Clark & Shiffrin, 1990; Shiffrin, Ratcliff & Clark, 1990).

1.2.2.1.5 New Generation Global Memory Models

Evidently, the global memory models cannot fully account for data observed in real recognition memory experiments, despite attempts at manipulating and adapting them. Consequently, new models were developed to overcome the phenomena described above, but which still accounted for the data in which the older models were successful. Shiffrin and Steyvers (1997) REM model and McClelland and Chappell's (1998) model were termed the new generation global memory models. Fundamentally they are similar to each other and to their predecessors; items are represented as vectors and the old / new decision is made at recognition by comparing the similarity value between studied and tested items to a criterion value.

The successfulness of these new generation global memory models lies with the assumptions they make. Firstly, they can accommodate errors in storage (and thus the fact that mismatch errors do occur) and secondly, the use of vectors enables the probability of a match to be calculated between the test item and another item in memory, whether the same or different to the test item. However, whilst they account for the problems which the earlier global memory models could not accommodate, the literature is still awaiting more critical tests on these new models.

1.2.2.2 Dual Process Models of Recognition Memory

These global memory models, however, did fail to account for data presented in many studies in which novel items were rejected on the basis of their similarity to previously presented stimuli. Consequently, this promoted the suggestion that there may also be some form of a recall process occurring during these recognition memory tasks, and dual-process models of recognition memory were developed.

In experimental design there is an obvious difference between tasks involving recognition and those requiring recall processes. Usually a free recall task involves participants firstly being presented with a list of words, for example, and then later being asked to remember as many of those words in any order. It can therefore be assumed that this recall process must involve some form of active searching of the memory stores. Recognition, on the other hand, involves a similar encoding process but for recognition, participants are re-presented with the stimuli, along with novel ones and asked to determine whether each is something they have seen before. It therefore involves a sense of familiarity for an item, without the need for active memory searching.

Many studies have demonstrated the advantage of recognition over recall, and one such theory is the two-stage / two-process theory (e.g. Mandler, 1980). Within the various versions of this theory, there is a consistent assumptions made by the model. Whilst recall involves a search or retrieval process, which is followed by a decision or recognition process based on the apparent appropriateness of the retrieval information, recognition involves only the second of these processes. Consequently, there is only point during recognition at which an error could occur, whilst for recall there are two occasions at which it could happen. Further evidence that there exist two-processes, a retrieval process followed by a decision-making recognition process, was shown by Rabinowitz, Mandler and Patterson (1977) in which their participants performed better under a generation-recognition strategy than under standard instructions.

Jones and Jacoby (2001) presented a series of experiments in which they investigated feature and conjunction errors within the realms of recognition memory. A dual-process theory was necessitated to account for their findings. They did acknowledge, however, that while other approaches on their own could not accommodate the findings, a combination of dual-process and item-associative distinction frameworks might be the way forward.

The two-process theory, however, although quite successful does have a number of questions that it cannot accommodate. Firstly, evidence exists (Muter, 1978) which demonstrates recall performance being superior to recognition performance, a phenomenon which according to the dual process model could not occur. Secondly, it has been demonstrated that following failure to recognise items from an encoded list, some of those unrecognised items are recalled in a subsequent recall test (Tulving & Thomson, 1973).

Recognition has been demonstrated to be easier than recall for many years (McDougall, 1904), but why is this so? It would seem logical that if psychologically a

clear superiority of recognition over recall can be demonstrated, thus highlighting a difference between these two processes, then the neural bases of these should also differ. Is it the case, therefore, that (1) they involve the same processes, but that recall occurs when these processes are stronger; (2) that all the processes involved in recognition are utilised during recall and that recall requires some extra processes; or is it (3) that there are some of the same components involved in both processes, and that there are also some unique to recognition and some unique to recall?

1.2.3 Tulving's Encoding Specificity Principle

Tulving assumed that there were basic similarities between recall and recognition and assumed that contextual factors played an important role in these processes. He claimed that an item is remembered well when information in memory is similar to information available at retrieval. Therefore, any changes that are made to the context between storage and testing can reduce the memory performance. Tulving claimed that this was true for both recall and recognition and this idea has much experimental support (see Bouton, Nelson & Rosas, 1999; Thomson & Tulving, 1970; Tulving & Thomson, 1973; Godden & Baddeley, 1975;1980).

According to Tulving's Specificity Principle, the superiority of recognition over recall can be explained in two main ways. Firstly, it is suggested that there is a greater overlap between information in the memory test and the memory trace on recognition memory tasks, than on recall tests. Secondly, more informational overlap is required for recall than for recognition because recall involves for example naming a previous event or recalling a previous list whereas recognition is only a judgement of familiarity. Tulving can also account for items being recalled but not recognised (see Tulving & Thomson, 1973). Evidence suggests that recall performance depends less on recognition performance than might be predicted by other dual-process models of recognition memory discussed later.

Tulving's theory emphasises the importance of contextual factors in recognition and recall. However, although there is evidence to suggest that the similarity of context at the encoding and retrieval stages plays an important role in recognition and recall, Tulving assumes that both recall and recognition are affected in the same way by contextual information. Baddeley (1982) however, presents research which suggests this may not be

the case, and makes a distinction between intrinsic (important factors such semantic characteristics) and extrinsic context (irrelevant characteristics such as the size of the experimental room). Baddeley claims that recall memory is affected by both intrinsic and extrinsic context but that recognition memory is affected only by the intrinsic context. This is demonstrated in two convincing studies by Godden and Baddeley (1975, 1980) who show that extrinsic context has very different effects on recall and recognition.

1.3 Cortical Regions Involved in Recognition Memory

Studies of brain-damaged individuals and also of animals with cortical lesions generated the first information about the neural correlates of memory functioning. They have been used in the development of these models of recognition memory and have principally guided the research undertaken within the field of neuroimaging today.

The case of HM (Scoville & Milner, 1957) is important in recognition memory research. It was used as evidence in support of the Multi-Store Model of Recognition Memory. The model suggests that if short term and long term memory stores are indeed distinct, then there should exist brain damage that disrupts one but not the other. HM's anterograde amnesia provides such evidence (Milner, Corkin, & Teuber, 1968). Furthermore, it provided one of the earliest indications that the hippocampus is involved in recognition memory (Scoville & Milner, 1957). HM experienced severe epilepsy and in 1955 underwent surgery to remove his hippocampi. Although this greatly reduced the number of epileptic episodes he later suffered, it left him with complete of episodic memory. This severe anterograde amnesia meant he had a profound failure to create new memories and thus had no memories following the surgery. Impairments were also seen to his semantic memory, with his language essentially frozen to the 1950s. Later studies indicated that his working memory was intact, HM performing within normal levels on digit span tasks, having a normal rate of forgetting (Wickelgren, 1968). He was also able to learn new motor tasks (Milner, 1962, 1965; Corkin, 1968) indicating that his procedural memory was also preserved. This ability to learn new motor tasks has also been demonstrated in studies of anterograde amnesiacs who are able to learn to play new pieces of music (Starr & Phillips, 1970). It is believed that these procedural tasks are associated with implicit memory processes, For HM studies involving the Gollin incomplete picture task (Milner et al, 1968) and the Tower of Hanoi (Cohen & Corkin, 1981) have indicated that these implicit processes remain intact, therefore suggesting that the impairments

observed are associated with explicit memory processing. HM also experienced temporally graded retrograde amnesia in which his child hood memories were preserved but he lost memories immediately preceding his lesions.

Animal studies which have investigated the robe of the hippocampus suggest that episodic memory is dependent upon a network of structures, including the hippocampus and adjacent medial temporal structures (Fletcher, Frith & Rugg, 1997). Bilateral lesions to the medial temporal lobes resulted in severe generalised impairment in acquiring new memories, and in the retrieval of events prior to the lesion (Squire, Knowlton & Musen, 1993). Mishkin (1978) also identified the importance of additional medial temporal structures in recognition memory, reporting that in monkeys, only removal of the amygdala as well as the hippocampus, produced recognition memory deficits. Several further animal lesion studies have confirmed the critical importance of the adjacent perirhinal cortex in test of recognition memory (Murray & Mishkin, 1986; Zola-Morgan et al, 1989; Murray, 1996).

As detailed previously, recall and to a lesser extent recognition, processes involve an active search for a specific target memory and a familiarity judgement made. These active search processes are believed to involve the regions of the frontal neocortex which are involved in top-down executive control processes. The specific location within the frontal lobes where these processes occur are not yet fully identified, with many different sites, such as dorsolateral, ventrolateral and orbito-frontal regions all being reported to be activated in retrieval tasks.

The executive role of the prefrontal cortex has been demonstrated in several lesion studies. Gershberg and Shimamura (1995) reported patients with frontal lobe lesions who were unable to select appropriate encoding strategies. Similarly, Stuss et al (1994) demonstrated that recognition memory can remain intact, despite frontal lobe lesions, unless a task requiring complex encoding or retrieval strategies is undertaken.

1.4 Neuroimaging Studies of Recognition Memory

Memory is a dynamic process involving primarily three distinct stages: encoding, storage and retrieval. With the development of neuroimaging techniques, much of the focus of memory research is on the identification of the cortical regions involved in these

stages and the specific roles that these regions have in mediating the memory process. Using these methodologies, it is now possible to evaluate the functional specialisation of these brain regions in two complementary ways: first by identifying the segregation of regions, in which anatomical areas are associated with specific cognitive processes; and second, by investigating the functional integration of these regions in which the interaction between cortical areas is assessed.

Before the development of Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI), neuroimaging studies utilising Computerised Tomography (CT) had proposed that medial temporal structures, especially those around the hippocampus, were involved in episodic memory. This was supported from many neuropsychological investigations of patients with medial temporal lesions. Early PET studies in which regional Cerebral Blood Flow (rCBF) measurements indicated that the most active structures were more anterior in location (Foster, 1999a,b,c), specifically regions within the PFC. A role for the medial temporal structures in recognition memory, however, is also still reported and it may be that the differences is brain activations reported are due to paradigm or task effects.

1.4.1 Encoding and Storage

Numerous PET and fMRI studies have demonstrated that regions within both the frontal and posterior neocortex play a significant role in the encoding of episodic memories. The specific regions which are activated during episodic encoding are dependent on the nature of the task itself and on the specific properties of the encoded material (Mayes & Montaldi, 1999). For example, different regions have been reported to be activated (for example passive viewing versus semantic discrimination) and on the specific properties of the encoded material (such as whether the to-be encoded items are for example words, complex objects, line drawings or faces) (Mayes & Montaldi, 1999).

The PFC has been shown to be involved in episodic encoding (Kapur, Craik, Tulving, Wilson, Houle, & Brown, 1994; Fletcher, Frith, Grasby, Shallice, Frackowiak, & Dolan, 1995; McDermott, Buckner, Peterson, Kelley & Sanders, 1999). Different regions of the frontal cortex are seen to be activated depending on whether the task is verbal or visual and it has further been suggested that there may be left / right hemispheric asymmetry associated with verbal and visual encoding. Specifically it is regions within the

left hemisphere which have been reported to be activated during verbal encoding and in tasks involving intentional learning (as opposed to the incidental learning which occurs in everyday life) (Fletcher et al, 1995) and conversely, it appears that in tasks of visual memory, it is the right frontal regions that show the greater activation (McDermott et al, 1999).

The specific role of the PFC is thought to be one which integrates with other cortical regions and controls executive functions, such as how attention is directed (Mayes and Roberts, 2001). These executive functions then influence and co-ordinate, through 'top-down' processes, which parts of the material are encoded by other brain regions, in particular the associations between contextual and sensory information (Squire & Kandel, 1999). If the PFC does play such an integral role in the encoding of information, disruption to this area or reduction in its activation, may offer an explanation for ineffective memory functioning, or suggest how inaccuracies sometimes occur during subsequent retrieval stages. Furthermore, if the PFC acts to co-ordinate memory, it should be active early in the memory process.

A role for medial temporal structures during encoding processes has also been reported (Montaldi, Mayes, Barnes, Pirie, Hadley, Patterson & Wyper, 1998; Montaldi, Mayes, Pirie, Barnes, Hadley, Patterson & Wyper, 1998). It is unclear whether the MTL are involved in the initial representation processes, or whether they have a role in the transfer of the information into long term memory (LTM). Murray and Bussey (1999) believe that its role is associated with the initial representation of the encoded material, enabling perception and identification of the stimuli, and suggest that without the MTL generating these visual representations, subsequent memory retrieval will be unsuccessful. Buckner, Kelley and Peterson (1999), however, propose that during the encoding stage of a recognition memory task, information is transferred to the MTL, including the hippocampus and structures adjacent to it. Evidence for this idea has been obtained through the study of patients with amnesia. Patient PS, reported by Buckner and Koustaal (1998), had a lesion within the MTL as identified through a MRI scan. FMRI scans during a word judgement and subsequent recollection task showed that although the PFC was significantly activated during the encoding part of the experiment, PS was unable to remember any of the stimuli. It was suggested that the lesion within the MTL did not enable PS to sufficiently form or store the memories during the encoding task. .

It has been postulated that the MTL and the hippocampus are involved in the consolidation and storage of encoded material (Mayes and Roberts, 2001). Gray (1982) suggests that these regions are activated by the novelty of the stimulus, probably through an orienting mechanism. This produces an increase in arousal which is necessary for the consolidation processes within long-term recognition memory to occur.

A number of studies have investigated the performance of amnesiacs with hippocampal or MTL damage on episodic memory tasks. It is often the case that they not only perform poorly on episodic memory tasks for items learned after the injury, but also for material encoded before it. Consequently, these lesion studies do not provide sufficient evidence for the exact role that these structures play in either encoding or storage (Riedel, Micheau, Lam, Roloff, Martin, Bridge, de Hoz, Poeschel, McCulloch & Morris, 1999).

The storage of encoded material is still believed to involve MTL and hippocampal structures (Mayes & Roberts, 2001; Morris & Frey, 1997). Storage is not restricted to this region though, with many studies offering support for areas within the posterior neocortex also having a role in this process (Squire & Alvarez, 1995; Nadel & Moscovitch, 1997).

Additional cortical regions have also been associated with episodic encoding. Krause, Taylor, Schmidt, Hautzel, Mottaghy, and Muller-Gartner (2000) discussed PET, fMRI and Magnetoencephalography (MEG) studies of episodic memory and observed that a number of regions were similarly activated during both encoding and recognition. These included the secondary visual cortex, parahippocampal cortex, left medial parietal structures and cingulate cortex. The medial parietal activation reported by Krause et al (2000) is of particular importance as the precuneus is also believed to be involved in episodic encoding (Fletcher, Frith, Baker, Shallice, Frackowiak & Dolan, 1995). Although the specific role of the precuneus is still yet to be fully identified, its activation has been linked with the subsequent success of retrieval processes (Montaldi, Mayes, Pirie et al, 1998). Mayes and Roberts (2001) also suggest that this region may be involved in the association between encoded stimuli and their semantic representations.

Interestingly, Krause et al (2000) observed differences between the two memory stages, using systems level modelling analyses and functional imaging, particularly with respect to the neural interactions between different cortical regions. Stronger links were reported between the posterior and prefrontal areas during encoding and between the left parahippocampal and posterior cingulate cortex during retrieval. Also during retrieval, interactions between the extrastriate cortex and posterior cingulate cortex were observed.

Another region within the limbic system that is believed to play an integral role in the encoding and storage of information is the amygdala (Gloor, Olivier, Quesney, Andermann & Horowitz, 1982). Specifically, it is associated with a change in emotional arousal during encoding, perhaps again through stimulus novelty, and is thought to have strong modulating connections with the hippocampus during this process, which facilitates subsequent episodic retrieval (Cahill, Haier, Alkire, Tang, Keator, Wu & McGaugh, 1996; Hamann, Ely, Grafton & Kilts, 1999).

1.4.2 Retrieval

Data from PET studies have consistently shown the activation of two main cortical areas during episodic retrieval: the anterior prefrontal cortex, of which activation is greater within the right hemisphere (Cabeza & Nyberg, 1997), and bilateral posterior medial parietal cortex (Fletcher, Frith & Rugg, 1997; Rugg, Fletcher, Frith, Frackowiak & Dolan, 1996; Fletcher, Frith, Grasby, Shallice, Frackowiak & Dolan, 1995; Markowitsch, 1997). Furthermore, it appears that it is only a small area of the right anterior prefrontal cortex, specifically a small region of anterior Brodmann Area (BA) 10, which is activated in episodic recognition memory tasks (Buckner, 1996).

The majority of recognition memory tasks detailed in this chapter involve item memory whereby participants are simply remembering what has happened previously. However, it must be noted that there are some PET studies that use source information tasks that involve remembering contextual information. McIntosh, Bookstein, Haxby and Grady (1996) compared these two forms of recognition memory. Although similar activations within the right prefrontal and midbrain regions could be seen, item and source retrieval differentially activated various frontal regions. For example, different source tasks evoked activation either in the left frontal lobe or in BA 24 and 32, the anterior cingulate gyrus. In contrast, BA 47 and 21 (the right inferior prefrontal region and anterior temporal region respectively) were differentially activated during item retrieval.

Other studies using different source and item measures have shown similar variation in brain activation (Cabeza, Mangels, Nyberg, Habib, Houle, McIntosh & Tulving, 1997). Together, these studies all suggest selective activation of temporal lobe and dorsal prefrontal regions for item and source memory tasks. Subsequent fMRI studies (Nolde, Johnson, & D'Esposito, 1998) have demonstrated that in line with the source / item

distinction, the level of prefrontal activation is correlated to the amount of episodic detail required for successful recognition.

Evidence from a study performed by McIntosh (1999) suggests that the right prefrontal cortex during episodic memory retrieval is functionally linked to other brain regions. This activation indicates that the role of the right prefrontal cortex in episodic memory retrieval may be one associated with the control of executive function, similar to that suggested for encoding processes. The data also further suggests that the other areas to which it is linked are the determining factors in distinguishing between retrieval mode and success, suggesting an interactive network for recognition memory processing.

PET studies have also demonstrated that episodic retrieval tasks also result in activation of the MTL (Fletcher et al, 1997; Buckner, Koustaal, Schacter, Wagner & Rosen, 1998). Other areas of the brain, such as regions within the left PFC, anterior cingulate and right lateral cerebellum (Buckner, 1996; Buckner et al, 1998), are also sometimes activated in episodic retrieval. The lack of consistency in the regions identified as being involved in recognition memory tasks between may be explained through differences in the studies themselves, such as the use of different tasks, stimuli, procedures, analysis techniques or variations in thresholding of data (Petrides, Alvisatos, & Evans, 1995; Buckner et al, 1998; and see Table 1.1).

Numerous EEG studies of recognition memory have demonstrated that event-related potentials (ERPs) for old words are more positive than for new words (Sanquist, Rohrbaugh, Syndulko & Lindsley, 1980; Neville, Snyder, Woods & Galambos, 1982; Neville, Kutas, Chesney & Schmidt, 1986; Rugg & Doyle, 1992; Smith, 1993; Ranganah, & Paller, 1999 and for reviews see Rugg, 1995; Johnson, 1995). This 'old / new' effect is largest over the temporo-parietal regions and is more predominant over the left hemisphere. This is thought to be indicative of episodic memory retrieval (Allan, Wilding, & Rugg, 1998; Paller & Kutas, 1992) and with respect to the dual process theory described previously, it appears that this old/new ERP effect is closely associated with recognition based on recollection rather than familiarity (Smith, 1993; Paller & Kutas, 1992). Evidence from PET studies also provides support for this. It is still unclear whether the hemispheric asymmetry of ERPs is specific to memory retrieval processes. Allan, Doyle and Rugg (1996) identified a cued-recall ERP effect which did not show this hemispheric asymmetry and suggested that the neural correlates of explicit retrieval processes are task-dependent.

However, it is also possible that it is differences in study procedures which are responsible (Allan & Rugg, 1997), such as the use of language stimuli activating the left hemisphere.

Recognition memory studies using MEG have replicated the ERP findings demonstrating a Magnetic Evoked Field (MEF) old / new effect (Tendolkar, Rugg, Fell, Vogt, Scholz, Hinrichs & Heinze, 2000). Tendolkar et al (2000) used a methodology in which words were visually presented on a screen. In the learning phase the words were to be incorporated into a sentence when they appeared. Between 400 and 1000 ms after stimulus onset, a significant difference between the correctly recognised old and new words was observed. As with the ERPs, the MEFs were larger to the old words over the left hemisphere and with time were more parietal in location. Similarly stronger fields were generated by dipole fitting over the scalp for old words, the strongest being in the region of the MTL. This supports earlier findings (Gabrieli, Brewer, Desmond, & Glover, 1997) that the MTL, whilst associated with both encoding and retrieval, responds more strongly to previously encoded stimuli. The importance of this area in recognition memory has been further demonstrated through studies of patients in which the MTL is damaged. In these cases the old / new effect is significantly reduced (Rugg, Roberts, Potter, Pickels, & Nagy, 1991; Allan et al, 1998).

In Tendolkar et al's (2000) experiment two other dipoles were identified. One was located to the left inferior parietal cortex, consistent with PET studies (Rugg, Fletcher, Frith, Frackowiak & Dolan, 1997; Tulving, Kapur, Markowitsch, Craig, Habib & Houle, 1994). The other was located to the right inferior frontal cortices, consistent with other neuroimaging studies which have shown that activation of this area is enhanced during successful retrieval (Fletcher et al, 1997). This study was the first to study recognition memory using MEG and elegantly shows the complementary data that can be generated from EEG, ERP, MEG and other functional imaging techniques such as PET and fMRI.

Episodic retrieval processes are believed to involve a feeling of familiarity for the previously encoded material (Mayes & Roberts, 2001). Moscovitch (2000) and Milner (1999) both suggest that two types of information are retrieved, during retrieval; the specific detail about the encoded material, and the components that generate the feeling of familiarity. The existence of this familiarity component, in addition to specific stimulus-related information, forms the basis for the dual-process theories of recognition memory (Mandler, 1980). It is has been suggested that these familiarity feelings are generated by the hippocampus and other MTL regions (Milner, 1999), although others suggest that these

regions may be more involved in remembering the detailed knowledge and that the familiarity component occurs in other neocortical regions such as the PFC (Aggleton & Brown, 1999; Eldridge, Knowlton, Furmanski, Bookheimer & Engel, 2000).

Within the large proportion of the studies associated with recognition memory, the strength of activation of cortical regions varies. It has been suggested that this may be the result of different retrieval processes, both related to individual participant and also to task variation, with particular emphasis placed on differences between retrieval effort and retrieval success (Rugg et al, 1996). Through neuroimaging, it should therefore be possible to identify the specific brain regions associated with these different retrieval processes. Some studies failed to show activation differences between retrieval effort and retrieval success within the right anterior prefrontal region (Kapur, Craik, Jones, Brown, Houle, & Tulving, 1995; Schacter, Alpert, Savage, Rauch, & Albert, 1996). Therefore, although obviously involved in recognition memory, there appears to be no substantial evidence to suggest "a differential role for anterior prefrontal cortex in either retrieval effort or retrieval success" (Buckner et al, 1998, p152).

One study, however, has managed to demonstrate this differential activation. Rugg et al (1996) manipulated a relatively standard PET recognition memory experiment (by varying the number of previously seen items across tasks) to obtain a gradient of retrieval success. There was an increase in anterior prefrontal cortical activation that positively correlated with an increase in level of retrieval success and since then fMRI studies have attempted to replicate these findings.

Buckner et al (1998), adopting a similar procedure to that used by Rugg et al (1996), incorporated shallow and deep encoding tasks as a method of producing different retrieval effort and success conditions. The results replicated earlier PET studies by clearly demonstrating activation of the left and right PFC during all recognition conditions. Furthermore, the condition requiring greater retrieval effort produced more activation in the left dorsal prefrontal region and in bilateral anterior insular regions. During successful retrieval, the right anterior PFC was most active.

PET studies comparing memory performance with levels of rCBF have reported that individuals who correctly recognised more words showed increased activation near the hippocampus, specifically the MTL. It has consequently been concluded that the MTL is primarily involved in successful retrieval, as opposed to in the process of retrieval effort (Schacter et al, 1996; Nyberg, 1999).

In addition to activation of specific cortical regions, numerous neuroimaging studies have reported that some brain structures show a *decrease* in activity (Buckner & Tulving, 1995) during recognition memory tasks. The brain structures involved in the recognition memory task require an increase in blood flow (as indicated through the PET rCBF recordings). Consequently, this blood may be 'drawn' from other cortical areas that are not involved in the memory task. Several studies have thus proposed that there is 'inhibition of irrelevant processes' (Nyberg, 1999; Fletcher, Frith, Grasby et al, 1995) during recognition memory. Subtraction analyses of PET data have been used to identify deactivation within regions; voxels showing less activity in the experimental condition compared to the baseline or control condition. Specifically, de-activation has been observed in the bilateral temporal regions (Nyberg, Tulving, Habib, Nilsson, Kapur, Houle & McIntosh, 1995). Support for this inhibition hypothesis can be obtained from observations of activation decreases during the recall stages of recognition memory (Nyberg, McIntosh, Cabeza, Nilsson, Houle, Habib & Tulving, 1996).

1.4.3 Explicit versus Implicit Memory

There is a substantial body of literature that demonstrates a dissociation between performance on explicit and implicit memory tasks. Recognition memory tasks are explicit in nature, as they require conscious recall of prior events or experiences. Identification tasks form a large proportion of the implicit tasks, priming manipulations often being incorporated. Variations in experimental paradigms can affect explicit and implicit memory measures differently. Specifically with respect to recognition memory, semantic encoding of words has been used to increase recall performance when compared to words encoded at a more shallow level (Hyde & Jenkins, 1973). There is, however, no obvious effect of this procedure on priming measures (Jacoby & Dallas, 1981). These differences are similarly observed in experiments manipulating focused and divided attention (Jacoby & Dallas, 1981).

Is it, therefore, that these memory tasks are governed by independent mechanisms, or is it the case that the same processes are involved, but with varying additional cognitive processes (not associated to memory)? There is some evidence from amnesic patients to suggest that it is the former. It has been reported that word priming is unaffected despite damage to the structures thought to be involved in explicit memory, primarily those in the limbic system (Schacter, Chiu & Ochsner, 1993). However, there is also other reliable

evidence from amnesic patients in which priming is significantly correlated with explicit memory performance, particularly when the priming tasks utilise less perceptual information (Ostergaard, 1998). Neuroimaging studies have attempted to identify the cortical areas involved in both implicit and explicit memory by manipulating the perceptual information of the stimuli to generate different levels of priming. Jernigan, Ostergaard, Law, Svarer, Gerlach and Paulson (1998) report such a study in which PET was used to measure changes in rCBF during word identification and recognition tasks. In-line with previous studies (such as that by Ostergaard, 1998) the word recognition task produced significantly more activation within the anterior PFC. It could also be seen that the effects of priming could be manipulated through changing the level of difficulty of the task (in this case, increasing the level of degradation). Unlike results from verbal recognition memory tasks (Petrides et al, 1995), the demands of this visual recognition memory task may not be sufficient to produce activation within the ventrolateral prefrontal regions. Consequently it is suggested that activation will occur only with a very 'active' recognition task and may relate to the verbal / visual hemispheric asymmetry reported in many neuroimaging studies.

1.4.4 Encoding and Recognition: Hemispheric Asymmetry?

Many neuroimaging studies have demonstrated similarly activated cortical regions during recognition and encoding (Krause et al, 2000). In particular, these include bilateral anterior cingulate, insular regions and also regions within the PFC (Nyberg et al, 1996). In Jernigan et al's (1998) study, there was evidence that some activation was hemispheric dependent. Activation within the left hemisphere was limited to a much smaller region than the activation seen across the entire posterior surface of the right hemisphere. These large right hemispheric, prefrontal activations substantiate earlier suggestions (Nyberg et al, 1996) of hemispheric asymmetry in recognition memory tasks.

The activation of prefrontal regions in both encoding and retrieval studies is consistently reported in PET studies. In a review of a number of these, Tulving, Kapur, Craik, Moscovitch, and Houle (1994) observed that many of these studies reported activation of the left prefrontal structures during encoding stages and activation of structures of the right prefrontal cortex during the subsequent retrieval stage. They proposed that these results provided evidence for a hemispheric encoding / retrieval asymmetry (HERA) model of PFC activation in episodic memory.

According to this model, the left and right PFC are part of an extensive neuronal network for episodic memory, but are differentially involved in the processes. It proposes that left (compared to right) PFC regions are more involved in retrieval of information from semantic memory and in encoding information from novel stimuli into episodic memory. It must be noted that the authors only suggest these left PFC roles for on verbal stimuli and make no assumptions about the involvement of the left PFC in processing visual information. Right (compared to left) PFC regions, are more involved in episodic memory retrieval, compared to retrieval of semantic information. No verbal or visual distinction is made in the role of the right PFC regions.

The proposal of this model has generated a significant amount of discussion within the recognition memory literature. A number of studies have offered support for this idea (Dolan & Fletcher, 1997; Fletcher et al, 1997; Nyberg, Cabeza & Tulving, 1996; Fletcher, Shallice & Dolan, 1998; Fletcher, Shallice, Frith, Frackowiak & Dolan, 1998; Blanchet, Desgranges, Denise, Lechevalier, Eustache & Faure, 2001), which is also sometimes referred to as the 'task-specific' hypothesis. Others have suggested that there may be a different kind of hemispheric asymmetry; one that is associated not with task, but with the type of stimulus used. This 'modality-specific' hypothesis proposes that the left and right hemispheres are specialised for verbal and visual material, respectively (McDermott, Buckner, Peterson, Kelley & Sanders, 1999; Lee, Robbins, Pickard & Owen, 2000).

Recently, the original HERA model has been updated to account for some of the criticisms generated by opposing studies (Habib, Nyberg & Tulving, 2003). Others still believe, however, that even with its revisions, the HERA model cannot fully account for the nature of hemispheric asymmetries reported (Owen, 2003).

On the following pages, Table 1.1 summarises a number of the studies which have been involved in the hemispheric asymmetry debate and outlines the location of any activation within the PFC that was reported by the authors.

It can be seen that in addition to the utilisation of different neuroimaging techniques there is also variation in the stimuli, encoding conditions / tasks and the analysis methods used. These differences may account for the variation in cortical regions reported to be involved in recognition memory.

Author and Year	Imaging Technique	Stimuli	Encoding Conditions / Tasks	Comparison	Areas Active During Encoding (E)	Areas Active During Recognition (R)
Casasanto (2002)	fMRI	4-Word Sentences	IL	Encoding vs. Retrieval	L IFG	L IFG
Epstein (2002)	TMS	Chinese Words	Word–pattern paired associations	N/A	R DLPFC*	*NT*
		Abstract Patterns				
Raye (2002)	fMRI	Words	Silent reading (using repetition, rehearsal & novel words)	Between Conditions	L DLPFC (for rehearsal)	*NT*
Reber (2002)	fMRI	Dot Patterns	Categorisation	Task vs. Control (counting)	R SFG; B IFG; MED SFG	R SFG; R MEDFG; R DLPFC
Vaidya (2002)	fMRI	Objects	Living vs. non-living	Between Conditions	*NS*	*NS*
		Words			*NS*	*NS*
Buckner (2001)	fMRI	Words	IL	Task vs. Fixation	*NT*	L PFC
Donaldson (2001)	fMRI	Words	Sentence generation (word-pair)	Encoding vs. Retrieval	*NT*	B IFG; MEDFG; L MFG
Grady (2001)	PET	Objects	Living / Non-Living (Deep) & Size judgment (Shallow)	Task vs. Baseline	*NT*	B OFC; B MFG; R APFC; L OFC; L IFG; B APFC
		Words	Living / Non-Living (Deep) & Size judgment (Shallow)	Task vs. Baseline	*NT*	L MFG; L OFC; R APFC; L IFG; R PFC
Otten (2001)	fMRI	Words	Animacy decisions	Task vs. Baseline	L PFC; MEDFG	*NT*
				Animacy vs. Syllable	MED PFC	MEDFG
				Remembered vs. Forgotten	*NT*	L IFG; MED IFG
			Syllable decisions	Task vs. Baseline	L PFC; MEDFG	*NT*
				Syllable vs. Animacy	L IFG	R IFG
				Remembered vs. Forgotten	*NT*	*NS*

Author and Year	Imaging Technique	Stimuli	Encoding Conditions / Tasks	Comparison	Areas Active During Encoding (E)	Areas Active During Recognition (R)
Simons (2001)	PET	Faces	IL	Faces vs. Objects	*NT*	DLPFC
				Familiar vs. Unfamiliar	*NT*	L VLPFC (familiar)
		Objects	IL	Objects vs. Faces	*NT*	L APFC
				Familiar vs. Unfamiliar	*NT*	L VLPFC (familiar)
Idiaka (2000)	fMRI	Japanese Words	Memorise through rehearsal	Task vs. Control	L DLPFC; B VLPFC	L IFG
				Word vs. Pattern	B IFG	*NT*
				Retrieval vs. Encoding	*NT*	*NS*
		Patterns	Memorise pattern	Task vs. Control	B MFG	R PFC
				Pattern vs. Word	B MFG	*NT*
				Retrieval vs. Encoding	*NT*	NS
Kohler (2000)	PET	Objects	Living Vs. Non-Living	Pictures Vs. Words	L MFG; L IFG	L MFG; L IFG
				Encoding vs. Retrieval	*NS*	R MFG; R IFG
		Words		N/A	*NS*	*NS*
Lee (2000)	PET	Unpronounceable Letter Strings	Look at stimulus for 2s	Encoding vs. Retrieval	B FPC; R VMPFC	*NS*
				Encoding vs. Retrieval	R DLPFC	*NS*
		Non-Words	Look at stimulus for 2s	Encoding vs. Retrieval	B FPC; R VMPFC	*NS*
				Encoding vs. Retrieval	B VMPFC; L AFP	*NS*
Ragland (2000)	PET	Words	IL	Task vs. Baseline (finger tapping)	L IFG; R APFC	R APFC; B IFG
				Encoding vs. Retrieval	*NS*	R APFC
Tendolkar (2000)	MEG	Words	Sentence production	N/A	*NS*	R IFG
McDermott (1999b)	fMRI	Words	Pleasant / unpleasant	Encoding vs. Retrieval	L IFG; L SFG; MEDFG	A MFG; R DLPFC
				Task vs. Baseline (fixation)	B FO	B FO
Fletcher (1998a)	PET	Words$^{\nabla}$	IL of organised & partially organised word list	Between Conditions	L PFC	*NT*
			IL of unorganised word list	Between Conditions	L PFC; L DLPFC	*NT*

Author and Year	Imaging Technique	Stimuli	Encoding Conditions / Tasks	Comparison	Areas Active During Encoding (E)	Areas Active During Recognition (R)
Fletcher (1998b)	PET	Word^	IL of Organised Word list (task1)	Task vs. Baseline	*NT*	R PFC
				Task 1 vs. Task2	*NT*	R DLPFC
			Paired associate words (task2)	Task vs. Baseline	*NT*	R PFC
				Task 2 vs. Task1	*NT*	R VMPFC
Grady (1998)	PET	Objects	Size judgment (Shallow)	N/a	*NS*	*NT*
			Living / Non-Living (Deep)	Deep vs. Shallow & Semantic vs. IL	VMPFC; DMPFC	*NT*
			IL –memorise	IL vs. Semantic	L PFC; L VLPFC	*NT*
		Words	Size judgment (Shallow)	Words vs. Pictures	B PFC; L OFC	*NT*
			Living / Non-Living (Deep)	Words vs. Pictures	B PFC; L OFC	*NT*
				Deep vs. Shallow & Semantic vs. IL	VMPFC; DMPFC	*NT*
			IL –memorise	Words vs. Pictures	B PFC; L OFC	*NT*
				IL vs. Semantic	L PFC; L VLPFC	*NT*
						NT
Kelley (1998)	fMRI	Words	IL	Task vs. Fixation	L DFC;	*NT*
	Exp 1	Objects	IL	Task vs. Fixation	B DFC	*NT*
		Unfamiliar Faces	IL	Task vs. Fixation	R DFC	*NT*
	fMRI	Words	IL & PL	Task vs. Fixation & IL vs. PL	L DFC	*NT*
	Exp 2	Objects	IL	Task vs. Fixation & IL vs. PL	B DFC	*NT*
			PL	Task vs. Fixation	*NS*	*NT*
		Unfamiliar Faces	IL	Task vs. Fixation & IL vs. PL	R DFC	*NT*
			PL	Task vs. Fixation	*NS*	*NT*

Table 1.1 Summary of prefrontal activations reported in recent neuroimaging studies.
Abbreviations used are as follows: IL = Intentional Learning; PL = Passive Learning; NT = Not Tested / Reported; NS = No significant areas identified; R = Right; L = Left; B = Bilateral; A = Anterior; P = Posterior; D = Dorsal; V = Ventral; MED – Medial; PFC = Prefrontal cortex; VLPFC = Ventral lateral PFC; DLPFC – Dorsal Lateral PFC; VMPFC = Ventral Medial PFC; DMPFC = Dorsal Medial PFC; IFG = Inferior Frontal Gyrus; SFG = Superior Frontal Gyrus; MEDFG = Medial Frontal Gyrus; MFG = Middle Frontal Gyrus; DFC = Dorsal Frontal Cortex; OFC = Orbito-Frontal Cortex; AFP = Anterior Frontal Pole; *Regions disrupted by administration of Transcranial Magnetic Stimulation (TMS); ^Auditory Stimuli (all other studies used visual stimuli)

1.5 Frequency-Specific Activations in Recognition Memory

The significance of frequency-specific activation is a topical issue in EEG research and there has been some evidence reported in the literature that suggests that activation during a memory task maybe be frequency-specific. Previous EEG studies (see for example; Burgess & Gruzelier, 1997, 2000; Klimesch, Vogt, & Doppelmayr, 1994; Klimesch, Doppelmayr, Pachinger & Russegger, 1997; Klimesch, Doppelmayr, Russegger & Pachinger, 1996; Klimesch, Doppelmayr, Schimke & Ripper, 1997; Klimesch, Schimke & Schwaiger, 1994); have focused on the alpha and theta bands in particular.

The most dominant EEG rhythm is the alpha wave, oscillating at 8-12Hz. It is seen under conditions of relative mental inactivity, such as during sleep, and has been shown to be disrupted by attention or increased mental activity. This disruption is observed as desynchronisation of the alpha rhythms, whereby the neurons which are usually active within the alpha band no longer oscillate at the same frequency or are no longer phase locked together. This is referred to as type 1 desynchronisation and synchronisation where the presence or absence of alpha rhythms indicates an inactive versus an active system.

The theta frequency band is between 4 and 7Hz and is often seen as synchronisation following response to cognitive demands. Primarily, it has been associated with mental inactivity and the encoding of simple episodic information. In awake humans, it is a weak rhythm induced by hippocampal-cortical pathways, which synchronises in response to cognitive demands.

The hippocampus has been shown to be involved in memory processes, as previously discussed, and EEG studies have demonstrated that it generates oscillations within the theta frequency range (Green & Arduini, 1954). Consequently, these hippocampal theta rhythms are thought to be important in memory processes (Burgess & Gruzelier, 2000), particularly encoding strategies.

Studies using ERPs have shown greater positivity of early P1 components for old words compared to new words, but do not offer accurate measurement of theta activity. Using a measure of Event-Related Desynchronisation (ERD), Burgess and Gruzelier (1997) supported previous ERP findings and demonstrated that power within the theta band was greater for old words compared to new words. This suggested that theta synchronisation may be involved in recognition processes. Importantly, they were also able to provide additional information about the temporal dynamics of this activity showing

power changes at 125-150ms and again at 500-750ms. Although the spatial location of this activation could not be explicitly determined, the authors postulated that the observed activation over the fronto-central electrodes may have been generated by the anterior cingulate. This work has been supported by a number of other studies which have demonstrated that during memory tasks, cortical synchronisation is evident in the narrow theta frequency band (4-7 Hz) (Klimesch, Doppelmayr, Schimke & Ripper, 1997). Furthermore, this activity is believed to correspond not only to working memory (Klimesch, Schimke & Schwaiger, 1994), but also to the encoding of new information (Burgess & Gruzelier, 1997; Klimesch et al, 1996; Klimesch, Doppelmayr, Schimke & Ripper, 1997).

The theta range is not the only frequency band believed to demonstrate memory-related changes. Desynchronisation within the alpha (8-12 Hz) range has been reported (Klimesch, Doppelmayr, Pachinger & Russegger, 1997) and EEG alpha oscillations are positively correlated with memory performance, higher alpha frequencies correlated to good memory performances (Klimesch et al, 1990, 1993, 1994). Similarly upper alpha desynchronisation (10-12 Hz) has been reported as being specific to semantic memory processes, whilst lower alpha (8-10Hz) changes have been linked with attentional processes (Klimesch, Doppelmayr, Pachinger & Russegger, 1997; Klimesch et al, 1994; 1996). This upper-lower alpha function dichotomy has not been replicated by all studies. Burgess and Gruzelier (2000), for example, showed a word repetition effect across both the upper and lower alpha frequency bands. There was also some evidence of hemispheric asymmetry for stimulus modality, although this was only present in the upper alpha frequency range. Nevertheless, the general bilateral nature of the alpha desynchronisation was consistent with previous non-EEG neuroimaging studies (for example, the PET study of Grasby et al, 1994), which is an important factor for neuroimaging studies of recognition memory. There is evidence that EEG alpha is related to thalamocortical oscillations, which thus suggests a role for a thalamocortical network in memory processes. Activation within the alpha band therefore, would indicate activity of some of these pathways. Frequency-specific activation would therefore appear to be an important consideration for neuroimaging studies. It might be that the frequency-specific memory activations reported previously (Klimesch, Vogt & Doppelmayr, 1999) may change during the task, or may be functionally specific and linked to particular components of memory tasks.

1.6 Concluding Remarks

Through the use of neuroimaging techniques it is possible to identify some of the regions associated with recognition memory, such as the PFC and the MTL regions. The extent to which each of these is activated either bilaterally or with an asymmetric response may be dependent upon the task or procedure involved. Differences in activated regions, particularly within frontal and medial temporal lobes, have been recorded between encoding and retrieval procedures, and also with the accuracy of recall; greater activation is shown for correctly recalled items. Furthermore, there is evidence to suggest the importance of frequency-specific activations, particularly those within the alpha and theta bands.

1.7 Research Aims and Hypotheses

This thesis aims to investigate the processes and mechanisms involved in recognition memory. Using a modern neuroimaging technique, MEG, the aim is to extend the current research and facilitate the identification of the neural correlates of recognition memory. Previous research has shown that prefrontal and medial temporal structures are significantly activated during the encoding and recognition phases and many have also reported that additional cortical areas are involved in memory processing. Table 1.1 highlighted the widespread activation reported in the literature and it is suggested that this variability may be due to factors such as differences in the neuroimaging technique, analysis procedures, the specific tasks and stimuli used.

The first aim of this thesis is therefore to perform several studies using the same neuroimaging technique, analysis parameters and experimental paradigms, thus producing reliable and replicated data about recognition memory. This is important for MEG research as to date there are only two studies which have used this neuroimaging technique to investigate recognition memory processes.

Secondly, these studies will use MEG to investigate the concept of hemispheric asymmetry in prefrontal regions, which has been reported in many of the previous neuroimaging studies. Specifically, conducting studies which involve encoding and recognition of objects and words will enable assessment of the 'task-specific' and 'modality-specific' hypotheses of hemispheric specialisation in prefrontal regions during

recognition memory tasks. It is predicted that if the 'task-specific' hypothesis is true, objects and words would both activate the left and the right PFC during encoding and recognition, respectively. In contrast, if the 'modality-specific' hypothesis is accurate words would activate the left PFC during both encoding and recognition, whereas objects would produce activation within the right hemisphere for both tasks.

Finally, the importance of frequency bands and temporal resolution in memory processes is well documented in EEG studies (see Klimesch et al). This thesis will therefore use MEG as a tool to investigate the temporal dynamics and frequency-specific activation. It is believed that this will provide further important information about the neural correlates of recognition memory processes.

2 NEUROIMAGING AND MEG

2.1 Overview

Neuroimaging techniques provide an excellent means of investi correlates of cognitive brain processes, providing both spatial and tem This chapter provides a brief summary of a number of structura neuroimaging methods used to obtain information about brain function account of the most popular methods is provided in the Technical Appe In a comparison of the relative advantages and disadvantages of the suggested that MEG, with its comparable spatial localisation to PE temporal information to EEG, may be the most appropriate tool in th order, complex cognitive tasks such as memory. As such, a detailed ov provided, which includes information about the theory of MEG r physiological source of the signals measured and the analysis technique source location. Finally, a short comparison of MEG with other imagin as EEG and fMRI is provided.

2.2 Summary of Neuroimaging Techniques

As reported in the previous chapter, neuroimaging techniques pr means of investigating where and when specific cognitive processes, i functioning, occur in the brain. Each of the techniques available vari physiological processes they measure. The common element is that measurement is correlated with task-performance, and they can all be us task, whether sensory, motor or cognitive in nature. This means it is becc possible to distinguish between different component processes, such retrieval, in the brain and task-specific regions within the brain can thus b

The standard imaging techniques of Computerised Tomography (Resonance Imaging (MRI) have been at the forefront of neurological years. They are very useful in providing anatomical information abo images produced are static so assessment of brain function is not possi this, brain scans have been developed which enable neurologists to do jus

Positron Emission Tomography (PET) is a useful tool in assessing cognitive function. It records information about the metabolic activity of specific brain regions, and by correlating this with task-performance, it is possible to investigate the specific function of many brain regions. The concept behind PET is that when part of the brain is being utilised, for example during a task, the tissue's in that region will require more energy and the blood flow to that region will increase. Therefore, a method through which it is possible to track the movement of the metabolic activity was developed. A radioactive isotope is injected into the patient and is tracked through the brain. By continuously providing three-dimensional images it is possible to identify the specific brain regions that are involved in a particular task.

The temporal resolution of PET scanning is determined by the decay. This therefore means that the temporal resolution is rarely less than about 1 minute. Furthermore, the anatomical and spatial resolution is quite limited, usually about 1cm. While the short half-lives of the isotopes is advantageous as it means the patients only receive low dosage radiation, the fact that radiation is involved is itself a disadvantage, time between repeat scans having to be quite long to account of this. There are also cost and timing issues, one scan taking anywhere from a couple of minutes to a couple of hours (Sawle, 1995).

Functional Magnetic Resonance Imaging (fMRI) is a comparatively newer technique for studying the brain, (compared to PET), involving the basic methodology of MRI scans and is primarily used to look specifically at brain function. It enables regional metabolism to be measured and it has proved to be a very useful tool in the study of various components of the brain, much attention being centred on the hippocampus and its' sub-regions (Gabrieli et al, 1997).

The principle of fMRI is that a series of images are taken in quick succession, enabling the visualisation of changes in the chemical composition of brain areas or the flow of fluid, such as blood, over time. Unfortunately, one of the disadvantages of fMRI is that this time-span is rarely less than about two seconds and so can provide little information about the temporal sequence of events.

Probably the most common fMRI technique is the blood oxygen dependent (BOLD) method (Ogawa, Tank, Menon, Ellermann, Kim, Merkle & Ugurbil, 1992), in which changes in oxygen levels within the brain are measured. As oxygen is one of the main components found within the blood, measuring the oxygen level can be used as indicator of blood flow. Furthermore, as it is assumed that an activated brain region will require

more oxygen, the blood flow to this region will increase and thus cortical activity can be inferred.

FMRI does provide excellent spatial resolution. However, in addition to its poor temporal resolution, it is also expensive and not widely available. Care must also be taken to ensure that the patient's head remains still as any movement can often produce spurious results. PET studies are also disadvantageous as they have poor repeatability. This is not only due to cost but also because of the use of radiation. Furthermore, unlike MRI scans, PET scans are invasive due to the injection of chemicals into the body.

In contrast electroencephalography (EEG) is a non-invasive technique which records volume currents produced by the activation of a large number of neurones within the brain. The electrical activity of the brain is measured by a number of electrodes placed on the scalp. The electrical activity is generated by the neurones in the brain as a signal is transmitted. The electrodes placed on the surface of the scalp detect this activity and the information is amplified onto either a computer or onto a moving paper. The spatial location of brain activity is determined by the position of the electrodes, for example, those at the front could be used for detecting electrical activity in the frontal lobe, those at the back for measuring occipital or visual activity. The changes in the electrical activity detected by any one electrode over time results in the generation of a brain wave. Therefore, whilst it has excellent temporal resolution, only topographical images are generated, which have relatively poor structural resolution (compared to fMRI).

Ideally then, what is required for investigations of memory is a technique that is non-invasive, does not require radiation and which provides functional, as well as anatomical information. Furthermore, for studies of cognitive functioning, it needs to obtain spatial resolution of the order provided by fMRI and the temporal resolution obtained during EEG. A number of researchers believe the solution is a technique called Magnetoencephalography (MEG). It is similar to EEG in that it records information about the electrical signals generated during neuronal transmission. Whilst these electrical signals themselves can be recorded (as in EEG), it is the magnetic field that the signals produce which is recorded in MEG. Consequently, the temporal resolution mirrors that of EEG and with the development of new analysis techniques, such as Synthetic Aperture Magnetometry (SAM) (Robinson & Vrba, 1998; described in detail in section 3.7), this resolution can be recorded on a millisecond (ms) by millisecond scale. The data recorded, however, do not initially provide any structural information. This potential problem can be

overcome through incorporating a procedure of coregistration, in which the functional MEG data is mapped onto a structural MR image. This produces a structural image upon which functional data is shown, the coregistration being accurate to within 5mm (Singh, Holliday, Furlong & Harding, 1997; Adjamian, Barnes, Hillebrand, Holliday, Singh, Furlong, Harrington, Barclay & Route, 2004).

In terms of temporal resolution, therefore, MEG is believed to be better than other brain scanning techniques and is comparable in terms of spatial resolution. Although not as easy to perform as EEG, it surpasses PET, SPECT and MRI in terms of the ease of use (Papanicolaou, Rogers & Baumann, 1991). It would therefore seem that MEG might be a useful tool in the study of complex tasks, when multiple brain regions are involved and when activity occurs within just a few hundred milliseconds, such as during higher order cognitive processes. Due to its necessity in everyday life, memory is one such cognitive function that has been extensively studied using functional neuroimaging, particularly PET and fMRI. Its complexity is due to the diverse number of brain regions involved and the small temporal latencies within which they interact. Through the use of MEG it may therefore be possible to build on the work previously reported using PET and fMRI to aid our understanding of memory and to ultimately identify a cortical network of memory functioning and the time scale within which the component processes interact.

MEG is therefore the chosen instrument for investigating recognition memory in the series of experiments presented in this thesis. As it is still relatively new, in comparison to the aforementioned methods, it will be useful to look at the technical aspects of MEG.

2.3 Magnetoencephalography (MEG)

2.3.1 What does MEG Measure?

As established in the previous section, "magnetoencephalography (MEG) is a non-invasive technique for investigating neuronal activity in the living human brain" (Hamalainen, Hari, Ilmoniemi, Knuutila & Lounasmaa, 1993, p413). It records the magnetic information associated with the electrical activity produced during neuronal transmission. Before discussing how the MEG records these signals, it may first be useful to understand how this electrical and magnetic activity occurs.

2.3.2 Neuroanatomy

2.3.2.1 Action Potential and Postsynaptic Potential

Two types of neuronal event can create an extracranial magnetic signal, an action potential and a postsynaptic potential. The production of a neuromagnetic field is due to the generation of an action potential brought about through movement of sodium (Na+) and potassium (K+) ions between neuronal cells (Figure 2.1 A and B) and the surrounding tissue. When no signal is being transmitted, the inside of the neurone is negatively charged. This changes as a pulse is presented and excitation changes the permeability of the cell to Na^+ and K^+ ions (Figure 2.1 C). Firstly, there is an increase in Na^+ ions (they 'move' from the surrounding, extra cellular tissue into the cell) during the depolarisation stage, resulting in a cell which is negatively charged. Consequently, the second stage of repolarisation occurs when K^+ ions 'move' out of the cell into the surrounding tissue, returning the charge to that of the resting state. This process occurs successively along the entire axon producing an intracellular or action potential current. However, due to the thickness of the skull and scalp, it is believed that hundred's of thousands of axons are required to generate a measurable signal. Furthermore, this process only lasts for a very brief period of time (usually about 1ms) and as such is fairly difficult to detect. Therefore, this short duration and lack of spatial synchrony suggests that the action potentials are unlikely to make significant contributions to the extra cranial signals.

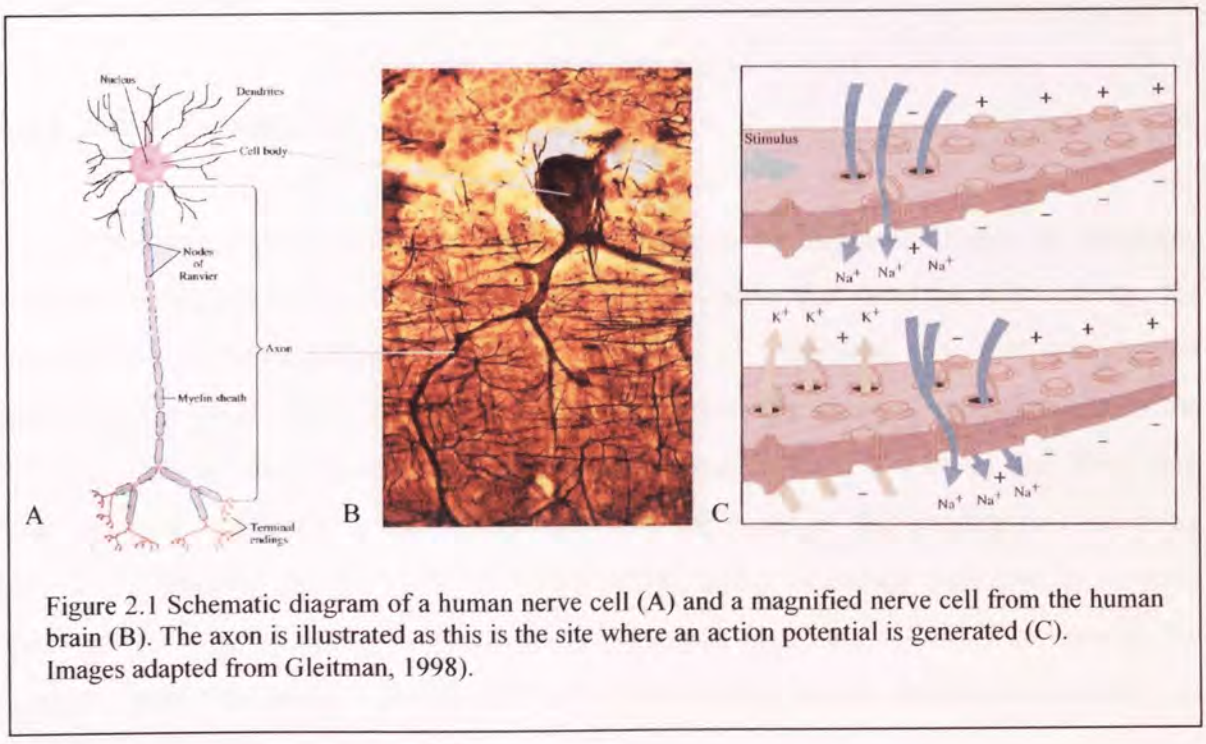


Figure 2.1 Schematic diagram of a human nerve cell (A) and a magnified nerve cell from the human brain (B). The axon is illustrated as this is the site where an action potential is generated (C). Images adapted from Gleitman, 1998).

This intracellular current will then reach the synapse of a neurone. There a presynaptic potential is set up at the membrane of the presynaptic cell. Some of the ions are then released into the synaptic cleft (resulting in repolarisation of the presynaptic cell) whereby the permeability of the postsynaptic neurone is altered. The electric current and field is now produced in this cell, and a postsynaptic potential has been generated. The postsynaptic potential is the process occurring within the brain that is responsible for the generation of the extracellular volume current which is measured by EEG, and intracellular magnetic field measured by MEG.

A postsynaptic potential can be measured provided about one million synapses are activated simultaneously at any one time. This equates to about one in one thousand neurones over one square millimetre (Hamalainen et al, 1993). Transmission between neurones takes considerably longer than the generation of the action potential along the axon, hence its classification as low frequency activity. This difference in time means that a postsynaptic potential does not have to occur simultaneously in as many neurones as the action potential in order for it to be detected. However, due to the numerous currents flowing in different directions (in several cortical areas) their electromagnetic fields often 'cancel each other out'. Therefore, in practice a large number do actually need to be firing at any one time for detection.

The amplitude of the action potential remains constant throughout, and so does not provide any useful information regarding the strength of the evoked potential. Rather, strength can be determined through the frequency of firing of the action potentials.

2.3.2.2 Cell Orientation

The orientation of the cells within the brain is an important factor in obtaining magnetic information. The neuromagnetic field outside the head mostly reflects the intracellular currents flowing in the apical dendrites of pyramidal cells that are oriented parallel to the skull. This tangential orientation permits the external measurement of the magnetic field as these pyramidal cells are positioned in such a way so that their long axons produce fields which will effectively 'cut' the plane of the sensing coil, enabling them to be detected (Reite, Teale & Rojas, 1999). MEG is mainly sensitive to currents produced by cells of this orientation, (Williamson & Kaufman, 1990). Conversely, the magnetic fields produced by cells of radial orientation simply surround the cell and

consequently it is suggested that only about 10% of the information from radial sources is detected by MEG (Lütkenhöner, Menninghaus, Steinsträter, Wienbruch, Gißler & Elbert, 1995; Eulitz, Eulitz & Elbert, 1997). A recent study by Hillebrand and Barnes (2002), however, has suggested that is the depth of the source and not the orientation which is the determining factor. They suggest that it is only the activity occurring at the crests of the gyri which are insensitive to MEG recording. As these only constitute a small proportion of the cortex it would therefore seem that MEG might be a more detailed neuroimaging tool than first reported.

2.3.3 Instrumentation

2.3.3.1 Dewars and Super Conducting Quantum Interference Device

Due to the small size of the magnetic signals produced, and recorded (Figure 2.2 A) (50-500 femo Tesla (fT), about 10^{-8} to 10^{-9} of the earth's magnetic field), it is necessary for a Super Conducting Quantum Interference Device (SQUID) to be used (Vrba & Robinson, 2001) to measure the extremely small variations in magnetic flux. The SQUID acts as a low-noise, high-gain current-to-voltage converter. The SQUIDs are submersed in liquid helium at –269°C. This temperature is critical in order for the superconducting sensor to function. The liquid helium is contained within a dewar (Figure 2.2 B). The material used to make the dewar is also essential. The use of a metallic element must not be implemented due to its interruption with the detection of the brain's magnetic field. Fibreglass therefore is a popular choice. Often there is more than one dewar within an MEG system, each comprising a relatively large number of SQUIDS, as the larger the number of SQUIDS, the better the spatial resolution of the magnetic field generated.

The SQUID itself is not usually the magnetic sensor and the set-up usually involves the coupling of a coil to the base of the SQUID. The coils can either comprise one loop, often used when magnetic shielding is exceptionally good (i.e. magnetometers), or two or more loops, gradiometers, which are useful in ascertaining local brain sources. The superconducting ring, i.e. the sensing component of the SQUID, generally comprises one or two Josephson junctions (Josephson, 1962) which are weak links in the ring responsible for limiting current flow. Most MEG systems either use radio frequency (rf) SQUIDs or direct current (dc) SQUIDs, the former having only one Josephson junction, the latter having two. The resulting difference in this relates to the direction of the limitation of the

current. While impedance within an rf SQUID is around the loop, the magnetic flux changes occur across the loop in a dc SQUID, resulting in reduced noise levels in dc SQUIDS (Clarke, 1966). The SQUID loops themselves also need to be relatively small in area. Although this does result in low sensitivity to changes in external flux, a larger loop would be significantly more affected by noise, which could not be sufficiently compensated by the noise reduction methods detailed below (Fagaly, 1990).

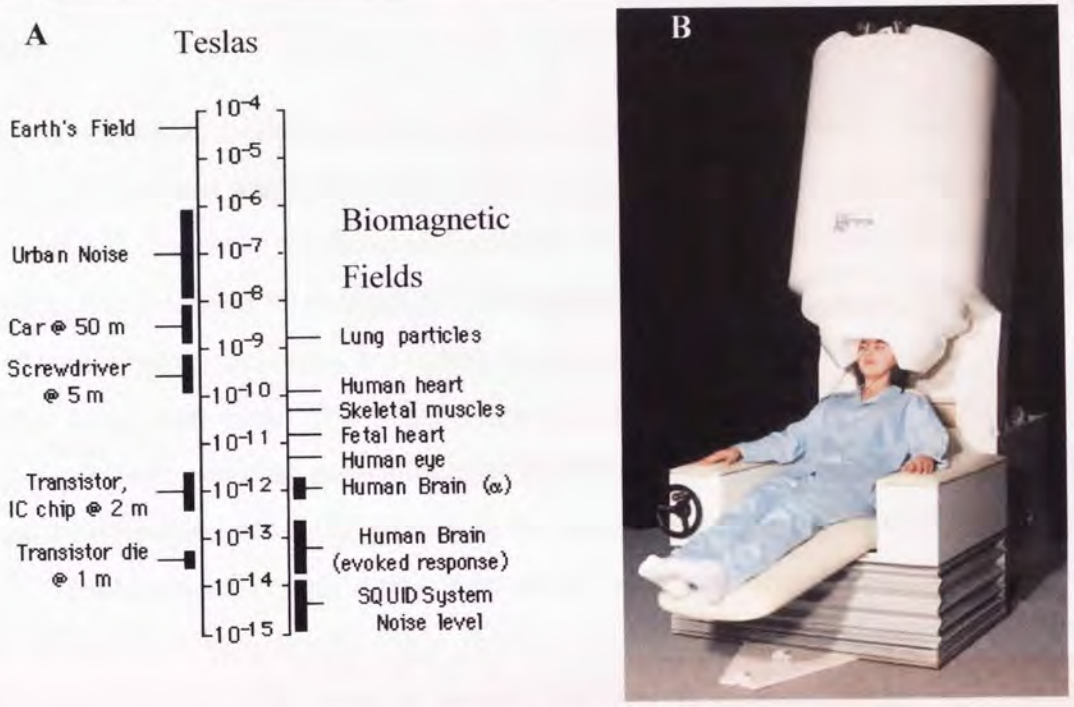


Figure 2.2 A represents a schematic diagram of the relative strengths of biomagnetic fields. SQUIDS are used to measure to the relatively small magnetic fields produced by cortical activity (~10^{-12}). These SQUIDS are located within a Dewar, similar to that depicted in B. Images courtesy of CTF Inc, Canada.

The signal produced by the current flow in the cortical neurones induces an electrical current within the wire loops of the detection coils positioned at the bottom of the SQUID, and then subsequently in the SQUID itself. Essentially the SQUID is responsible for amplifying the current-to-voltage relationship and facilitating detection of the magnitude of the signal.

The use of SQUIDS and consequently liquid helium significantly increases the cost of the MEG machines. Expense has further increased with the development of multi-channel sensors, 151 channel MEG scanners are frequently used today.

2.3.3.2 Current Dipoles

MEG produces topographic images of activation, compared to the internal tomographic images produced by PET and fMRI. Therefore, once the magnetic field has been measured, it is necessary to then locate the specific region of the cortex that has been activated. In the literature this is sometimes referred to as the inverse problem: we must use this external information to trace the source location back through the skull to a specific brain region.

By mathematical modelling of the magnetic field, it is possible to infer the spatial location, orientation and strength of neuronal currents that generate the recorded data. The most popular and successful model used for source localisation is the current dipole model. The dipole is characterised by position and location and its popularity is partially related to the use of an averaging technique for a large number of stimulus responses and also to the millisecond time resolution. The MEG literature suggests that a single current dipole produces a relatively accurate source location (Darvas et al, 2005); statistical analyses are often used to determine this. The procedure for dipole modelling is reported in detail in section 3.5. Problems arise with dipole modelling, however, when activity is distributed over the different hemispheres. Multiple dipole models are being developed but these are often significantly affected by noise in the data (Jerbi et al, 2004). Current MEG research is investigating new ways to solve this inverse location problem and one successful method to date is Synthetic Aperture Magnetometry (SAM; Robinson & Vrba, 1998). This uses a beamformer technique and enables superior millisecond time resolution. This procedure is described in more detail in section 3.7.

2.3.3.3 Noise Reduction

Magnetic fields are also produced by other environmental sources; those produced by the brain are relatively weak in comparison. Consequently, efforts must be made to reduce the amount of external magnetic noise present. One such way concerns the specific construction of the SQUID sensors. Ideally, there will be two detecting coils attached to the MEG sensor in series, referred to as a gradiometer coil. Although they are identical in size, they differ in the orientation in which they are wound around the sensor. The first, lower coil is responsible for detecting the brain's signal, while the second, upper, coil compensates for the other noise in the environment.

Further noise reduction methods involve the placing of the MEG system within a magnetically shielded room in order to limit any confounding noise from the data sets collected. Standard shielding rooms combine aluminium, which produces currents to cancel out those generated by the environment, surrounded (either externally or internally, or sometimes both) by high permeability iron which directs the noise away from the interior of the room. Standard magnetic shielding equipment used for EEG is not good enough to omit all the noise involved in MEG recordings. However, there are a number of systems (including the scanner at Aston University, Birmingham, UK, which was produced by CTF systems, Vancouver, BC, Canada) which incorporate a set of sensing coils to monitor the magnetic noise and employ analysis software to annul them.

2.4 Comparison of MEG with Other Neuroimaging Techniques

2.4.1 Comparison to EEG

The large number of similarities between MEG and EEG often provokes a comparison of the two methods. Possibly the most significant difference between the two corresponds to the cell orientation from which optimum signal detection is obtained. As stated previously, MEG is primarily sensitive to intracellular currents that flow in parallel (tangential) to the scalp surface (Ueno, 1999). Extra-neuronal currents also exist but these magnetic fields produced can not be identified as well and thus with MEG activity of cells of radial orientation is virtually undetectable. In contrast, because EEG measures electrical activity, which moves in a different direction to magnetic currents, the EEG electrodes are perfectly placed to detect any activity within these radial cells (Reite et al, 1999). Tangentially oriented cells, however, are undetectable by EEG because of this difference in current direction. This orthogonal nature demonstrates the compatibility of MEG and EEG data, and furthermore, the necessity for both. MEG does surpass EEG with respect to the spatial resolution of the activation recorded; the resolution of MEG being ~5mm, compared to 1-2cm for EEG (Lewine & Orrison, 1995).

The recording of magnetic, in comparison to electrical, activity is less affected or disrupted by the brain components they pass through, such as tissues, fluids and primarily the skull. The fact that EEG recordings are obtained from surface electrodes on the skull

puts it at an immediate disadvantage to MEG. Furthermore, the absence in recording magnetic signals enables very high frequencies to be recor something which is not possible using EEG. Indeed, the examination frequencies has proven to be very useful for studies of auditory proces patient studies (see for example, Ribary, Ioannides, Singh, Hasson, Bolton & Llinas, 1991).

2.4.2 Coregistration of MEG with MRI

MEG and MRI appear to complement each other with MEG provi temporal resolution not seen in fMRI, which itself can provide very high s Activity produced by a large number of neurones can be recorded by time, accounting for its good temporal resolution, fMRI being affec haemodynamic response. Looking at the possibility of combining thes been the focus of much investigation (George, Aine, Mosher, Schmidt Beisteiner, Gomiscek, Erdler, Teichmeister, Moser & Deecke 1995; Mor Mizushima, Tombimatsu, Shigeto, Hasuo, Nishio, Fujii & Fukui, 1995; Lewine, Caprihan & Aine, 1995; Sanders, Lewine & Orrison, 199(Hillebrand, Forde & Williams, 2002). In simple investigations somatosensory cortex using the evoked response, the accuracy of the loc differed only slightly between the two techniques. Again the differ information yielded by the two methods was demonstrated, fMRI showin location but providing information over a relatively long period of activat Recently Singh et al (2002) have shown that there is good consistency l areas identified by SAM and fMRI in both visual (biological motion) fluency) tasks, and they also highlighted the potential of MEG, co-re images, as a cognitive neuroimaging technique. Furthermore, successl procedures in which a structural MR image is mapped onto the functic from the MEG have been detailed, with localisation accuracy shown to w et al, 1997; Adjamian et al, 2004).

2.5 Concluding Remarks

In comparison to other well-established functional imaging techniques, MEG seems to be able to provide a relatively detailed account of the working brain in terms of generating information about both temporal and spatial resolution. Its similarities to EEG enable earlier findings to be replicated and studies have indicated that comparable data can be generated from MEG and fMRI studies. The compatibility of MEG and EEG and co-registration between MEG and MRI data suggests that combining methodologies is extremely beneficial. Furthermore, with the continuing development of more sophisticated analysis techniques, the accuracy and comprehensiveness of research and understanding into neuropsychology will benefit from the development of these neuroimaging procedures.

3 ANALYSIS TECHNIQUES

3.1 Overview

This chapter provides details of the experimental recording and analysis techniques used in the subsequent studies. It provides information about the general recording process and basic data analysis performed on the raw MEG data. Using the raw data it is possible to perform event-related potential analysis similar to that used in many EEG studies. To generate information about the spatial location of sources, the MEG data is first co-registered with previously acquired anatomical MR scans. Many MEG studies use dipole fitting as a way of analysing the data, although a beamformer technique, Synthetic Aperture Magnetometry, has recently been developed as an effective analysis tool. Detailed analysis of the SAM activations can be achieved by generating group images in which individual images are normalised and the information from all participants averaged. Recently, statistical procedures have been applied to determine the significance of these group activations. One of the advantages of SAM is that it provides detailed temporal information and, through the use of Virtual Electrodes (VEs) and Spectrograms, this can be illustrated on a millisecond-by-millisecond time scale.

3.2 MEG Recording and Data Analysis

For all studies, participants were seated in a magnetically shielded room and viewed the stimuli, presented on an Eizo T662 computer monitor, through a mirror. Viewing was at a distance of two metres and the stimuli subtended approximately 2^{o} x 2^{o} of visual angle. Neural activity was recorded using a 151-channel CTF Omega MEG System (CTF Systems Inc, Vancouver, Canada) at a sampling rate of 312Hz.

After each recording, a DC correction was first performed on the unaveraged raw data, which was then filtered. The low and high band-pass filters were 2Hz and 100Hz respectively. 2Hz was selected as the low-pass filter to remove as many eye-blink artefacts from the data as possible. Any trials containing eye-blinks following this filtering procedure were removed manually. A 50Hz mains power-line filter (width 3.5Hz) was also applied to remove any effects that this might have had on the data.

3.3 Event-Related Potentials (ERPs)

Event-Related Potentials (ERPs) are peaks of activation that occur at a certain tim following exposure to a stimulus (see Figure 3.1). For cognitive paradigms, evoked potential type responses are less obvious than in visual or somatosensory stimulatio studies, but through averaging across trials signal to noise ratio is increased and ERPs ca be recorded.

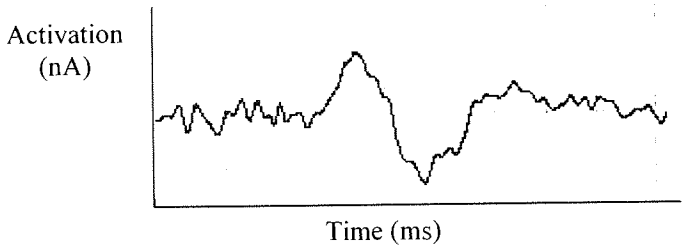


Figure 3.1 An Event-Related Potential (ERP). The activation recorded by one of the 151 MEG sensors for each trial was averaged together to produce this ERP

The 151 channels of the MEG Scanner are positioned so that frontal, tempora parietal, occipital and central cortical activity can be recorded from both the left and rig hemispheres. The raw data obtained during scanning (after the filtering procedu described in Section 3.2 above) displays traces of neural activity recorded by each of tl 151 sensors for each trial. Averaging across trials increases the signal to noise ratio ai enables peaks in cortical activity to be observed. It is also then possible to average acro several, or all, of the sensors.

For the ERP data presented in this thesis, the neural activity recorded by each grou of sensors within each hemisphere was averaged together for each trial. This provided EF traces for left and right, frontal, temporal, occipital, parietal and central channels. T activity for each of these from each trial was then averaged.

The peak activation value (nanoAmps, nA) was then obtained for each 100ms tir period across the trial; that is 0-100ms, 100-200ms and then every 100ms until 9C 1000ms post stimulus-onset. These values could then be compared across stimulus a task conditions depending on the study: objects versus words; encoding versus recognitic living versus non-living; old versus new. The peak activation values were in the region 1^{-14} to 1^{-13} nA, so for graphical illustration purposes, the peak activation values were ea multiplied by 10^{13} so that small positive values greater than zero could be displayed.

3.4 Co-Registration of MEG Data with an Anatomical MRI

During MEG scanning participants wear a small set of three localization coils (electrodes) around the head, which are fixed in position through use of Velcro bands. These coils act as fiducial markers which enable the position of the participant's head to be determined with respect to the 151 MEG sensors (Ahlfors & Ilmoniemi, 1990). The head position is taken as the average of pre- and post-scanning locations, and a maximum of 5mm movement throughout the scan is permitted. Runs in which there were deviances greater than 5mm between the two head localisations were rejected as this movement would create artefacts in the subsequent analysis of the spatial localisations of sources.

Outside the scan room, a dental impression is provided by each participant and fixed to a 'bite-bar'. The 'bite-bar' is mounted on a static platform and the participant required to be seated with their dental impression part of the 'bite-bar' in their mouth. This provides a consistently stable environment which is necessary for accurate co-registration.

Four markers along this 'bite-bar' are used to reference a co-ordinate system in 3-D space. This is done using a 3-D digitiser pen (Polhemus Isotrak system, Kaiser Aerospace Inc., Colchester, Vermont, USA). The location of the three fiducial points surrounding the participant's head are then located within this co-ordinate system using the 3-D digitiser. Finally, the digitiser pen is moved across the scalp surface of the individual in a systematic manner, creating a 3-D head shape for that individual (Pelizzari, Chen, Spelbring, Weichselbaum & Chen, 1989).

Using Align (www.ece.drexel.edu/ICVC/Align.align11.html) this digitised head shape is then matched to a head shape extracted previously from the participant's MRI (Pelizzari et al, 1989; Schwartz, Lemoine, Poiseau & Barillot, 1996; Huppertz, Otte, Grimm, Kristeva-Feige, Mergner & Luking, 1998) and thus the MEG data is co-registered with the participant's anatomical MRI. Investigations have demonstrated that the co-registration is accurate to within 5mm (Singh et al, 1997; Adjamian et al, 2004).

3.5 Dipole Fitting

The magnetic field pattern evoked in a specific region of interest (ROI) following stimulus presentation is known to be dipolar (Brenner, Lipton, Kaufman & Williamson,

1978). A method of non-linear least squares searching, or moving dipole, (Tuomisto, Hari, Katila, Poutanen & Varpula, 1983) has been established as a tool for estimating the source location of the dipole. An equivalent current dipole is generated and fitted to the data for specific time windows. Comparing these current dipoles to the magnetic field patterns obtained during MEG scanning produces a cortical map of residual field variance: the difference between the theoretical dipole and the measured field pattern. It is assumed that some differences between the expected and recorded data will be due to noise artefacts. Therefore, once this residual pattern can be satisfactorily explained through noise in the data, it can be concluded that the source location has been identified.

Several analyses are performed on the dipole solution to assess stability. The mathematical error of the dipole location is calculated and displayed as a χ^2 value, which for stable solutions should be less than or equal to 1. The robustness of the dipole is then further assessed through Monte-Carlo (MC) analysis, a statistical procedure during which variable levels of noise are repeatedly added to the data (usually about 1000 different permutations) and the dipole refitted multiple times. This produces an error volume (cm^3) which provides a measure of the volume within which the stable solution can be found; a volume of less than $1cm^3$ being ideal but less than $3cm^3$ generally acceptable.

Dipole fitting has been successfully used in identifying regions involved in sensory processing (Brenner et al, 1978; Hari, Reinikainen, Kaukoranta, Hamalainen, Ilmoniemi, Pettinen, Salminen & Teszner, 1984) when it is expected that only a few areas will be activated and any multiple sources are located far away from each other (Hamalainen et al, 1993). As the complexity of the task increases however, and multiple brain regions are involved, the reliability of current dipole modelling techniques decreases. The active cells to which a dipole is fitted must not exceed more than a few square centimetres (Hari & Lounasmaa, 1989) so any task producing widespread non-discrete neural activation cannot reliably be analysed using this technique. Furthermore, the experimenter requires *a priori* knowledge of the location of neuronal sources before dipole fitting can be completed.

3.6 Synthetic Aperture Magnetometry (SAM)

SAM is a nonlinear adaptive beamforming analysis technique (Van Veen, Van Drongelen, Yuchtman, & Suzuki, 1997; Sekihara, Nagarajan, Poeppel, Marantz, & Miyashita, 2002; Robinson & Vrba, 1999; Vrba & Robinson, 2001; Barnes & Hillebrand,

2003) in which an optimum spatial filter is constructed for each location in the brain. Each of these brain voxels are thus linked to MEG sensors. This optimum spatial filter is determined from a set of weights, which are calculated from the covariance matrix of the data. This weighting procedure ensures that at each voxel there is maximum sensitivity to the source and minimal output power from the filter.

Once the spatial filter parameters for a given voxel in the bran have been determined, the MEG signals can be projected through this filter to give an estimated measure of electrical activity at that cortical location. This in essence produces a narrow beamformer, or virtual electrode (VE), for each voxel, which has been placed at the location of the neuronal source (Barnes & Hillebrand, 2003; Barnes, Hillebrand, Singh, Furlong & Cheyne, 2001). The output of this virtual electrode has the same millisecond time-resolution as the MEG recordings. By applying SAM to each voxel over the whole brain, a three-dimensional image of activity can be produced (Taniguchi, Kato, Fujita, Hirata, Tanaka, Kihara, Ninomiya, Hirabuki, Nakamura, Robinson, Cheyne & Yoshimine, 2000; Singh, Barnes, Hillebrand, Forde & Williams, 2002). The resolution of the image is determined by the voxel size of 5mm, creating a 5x5x5mm grid of activation across the entire brain.

Evoked electrical activity is that which occurs following sensory input and is phase- and time-locked to the stimulus. Such activations produced obvious peaks which when averaged, for example, can be easily identified from the background neural activity. Induced activation is time-locked to the onset of the sensory stimulus but is not phase-locked and therefore requires more in depth analysis than the evoked activations. SAM has proved to be most powerful in localising task induced changes in cortical oscillatory power within specific frequency ranges. There is increasing evidence that these power increases and decreases, termed event-related synchronisation (ERS) and event-related desynchronisation (ERD) respectively (Pfurtscheller & Lopes da Silva, 1999), are important correlates of both sensory and cognitive processing within the brain. ERS and ERD are discussed in more detail in section 3.7.

In the simplest form of SAM analysis, the output of each voxel for one state or condition (active) can be compared with another (passive) and the difference in power (amount of ERS and ERD) can be quantified. A voxelwise t-statistic is used to indicate differences in frequency-specific oscillatory power between these two states. Positive and negative t-statistics reflect ERS and ERD, respectively. SAM also incorporates a method of

noise-normalisation to overcome the increase in intensity which is seen with increasing depth when non-uniform beamformers are used (Singh, Barnes & Hillebrand, 2003; Vrba & Robinson, 2001; Van Veen et al, 1997). It is these noise-normalised t-images which are displayed. It must be noted that the t-images themselves do not provide true t-statistical values. They do not accommodate any measure of signal variance, so perhaps a true description is that they are pseudo-t statistics, or the values of a neural activation index (NAI; Van Veen et al, 1997).

3.7 Event Related Synchronisation and Desychronisation

At baseline (i.e. during a passive epoch), neurones within a cortical region fire synchronously at a resting frequency. This synchronous activation may or may not occur as oscillations as this is dependent upon the state of the system and the frequency of activations (Lopes da Silva & Pfurtscheller, 1999). When these neurones process information about a task (i.e. in an active epoch), the frequency at which they fire changes causing a reduction in resting activity (phase coherence). This is termed event-related desynchronisation (ERD; Pfurtscheller & Araniber, 1977) and is believed to indicate an activated cortical network (Pfurtscheller & Lobes Da Silva, 1999), or one which is maximally ready to receive and process information (Thatcher, McAlaster, Lester, Horst & Cantor, 1983).

ERD and ERS can occur in two ways; evoked or induced. As stated in the previous section, evoked electrical activity is that which occurs following sensory input and is phase- and time-locked to the stimulus. Such activations produced obvious peaks which when averaged, for example, can be easily identified from the background neural activity. Induced activation is time-locked to the onset of the sensory stimulus but is not phase-locked and therefore requires more in depth analysis than the evoked activations. Analysis tools such as SAM are ideal for such induced activation (see section 3.6). Furthermore, because the effects can be determined (using SAM) without assuming that the cortical response is tightly time- and phase-locked to a brief stimulus presentation, ERS and ERD can be studied in the context of any given cognitive paradigm, even if the cortical activation changes associated with the task of interest are poorly time-locked.

Lopes da Silva & Pfurtscheller (1999) highlight the difficulties in interpreting cortical activations from MEG and EEG as ERD or ERS. Consequently, for the purpose of

this research, in the succeeding studies, increases in cortical activation will be referred to as ERD, decreases as ERS (and therefore should not be confused with increases or decreases in the power of the system). It is expected that ERD will be observed in the later studies as the cortical networks begin processing the cognitive task, previous EEG studies of recognition memory showing that desynchronisation occurs during the recognition of old words, indicating activated memory processes (Burgess & Gruzelier, 1999, 2000).

3.8 Normalisation and Group Averages

SAM produces similar 3-D cortical activation maps for each individual so it is possible to generate group images of activation. This is achieved by re-slicing the participant's anatomical MRI in the same plane as the SAM volume. SPM99 (Friston, Worsley, Poline, Frith & Frackowiak, 1995) is then used to spatially normalise the SAM image into a standard 3-D template space. Once the SAM images are in the same template space, they can be viewed using mri3dX (www.aston.ac.uk/lhs/staff/singhkd/mri3dX), or a voxelwise analysis of group effects can be performed.

Two different group averages can be calculated. The first simply calculates the average activation across all participants for each voxel in the brain and generates a 'simple effects' image. With this method, however, there are problems with variability across participants. To overcome this, a second group average can be calculated which uses a t-test calculation to determine the reliability of any activation. This is a very stringent measure and necessitates a large participant population to produce reliable and valid results. Furthermore, its assumption that the noise in the data is normally distributed increases the difficulty in this method of producing significant activations. Nevertheless, studies have shown the effectiveness of these group activations in illustrating task-related cortical activations and the results have been comparable to previously reported fMRI data (Singh et al, 2002).

3.9 Statistical Non-Parametric Mapping – Group Studies

In order to statistically threshold group activation maps, a method of non-parametric permutation testing (SnPM) has been specifically developed for volumetric neuroimaging data (Nichols & Holmes, 2002). This has been successfully used on group SAM data

(Singh et al, 2003). Unlike classical parametric methods, which require an assumption to be made about the form of the probability distribution for the null-hypothesis, SnPM estimates the distribution for the Null-Hypothesis from the data itself using a randomisation approach. For the simple design used in the following studies (which involve assessing a single group effect from multiple participants) the randomisation strategy involves negating the activation values for half of the participants.

If there truly is no statistically significant group activation within a voxel, manipulating half of the participants' values in this way (i.e. negating the activation values) should not have an effect and thus the Null-Hypothesis would not be rejected. All possible (2^N, for N participants) permutations of this negation strategy are performed. For example, for 6 participants, 64 permutations would be performed in order to generate an estimate of the statistical distribution. This distribution is then used to determine the significance of the originally calculated un-permuted t-value, with the observed t-value needing to be greater than the threshold value calculated in the permutation process. Note that this approach can be easily extended to account for the problem of multiple comparisons that occurs in volumetric neuroimaging data because of the thousands of voxelwise statistical tests that are performed (Nichols & Homes, 2002). It is also important to note that, using the same procedure, SnPM can be extended to assess the significance of a cluster of activation.

3.10 Spectrograms

SAM analysis is capable of illustrating cortical activity on a millisecond-by-millisecond time scale. Voxels of interest can be subjected to additional analyses so that time-frequency representations, referred to as spectrograms, can be generated for that voxel across the trial. Morlet wavelet analysis is used to generate these spectrograms. For every 5ms, the activation level of the voxel, in each 1Hz frequency band, usually between 0 and 100Hz is calculated. Using a Mann-Whitney statistical calculation the activation is analysed and a z score generated. It is these z scores which are represented on the time-frequency wavelet spectrograms.

4 DIPOLE FITTING VERSUS SYNTHETIC APERTURE MAGNETOMETRY

4.1 Overview

There is a large amount of neuroimaging literature detailing investigations of recognition memory using techniques such as EEG, PET and fMRI. Only a few studies, however, have used MEG, to investigate these processes. This preliminary study, was designed to determine the suitability of MEG to interrogate memory functioning. For the majority of MEG studies the source location of neural activity recorded is determined using various dipole fitting methods, one of the most popular being the equivalent current dipole (ECD) model. Whilst it has proven to be very successful in localising visual and somatosensory cortical activity only a few studies have used MEG and the ECD model to investigate cognitive functioning, such as memory processing. Synthetic Aperture Magnetometry (SAM) offers a novel way of analysing cognitive neural activation. To date, however, no study has directly compared the effectiveness of the two techniques for analysing recognition memory processes.

In this study, the neural activation produced when correctly identifying new stimuli during a recognition task were separately analysed using a current dipole procedure and SAM. It was expected that both the ECD and SAM analyses of MEG data would identify the prefrontal and medial temporal activations, consistent with previous neuroimaging studies. However, the different assumptions for the ECD and SAM indicated that different cortical activations may be identified by the two groups.

Stable dipoles were found for the early component of the response, believed to reflect the early visual processing following stimulus presentation. This was similar to the visual evoked potential responses seen in MEG and EEG studies of visual processing. For the remainder of the response, the dipoles identified were not found to be completely stable. These occurred during latencies consistent with memory processing and suggested that dipole modelling may not be successful for analysing cortical areas involved in cognitive processing. SAM analysis revealed multiple cortical regions of activation throughout the task. The location of the SAM activations was similar to the location of the dipoles for the visual component of the task (stimulus presentation) and for the motor task

(button-press). Differences were observed during the part of the task that required cognitive processing, SAM analysis revealing sites of activation where dipole modelling could not. This suggests that because higher order cognitive tasks, such as recognition memory, do not elicit a strong evoked-type response, dipole fitting may not be the most appropriate analysis tool. Instead, the relatively new technique of Synthetic Aperture Magnetometry (SAM) offers a way of identifying multiple activated cortical regions on a millisecond time-scale.

4.2 Introduction

As previously discussed (2.3.3.2), one significant problem that MEG has to overcome is solving the inverse problem, i.e. using the external magnetic field information to effectively trace the source location back through the skull. Various methods of dipole modelling have been developed for doing this. Multiple Signal Classification (MUSIC) is a method which involves the search for independent sources. All noise is removed from the data, which includes any activity which cannot be assigned to a specific source. The remaining data is assessed for the location of dipoles. Its assumption that all sources are independent has the potential to generate false results, especially if the signal is actually due to multiple sources occurring synchronously. Low resolution electromagnetic tomography (LORETA) (Pascual-Marqui, Michel & Lehmann, 1994) assumes that the measured signals are generated by multiple distributed sources. These source locations, however, need to be determined *a priori* as a number of different parameters have to be calculated for each location. The assumption that enables these *a priori* estimations is that neighbouring neurones will be activated synchronously and can thus be identified. The parameters that are applied identify sources that possess the lowest electrical activity. These sources are thus identified as the cortical regions responsible for the neural activity recorded.

Probably the most popular model used for assessing MEG activity has been the current dipole model. The dipole is characterised by position and location and its success is partially related to the use of an averaging technique for a large number of stimulus responses, and also to the millisecond time resolution. The MEG literature suggests that a single current dipole produces a relatively accurate source location; statistical analyses are often used to determine this. Problems arise, however, when activity is distributed over the different hemispheres. Consequently, multiple dipole models are being developed but these

are often significantly affected by noise in the data. Dipole modelling has been used in the recognition memory literature, specifically by Tendolkar et al (2000). It is suggested, however, that dipole fitting can be problematic in isolating the areas involved in 'higher-order' cognitive functioning, such as recognition memory, for a number of reasons. Firstly, as the complexity of the task increases and multiple brain regions are likely to be involved, the reliability of current dipole modelling techniques decreases significantly. The area to which a dipole can be fitted reliably must not exceed more than a few square centimetres (Hari and Lounasmaa, 1989) so any task producing widespread, non-discrete neural activation cannot be analysed reliably using these techniques. Secondly, the experimenter requires *a priori* knowledge of the location of neuronal sources before dipole fitting can be completed to ensure that a plausible, stable solution for the inverse problem is reached. Finally, it is likely that activation related to cognitive processing may not be tightly phase-locked to the initial stimulus presentation. This means that standard evoked-response paradigms, which rely on averaging of brief events to differentially enhance phase-locked activity, may not be the best approach for studying cognitive paradigms.

Current MEG research is investigating new ways to approach this inverse location. One method to date is Synthetic Aperture Magnetometry (SAM), which uses a beamformer technique and also enables millisecond time resolution. SAM provides an alternative approach to designing and analysing data from MEG experiments, which does not depend on activity being phase-locked to a stimulus and does not require *a priori* assumptions about the spatial distribution of the cortical activity. SAM has been successfully used in a number of studies (Singh et al, 2003; Ishii, Schulz, Xiang, Takeda, Shinosaki, Stuss & Pantev, 2002; Ishii, Shinosaki, Ukai, Inouye, Ishihara, Yoshimine, Hirabuki, Asada, Kihara, Robinson & Takeda, 1999; Vrba & Robinson, 2001), including motor (Taniguchi, Kato, Fujita, Hirata, Tanaka, Kihara, Ninomiya, Hirabki, Nakamura, Robinson, Cheyne & Yoshimine, 2000), sensory (Barnes, Hillebrand, Singh, Furlong, Holliday & Cheyne, 2001; Gaetz & Cheyne, 2003; Hirata, Kato, Taniguchi, Ninomiya, Cheyne, Robinson, Maruno, Kumura, Ishii, Hirabuki, Nakamura & Yoshimine, 2002), visual (Fawcett, Barnes, Hillebrand & Singh, 2004) and language (Singh et al, 2002; Xiang, Wilson, Otsubo, Ishii & Chuang, 2001) tasks. Furthermore, the potential for use as a cognitive neuroimaging technique has already been detailed (Singh et al, 2002). Singh et al (2002) have also shown that there is good consistency, particular in terms of spatial resolution, between the brain areas identified by SAM and fMRI in both visual (biological motion) and verbal (letter

fluency) tasks. SAM, therefore, could also be a successful tool for investigating cognitively demanding paradigms, such as recognition memory.

4.2.1 Aims and Hypotheses

This pilot experiment was conducted to determine whether two methods of MEG analysis, ECD and SAM, could be used to identify the functional areas reported in previous fMRI, PET and EEG studies of recognition memory. This experiment aimed to do this by simultaneously analysing the same recognition memory data with both SAM and a current dipole modelling procedure. It was hypothesised that both the dipole and SAM analyses of MEG data would identify the prefrontal and medial temporal activations, consistent with previous neuroimaging studies. It was further predicted, that as the successfulness of both procedures for analysing data involving evoked responses has been previously documented, both methods should be successful in locating the neural activity for the evoked-type-responses of the recognition memory task, i.e. the stimulus onset and the button-press response. However, the different assumptions for the ECD and SAM indicated that for the more cognitive demanding component of the task, different cortical activations, in terms of location and latency, may be identified by the two techniques. The technical details of SAM and dipole modelling are described briefly in the methods section and in more detail in chapter 3.

4.3 Methods

4.3.1 Participant

The data was collected from ES, a right-handed female participant (age 23 years). An anatomical MRI scan had previously been obtained for this individual and was made available for the analysis.

4.3.2 Stimuli

ES was presented with pictures taken from the Snodgrass and Vanderwart (1980) line drawings. As the cognitive task selected was an object recognition memory experiment, ES performed an encoding and recognition task. 52 pictures (26 living and 26

non-living matched for frequency (Kucera and Francis, 1967)) were presented in the encoding phase. Immediately following this, these same 52 images were shown, intermingled with 52 new images (also 26 living and 26 non-living frequency matched to each other and to those presented in the encoding phase).

4.3.2.1 Presentation of Stimuli

ES was seated in a magnetically shielded room and viewed the stimuli, presented on an Eizo T662 monitor, on a mirror, at a distance of two metres. In both the encoding and recognition phases of the experiment, ES fixated on a centrally presented small white square for 1000ms. A stimulus was then centrally presented for 200ms, before the fixation point changed from white to black. This was the cue for ES to make a button-press response using the dominant (right) hand. In the encoding phase, ES made an animacy judgement on the picture, categorising the stimulus as living or non-living, whilst in the recognition phase, the judgment was whether it was an old or new item (where old and new represent a previously seen or novel item in the set, respectively. ES had 2000ms to respond before the fixation point turned white again and signalled the beginning of the next trial.

4.3.3 MEG Recording and Analysis

Neural activity was recorded using a 151-channel CTF Omega MEG System (CTF Systems Inc, Canada). Neural activity was recorded for encoding and recognition phases. For analysis, however, only the recognition data was considered as this was the most cognitively demanding component of the task and believed to most closely resemble the recognition memory experiments designed for subsequent studies. Following recording, a Polhemus Isotrak System was used to digitise the surface shape of ES's head and this information was used to co-register the MEG data with the previously acquired anatomical MRI (see section 3.4 for details on this co-registration procedure).

For analysis purposes, accuracy and reaction time responses were recorded. The trials on which ES responded: before the cue, had a reaction time greater than 2000ms or made an incorrect response, were removed from the analysis. Correctly recognised objects were divided into four different datasets, (1) correctly recognised, previously seen living items, (2) correctly recognised, previously seen non-living items, (3) correctly identified,

novel living items, and (4) correctly identified, novel non-living items. The group with the most correct trials, thus the largest signal to noise ratio, was selected for the dipole and SAM analyses. This was the correctly identified novel items.

4.3.3.1 Dipole Fitting

All the 151 channels from the MEG recording were averaged. This revealed some peaks within the data, as illustrated in Figure 4.1. Each of these peaks was systematically analysed using dipole fitting. Generally it is anticipated that a smaller time window is better as there is less room for noise to be incorporated into the solution. This reduces the number of trials that are involved in the dipole solution and so could potentially be detrimental to the analysis. Consequently, for each peak, it was decided that two time windows should be analysed, the first being a relatively long time window that covered the entirety of the peak, and the second a much shorter one, to be identified following the results of the previous longer window.

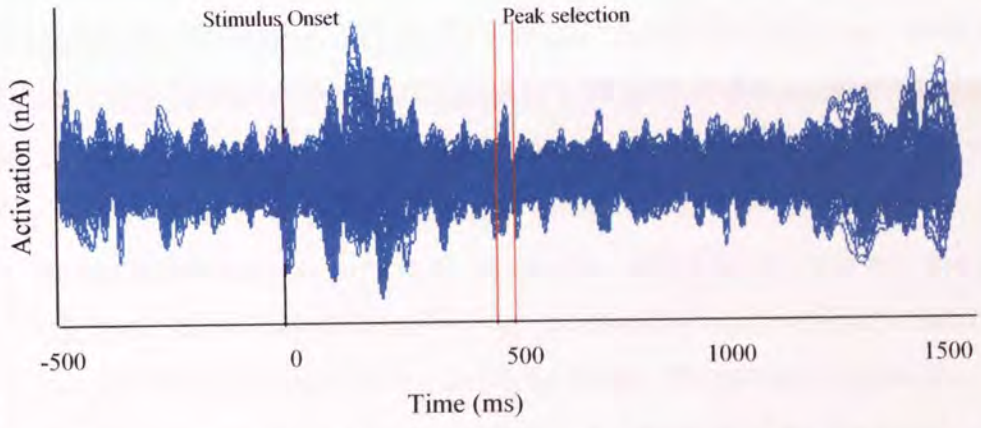


Figure 4.1 Averaged neural trace. The activation (nA) from each MEG sensor for all trials was averaged, and then the average of all sensors calculated. This activation (nA) was plotted against time for the entire trial. Peaks of activation can be seen, and the nine strongest were systematically analysed using dipole fitting.

Using the co-registered MRI, a best-fitting sphere was created over the shape of the head. This provided the area within which the dipoles would be fitted. The time windows analysed were decided through visual identification of the largest peaks across the entire 1500ms of MEG recording. The shorter time windows were identified through the dipolar activation in the field map. These nine peaks are illustrated in Figure 4.2.

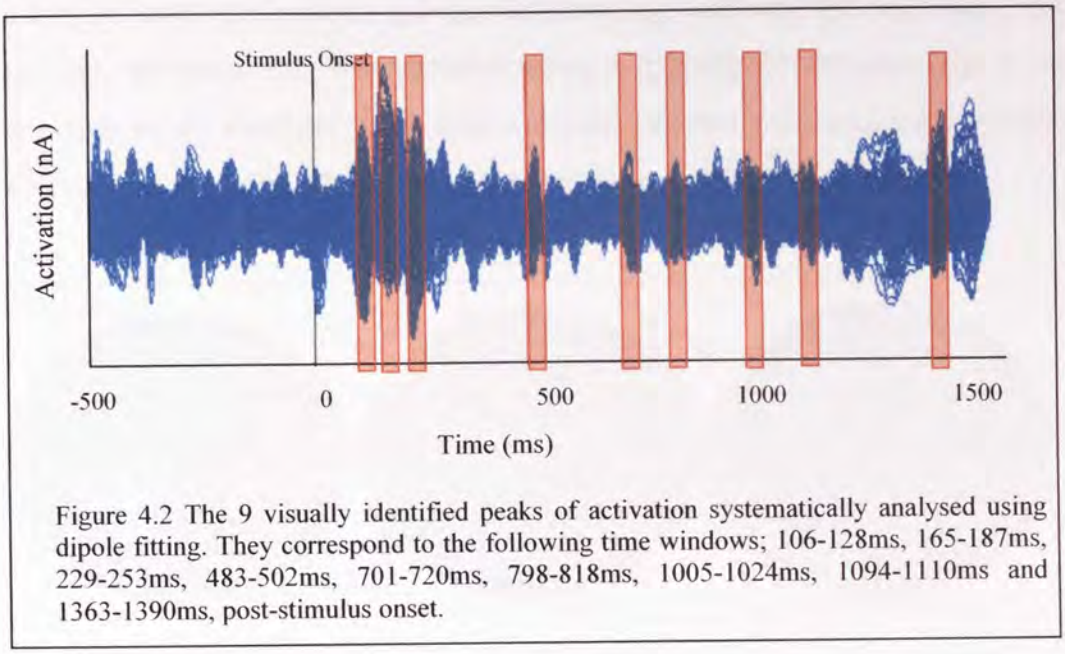


Figure 4.2 The 9 visually identified peaks of activation systematically analysed using dipole fitting. They correspond to the following time windows; 106-128ms, 165-187ms, 229-253ms, 483-502ms, 701-720ms, 798-818ms, 1005-1024ms, 1094-1110ms and 1363-1390ms, post-stimulus onset.

Once the time window had been identified, a dipole was added to the area that approximated the area of dipolar activation in the field map. Once the spatio-temporal fit was completed, the dipole moved to a location thought to best explain the field. Three images are produced (Figure 4.3) which show (A) the field pattern of the latency being fitted to, (B) the field pattern of the dipole fitted, and (C) the difference between these two field patterns. Ideally the images (A) and (B) should mirror each other and there should be no dipolar source observed in the third image (C). A plot of the error of the dipoles was also obtained. This is a χ^2 value and for stable solutions should be around 1. The robustness of the dipole was further assessed through Monte-Carlo (MC) analysis, a statistical procedure during which variable levels of noise were added to the data and the dipole re-fitted multiple times. Error volumes (cm^3) were produced which provided a measure of the volume within which the stable solution could be found. Therefore, a volume of less than $1cm^3$ was determined to be ideal, with acceptable volumes being less than $3cm^3$.

For this analysis, the long time window across each peak was fitted with a dipole and the co-ordinates of the final position, the χ^2 error and the MC volume recorded for subsequent analysis. A smaller time window for each peak was then analysed and the same information recorded. For each of the peaks it was found that the smaller time windows produced more stable dipole solutions. Consequently, further assessment of the dipole solutions was performed on each of these smaller time windows.

To determine the stability of the solution, the single dipole was positioned in five different starting locations and the co-ordinates, χ^2 error and MC volume recorded for each of the 5 fits. The stability of the solution was indicated by the number of times the dipole

returned to the same end location and the variation in χ^2 error and MC volumes. Following on from this, the procedure was repeated using a two-dipole solution with 5 different starting locations. In summary, therefore, a dipole solution was obtained for each of the nine peaks across the entire trial and the stability of each solution assessed.

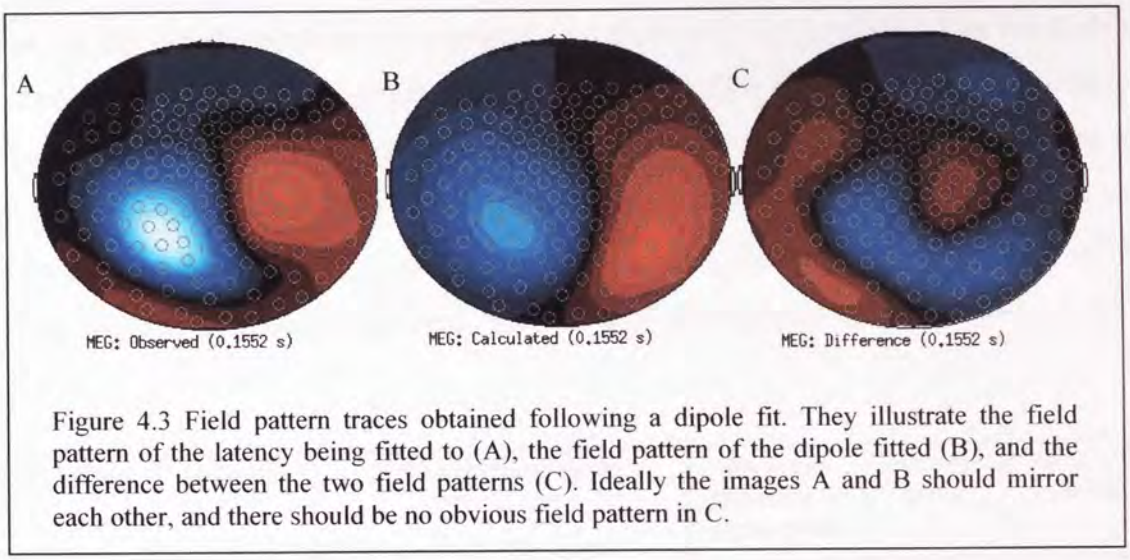


Figure 4.3 Field pattern traces obtained following a dipole fit. They illustrate the field pattern of the latency being fitted to (A), the field pattern of the dipole fitted (B), and the difference between the two field patterns (C). Ideally the images A and B should mirror each other, and there should be no obvious field pattern in C.

4.3.3.2 Synthetic Aperture Magnetometry (SAM)

In the simplest form of SAM Analysis, one state or condition (active) can be compared with another (passive) and the amount of ERS and ERD can be quantified using a voxelwise t-statistic to indicate statistically significant differences in frequency-specific activity between these two states. Positive and negative pseudo-t statistics reflect ERS and ERD, respectively. In the current experiment, SAM comparisons were made between the active recognition state and the passive pre-stimulus fixation in six overlapping 10Hz frequency bands; 5-15Hz, 10-20Hz, 15-25Hz, 20-30Hz, 25-35Hz and 30-40Hz. These were assessed across three time windows, 0-500ms (comprising the initial processing of the stimulus), 500-1000ms (cognitive activation) and 1000-1500ms (reflecting button-press response activation). The comparison of active and passive states produced a t-statistic for each peak of activation; the larger the value the greater the strength of the neural activity in that area. The co-ordinates and the spatial locations for the strongest peaks were recorded for each frequency band within each time window. Wavelet spectrograms depicting Mann-Whitney z scores were also generated for the strongest SAM peaks. See section 3.10 for a detailed explanation of spectrograms.

4.4 Results

4.4.1 Results for Dipole Fit

The data presented in Table 4.1. are from the smaller time windows. For each window, all the dipole solutions are reported, and their stability determined by the number of times (out of 5) that they returned to the same end location (i.e. same xyz co-ordinates), their average, their average χ^2 error and the MC volume. If the number of times that the end dipole location was the same for each of the five starting positions is first considered, for eight of the peaks, the exact end dipole location was produced on either four or five occasions (Figure 4.4). Only one peak showed less consistency than this, that at 1094-1110ms.

Time Window	Solution No	Solution co-ordinates			No times returned to same place	Mean χ^2 error	Mean MC Volume
106-128 ms	1	-0.38	-1.54	2.46	4	1.169	1.877
	2	2.26	0.65	0.79	1	1.997	0.000
165-187 ms	1	-1.02	-0.96	1.39	5	1.416	0.915
229-253 ms	1	-0.24	-1.32	3.15	4	1.011	3.042
	2	2.26	0.65	0.79	1	1.458	1.702
483-502 ms	1	-0.00	-0.06	4.01	4	0.258	4.855
	2	2.26	0.65	0.28	1	0.450	188.039
701-720 ms	1	1.17	-0.19	2.41	5	0.500	24.916
798-818 ms	1	1.47	-2.21	-0.70	4	0.652	167.130
	2	14.4	-1.87	11.44*	1	0.883	5361.029
1005-1024 ms	1	2.10	-2.40	2.62	5	0.684	11.800
1094-1110 ms	1	-0.64	0.93	-2.68	3	0.735	1899.833
	2	-1.69	-3.91	2.40	2	0.485	5.766
1363-1390 ms	1	-3.81	0.53	4.21	5	0.902	1.904

Table 4.1 Data for single dipole solutions. For each of the small time windows, the location of dipoles are reported and their stability indicated by the number of times (out of 5) they returned to exactly the same location, their average χ^2 error and MC Value. * Indicates that the end dipole location was not within the participant's brain. (Data are presented to 3 decimal places).

If, however, the average χ^2 error produced for each different end location across the time windows is analysed, there is much less consistency, as illustrated in Figure 4.5. It was stated that the ideal χ^2 error value should be less than 1 to indicate stability. For this data, however, all of the error values were less than 2 with the values for all the peaks

tested between 400 and 1500ms showing ideal χ^2 values of less than 1. This was found regardless of whether it was the dipole with a consistent end location, and thus a stable dipole in the previous graph, or whether it was determined to be unstable.

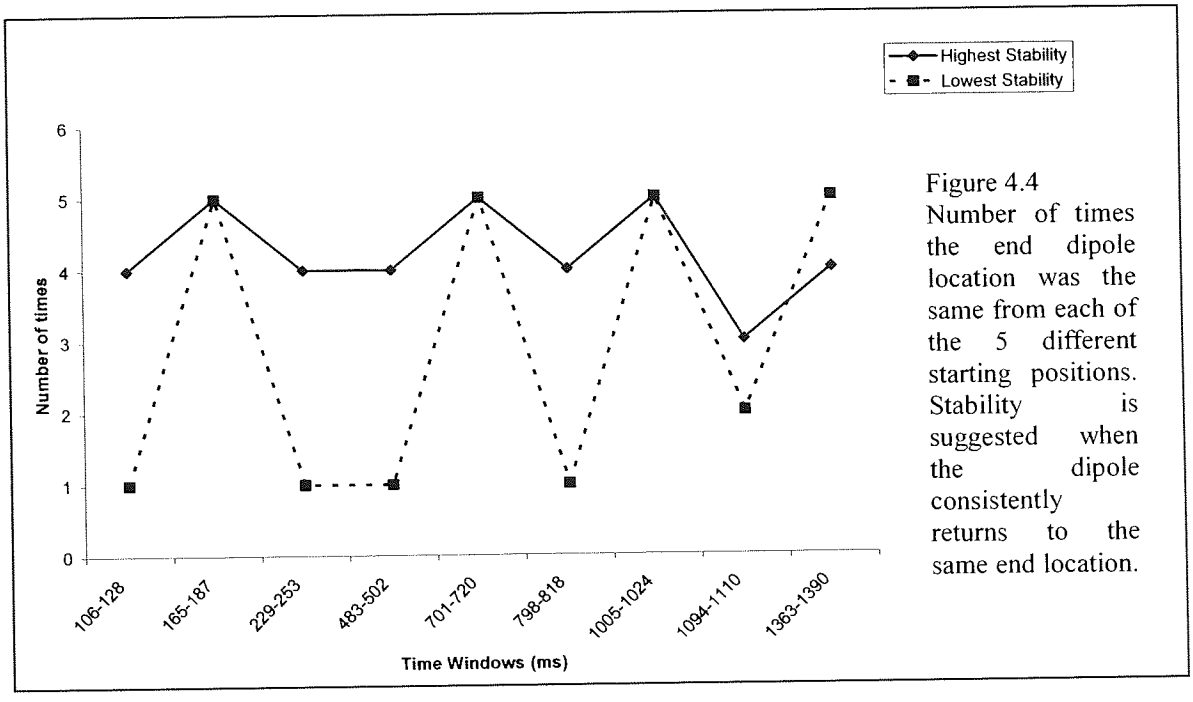


Figure 4.4
Number of times the end dipole location was the same from each of the 5 different starting positions. Stability is suggested when the dipole consistently returns to the same end location.

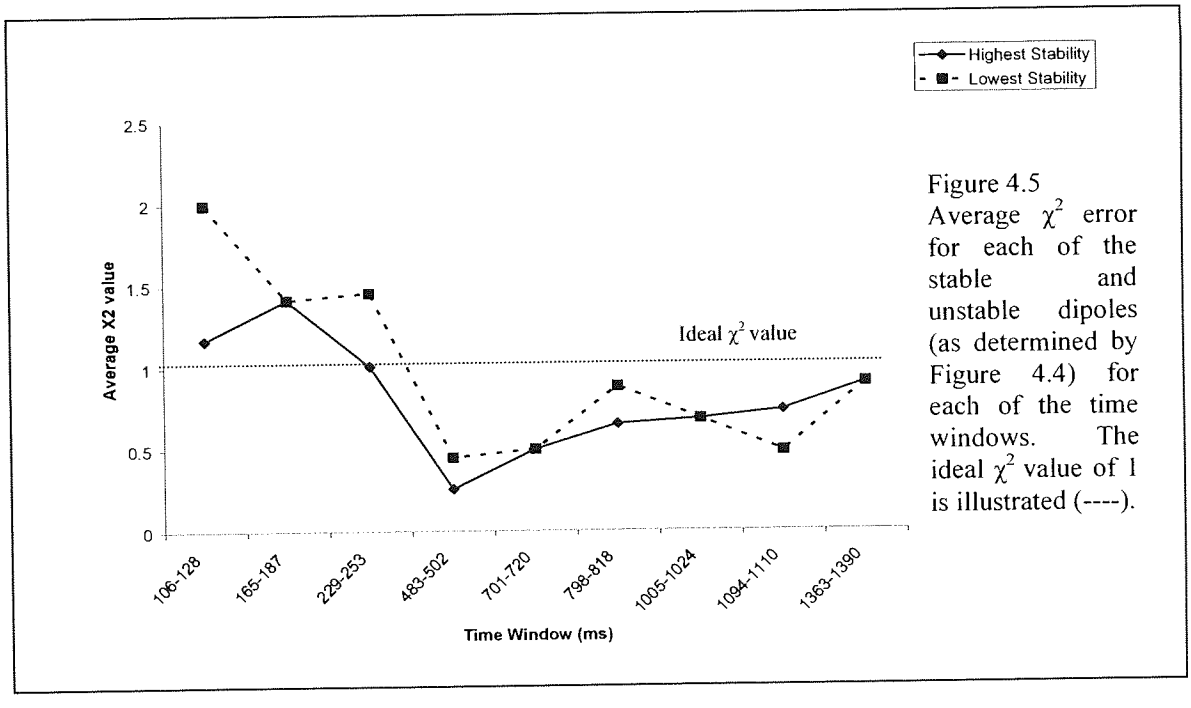


Figure 4.5
Average χ^2 error for each of the stable and unstable dipoles (as determined by Figure 4.4) for each of the time windows. The ideal χ^2 value of 1 is illustrated (----).

Perhaps, therefore, the MC volume should be used as an indication of stability. The ideal volume was less than $1cm^3$, with acceptable values being less than $3cm^3$. For the peaks spanning 0 to 400ms, the MC volumes produced were acceptable. Even within this, however, there was some discrepancy as the χ^2 values were not ideal and the lowest MC volumes were produced for dipole locations that were found only once in the 106-128ms and 229-253ms time windows. Nevertheless, the spatial locations of these dipoles did correspond to the visual cortex, which would be consistent with the image being present on the screen for 200ms.

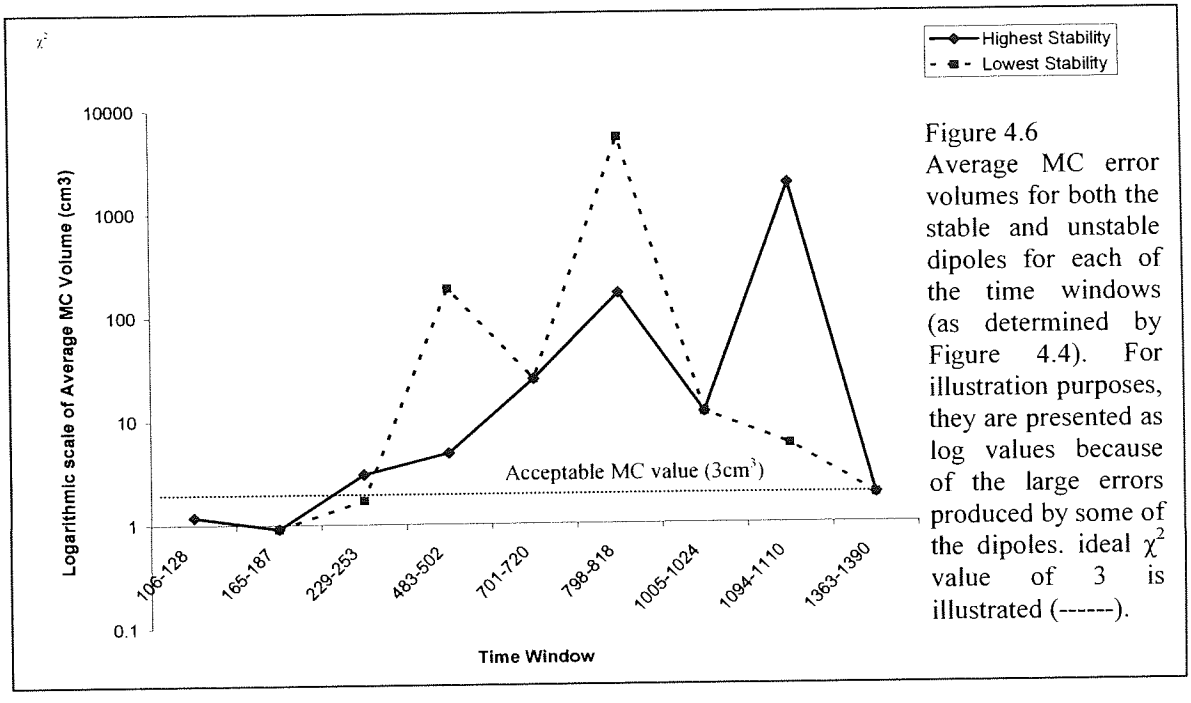


Figure 4.6
Average MC error volumes for both the stable and unstable dipoles for each of the time windows (as determined by Figure 4.4). For illustration purposes, they are presented as log values because of the large errors produced by some of the dipoles. ideal χ^2 value of 3 is illustrated (------).

For the 483-502ms time window, the dipole location found four of the five times could potentially have been rejected because of the large MC volume. For the peaks considered between 700-1300ms, although the χ^2 error values are excellent and for some of the peaks the same dipole location was observed on at least four of the five occasions, the MC volumes calculated were relatively large. For the final time window, 1363-1390ms, it would appear that a stable solution had been located. The dipole was fitted to the same location from each of the five different starting positions, the χ^2 value was at an ideal level of less than 1, and although the MC volume was not ideal, it was below an acceptable level.

Time Window	Solution	Solution co-ordinates			No times returned to same place	Mean χ^2 error	Mean MC Volume
106-128 ms	2 dipole solution	-0.31	-1.55	1.45	3	0.745	4209.595
		-2.4	-2.73	5.19		0.745	1105.252
165-187 ms	1 dipole	-0.75	-0.16	0.44	2	0.939	39.410
229-253 ms	1 dipole	2.14	0.07	3.5	2	0.806	15.324
	2 dipole solution	-0.11	-1.8	3.52	2	0.627	3.296
		3.4	-0.1	-5.35		0.627	314.957
483-502 ms	2 dipole solution	6.15	0.67	1.49	2	0.210	6653.267
		0.7	-0.22	3.68	2	0.210	135.211
701-720 ms	No consistent dipole solution						
798-818 ms	1 dipole	2.3	0.65	0.8	2	0.422	39.410
	1 dipole	2.5	-0.1	0.8	2	0.408	271.414
1005-1024 ms	2 dipole	1.46	-0.6	1.4	2	0.384	20.300
		-0.8	1.45	1.52	2	0.384	14.191
1094-1110 ms	2 dipole	-1.04	-2.85	2.3	3	0.291	429.158
		3.44	1.7	1.44	3	0.291	430.256
1363-1390 ms	2 dipole	-2.02	0.45	1.45	2	0.406	92.551
		-1.98	0.45	1.38	2	0.406	1755.367

Table 4.2 Data for two dipole solutions. For each of the small time windows, the location of both dipoles are reported and their stability indicated by the number of times (out of 5) they returned to exactly the same location, their average χ^2 error and MC Value. No two-dipole solution could be found for the peak at time window 701-720ms and for 4 of the time-windows, both dipoles returned to the same location and thus were interpreted as a I dipole solution. (Data are presented to 3 decimal places).

The data was also analysed using two dipoles. Table 4.2. presents any dipole solution that was found on more than one occasion. For all except one of the time windows (that between 701-720ms), dipole solutions were observed that occurred more than once. None of the solutions, however, occurred more than three times, although all solutions produced ideal $\chi 2$ values. Furthermore, for only one of the dipoles was the MC close to an ideal level and this was for only one of the dipoles in a two-dipole solution. Consequently, none of these dipole solutions satisfied the criteria for stability.

4.4.2 Results for SAM Analysis

Time Window	Frequency Band	Co-ordinates			Peak T value	Location
0-500ms	5-15Hz	-1.5	-2.5	6.0	2.3	Parietal
		0.5	4.5	6.0	2.0	Parietal
	10-20Hz	-3.5	3.5	2.5	2.0	Occipital – Temporal
		7.0	-0.5	6.0	1.9	Frontal
	15-25Hz	-3.5	3.0	1.5	2.6	Occipital – Temporal
		2.0	1.5	2.0	2.2	Superior Temporal / Cingulate Gyrus
	20-30Hz	0.5	2.5	6.5	2.3	Posterior Parietal
		7.0	3.5	3.5	1.9	Frontal
	25-35Hz	-2.0	-2.0	5.0	2.5	Parietal / Occipital
		-2.0	4.0	4.0	1.5	Parietal
	30-40Hz	-0.5	3.0	6.0	2.6	Parietal
		0.5	-4.0	5.0	2.2	Superior Parietal
500-1000ms	5-15Hz	8.5	-0.5	4.0	2.2	Prefrontal Cortex
		4.5	-3.5	4.0	2.0	Precentral Gyrus
	10-20Hz	-3.5	3.0	2.5	2.1	Occipital
		-2.0	-3.0	6.5	2.0	Superior Parietal
	15-25Hz	2.0	5.0	4.0	3.2	Frontal – Temporal
		-5.0	-0.5	1.0	1.9	Occipital
	20-30Hz	0.5	2.5	6.5	2.3	Parietal
		7.0	3.5	3.5	1.9	Frontal
	25-35Hz	2.5	5.5	4.0	2.5	Parietal – Temporal
		1.0	4.0	5.5	2.3	Parietal
	30-40Hz	0.5	2.0	6.5	2.0	Parietal
		4.0	1.0	6.5	2.0	Frontal
1000-1500ms	5-15Hz	6.5	3.5	3.0	1.8	Frontal
	10-20Hz	2.0	5.0	6.0	1.9	Parietal
	15-25Hz	0.5	5.0	5.0	2.3	Parietal
		2.0	1.5	2.0	1.8	Limbic
	20-30Hz	0.5	2.5	6.5	2.5	Parietal
		7.5	4.5	3.5	2.2	Frontal
	25-35Hz	0.0	4.0	5.5	2.3	Parietal
		-2.0	-2.5	5.0	1.8	Parietal
	30-40Hz	0.0	2.5	6.0	3.6	Parietal
		1.5	-3.0	4.5	2.0	Parietal

Table 4.3 Summary of SAM Analysis results. The two largest peaks of activation (with pseudo-t values of greater than 1.5) are presented for each of the 10Hz frequency bands in the three 500ms time windows. Co-ordinates are in standard CTF space (cm). A location estimate is also provided

SAM comparisons were made between the active recognition phase and the passive fixation (baseline) phase. As only 500ms of baseline activity was recorded, comparisons were split into three time windows to ensure that there was the same amount of time being compared across the two phases (i.e. 500ms). Furthermore, the analysis was conducted

over six overlapping 10Hz frequency bands, 5-15, 10-20, 15-25, 20-30, 25-35 and 30-40 Hz. A large number of peaks were observed, although only those exceeding a pseudo-t value statistic of greater than 1.5 were considered. This value was selected as this ensured that only values exceeding the 75th percentile were analysed. Data presented in Table 4.3 summarises the two strongest activations for each frequency band (as indicated by the pseudo-t value) within the three time windows. It can be seen that considerably more activation was suggested by the SAM analysis than from the dipole fitting.

Wavelet Mann-Whitney spectrograms were computed for the five strongest SAM peaks in each of the three time windows (summarised in Table 4.4).

Peak	Frequency Band	Co-ordinates			Peak T value	Location
0-500ms						
A	15-25 Hz	-3.5	3.0	1.5	2.6	Occipital
B	30-40 Hz	-0.5	3.0	6.0	2.6	Parietal
C	25-35 Hz	-2.0	-2.0	5.0	2.5	Parietal / Occipital
D	5-15 Hz	-1.5	-2.5	6.0	2.3	Parietal
E	20-30 Hz	0.5	2.5	6.5	2.3	Posterior Parietal
500-1000ms						
A	15-25 Hz	2.0	5.0	4.0	3.2	Frontal / Temporal
B	25-35 Hz	2.5	5.5	4.0	2.5	Parietal / Temporal
C	20-30 Hz	0.5	2.5	6.5	2.3	Parietal
D	25-35 Hz	1.0	4.0	5.5	2.3	Parietal
E	5-15 Hz	8.5	-0.5	4.0	2.2	Prefrontal Cortex
1000-1500ms						
A	30-40 Hz	0.0	2.5	6.0	3.6	Parietal
B	20-30 Hz	0.5	2.5	6.5	2.5	Parietal
C	15-25 Hz	0.5	5.0	5.0	2.3	Parietal
D	25-35 Hz	0.0	4.0	5.5	2.3	Parietal
E	20-30 Hz	7.5	4.5	3.5	2.2	Frontal

Table 4.4 Summary of the 5 strongest SAM peaks within each of the three 500ms time-windows. Pseudo-t statistics provide this measurement of strength, the strongest peaks having the largest pseudo-t values.

For each of the spectrograms in the 0-500ms time window (Figure 4.7), significant ERD could be seen within the frequency band from which the initial peak of activation was identified. This was more evident in the strongest peak spectrograms. For example in Figure 4.7A, a band of ERD was seen in the 15-25Hz range at 200-400ms. There was also a band of ERD covering 10-20Hz from 200-600ms. The pattern of activation in Figure 4.7B was more event-related with bursts of ERD occurring between 0-500ms in the 30-40Hz range. This was similar to the pattern in Figure 4.7C, with spikes of ERD in the 25-

35Hz range. The ERD was less obvious in the desired frequency band in Figure 4.7D, although ERD did extend from 10Hz to 30Hz between 0-500ms. There was definite ERD in the 20-30Hz range for Figure 4.7E, specifically a band at 200-300ms and again covering 500ms.

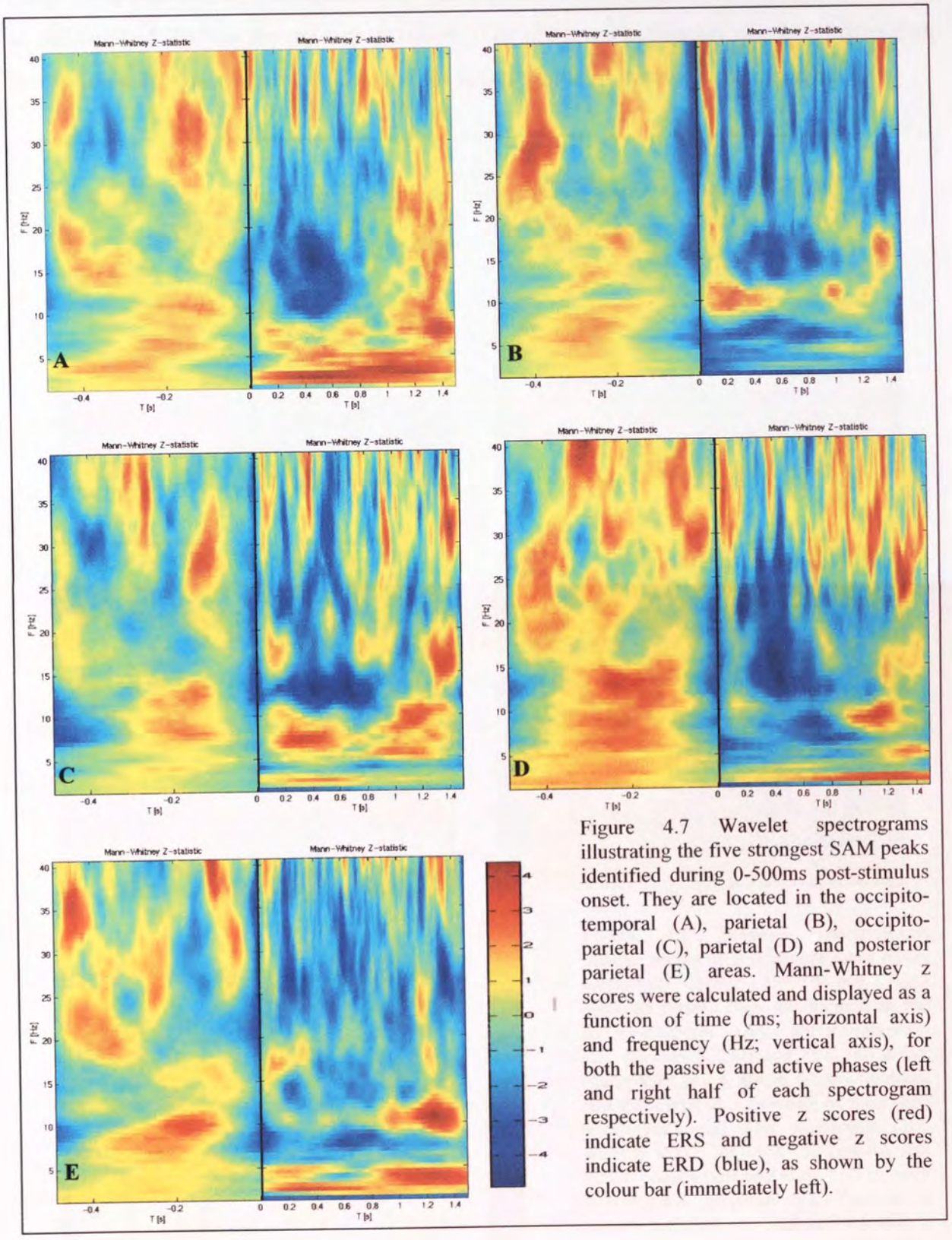


Figure 4.7 Wavelet spectrograms illustrating the five strongest SAM peaks identified during 0-500ms post-stimulus onset. They are located in the occipito-temporal (A), parietal (B), occipito-parietal (C), parietal (D) and posterior parietal (E) areas. Mann-Whitney z scores were calculated and displayed as a function of time (ms; horizontal axis) and frequency (Hz; vertical axis), for both the passive and active phases (left and right half of each spectrogram respectively). Positive z scores (red) indicate ERS and negative z scores indicate ERD (blue), as shown by the colour bar (immediately left).

In the 500-100ms band (Figure 4.8.), the reported ERD was also more evident in the strongest peak spectrograms. For Figure 4.8.A, the block of ERD was within the 15-25Hz range and covered the entire 500-1000ms time window. In Figure 4.8B it was less obvious although there was some indication of ERD spikes within a band of ERS in the 25-35Hz range. This was similar for Figures 4.7C and D, the onset more obvious in Figure 4.7D due to the band of ERS in the preceding 500ms. The observed activation was less obvious in the Figure 4.8E spectrogram, which had the lowest value of the five peaks analysed.

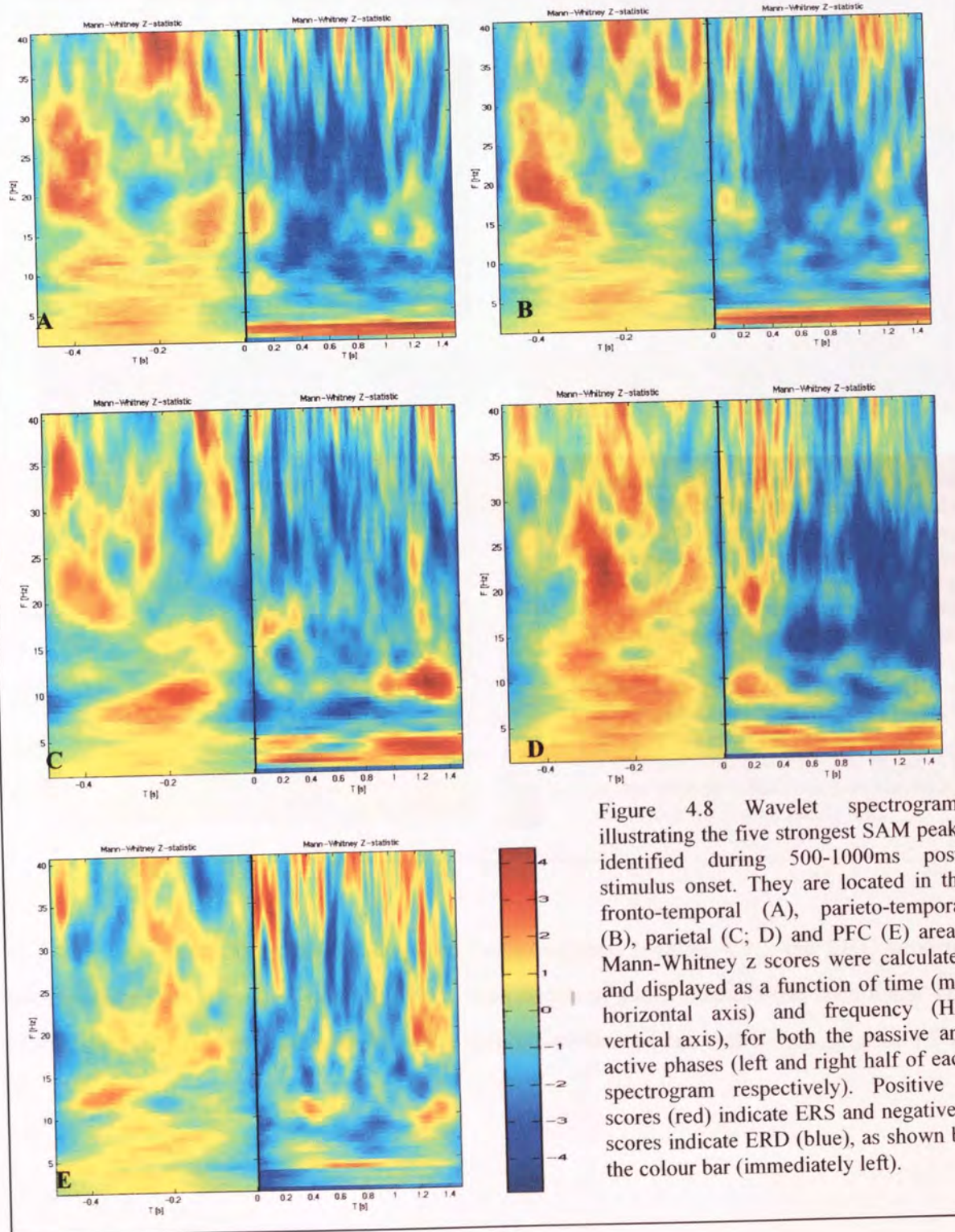


Figure 4.8 Wavelet spectrograms illustrating the five strongest SAM peaks identified during 500-1000ms post-stimulus onset. They are located in the fronto-temporal (A), parieto-temporal (B), parietal (C; D) and PFC (E) areas. Mann-Whitney z scores were calculated and displayed as a function of time (ms; horizontal axis) and frequency (Hz; vertical axis), for both the passive and active phases (left and right half of each spectrogram respectively). Positive z scores (red) indicate ERS and negative z scores indicate ERD (blue), as shown by the colour bar (immediately left).

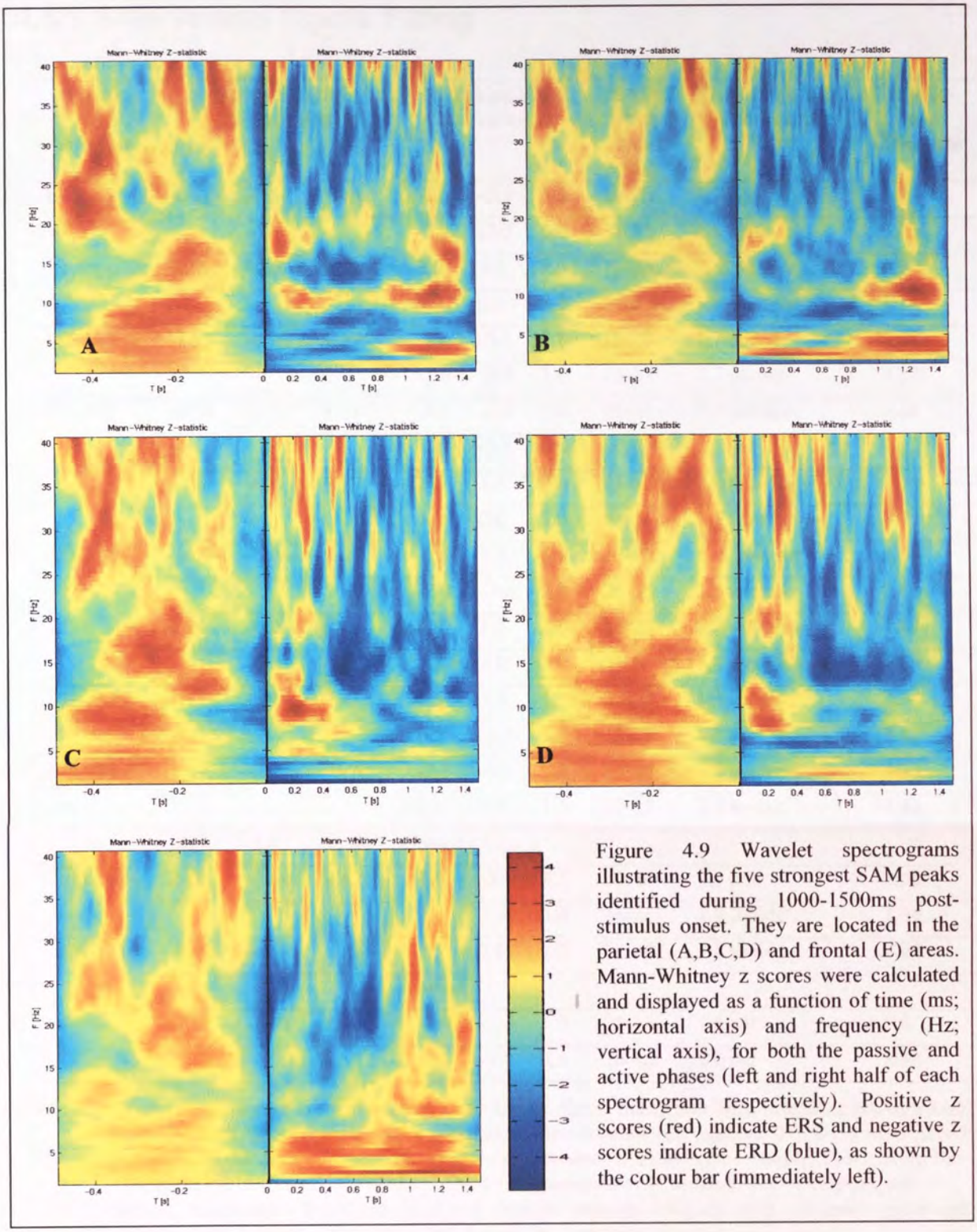


Figure 4.9 Wavelet spectrograms illustrating the five strongest SAM peaks identified during 1000-1500ms post-stimulus onset. They are located in the parietal (A,B,C,D) and frontal (E) areas. Mann-Whitney z scores were calculated and displayed as a function of time (ms; horizontal axis) and frequency (Hz; vertical axis), for both the passive and active phases (left and right half of each spectrogram respectively). Positive z scores (red) indicate ERS and negative z scores indicate ERD (blue), as shown by the colour bar (immediately left).

For the final 500ms, for all displayed spectrograms (Figure 4.9.), the ERD reported was illustrated in an evoked-potential way, with bands of ERD interspersed with ERS. This was particularly evident in the SAM peaks located within the parietal cortex (Figure 4.9 A-D).

4.4.3 SAM versus Dipole Fitting

Dipole Time Window (ms)	Dipole Solution Co-ordinates			Matching SAM co-ordinates			SAM Freq Band (Hz)	SAM Peak Value and location	Euclid-ean Distance
106-128	-0.38	-1.54	2.46	-3.0	-3.5	3.5	10-20	1.7 occ	3.43
				-2.0	-2.0	5.0	25-35	2.5 par/occ	3.05
	2.26	0.65	0.79	2.0	1.5	2.0	15-25	2. 2 mtl-cing	1.5
				5.0	2.0	3.0	5-15	1.5 front/temp	3.77
165-187	-1.02	-0.96	1.39	-3.0	-3.5	3.5	10-20	1.7 occ	3.85
				-2.0	-2.0	5.0	25-35	2.5 par/occ	3.88
229-253	-0.24	-1.32	3.15	-2.0	-2.0	5.0	25-35	2.5 par/occ	2.64
				-1.5	-2.5	6.0	5-15	2.3 par	3.33
	2.26	0.65	0.79	2.0	1.5	2.0	15-25	2.2 mtl-cing	1.50
				5.0	2.0	3.0	5-15	1.5 front/temp	3.77
483-502	-0.00	-0.06	4.01	-2.0	1.5	5.5	10-20	1. 5 post par	2.94
				-2.0	-2.0	5.0	25-35	2.5 par/occ	2.96
	2.26	0.65	0.28	2.0	1.5	2.0	15-25	2.2 mtl-cing	1.94
				5.0	2.0	3.0	5-15	1.5 front/temp	4.09
701-720	1.17	-0.19	2.41	2.5	1.5	1.5	25-35	1.5 limbic	2.34
				0.5	-1.5	5.5	15-25	1.7 par	3.42
798-818	1.47	-2.21	-0.70	-2.5	-3.5	0.0	15-25	1.5 occ/temp	4.23
				2.5	1.5	1.5	25-35	1.5 limbic	4.43
	14.4	-1.87	11.44*	None					
1005-1024	2.10	-2.40	2.62	1.5	-3.0	4.5	30-40	2.0 par	2.06
				2.0	1.5	2.0	15-25	1.8 limbic	3.95
1094-1110	-0.64	0.93	-2.68	2.5	2.0	1.0	30-40	1.8 limbic	4.95
				None					
	-1.69	-3.91	2.40	-2.0	-2.5	5.0	25-35	1.8 par	2.8
				1.5	-3.0	4.5	30-40	2.0 par	3.93

Table 4.5 Direct comparison of cortical sources identified by dipole fitting and those identified through SAM analysis. All SAM peaks within the appropriate time-window (for example 0-500ms) were directly compared to the dipole solution locations in similar time windows (for example, 106-128ms, 165-187ms, 229-253ms and 483-502ms). Abbreviations used are as follows; occ – occipital, par – parietal, front/temp – fronto-temporal, mtl – medial temporal lobe, mtl-cing – cingulate gyrus and mtl structures, par/occ – parieto-occipital, post par – posterior parietal.

In order to determine which method of analysis was most suitable for recognition memory experiments, the co-ordinates of the peaks obtained from the SAM analysis were directly compared to those obtained from the dipole fitting procedure. This was done through calculation of the Euclidean distance between these co-ordinates, i.e. the distance between two points in three dimensional space. This essentially computes a distance between these values, measured in cm^3. All SAM peaks were directly compared to all

dipole peaks in the relevant time windows. The data are summarised in Table 4.5. Only those comparisons that produced Euclidean distances of less than 5cm3 are reported as it was believed that sources located any further away from each other were unlikely to be related to the same cortical process.

Figure 4.10 illustrates the calculated Euclidean distances. For the most stable dipoles, as determined by the number of times they returned to the same place, it was clear that a SAM peak was not necessarily located any closer to this peak than for the less stable dipole solution. For example, for all of the time windows, with the exception of that between 798 – 818ms, the smallest Euclidean distance was for the less stable dipole. The data was further analysed by considering each of the time windows individually and directly comparing the SAM and dipole data. Each co-ordinate of the dipole locations found and their closest SAM peak were further analysed. Wavelet spectrograms were calculated for each co-ordinate illustrating the activation over time of that particular brain region.

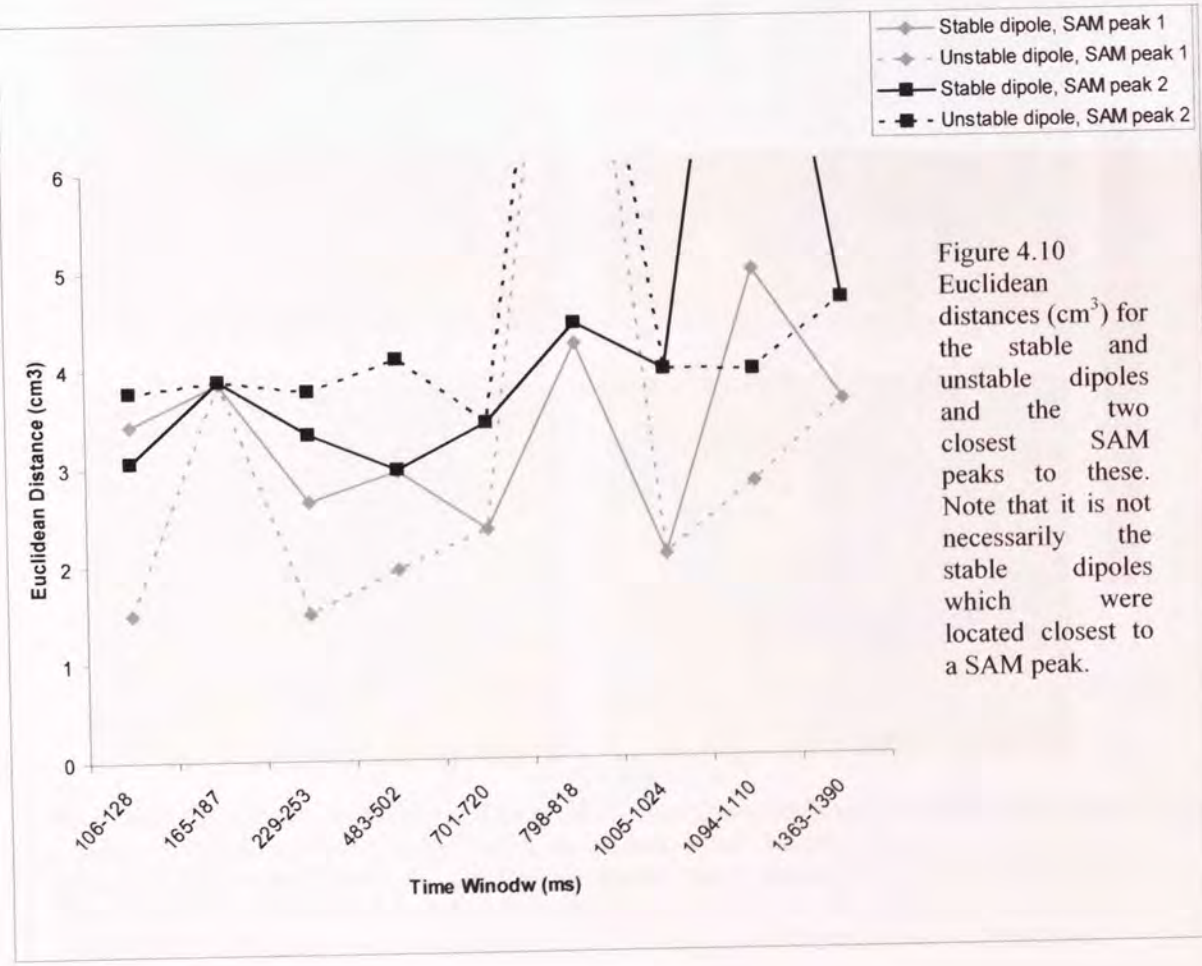


Figure 4.10 Euclidean distances (cm^3) for the stable and unstable dipoles and the two closest SAM peaks to these. Note that it is not necessarily the stable dipoles which were located closest to a SAM peak.

For the first peak after stimulus onset (106-128ms), the smallest Euclidean distance (1.5cm) was found between the second dipole location and a SAM peak in the 15-25Hz band. In the spectrograms (Figure 4.11) for the first dipole, located in the 106-128ms time window and corresponding SAM peak (Figure 4.11 A and B), it can be seen that for both locations, there was significant ERD (negative/blue) in the 10-25Hz range, beginning shortly after stimulus onset ~100ms and lasting until ~800ms post-stimulus onset. Although there was no definite activation between 106-128ms for the dipole spectrogram, there was a band of ERS covering 5-20Hz and ~28-40Hz at the time of dipole peak, with ERD seen covering the 20-28Hz range at the same point in time. It is feasible that this may have been the source of the dipole location. The SAM peak occurring in the 0-500ms time window was measured as 3.43cm from the centre of the dipole and the peak was clearly seen in the spectrogram covering the 10-20Hz range and lasting between 100-800ms post-stimulus onset.

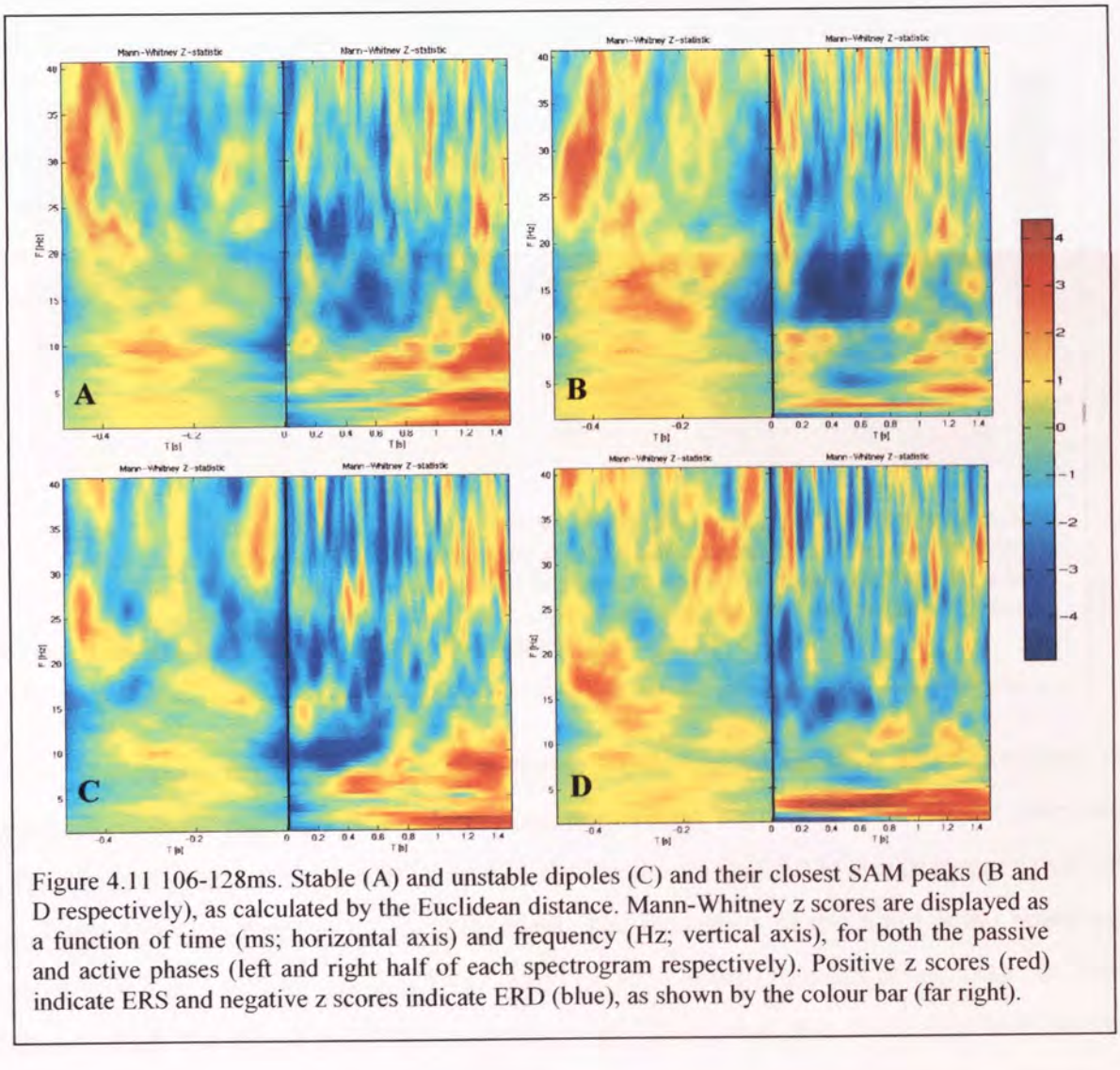


Figure 4.11 106-128ms. Stable (A) and unstable dipoles (C) and their closest SAM peaks (B and D respectively), as calculated by the Euclidean distance. Mann-Whitney z scores are displayed as a function of time (ms; horizontal axis) and frequency (Hz; vertical axis), for both the passive and active phases (left and right half of each spectrogram respectively). Positive z scores (red) indicate ERS and negative z scores indicate ERD (blue), as shown by the colour bar (far right).

Although dipole 2 for 106-128ms time window was considered to be less stable, a SAM peak was located only 1.5cm away from the centre of the dipole. Furthermore, the spectrograms for the two locations follow a similar pattern (Figure 4.11.C and D for the dipole and SAM peaks respectively), particularly in the 15-25Hz band, with a band of ERD at about 100ms.

The dipole located at 165-187ms had a corresponding SAM peak 3.85cm away. As with the first time window, it appeared that in the spectrogram for the dipole (Figure 4.12.A), a band of ERS at about 150ms covered 0-15HZ and 25-40Hz, with ERD between 15and 20Hz. There was also a block of ERD between 10and 20Hz from 200-600ms, which corresponded in part to the SAM spectrogram (Figure 4.12.B) where ERD could be seen in the 10-20Hz range from 200ms to 800ms. Of further interest was the location of the SAM dipole in the occipital cortex and the fact that this same SAM peak was the closest SAM peak to both the dipoles located at 106-128ms and 165-187ms.

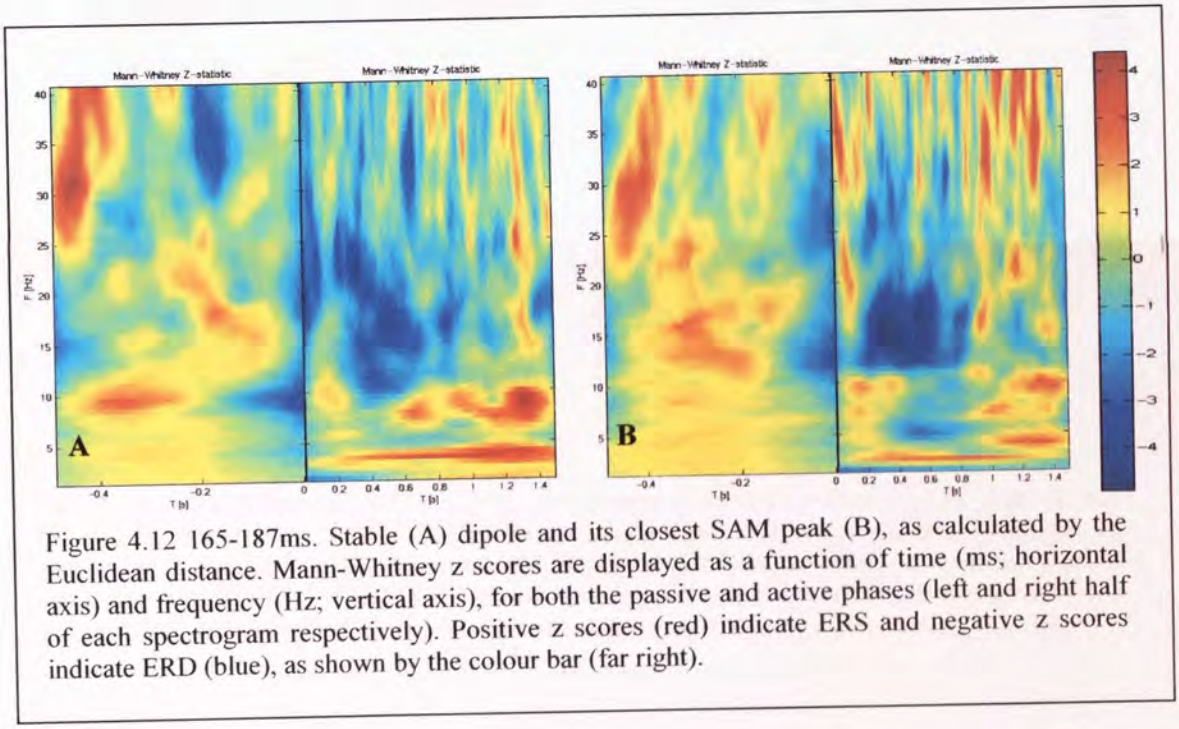


Figure 4.12 165-187ms. Stable (A) dipole and its closest SAM peak (B), as calculated by the Euclidean distance. Mann-Whitney z scores are displayed as a function of time (ms; horizontal axis) and frequency (Hz; vertical axis), for both the passive and active phases (left and right half of each spectrogram respectively). Positive z scores (red) indicate ERS and negative z scores indicate ERD (blue), as shown by the colour bar (far right).

The closest SAM peak to the most stable dipole located between 229-253ms was in a parietal-occipital region, 2.64cm way. A corresponding band of ERD could be observed in both spectrograms (Figure 4.13 A and B for the dipole and SAM peaks respectively) at about 200-400ms, covering the 10-25Hz band. The frequency of the SAM peak, however, was 25-35HZ and a small band of ERD could be seen within this frequency range at 200-250ms in both the dipole and SAM spectrograms. There was also some similarity in the pattern of activation for these locations within the slower frequency bands, specifically a

band of ERS continuing across the entire time window (0-1500ms) in 0-10Hz range and then a band of ERD in the 10-15Hz range covering 0-1800ms. Although the second dipole was located only 1.5cm away from a SAM peak, the patterns of activation between the two locations were not as similar (Figure 4.13.C and D for the dipole and SAM peak respectively). There was some evidence of ERD in the 15-25Hz range in both locations at about 150-200ms for the SAM peak and between 200-250ms in the dipole peak.

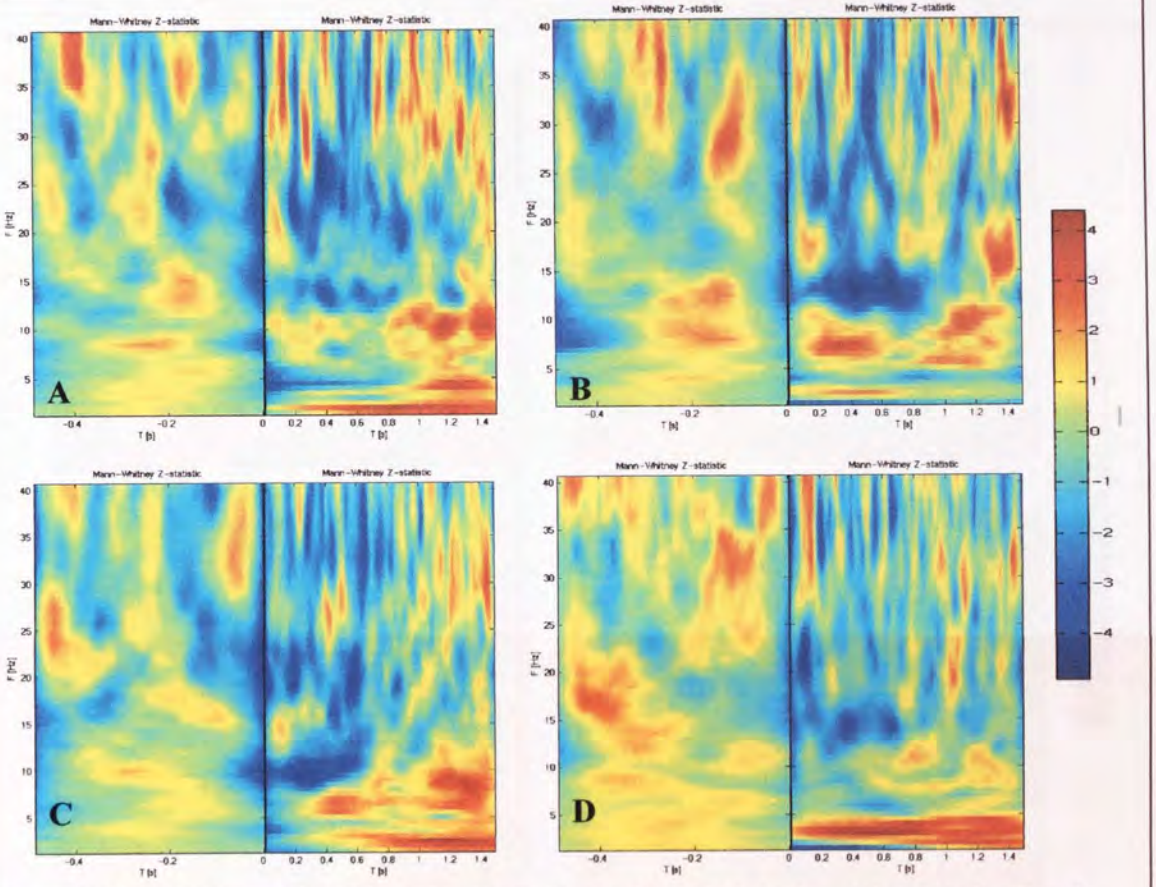


Figure 4.13 229-253ms. Stable (A) and unstable dipoles (C) and their closest SAM peaks (B and D respectively), as calculated by the Euclidean distance. Mann-Whitney z scores are displayed as a function of time (ms; horizontal axis) and frequency (Hz; vertical axis), for both the passive and active phases (left and right half of each spectrogram respectively). Positive z scores (red) indicate ERS and negative z scores indicate ERD (blue), as shown by the colour bar (far right).

Two dipoles were located separately in the time window 483-502ms. SAM peaks were located 2.94cm and 1.94cm away from the first and second dipoles respectively. Furthermore, these were located in different cortical regions, posterior parietal and superior temporal extending into the cingulate cortex, respectively. For dipole1, ERD could be seen at the reported time window (Figure 4.14.A), around 500ms covering the 20Hz frequency band. For the corresponding SAM peak (Figure 4.14.B), ERD was more obvious and covering the 5-25Hz bands between 300ms and 800ms, with the strongest activation covering the 10-20Hz band at around 500ms.

The less stable second dipole was located 1.94cm away from a SAM peak. Considering the two spectrograms, there was very little similarity in the reported time window (Figure 4.14.C.and D for the dipole and SAM peak respectively). Between 0-200ms, the SAM spectrogram revealed a band of ERD in the desired 15-25Hz band. There was a small amount of ERD in the same time window for the dipole spectrogram but at the desired 483-502ms time window, no definite ERD could be seen, with a small amount in the 30-40Hz band.

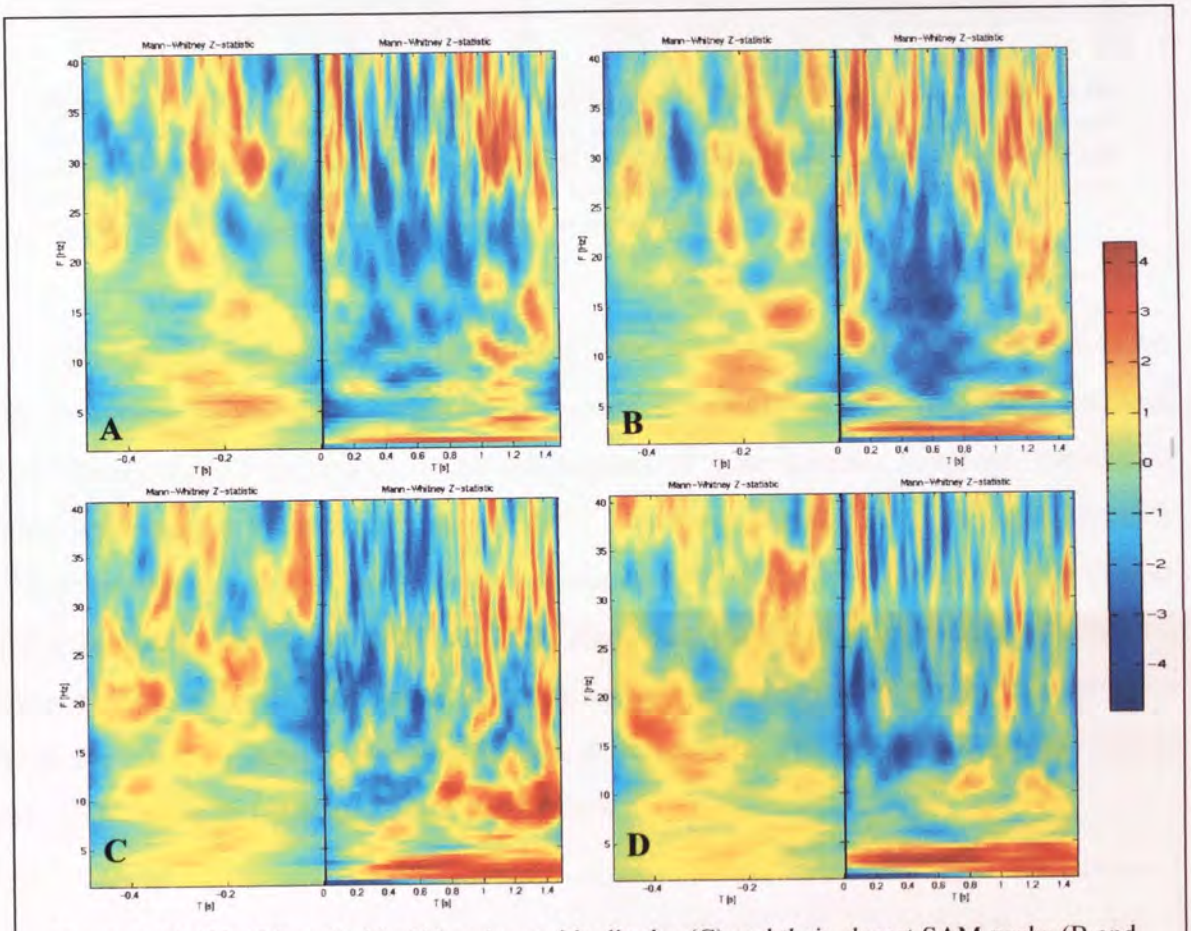


Figure 4.14 483-502ms. Stable (A) and unstable dipoles (C) and their closest SAM peaks (B and D respectively), as calculated by the Euclidean distance. Mann-Whitney z scores are displayed as a function of time (ms; horizontal axis) and frequency (Hz; vertical axis), for both the passive and active phases (left and right half of each spectrogram respectively). Positive z scores (red) indicate ERS and negative z scores indicate ERD (blue), as shown by the colour bar (far right).

The closest SAM peak to the dipole located in the 701-720ms time window was 2.34cm away and situated in the limbic cortex. The dipole spectrogram (Figure 4.15.A) indicated that the dipole was in the 30-40Hz band, this being the only band of ERD during the desired time window. For the SAM peak (Figure 4.15.B), there was no obvious band of ERD in the 25-35Hz band in the 500-1000ms time window. This may be due to the peak value only being 1.5, and possibly not being significant.

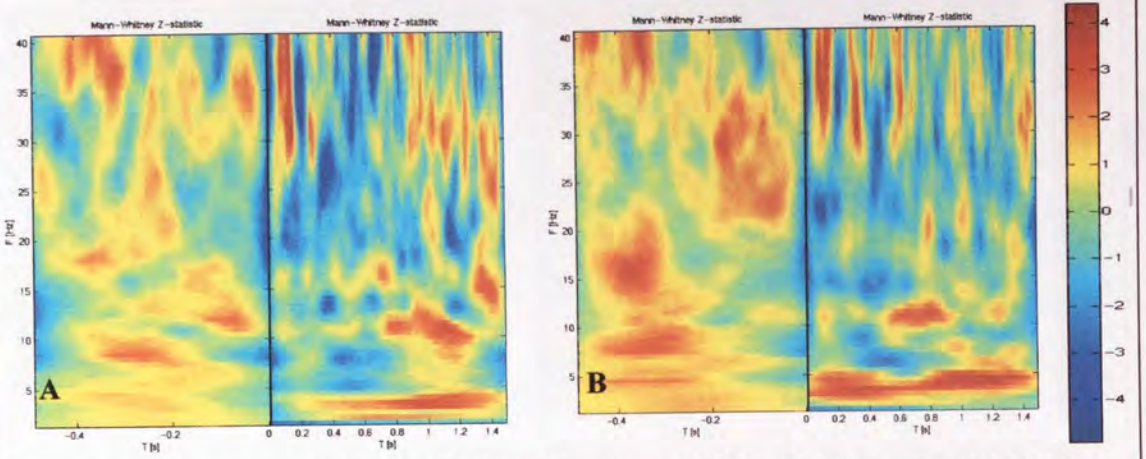


Figure 4.15. 701-720ms. Stable (A) dipole and its closest SAM peak (B), as calculated by the Euclidean distance. Mann-Whitney z scores are displayed as a function of time (ms; horizontal axis) and frequency (Hz; vertical axis), for both the passive and active phases (left and right half of each spectrogram respectively). Positive z scores (red) indicate ERS and negative z scores indicate ERD (blue), as shown by the colour bar (far right).

The dipole located in the 798-818ms time window was considered to be quite stable, returning to the same location on four of the five occasions (the other locating outside the head and being rejected). Its spectrogram (Figure 4.16.A), however, showed no definite activation at the desired time window. There was a small band of ERD covering the 25-35Hz frequency band and a large amount of ERS in the 15-25Hz band. The closest SAM peak was 4.23cm away in the 15-25Hz frequency band and in an occipital / temporal location (Figure 4.16.B). The small 1.5 peak value was mirrored by the lack of obvious ERD in the 15-25Hz band in the 500-1000ms time window. The majority if activation was in the 10-20Hz range between 200ms and 700ms.

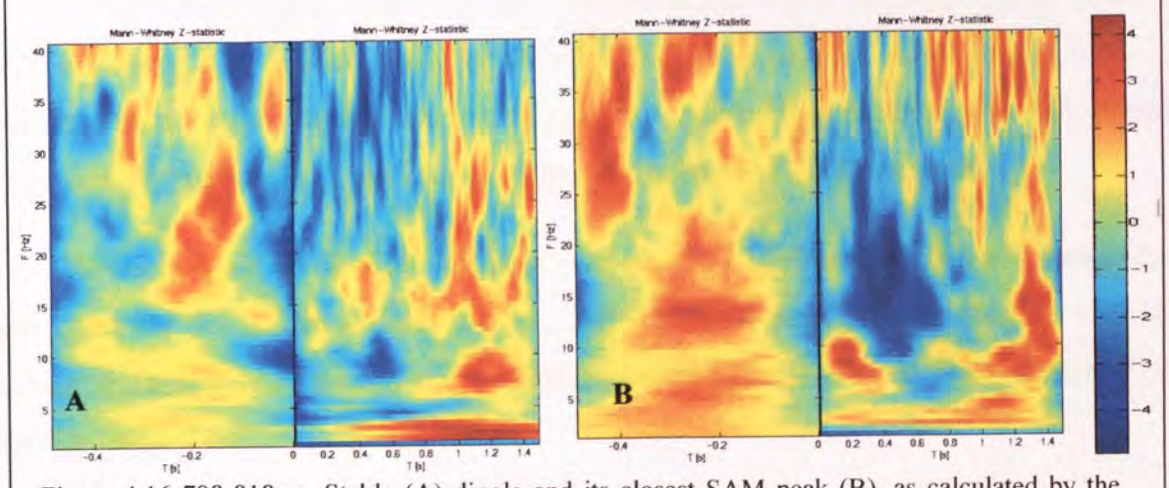


Figure 4.16 798-818ms. Stable (A) dipole and its closest SAM peak (B), as calculated by the Euclidean distance. Mann-Whitney z scores are displayed as a function of time (ms; horizontal axis) and frequency (Hz; vertical axis), for both the passive and active phases (left and right half of each spectrogram respectively). Positive z scores (red) indicate ERS and negative z scores indicate ERD (blue), as shown by the colour bar (far right).

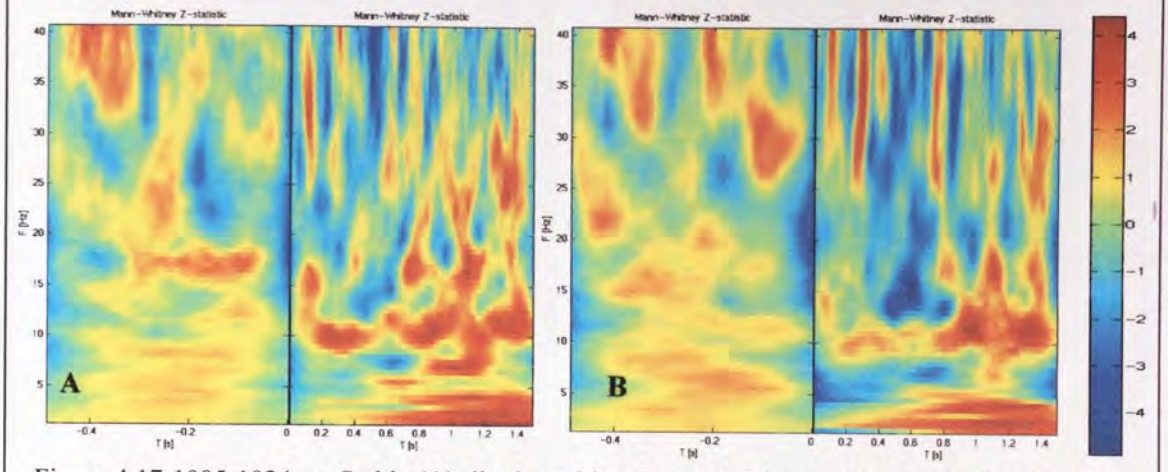


Figure 4.17 1005-1024ms. Stable (A) dipole and its closest SAM peak (B), as calculated by the Euclidean distance. Mann-Whitney z scores are displayed as a function of time (ms; horizontal axis) and frequency (Hz; vertical axis), for both the passive and active phases (left and right half of each spectrogram respectively). Positive z scores (red) indicate ERS and negative z scores indicate ERD (blue), as shown by the colour bar (far right).

In the 1005-1024ms time window, one dipole was located. The spectrogram, however, did not show any significant activation at the specified time window (Figure 4.17.A). The closest SAM peak was 2,06cm away but the spectrogram for this too did not show any significant activation at the specific time window (Figure 4.17.B.).

The spectrogram for the most stable dipole in the 1094-1110ms time window did not show any significant activation at the identified time (Figure 4.18.A). It had a SAM peak 4.95cm away, located in the limbic region (Figure 4.18.B.). This peak was identified as being ERS. Between 1000-1500ms ERS was observed in the desired frequency band of 30-40Hz at 1100-1200ms and 1300-1500ms.

For the second dipole (Figure 4.18.C), its corresponding SAM peak (Figure 4.18.D) was 2.8cm away. The spectrograms for these cortical regions were more similar in their appearance than the first dipole. There was still no identifiable activation, however, at the desired time for the dipole or in the desired frequency band of the SAM peak.

The final peak fitted with a dipole was at 1363-1390ms. Although visually the spectrogram for the dipole (Figure 4.19.A) and the SAM peak 3.62cm (Figure 4.19.B) away are quite similar, there is no specific activation at the desired time windows or frequency bands.

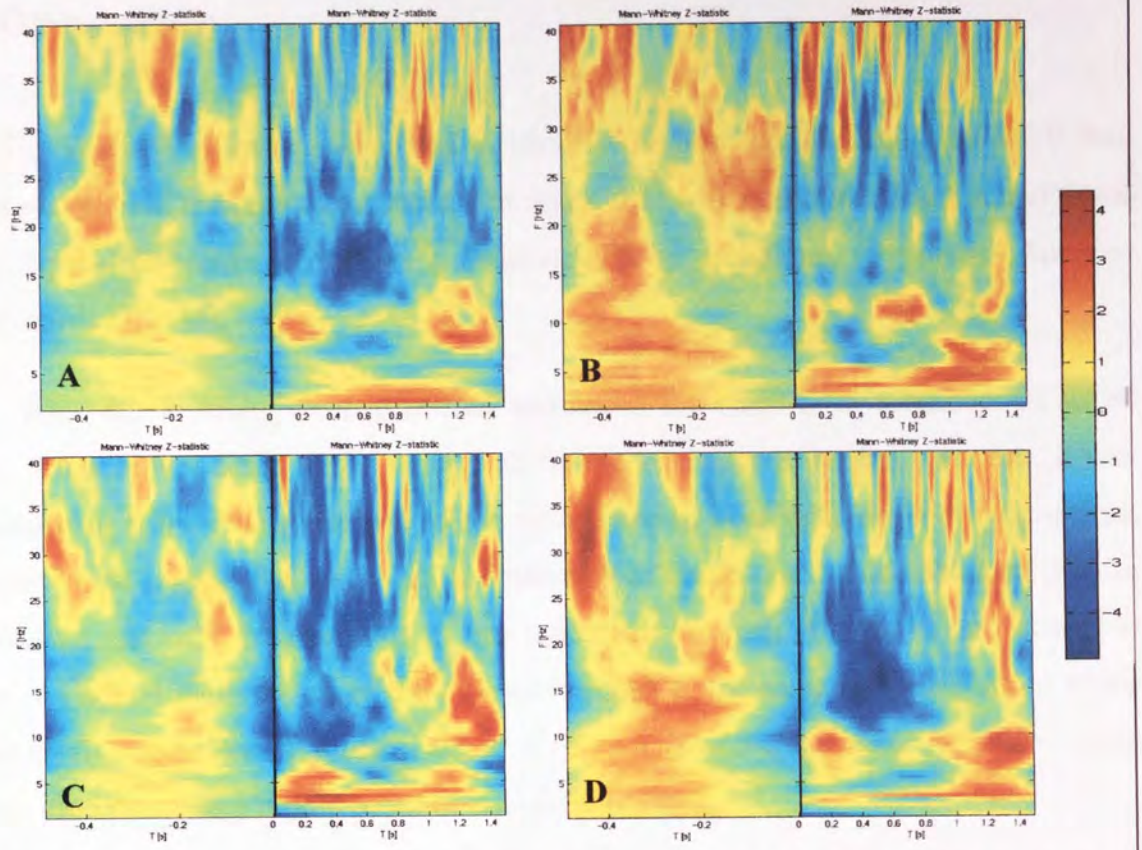


Figure 4.18. 1094-1110ms. Stable (A) and unstable dipoles (C) and their closest SAM peaks (B and D respectively), as calculated by the Euclidean distance. Mann-Whitney z scores are displayed as a function of time (ms; horizontal axis) and frequency (Hz; vertical axis), for both the passive and active phases (left and right half of each spectrogram respectively). Positive z scores (red) indicate ERS and negative z scores indicate ERD (blue), as shown by the colour bar (far right)

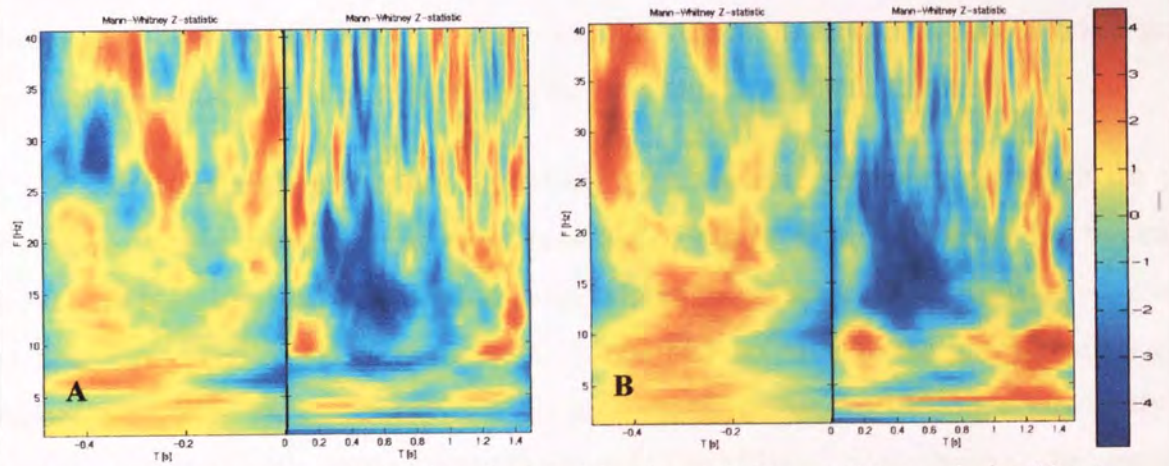


Figure 4.19 1363-1390ms. Stable (A) dipole and its closest SAM peak (B), as calculated by the Euclidean distance. Mann-Whitney z scores are displayed as a function of time (ms; horizontal axis) and frequency (Hz; vertical axis), for both the passive and active phases (left and right half of each spectrogram respectively). Positive z scores (red) indicate ERS and negative z scores indicate ERD (blue), as shown by the colour bar (far right)

4.5 Discussion

The aim of this investigation was to identify the best tool for analysing MEG data from a recognition memory experiment. The same data was analysed using the traditional MEG dipole fit tool and with a relatively new technique, Synthetic Aperture Magnetometry (SAM).

Nine dipole peaks were identified and tested for stability in a number of ways. Firstly, a dipole was fitted to the same peak from five different starting positions. It was suggested that if the dipole returned to the same location from different starting positions then this would suggest that the solution obtained was stable. The results obtained (Figure 4.4) showed that with the exception of one peak (that between 1094-1110 ms, located to limbic or parietal regions), all of the dipoles returned to the same end location on either four or all five occasions. Therefore, taken on its own, it would seem that for at least eight of these time windows a dipole could be consistently fitted.

The second analysis of the dipole fit data involved assessment of the χ^2 values obtained. Ideally a stable dipole solution should produce a χ^2 error of less than 1. The data (Figure 4.5) showed that all of the dipole solutions, whether the most stable dipole or not (as identified from the number of occasions the dipole returned to the same location), had a value of less than 2 and for those peaks between 400ms and 1500ms, below the ideal value. Consequently, if the χ^2 error value was simply used as the measure of consistency, the solution identified may have been a dipole location that on four other occasions might not have been found (as for the peaks covering the time windows 400 to 1500ms).

It was therefore hypothesised, that using a MC volume, in conjunction with the χ^2 error value, would provide an accurate measure of dipole stability. Ideally the volume should have been less than $1cm^3$, although acceptable values were usually considered to be less than $3cm^3$. The peaks between 0-400ms had MC volumes in the acceptable range, although they were not necessarily for the most stable dipole (as identified previously), especially for the early peaks (106-128ms and 229-253ms). Nevertheless, the spatial locations of these dipoles did correspond to the visual cortex, which is consistent with the image being present on the screen for 200ms.

Between 400-1300ms, the MC volumes for all of the dipole solutions, whether stable or not, significantly exceeded the acceptable volume. Consequently, it was difficult to

conclude that a stable solution has been located. For the final time window, a stable dipole location was indicated, the dipole locating to the same position five times and the χ^2 value and Monte Carlo volume were at acceptable levels. Looking at the spatial location of the dipole, it was located within the somatosensory area associated with finger movement, and as this time window corresponded with ES making a button-press response, it is possible to be confident about the dipole location.

It would seem that relatively stable solutions were found in the visual processing areas during the initial 200ms and in the somatosensory area between 1300 and 1500ms. There, was not however, any indication of such stable solutions between 400 and 1300ms. Perhaps, as this is the more demanding cognitive component of the task, stable solutions could not be found with only one dipole. This does not appear to be the case as although all had acceptable χ^2 values, none of the Monte Carlo volumes for the two-dipole solutions were acceptable and for only one peak was the same solution reached on more than one occasion.

Considering the data from the one and two dipole solutions, it would seem that relatively stable single dipole models were observed during the early and late time windows (specifically, 0-200ms and 1300-1500ms). No dipole solutions (either using single or multiple dipole models) met the criteria for stability during the cognitive component of the task (400-1300ms). This the highlights the potential disadvantage of dipole modelling for analysing cognitive function as it may be that multiple dipoles were present but not found due to their disruption of each other.

The SAM analyses produced data in three 500ms time windows and across six frequency bands. Only the strongest 25% of the peaks (i.e. peaks with a pseudo t-statistic of greater than 1.5) were recorded. In total, 32, 44, and 16 SAM peaks were identified in the 0-500ms, 500-1000ms and 1000-1500ms time-windows, respectively, and the two strongest in each frequency band for each time window were reported. Further analyses were then conducted on the five strongest peaks in each time window.

For the 0-500ms time window, the strongest peak (a t-statistic of 2.6) was located in the occipital cortex, the remaining four extending over different regions of the parietal cortex. The spectrograms for these peaks, especially those with the largest values, displayed the reported activation in the appropriate frequency bands. It is suggested that these SAM peaks represented the presentation of the stimuli, resulting in activation of the

visual cortex and related occipital regions, with the parietal activation demonstrating engagement of attentional processes.

The activation displayed by the SAM analyses for the 500-1000ms was more widespread, extending over prefrontal, fronto-temporal, and parietal regions. Activation of these areas is consistent with the completion of a higher-order cognitive task (Table 1.1). This was further shown by the Mann-Whitney Wavelet spectrograms for the strongest peaks. The final time-window produced predominantly parietal activation. As for the dipole fit, it could be concluded that this represented the activation of the somatosensory and motor regions situated within the parietal cortex as ES prepared to make and completed the button-press response.

One point to note for all of the spectrograms shown is their ability to show the activation of the specific cortical region, as identified from the co-ordinates, in any time window and frequency band. This is an advantage of SAM, compared to dipole fitting, because the pattern of activation of multiple areas can be mapped over time, irrespective of how close together they are. It is possible to see the temporal resolution of when a brain region becomes activated and deactivated, therefore providing an indication of how long the region is active for, and eventually identify the specific role it has in. and determine how long it is activated for at any one time. This may enable more detailed cortical networks to be identified, which would be especially useful in cognitive paradigms such as recognition memory.

The dipole fit and SAM analysis data were directly compared through the calculation of the Euclidean distance between each dipole location and all identified SAM locations. The two closest SAM peaks to each dipole (both stable and unstable) were reported. Wavelet spectrograms were then computed for each dipole and its closest SAM peak. It was predicted that this would demonstrate any similarities between the dipole data and SAM data.

Looking at the Euclidean distances independently, it was demonstrated that some of the smallest distances were between SAM peaks and the dipole considered to be less stable. This is interesting for the fact that it suggests that although the dipole data is not particularly reliable for these locations, the SAM data would suggests that there is some activation close to that region.

Although some similarities were seen between the dipole spectrograms and the corresponding SAM spectrograms, even those with relatively short Euclidean distances it does not appear that the dipole located to the exact same location as a SAM peak. Some of this error may be due to the fact that for some of the dipoles, the closest SAM peak only had small t-statistic values, for example of about 1.5. From the analysis of the SAM data alone, it was suggested that only the strongest SAM peaks provided accurate representation of activation. Other peaks with pseudo-t values of 1.5 were identified, indicating that there was also a change in activation from baseline measures for other regions. However, they may not necessarily be directly involved in memory processing, for example, but may reflect other processes such as attention. It may therefore be that this associative activation interferes with the dipolar field of the activity and results in error in the location of the dipole solutions.

What can be concluded from these findings? This pilot experiment was conducted to determine whether two methods of MEG analysis, ECD and SAM, could be used to identify the functional areas reported in previous fMRI, PET and EEG studies of recognition memory. This experiment did this by simultaneously analysing the same recognition memory data with both SAM and a current dipole modelling procedure. As hypothesised, both the dipole and SAM analyses of MEG data identified the prefrontal and medial temporal activations, consistent with previous neuroimaging studies.

It was further predicted, that as the successfulness of both procedures for analysing data involving evoked responses has been previously documented, both methods should be successful in locating the neural activity for the evoked-type-responses of the recognition memory task, i.e. the stimulus onset and the button-press response. In this study, the most evoked-type response was for the onset of the stimulus in occipital regions and it was within the corresponding time-windows that the dipole solutions were reasonably stable. Although an identical corresponding SAM peak was not identified, the large number of occipital and parietal SAM peaks within the same time frame is encouraging. It might be that these represented association visual and attentional areas, which the dipole fit could not detect. The same could also be said for the final time-window during which ES was required to perform a button-press response.

However, the different assumptions for the ECD and SAM indicated that for the more cognitive demanding component of the task, different cortical activations, in terms of location and latency, may be identified by the two techniques. As hypothesised, for the

main cognitive component of the task, several dipole solutions were identified in frontal and temporal regions, although these did not satisfy the criteria for stability. The large number of SAM peaks identified, which extended over different regions of the cortex suggests that because of the complexity of the task, the activity is widespread, consistent with the diverse activation reported by previous neuroimaging studies.

This data suggests that both dipole modelling and SAM analysis can be used to analyse the cortical activation recorded by MEG, particularly for sensory stimuli. However, the lack of stability for the dipole solutions during the cognitive part of the task suggests that neighbouring activations disrupt closely located dipoles. For dipole modelling to work for recognition memory studies, therefore, a successful dipole fit analysis would have to enable a large number of overlapping dipoles to be located, and thus is very unrealistic. SAM provides a way of doing this as multiple, closely located regions can be identified on a millisecond time-scale, and do not disrupt each other. Although the strength of the peaks varies, some not reaching significance, a large number of strong peaks are identified and can be used for further analyses. This study has shown that SAM has successfully identified similar cortical regions to those displayed in previous neuroimaging studies. For the subsequent MEG studies, therefore, SAM is an appropriate analysis tool to use to interrogate the neural correlates of recognition memory.

4.6 Concluding Remarks

This data suggests that both dipole modelling and SAM analysis can be used to analyse the cortical activation recorded by MEG, particularly for sensory stimuli. However, the lack of stability for the dipole solutions during the cognitive part of the task suggests that neighbouring activations disrupt closely located dipoles. For dipole modelling to work for recognition memory studies, therefore, a successful dipole fit analysis would have to enable a large number of overlapping dipoles to be located, and thus is very unrealistic. SAM provides a way of doing this as multiple, closely located regions can be identified on a millisecond time-scale, and do not disrupt each other. Although the strength of the peaks varies, some not reaching significance, a large number of strong peaks are identified and can be used for further analyses. This is essential for the development of our understanding of recognition memory processes, with the ultimate aim of determining a cortical network for this complex process. This study has shown that SAM has successfully identified similar cortical regions to those displayed in previous neuroimaging studies. For the subsequent MEG studies, therefore, SAM is an appropriate analysis tool to use to interrogate the neural correlates of recognition memory.

5 VISUAL RECOGNITION MEMORY OF OBJECTS AND WORDS: AN INVESTIGATION OF HEMISPHERIC ASYMMETRY

5.1 Overview

Neuroimaging literature indicates that there is some controversy over the roles of the left and right hemispheres in recognition memory tasks. Some authors suggest that the left and right hemispheres (particularly in the frontal and temporal lobes) are specialised for encoding and retrieval respectively (the 'task-specific' hypothesis) (Tulving, Kapur, Craik et al, 1994). Others suggest that the left and right hemispheres are involved in recognition memory for words and objects, respectively (the 'modality-specific' hypothesis) (McDermott, Buckner et al, 1999; Lee et al, 2000). The aims of this study were to demonstrate the effectiveness of magnetoencephalography (MEG) as a tool for studying higher-order cognitive tasks, extend the research on recognition memory and test the 'task-specific' and 'modality-specific' hypotheses.

Objects and their corresponding names were presented separately as stimuli in two recognition memory experiments. In each experiment, a fixation point was presented for 1000ms, followed by the stimulus for 200ms, the fixation point for a further 1000ms, and finally a cue indicating that participants should respond. The responses were living / non-living categorisation and old / new identification in the encoding and recognition phases, respectively. In the current study, a relatively new analysis technique, Synthetic Aperture Magnetometry (SAM) was used to identify the brain areas activated during encoding and recognition for both words and objects.

Direct comparisons between encoding and recognition revealed event-related desynchronisation (ERD) during the recognition phase. Hemispheric and regional differences within this recognition phase were observed between objects and words, especially within two smaller 500ms windows. Specifically, objects activated the left superior and medial frontal gyri, whilst words activated the left inferior frontal and temporal gyri. Within the right hemisphere, ERD was seen in middle, frontal, precentral and fusiform gyri for objects and in the middle temporal lobe for words. However both stimulus modalities also elicited ERD in identical cortical regions. In addition, no old / new

effect during the recognition phase was observed for either objects or words. The results are considered with respect to previous neuroimaging literature and the implications for hemispheric specialisation in encoding and recognition are discussed. It is suggested that neither the 'task-specific' nor the 'modality-specific' hypothesis can account fully for the hemispheric differences observed in recognition memory tasks. Furthermore, the pattern of activation observed in these tasks may reflect a distributed cortical network for recognition memory, which includes modality specific areas, and which is dependent upon encoding strategy, the development of semantic associations and also the temporal dynamics of the system.

5.2 Introduction

In everyday life, episodic memory is associated with the recall of previously learned or encountered material and in recent years, functional imaging techniques have enabled us to investigate the brain areas involved when recalling or recognising information. In general, these neuroimaging studies have demonstrated differential involvement of frontal, parietal and temporal regions in accurate encoding, retrieval and recognition. In particular, the anterior prefrontal cortex (e.g. Cabeza and Nyberg, 1997), medial temporal lobe (MTL) (e.g. Fletcher et al, 1997; Schacter and Wagner, 1999) and posterior medial parietal cortex (e.g. Fletcher et al 1997; Rugg et al, 1996; Fletcher, Frith, Grasby et al, 1995; Markowitsch, 1997) have been identified as the important cortical regions involved in encoding and retrieval in recognition memory.

The prefrontal cortex is involved in both encoding and recognition tasks. Cabeza and Nyberg (1997) demonstrated that there is greater left lateralised activation evident during encoding and right during episodic memory retrieval. Furthermore, it appears that only a localised area of the right anterior prefrontal cortex is involved in recognition memory tasks, specifically a small region of anterior Brodmann area (BA) 10 (Buckner, 1996).

PET studies have also demonstrated that the MTL is activated in recognition memory tasks (reviewed in Fletcher et al, 1997). In addition, patient studies using fMRI have indicated that medial temporal structures are important in recognition memory. For example, Buckner and Koustaal (1998) reported a patient (PS) who had a lesion in the MTL. Imaging during a word judgement and subsequent recognition memory task showed that, although the prefrontal cortex was significantly activated during the encoding task, PS

was unable to remember any of the stimuli. The authors concluded that the lesion within the MTL was responsible for this impairment in word recognition, thus suggesting the importance of this region for accurate recognition memory.

The involvement of other areas during recognition memory tasks have also been documented, specifically the medial parietal (Tendolkar et al, 2000; Rugg et al, 1997; Tulving, Kapur, Markowitsch, et al, 1994) and the right inferior frontal cortices (Tendolkar et al, 2000; Fletcher et al, 1997). The specific role that the medial parietal region plays in recognition memory still remains unidentified, as to date there have being no patient / lesion studies that address this issue. However, it has been suggested that medial parietal activation might reflect processes such as visual imagery and mnemonics adopted by individuals during recognition memory tasks (Fletcher et al, 1997).

One topical issue in functional imaging research on recognition memory is the role of the right and left hemispheres in encoding and recognition of material. For instance, some studies have suggested that the left and right hemispheres are specialised for encoding and retrieval, respectively (Dolan and Fletcher, 1997; Fletcher et al, 1997; Nyberg, Cabeza and Tulving, 1996; Tulving, Kapur, Craik, et al, 1994). This HERA model is referred to as the 'task-specific' hypothesis. Fletcher, Shallice and Dolan (1998) claimed that the left prefrontal cortex (PFC) activation in encoding and right PFC activation in recognition / recall (Fletcher, Shallice, Frith, et al, 1998) was not linked to the type of material presented to participants (e.g. visual versus verbal) or to strategic factors, such as the intention to recall information. Instead they suggested that the left PFC activation observed during encoding tasks reflected a "requirement for processing study material with respect to memory" (p1244). Consistent with this, they found that increasing the involvement of semantic processes in the encoding task also resulted in an increase in left PFC (particularly in dorsolateral PFC (DLPFC)). Fletcher, Shallice, Frith et al (1998) suggested that the right PFC activation observed in recall or recognition phases of recognition memory tasks reflected the monitoring process required to optimise recall.

In contrast, others have suggested that the left and right hemispheres are specialised for verbal and visual material, respectively (the 'modality-specific' hypothesis) (McDermott, Buckner, et al, 1999; Lee, et al, 2000). For example, Lee et al (2000) reported a PET study that investigated the asymmetric involvement of frontal regions during episodic memory encoding and retrieval processes. Participants were scanned during encoding and recognition tasks for visual and verbal material. The stimuli were either

unpronounceable letter strings (e.g. ZXPQDF) or pronounceable non-words (e.g. pelnel) designed to encourage visual or verbal strategies, respectively. Regional cerebral blood flow (rCBF) was recorded during four conditions (visual and verbal stimuli in both encoding and recognition tasks). Conjunction analyses (Price & Friston, 1997) enabled the authors to identify regional cerebral blood flow (rCBF) which was specific to encoding and retrieval irrespective of stimulus modality and also rCBF specific to stimulus modality regardless of encoding or retrieval processes. During encoding, for both verbal and visual stimuli, significant rCBF changes were observed bilaterally within the PFC. For recognition, however, no significant PFC activity was observed for either class of stimuli. Furthermore, conjunction analyses revealed that, irrespective of task, significant rCBF changes were left-lateralised in the inferior frontal and middle temporal gyri for verbal material. Activation for the visual stimuli was predominantly right-lateralised in the DLPFC and inferior temporal gyrus. The authors concluded that this provided direct evidence for asymmetric frontal activation being dependent upon stimulus modality, and not the nature of the task (i.e. encoding versus retrieval).

In a recent study, Kohler et al (2002) tested whether there was hemispheric specialisation within the middle temporal lobe (MTL) structures, and if this was 'task-specific' or 'modality-specific'. Kohler et al (2002) used a PET study with objects and words. In the encoding phase, participants were presented with pictures of objects, or their corresponding names, and were asked to make a semantic judgement about the item (living or nonliving thing?). In the recognition phase, participants were presented with objects or words and asked to judge if the item had been presented in the encoding phase. Kohler et al suggested that the posterior right parahippocampal gyrus was involved in setting up memory traces for pictorial stimuli during encoding and in accessing these memory traces from pictorial cues during recognition. They also suggested that a more anterior region in the right parahippocampal gyrus may be specifically involved in accessing stored pictorial representations irrespective of modality at recognition phase. Objects, however, also activated the left MTL, and Kohler et al suggested that these regions may be involved in establishing an episodic record of objects based on their meaning, rather than their visual appearance. The role of the right and left hemispheres, and of different sub-regions of MTL in encoding and recognition of words was less clear. This study, however, did not find any clear evidence to support either the 'task-specific' or 'modality-specific' hypotheses of PFC activation as there was no predominantly left- or right-lateralised activation for either stimulus class or for either encoding or recognition tasks. .

5.2.1 MEG Studies of Recognition Memory

In addition to functional neuroimaging work using PET and fMRI, MEG has also been used as a tool to study recognition memory. In Tendolkar et al's (2000) study, words were visually presented (500ms) during the encoding and recognition phases. During the encoding phases, participants were presented with a series of 100 words and asked to create a short sentence with each word. In the recognition phases, participants were presented with a series of 200 stimuli (100 'old' and 100 'new') and asked to judge if the word had previously been shown or not (using a button-press response). The focus of Tendolkar et al's study was on the difference in the magnetic evoked fields (MEFs) for correctly recognised old (previously seen during an encoding task) and new (novel words only presented in the recognition phase words. They did not report on the different brain areas involved in episodic encoding and recognition tasks. However, using dipole fitting they did identify three dipoles during the recognition of 'old' stimuli. These were located in the right parahippocampal gyrus, right inferior frontal gyrus and left inferior parietal gyrus.

Tendolkar et al reported that, between 400 and 1000 ms after stimulus onset, there was a significant difference in the magnetic evoked fields (MEFs) for correctly recognised old and new words, and there was also an interaction between hemisphere and region. Dipole fitting was used to identify the location of differences between old and new items in more detail. For both old and new words, there were three dipoles identified in the right parahippocampal gyrus, right inferior frontal gyrus and left inferior parietal gyrus, respectively (see Table 5.1), but the strength of these dipoles was greater for old compared to new items. This supports earlier research, which showed that the MTL was associated with both encoding and retrieval, but responded more strongly to previously encountered stimuli (Gabrieli et al, 1997).

Region	Old words	New words
Left Inferior Parietal Gyrus	-35 -55 38	-34 -51 34
Right Hippocampal Gyrus	43 -19 4	44 -24 5
Right Inferior Frontal Gyrus	21 48 -10	27 45 -2

Table 5.1 Talairach co-ordinates of dipoles located by Tendolkar et al (2000) for old and new words

Duzel, Habib, Schott, Schoenfeld, Lobaugh, McIntosh, Scholz and Heinze (2003) performed a multivariate, spatio-temporal analysis of MEG time-frequency recognition memory data. An explicit word recognition memory experiment was conducted with participants required to perform a button press response to indicate whether a word was old or new. Their analysis revealed that the neural constructs of recognition memory were in the theta (4.5–7.5Hz) alpha (8–11.5Hz) and in some beta (12–19.5Hz) frequency bandwidths. At 400ms these neural oscillations were shown to be in the frontal lobe, with activity spreading across the temporal, parietal and occipital areas between 500ms and 700ms. Between 200–300 ms, gamma oscillations were observed in the left frontal lobe. Duzel et al reported that the occurrence of gamma and theta oscillations together in the early stages of the task was linked to the interaction between the hippocampus and the entorhinal and perirhinal cortices.

5.2.2 Aims and Hypotheses

The first aim of this study was to extend the research on recognition memory using MEG. Previous research has shown that prefrontal and medial temporal structures are significantly activated during the encoding and recognition phases and have also reported that additional cortical areas are involved in memory processing. Using Synthetic Aperture Magnetometry (SAM) (Robinson & Vrba, 1999), rather than the standard dipole fitting of the evoked response it is hypothesised that the involvement of prefrontal and medial temporal structures in encoding and recognition tasks would be identified and furthermore that the MEG data can be used to identify the additional cortical areas involved in recognition memory. Secondly, this study aimed to use MEG to assess the 'task-specific' and 'modality-specific' hypotheses of hemispheric specialisation in prefrontal regions during recognition memory tasks. It was predicted that if the 'task-specific' hypothesis was true, objects and words would both activate the left and the right PFC during encoding and recognition, respectively. In contrast, if the 'modality-specific' hypothesis was accurate words would activate the left PFC during both encoding and recognition, whereas objects would produce activation within the right hemisphere for both tasks. The technical details of SAM are summarised in the methods section (chapter 3) and described in detail in Robinson and Vrba (1999).

5.3 Methods

5.3.1 Participants

Thirteen healthy participants (nine females and five males, age range 22-51 years) volunteered to participate in the study. Six right-handed participants (four females and two males) were scanned during Experiment 1 (with objects as stimuli), and seven participants (four right-handed females, and three right-handed males) during Experiment 2 (with words as stimuli). Anatomical MRI scans had previously been taken for each of these individuals and were made available for the analysis.

5.3.2 Stimuli

In Experiment 1, participants were presented with objects taken from the Snodgrass and Vanderwart (1980) set of line drawings. In the encoding phase, there were 52 objects, 26 living and 26 non-living matched for frequency (Kučera and Francis, 1967). In the recognition phase, participants were presented with the same 52 stimuli and 52 new objects. The new items were 26 living and 26 non-living, matched for frequency to the stimuli presented in the encoding phase. The corresponding names of these objects were presented as words in Experiment 2.

5.3.3 Presentation of Stimuli

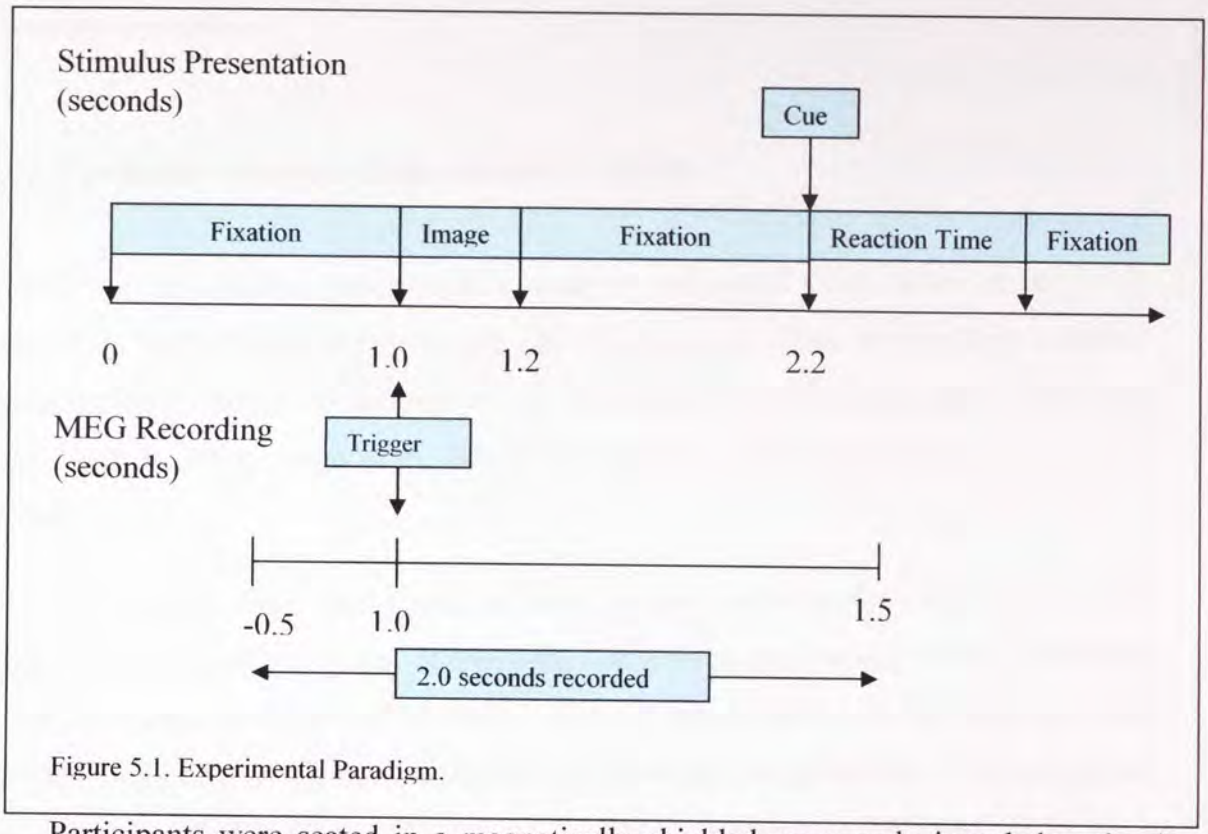


Figure 5.1. Experimental Paradigm.

Participants were seated in a magnetically shielded room and viewed the stimuli, presented on an Eizo T662 monitor, at a distance of two meters. In both the encoding and recognition phases of the experiment, the participants were required to fixate on a centrally presented small white square for a period of 1000 ms. A stimulus was then presented on the centre of the screen for 200 ms before the fixation point returned for another period of 1000 ms. The fixation point then changed from white to black, and this was the cue to make a response with a button press using their dominant hand. In the encoding phase, participants were asked to categorise the stimulus as a living or non-living thing and, in the recognition phase, as an old or new item. Accuracy and reaction time responses were recorded. Participants had 2000 ms to respond before the fixation point turned white again. This marked the onset of the next trial. The timing is illustrated in Figure 5.1. Stimuli were presented in a different random order for each participant. The same procedure was followed for words and objects.

5.3.4 MEG Recording and Analysis

Neural activity was recorded using a 151-channel CTF Omega MEG system (CTF Systems Inc, Canada.). Following MEG recording, a Polhemus Isotrak system was used to

digitise the surface shape of the participant's head and this information was used to co-register the MEG data with the participant's anatomical MRI (see chapter 3 for further details of this procedure).

5.3.4.1 Synthetic Aperture Magnetometry (SAM)

SAM is an adaptive beamforming analysis technique (Van Veen et al, 1997; Sekihara et al, 2002; Barnes & Hillebrand, 2003; Robinson & Vrba, 1999) which enables a three-dimensional image of activity to be produced in millisecond time resolution (Taniguchi et al, 2000; Singh et al, 2002). See chapter 3 for a detailed account of this technique.

In the current study, SAM comparisons between active and passive states were created for each participant in six overlapping 10Hz frequency bands; 5-15Hz, 10-20Hz, 15-25Hz, 20-30Hz, 25-35Hz and 30-40Hz. The 3-D images produced illustrate ERD and ERS, which were interpreted as increases and decreases in cortical activity (Pfurtscheller & Lopes Da Silva, 1999; refer to chapter 3 for further explanation of ERD and ERS). Each participant's SAM images were then spatially normalised into a standard template space using SPM99 (Friston, et al, 1995), which allows a voxel-wise analysis of group effects (see chapter 3 for further details).

5.3.4.2 Statistical Non-Parametric Mapping (SnPM)

In order to statistically threshold the group activation maps, a method of non-parametric permutation testing (SnPM) was used. It has been specifically developed for volumetric neuroimaging data (Nichols and Holmes, 2002), and has been successfully used on group SAM data (Singh et al, 2003). Essentially it enables statistical significance of group data to be determined. (For a detailed account of SnPM refer to chapter 3). In the current study, data is provided on statistically significant differences in ERS / ERD from a group of participants using this technique for analysing SAM.

5.3.4.3 *Additional Analysis Parameters*

In the analysis, incorrect responses were removed and several SAM comparisons made on the raw data for both objects and words. Previous research has suggested that different locations within the brain's visual pathway are activated when an old item is correctly recognised, compared to when a new item is falsely reported to be recognised, or an old item is failed to be recognised (Slotnick & Schacter, 2004). Therefore, neural activity observed by only analysing correct responses should not be contaminated by these variations.

In addition to analysing the entire trial (0-1500ms), the timing of brain activity during encoding and recognition memory was investigated with the first (0-500ms) and second (500-1000ms) epochs analysed separately. Analysis was conducted in these two 500ms time-windows because previous research suggests that there may be both an initial peak of activation (up to about 400ms post-stimulus onset), and a later peak (around 700ms post-stimulus onset). The third 500ms epochs was not analysed for two reasons. Firstly, a button-press response was performed at 1000ms post-stimulus onset and it was expected that this would contaminate any data in the final 500ms time span. Secondly, previous neuroimaging research suggested that recognition memory processing is probably finished by 1000ms post stimulus onset.

Encoding versus Recognition

1. Direct comparison of encoding versus recognition of 'old' stimuli across the entire trial (0-1500ms)

2. Encoding versus recognition during the first and second 500 ms post-stimulus onset

3. 4 baseline comparisons of encoding / recognition during first / second 500 ms compared to 500ms fixation (baseline)

Old versus New

4. Direct comparison of 'old' versus 'new' stimuli across the entire trial in the recognition phase (0-1500ms)

5. Encoding versus recognition during the first and second 500 ms onset

6. 4 baseline comparisons of encoding / recognition during first / se compared to 500ms fixation (baseline)

All power changes were calculated in six overlapping 10Hz frequen 15Hz, 10-20Hz, 15-25Hz, 20-30Hz, 25-35Hz and 30-40Hz.

5.4 Results

5.4.1 Behavioural Data

Behavioural data was collected from the thirteen participants. Tri participants responded before the cue, had reaction times greater than 2000m incorrect response, were removed from the analysis. Participants were highl both the encoding and recognition tasks for the two experiments (for objec 84.9%, respectively and for words, 94.2% and 83.2%, respectively). Chi-squa the recognition data showed this level of accuracy to be above chance for bc (df1) = 30.33; $p < 0.01$) and for words ($\chi 2$ (df1) = 23.66; $p < 0.01$). Fo percentage of correct responses for old and new stimuli was the same (84 words were not significantly different (83.7% and 82.7% for old anc respectively, $p > 0.05$). A chi-square analysis revealed no statistically signific in accuracy between old and new words (χ^2 (df1) = 0.14; p = 0.71) i participants could respond with equal accuracy to recognising an item as old

These similarities between the modalities (objects and words) an (encoding and recognition) were also reflected in the reaction times. Participa slightly faster when encoding the stimuli for both objects and words 263.2ms, respectively) than when recognising them later (322.5ms and objects and words respectively). Reaction times for words, irrespective of n on average faster than for objects. However, Analyses of Variance (ANOV on the reaction times for all participants found no statistically significant m either modality (F (1,24) = 0.57, p = 0.46) or for task (F (1,24) = 1.4 Furthermore, there was no statistically significant interaction between moda

(F (1,24) = 0.09, p = 0.76). Reaction times for recognising 'old' stimuli were slightly faster for both objects and words (255.1ms and 288.6ms, respectively) than for identifying 'new' stimuli (291.8ms and 304.3ms, respectively). However, again ANOVAs failed to show any statistically significant main effect for either modality (F (1.24) = 0.59, p = 0.45) or for task (old / new) (F (1,24) = 0.45, p = 0.51) and there was no interaction between these two factors (F (1,24) = 0.094, p = 0.76).

In addition to a direct comparison between encoding and recognition across the entire trial (0 – 1500ms post stimulus onset), two 500ms time-span SAM comparisons were also made on the raw (un-averaged), correctly categorised and recognised data for both objects and words. These were 0-500ms, and 500-1000ms post stimulus onset.

5.4.2 Encoding versus Recognition

5.4.2.1 Comparison across Entire Trial (0-1500ms)

A direct comparison between encoding and recognition across the entire trial (0 – 1500ms post stimulus onset) was conducted for both objects and words. The SAM analysis for both stimulus types compared the recognition phase (active) with the categorisation (encoding) phase (passive). Detailed results are presented below, and a summary of the activation revealed by directly comparing encoding with recognition is presented in section 5.4.2.4. Figure 5.2.A and 5.2.B show areas that were differentially activated between these two tasks, for words and objects respectively. SAM analysis for recognition versus encoding only revealed ERD, but this could reflect either greater ERS during the passive stage (encoding), or more ERD in the recognition phase. To distinguish between the two possibilities, comparisons were made between encoding (active) and baseline (fixation, passive) and recognition and baseline. All baseline comparisons (see section 5.4.2.3) revealed ERD in the recognition phase indicating that there was an increase in ERD when participants were recognising previously seen items, compared to when they were categorising them.

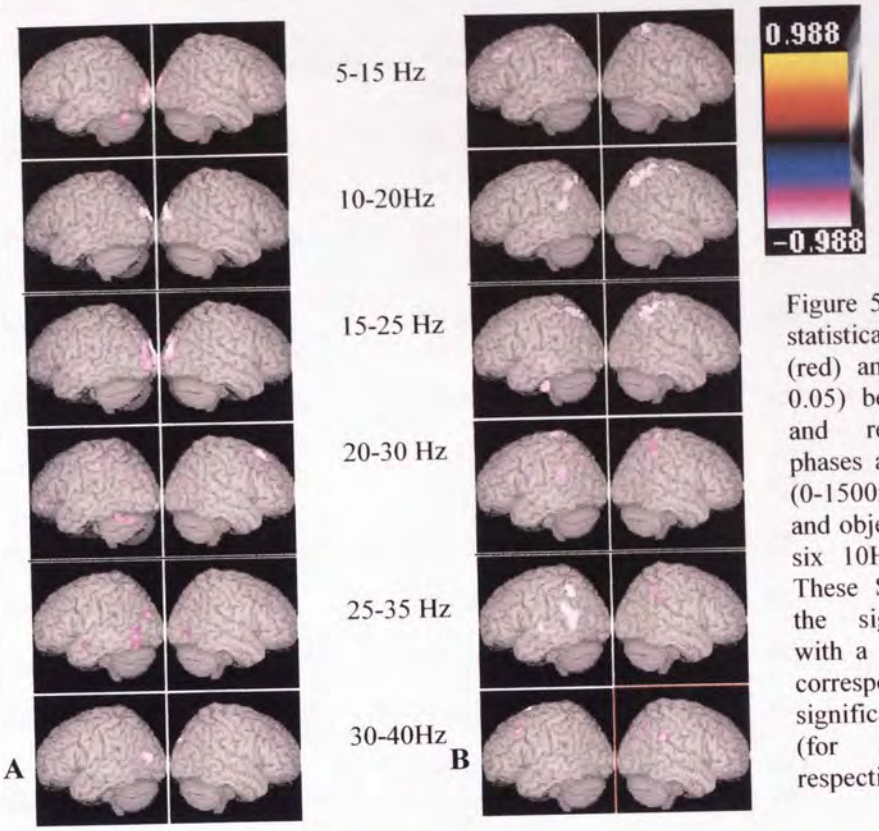


Figure 5.2. Regions showing statistically significant ERS (red) and ERD (blue) ($p < 0.05$) between the encoding and recognition memory phases across the entire trial (0-1500ms) for words (A) and objects (B) in each of the six 10Hz Frequency bands. These SAM images display the significant activations with a value of 0.95 / -0.95 corresponding to a significance value of $p < 0.05$ (for ERS and ERD respectively)

Words

The regions in which ERD was statistically significantly different between encoding and recognition for words are shown in Table 5.2. Significant ERD differences were only observed bilaterally within the occipital lobes, specifically the middle and inferior occipital gyri and the cuneus (see Figure 5.2.A).

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P value	BA
Middle Occipital Gyrus	Left	5-15	-27 -93 -3	33	6.06	0.023	18
		25-35	-45 -66 -12	4	5.67	0.047	
	Right	15-25	24 -94 15	42	6.14	0.047	18
Inferior Occipital Gyrus	Left	5-15	-18 -101 9	5	5.76	0.031	
Cuneus	Right	15-25	6 -99 0	3	5.55	0.047	17

Table 5.2 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and recognition memory phases across the entire trial for words

Objects

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P value	BA
Precentral Gyrus	Left Right	20-30 Hz 25-35 Hz	-15 -33 63 9 -21 72	517 163	7.61 7.11	0.031 0.016	4 6
Medial Frontal Gyrus	Left	5-15 Hz 20-30 Hz	-18 45 15 -12 36 30	8 48	6.41 8.54	0.031 0.016	
Middle Frontal Gyrus	Left Right	25-35 Hz 10-20 Hz	-12 -15 69 36 33 48	163 7	6.53 6.02	0.031 0.047	6/9/ 10/4
Prefrontal Cortex/Insula	Right	10-20 Hz	33 -6 21	1262	8.61	0.016	13
Precuneus	Left	5-15 Hz 15-25 Hz	-12 -63 51 -3 -66 42	1688 4828	7.96 8.48	0.016 0.016	7
Supramarginal Gyrus	Left	10-20 Hz	-60 -51 21	29	6.80	0.031	40
Inferior Parietal Lobule	Left	10-20 Hz	-48 -60 48	32	6.43	0.031	40
Paracentral Lobule	Left	15-25	-12 -33 60	4828	8.66	0.016	
Superior Parietal Lobule	Right	5-15	24 -45 63	128	7.30	0.016	5
Superior Temporal Gyrus	Left	10-20 25-35	-48 0 -9 -63 -12 -3	58 45	7.23 7.16	0.031 0.016	21
Middle Temporal Gyrus	Left	25-35	-48 -42 0	479	9.55	0.016	21
Inferior Occipital Gyrus	Left	5-15	-27 -87 -12	49	7.24	0.016	37
Posterior Lobe	Left	10-20	-9 -75 -18	3086	9.16	0.016	
Corpus Callosum	Right	5-15	15 -36 21	118	7.18	0.016	
Lingual Gyrus	Right	10-20	0 -81 -12	3086	9.84	0.016	

Table 5.3 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and recognition memory phases across the entire trial for objects

Table 5.3 highlights the major regions in which ERD was statistically significantly different ($p < 0.05$) between encoding and recognition for objects. There was extensive ERD in the left hemisphere and only a small amount of ERD in the right middle and pre-frontal gyri and the right pre- and postcentral gyri, extending into the superior parietal lobule. The largest clusters in the left hemisphere were in the frontal and parietal lobes (see Figure 5.2.B), in particular, the precentral, middle and medial frontal gyri, precuneus and the inferior parietal lobule (including the supramarginal gyrus and paracentral lobule). Further significant clusters were identified in the left temporal lobe, (specifically the middle and superior temporal gyri), areas of the corpus striatum (putamen and lentiform nucleus) and occipital lobe (including the lingual gyrus, extending towards the cuneus and over the posterior lobe).

5.4.2.2 Time Span Comparisons

Direct SAM comparisons between encoding (passive) and recognition of 'old' items (active) were conducted for two 500ms time spans to provide detail on the temporal sequence of brain activity. The first (0-500ms) and second (500-1000ms) 500ms post stimulus onset blocks were analysed separately for objects and words and both showed widespread ERD. This could reflect either greater ERS during the passive stage (encoding), or more ERD in the recognition phase. To distinguish between these two possibilities, comparisons were made between encoding (active) and baseline (fixation, passive) phases and between recognition and baseline phases. The SAM analysis for the entire trial (see previous section; 5.4.2.1) and all baseline comparisons (see section 5.4.2.3) produced ERD indicating that differences between encoding and recognition reflected an increase in ERD when participants were recognising previously seen items, compared to when they were categorising them. Figures 5.3 and 5.4 and Tables 5.4-5.7 highlight the areas that showed statistically significant ERD between encoding and recognition for both objects and words over the two 500ms time-windows.

0-500ms

Words

There was widespread bilateral ERD. Whilst virtually identical temporal (inferior, middle and superior temporal gyrus) and occipital (middle occipital gyrus and cuneus) regions were bilaterally activated, more hemispheric differences were observed within frontal and parietal regions. In particular, the inferior frontal gyrus was the only frontal region bilaterally activated during this initial 500ms time window. There was left lateralised ERD in the middle and prefrontal gyri but right lateralised ERD in the superior and medial frontal gyri (Table 5.4; Figure 5.3.A).

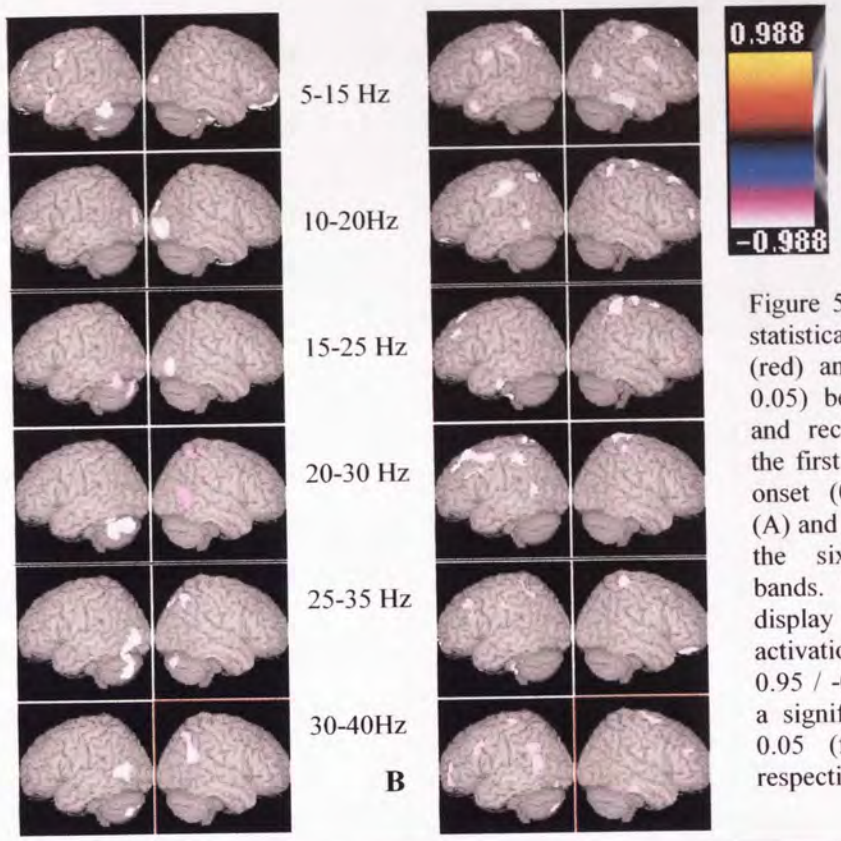


Figure 5.3. Regions showing statistically significant ERS (red) and ERD (blue) ($p < 0.05$) between the encoding and recognition memory in the first 500ms post-stimulus onset (0-500ms) for words (A) and objects (B) in each of the six 10Hz Frequency bands. These SAM images display the significant activation, with a value of 0.95 / -0.95 corresponding to a significance value of $p < 0.05$ (for ERS and ERD respectively).

Within the parietal lobe, the postcentral gyrus was bilaterally activated but there was also left lateralised ERD in the superior parietal lobule and right lateralised ERD in the supramarginal gyri. Further bilateral activation was observed in the limbic lobe, but again specific regions showed lateralised ERD (right parahippocampal gyrus and left posterior cingulate). Finally, both the left and right cerebellar also showed some ERD.

Objects

During the initial 500ms post stimulus onset SAM comparison between encoding and recognition of 'old' items, there was also extensive bilateral ERD when objects were presented as stimuli (see Figure 5.3.B and Table 5.5).

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Frontal Gyrus	Left	5-15	-45 1 47	295	5.78	0.035	6
Superior Parietal Lobule	Right	5-15	15 -57 66	74	5.50	0.031	7
		25-35	42 -66 57	134	5.97	0.047	
Superior Frontal Gyrus	Right	5-15	18 64 -11	3257	7.49	0.031	11
Inferior Frontal Gyrus	Right	5-15	18 30 -19	3257	7.49	0.016	47
		10-20	51 27 -3	43	4.95	0.043	
	Left	5-15	-51 46 3	617	5.43	0.047	44
Superior Temporal Gyrus	Left	5-15	-55 13 -6	617	5.17	0.043	22/38
		10-20	-52 -30 15	13	4.75	0.047	
	Right	30-40	60 -59 27	67	5.40	0.047	
Inferior Temporal Gyrus	Left	5-15	-54 -55 -18	1374	6.85	0.016	20
	Right	10-20	33 -12 -48	481	6.43	0.008	20
		15-25	51 -74 -1	128	6.16	0.027	37
Insula	Left	10-20	-54 -33 18	13	4.75	0.047	13
Limbic Lobe – Uncus	Right	5-15	24 -8 -44	653	6.03	0.020	36
Precentral Gyrus	Left	5-15	-48 -3 45	295	5.78	0.020	6
Supramarginal Gyrus	Right	30-40	63 -56 24	67	5.86	0.047	40
Fusiform Gyrus	Left	5-15	-54 -54 -21	1374	6.85	0.016	
		25-35	-51 -69 -18	1099	6.02	0.016	19/37
Postcentral Gyrus	Right	5-15	15 -56 73	74	5.50	0.043	7
	Left	10-20	-52 -30 15	13	4.75	0.047	40
Middle Temporal Gyrus	Left	5-15	-54 -43 -16	1374	6.85	0.039	20
		25-35	-39 -76 9	1099	6.70	0.016	39/37
	Right	10-20	33 1 -46	481	5.91	0.027	20
Cerebellum	Left	5-15	-18 -66 -36	1374	7.52	0.012	
		20-30	-45 -81 -30	718	6.83	0.016	
	Right	25-35	48 -77 -27	77	5.86	0.039	
		30-40	6 -57 -51	73	5.79	0.039	
Medial Frontal Gyrus	Right	25-35	6 51 39	11	5.22	0.035	
Parahippocampal Gyrus	Right	10-20	33 -11 -30	481	6.43	0.035	30
Posterior Cingulate	Left	25-35	25 -69 9	1099	6.70	0.031	30
Inferior Occipital Gyrus	Right	10-20	38 -85 -8	1299	7.86	0.023	18
Middle Occipital Gyrus	Right	10-20	39 -88 -3	1299	7.86	0.004	18
		15-25	51 -78 -3	128	6.16	0.023	
	Left	10-20	-34 -94 12	974	5.15	0.047	19
Superior Occipital Gyrus	Left	10-20	-31 -87 21	974	5.03	0.047	19
Lingual Gyrus	Right	5-15	6 -81 -12	340	5.78	0.020	18
Cuneus	Right	10-20	-15 -78 15	974	6.78	0.004	18/19
	Left	5-15	-12 -81 9	340	5.43	0.035	17/18

Table 5.4 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and recognition memory phases for words, 0 – 500ms post stimulus onset

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Frontal Gyrus	Right	5-15	33 -9 63	86	7.03	0.031	6
		10-20	27 54 12	116	7.79	0.016	
	Left	15-25	-39 37 39	73	7.77	0.031	9
		20-30	-45 21 27	1286	7.48	0.031	
Superior Parietal Lobule	Left	5-15	-27 -60 63	250	6.98	0.031	7
		10-20	-30 -63 57	449	7.76	0.016	
Inferior Parietal Lobule	Right	15-25	54 -48 45	65	6.95	0.031	40
	Left	20-30	-36 -39 42	1233	8.13	0.016	40
Precuneus	Left	5-15	-21 -75 36	250	6.92	0.031	
Superior Frontal Gyrus	Right	10-20	18 -18 75	210	7.62	0.031	6
		15-25	18 11 65	858	8.31	0.031	
	Left	15-25	-20 35 56	75	7.45	0.031	8
		20-30	-27 30 57	1286	8.03	0.016	
Inferior Frontal Gyrus	Right	5-15	39 24 9	40	6.90	0.031	13/45
Inferior Temporal Gyrus	Right	5-15	63 -21 -30	70	6.61	0.031	20
Superior Temporal Gyrus	Right	5-15	60 -63 15	11	6.50	0.031	39
		10-20	9 45 54	309	8.48	0.016	
	Left	20-30	-57 -57 12	117	7.03	0.031	
Insula	Left	5-15	-33 -18 15	36	6.64	0.031	
		10-20	45 -21 21	279	8.41	0.016	
	Right	20-30	48 6 6	203	5.86	0.047	
Precentral Gyrus	Right	15-25	21 -15 78	858	8.36	0.031	6
	Left	5-15	-60 -6 39	8	6.45	0.031	
		15-25	-45 -15 30	121	7.89	0.031	
Fusiform Gyrus	Right	5-15	51 -21 -33	70	6.70	0.031	20
	Left	15-25	-60 -15 -27	256	8.29	0.031	20
Postcentral Gyrus	Right	10-20	36 42 63	165	8.74	0.016	3
		15-25	36 –36 60	858	10.64	0.016	
		20-30	19 -48 75	1440	7.32	0.031	2
	Left	20-30	-18 -48 72	1440	7.65	0.016	
Anterior Cingulate	Right	10-20	9 27 27	309	6.15	0.047	32
		25-35	12 32 -10	321	9.39	0.031	
Middle Temporal Gyrus	Left	10-20	-63 -54 -3	53	7.50	0.031	21
		20-30	-63 -51 -9	117	5.64	0.047	
Cerebellum	Left	15-25	-24 -63 -42	136	7.30	0.031	
		20-30	-15 -42 -12	1233	7.37	0.031	
Medial Frontal Gyrus	Left	15-25	-6 -27 75	63	7.20	0.031	6
	Right	25-35	12 38 -7	321	9.39	0.031	10/25
Parahippocampal Gyrus	Right	20-30	33 0 -24	203	6.12	0.047	
Lingual Gyrus	Right	20-30	3 -93 -21	29	6.00	0.047	18
Cuneus	Left	20-30	-6 -87 6	29	5.99	0.047	18
	Right	15-25	6 -87 9	59	6.99	0.031	18

Table 5.5 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and recognition memory phases for objects, 0 – 500ms post stimulus onset

In particular, there was bilateral frontal (middle, superior and medial frontal and precentral) and temporal (superior temporal and fusiform gyri) ERD. There was also some ERD in parietal (inferior parietal lobule and postcentral gyrus) and occipital (cuneus) regions. However, there was also some ERD restricted to one hemisphere. For instance, there was ERD in the right inferior frontal gyrus as well as the left middle and right inferior temporal gyri. There was also left-lateralised ERD in the precuneus and superior parietal lobule, and right-lateralised ERD in the anterior cingulate and parahippocampal gyrus.

500-1000ms

Words

A comparison between encoding and recognition during the second 500ms time window for words also showed extensive bilateral activation (See Figure 5.4.A). The specific regions showing statistically significant differences between the two tasks, however, showed many more hemispheric differences (see Table 5.6).

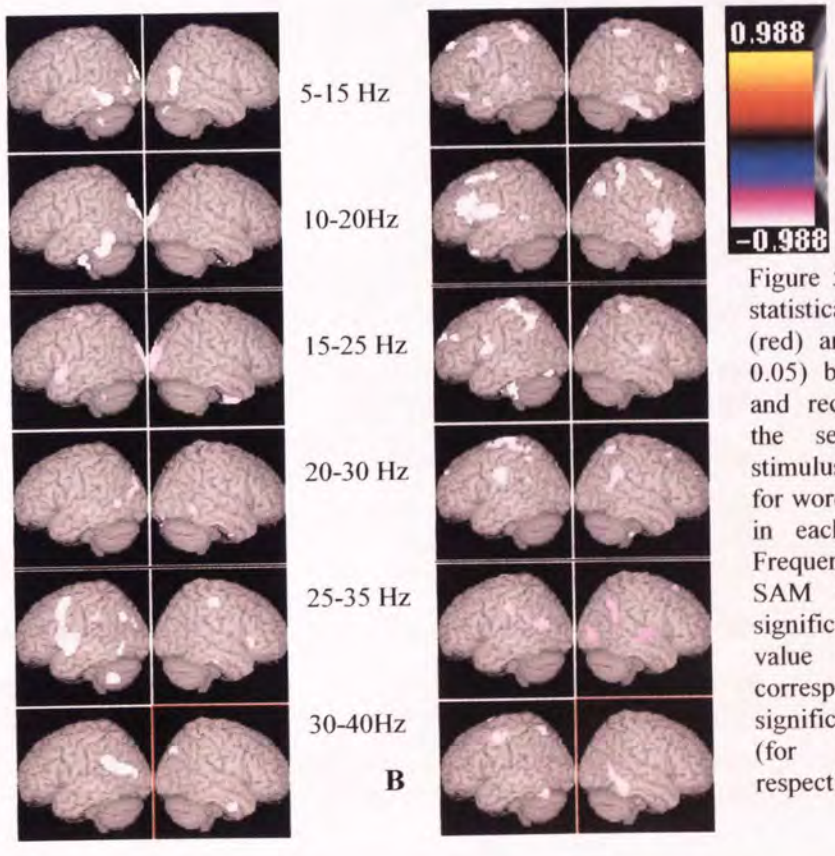


Figure 5.4. Regions showing statistically significant ERS (red) and ERD (blue) ($p < 0.05$) between the encoding and recognition memory in the second 500ms post-stimulus onset (500-1000ms) for words (A) and objects (B) in each of the six 10Hz Frequency bands. These SAM images display the significant activation, with a value of 0.95 / -0.95 corresponding to a significance value of $p < 0.05$ (for ERS and ERD respectively).

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Frontal Gyrus	Left	5-15	-23 -10 49	87	5.12	0.039	6/9/8
		25-35	-40 0 63	2626	6.24	0.043	
Inferior Parietal Lobule	Left	25-35	-50 -66 39	1876	6.34	0.043	39
		30-40	-62 -41 30	882	5.80	0.043	40
Inferior Temporal Gyrus	Right	5-15	44 -66 -2	863	5.78	0.035	37
		15-25	33 -6 -43	227	6.83	0.031	20
	Left	10-20	-56 -58 -15	8402	6.80	0.012	37
		25-35	-58 -62 -12	1876	5.83	0.043	
Precuneus	Left	25-35	-18 -78 24	1876	7.43	0.012	31
	Right	30-40	39 -75 36	43	5.26	0.043	
Inferior Frontal Gyrus	Left	25-35	-54 9 35	2626	6.24	0.039	9
	Right	25-35	54 21 0	50	4.96	0.043	47
Superior Temporal Gyrus	Right	5-15	55 -58 21	863	5.81	0.043	39
	Left	20-30	-54 0 -3	2626	6.25	0.012	22
		30-40	-45 -59 16	882	6.22	0.035	
Insula	Left	25-35	-39 -3 12	2626	6.34	0.012	13
Precentral Gyrus	Left	25-35	-41 10 8	2626	6.34	0.012	44
Fusiform Gyrus	Right	30-40	62 -7 -33	35	5.28	0.047	20
Postcentral Gyrus	right	25-35	54 -24 52	146	5.45	0.027	2
Anterior Cingulate	Right	10-20	3 7 -12	8402	7.71	0.027	
Middle Temporal Gyrus	Right	5-15	51 -66 21	863	5.81	0.031	39/19/
		15-25	33 2 -43	227	6.83	0.008	37
	Left	10-20	-54 -54 -15	8402	6.80	0.012	37/19
		30-40	-45 -66 12	882	6.22	0.027	
							19/39
Cerebellum	Right	5-15	42 -75 -30	42	4.67	0.043	
	Left	25-35	-49 -60 -43	339	5.90	0.039	
Medial Frontal Gyrus	Right	10-20	3 9 -21	8402	7.71	0.012	25
Parahippocampal Gyrus	Right	5-15	31 -1 -26	32	4.80	0.039	34
		10-20	3 7 -12	8402	7.71	0.047	
Cingulate Gyrus	Left	5-15	-20 -10 41	87	5.12	0.035	
Middle Occipital Gyrus	Left	25-35	-56 -63 -12	1876	5.83	0.043	37
		30-40	-45 -79 13	882	5.74	0.031	
Lingual Gyrus	Left	20-30	-15 -81 -12	106	5.45	0.027	18
Cuneus	Left	5-15	-12 -90 30	282	5.54	0.031	19
		20-30	-18 -76 31	1876	7.43	0.020	17
	Right	15-25	15 -100 6	395	6.30	0.027	18
Supramarginal Gyrus	Left	30-40	-60 -48 30	882	5.80	0.031	40
Posterior Cingulate	Left	5-15	-15 -54 9	135	4.93	0.035	
		10-20	-15 -63 12	8402	7.65	0.008	

Table 5.6 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and recognition memory phases for words, 500-1000ms post stimulus onset

This was particularly noticeable in the frontal lobe: there was left-lateralised ERD in the middle frontal and precentral gyri, and bilateral ERD in the inferior frontal gyri. The ERD in the temporal lobes was predominantly bilateral (inferior, superior and middle temporal gyri) with some right fusiform activity also being observed. Within the parietal lobes, whilst there was bilateral precuneus ERD, as well as in the left inferior parietal lobe, left supramarginal gyrus and right postcentral gyrus. The anterior and posterior cingulate showed right and left lateralised ERD, respectively. In addition, parahippocampal activity was only observed within the right hemisphere.

Objects

The statistically significant differences in ERD between encoding and recognition of objects (between 500 and 1000ms post stimulus onset) were observed in a range of areas (see Figure 5.4.B and Table 5.7). Within the frontal lobes, there was bilateral ERD in the middle, superior and medial frontal gyri and left-lateralised ERD in the inferior frontal gyrus. Similarly, across the temporal regions, superior and middle frontal gyri showed bilateral activation, with some right lateralised ERD in the transverse temporal and fusiform gyri. There was also bilateral ERD in parietal (superior and inferior parietal lobules and postcentral gyri), occipital (middle occipital gyrus and cuneus) and limbic regions (insula). In addition there was ERD in the right precuneus, left cuneus, left lingual gyrus, the right cingulate gyrus, both anterior and posterior cingulate, and right parahippocampal gyrus.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	Va
Middle Frontal Gyrus	Right	5-15	33 39 42	126	8.19	0.0
	Left	10-20	-39 -3 63	2201	7.23	0.0
		20-30	-21 -16 60	428	9.69	0.0
Superior Parietal Lobule	Right	20-30	39 -56 66	8	7.39	0.0
	Left	30-40	-30 -57 57	104	7.69	0.0
Inferior Parietal Lobule	Right	10-20	54 -60 42	114	6.55	0.0
	Left	30-40	-30 -50 58	104	7.69	0.0
Precuneus	Right	10-20	18 -78 54	308	6.24	0.0
Superior Frontal Gyrus	Left	5-15	-15 42 51	86	8.60	0.0
	Right	25-35	3 -7 70	50	7.99	0.0
Inferior Frontal Gyrus	Left	10-20	-51 9 15	2201	8.16	0.0
Transverse Temporal gyrus	Right	15-25	64 -11 14	124	6.70	0.0
Superior Temporal Gyrus	Right	10-20	51 15 -12	4828	10.13	0.0
		20-30	35 -50 15	765	13.91	0.0
	Left	10-20	-45 19 -34	137	7.04	0.0
Insula	Right	25-35	34 -39 19	765	13.91	0.0
	Left	15-25	-33 -18 12	3751	8.01	0.0
Precentral Gyrus	Right	15-25	57 -12 12	124	6.70	0.
	Left	20-30	-9 -24 75	428	9.20	0.
Fusiform Gyrus	Right	5-15	24 -63 -12	9	6.64	0.
Postcentral Gyrus	Right	5-15	39 -33 66	282	11.88	0.
	Left	30-40	-51 -13 52	203	7.01	0.
Anterior Cingulate	Right	5-15	12 22 -9	2338	9.86	0.
Middle Temporal Gyrus	Right	5-15	45 –21 -24	2338	9.15	0.
		30-40	57 -48 -9	1434	9.64	0.
	Left	30-40	-49 -51 -3	459	8.94	0.
Cerebellum	Left	15-25	-24 -34 -45	3751	9.44	0
	Right	25-35	21 -33 -24	1434	7.38	0
Medial Frontal Gyrus	Left	20-30	-12 42 30	267	8.47	0
	Right	20-30	12 -3 51	30	7.60	0
Parahippocampal Gyrus	Right	5-15	25 -54 1	2338	9.86	0
Cingulate Gyrus	Right	20-30	13 -3 48	30	7.60	0
Inferior Occipital Gyrus	Left	10-20	-30 -81 -9	132	6.65	0
Middle Occipital Gyrus	Left	15-25	-39 -75 -15	216	7.63	0
	Right	30-40	27 -75 3	1434	9.83	0
Lingual Gyrus	Left	5-15	-9 -81 -3	429	8.03	0
Cuneus	Right	5-15	18 84 18	429	8.67	0
	Left	30-40	-6 -76 32	134	6.76	0
Posterior Cingulate	Right	5-15	12 -45 12	715	7.09	0

Table 5.7 Regions showing statistically significant differences in activation ($p < 0.05$) betw and recognition memory phases for objects, 500-1000ms post stimulus onset

5.4.2.3 Baseline Comparisons

Several SAM comparisons were computed for both words and objects comparing baseline activation (500ms pre-stimulus onset) with the first and second 500ms epochs for encoding and recognition of 'old' items. These comparisons are detailed below and Tables 5.15 – 5.17 (section 5.4.2.4) summarise the areas observed to show statistically significant differences ($p < 0.05$) for words and objects during encoding and recognition, within these two time frames. Figures 5.5. and 5.6 illustrate activation (ERD) in the first and second 500ms, respectively, for encoding and recognition (versus baseline) for objects and words.

5.4.2.3.1 Baseline versus Encoding

0-500ms

Words

During the initial 500ms epoch, encoding of words (when compared to baseline activity) produced statistically significant ERD that was completely right-lateralised and focused within the parietal (inferior parietal lobule and supramarginal gyrus) and occipital (middle occipital gyrus and cuneus) regions (Table 5.8).

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Inferior parietal lobule	Right	25-35	67 -33 27	12	6.50	0.031	40
Supramarginal Gyrus	Right	25-35	68 -48 24	1	6.08	0.031	
Middle occipital gyrus	Right	15-25	27 -188 6	114	7.59	0.008	
Cuneus	Right	15-25	19 -81 7	114	7.59	0.008	17

Table 5.8 Baseline activity (passive) versus 0 to 500 ms post stimulus onset encoding activation (active) for words

Objects

Statistically significant ERD during encoding of objects was observed across all cortical regions (Table 5.9). Whilst ERD within the frontal lobes was bilateral (inferior frontal gyrus), all temporal (middle and superior temporal gyri) and limbic (insula and cingulate gyrus) activity was right-lateralised. Although parietal and occipital regions were

also bilaterally activated, specific areas within these showed more specific hemispheric differences. In particular, ERD was observed within the left postcentral gyrus, the right inferior parietal lobule and middle occipital gyrus, and bilaterally in the lingual gyrus. Finally, both the left and right cerebellar also showed statistically significant ERD.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Inferior Frontal Gyrus	Right	25-35	51 15 12	175	9.06	0.016	44
Parietal Lobe	Left	15-25	-30 -87 -6	9	8.96	0.031	
Superior Parietal Lobule	Left	10-20	-21 -72 45	267	8.82	0.016	7
Inferior Parietal Lobule	Right	25-35	45 -36 48	2	6.89	0.047	40
Postcentral Gyrus	Left	25-35	-48 -21 45	15	7.26	0.031	2
Middle Temporal Gyrus	Right	15-25	51 -66 15	164	9.12	0.031	39
Superior Temporal Gyrus	Right	25-35	66 -15 3	48	7.36	0.031	22
Occipital Lobe	Right	10-20	36 -81 -6	98	7.88	0.016	
Middle Occipital Gyrus	Right	15-25	39 -78 3	184	7.29	0.031	
Lingual Gyrus	Right	15-25	3 -93 -18	78	9.05	0.031	18
	Left	15-25	-12 -90 0	62	7.84	0.031	17
Cerebellum	Left	5-15	-18 -72 -24	168	8.66	0.016	
		10-20	-33 -78 -33	21	6.16	0.047	
	Right	20-30	45 -63 -33	6	7.65	0.047	
Insula	Right	25-35	42 -9 0	48	7.07	0.031	
Cingulate Gyrus	Right	25-35	3 -18 36	299	10.01	0.016	24

Table 5.9 Baseline activity (passive) versus 0 to 500 ms post stimulus onset encoding activation (active) for objects

500-1000ms

Words

No statistically significant ERD was observed during the second 500ms epoch for encoding of words.

Objects

Between 500ms and 1000ms post-stimulus onset, statistically significant ERD for encoding objects was observed over much of the frontal lobe (Table 5.10). Whilst the middle frontal and precentral gyri were bilaterally activated, other areas showed

hemispheric specialisation (in particular, the left superior and right inferior and medial frontal gyri). Temporal and limbic activity was only observed in the right hemisphere (fusiform and cingulate gyri, respectively). Similar hemispheric differences were observed in the parietal (left postcentral and right supramarginal gyri) and occipital (left inferior occipital gyrus) lobes, and also the left cerebellum.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Precentral Gyrus	Left	15-25	-51 -9 45	1259	8.48	0.016	
		25-35	-45 -6 39	513	7.43	0.016	6
	Right	15-25	30 -27 66	118	7.78	0.016	
Middle Frontal Gyrus	Left	25-35	-36 -3 48	513	7.02	0.016	
	Right	25-35	21 -9 63	2	6.45	0.047	6
Inferior Frontal Gyrus	Right	25-35	39 3 30	764	8.97	0.016	
Medial Frontal Gyrus	Right	25-35	3 15 51	43	6.49	0.047	
Superior Frontal Gyrus	Left	25-35	-24 39 36	8	6.47	0.047	
Parietal Lobe	Left	15-25	-54 -18 15	1259	7.98	0.016	
		25-35	-45 -30 54	513	9.13	0.016	
	Right	25-35	42 -42 30	35	6.95	0.016	
Postcentral Gyrus	Left	15-25	-54 -18 15	1259	7.98	0.016	
		25-35	-45 -30 54	513	9.13	0.016	
Supramarginal Gyrus	Right	25-35	42 -42 30	35	6.95	0.016	
Fusiform Gyrus	Right	15-25	48 -9 -30	34	7.27	0.016	20
Inferior Occipital Gyrus	Left	20-30	-33 -78 -9	7	7.05	0.047	
Cerebellum	Left	15-25	-33 -51 -45	142	7.31	0.016	
Posterior Lobe	Left	15-25	-33 -51 -45	142	7.31	0.016	
Cingulate Gyrus	Right	25-35	12 -3 45	43	6.86	0.016	

Table 5.10 Baseline activity (passive) versus 500 to 1000 ms post stimulus onset encoding activation (active) for objects

5.4.2.3.2 Baseline versus Recognition

0-500ms

Words

The baseline comparison for words during the first 500ms-recognition epoch showed ERD in all cortical regions, but also more hemispheric specialisation (Table 5.11). Frontal activity (middle frontal gyrus) was only observed in the left hemisphere, whilst all

statistically significant temporal (inferior temporal and fusiform gyri) and limbic (parahippocampal gyrus) ERD was right-lateralised. Some bilateral parietal ERD was seen (precuneus), in addition to the left inferior parietal lobule, right middle occipital gyrus and right cerebellum being involved.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Middle Frontal Gyrus	Left	15-25	-47 9 41	7	5.77	0.047	8
Inferior Temporal Gyrus	Right	15-25	45 -71 -6	863	6.46	0.016	
Fusiform Gyrus	Right	5-15	37 -33 -23	166	8.82	0.016	37 / 20
		15-25	46 -69 -18	863	6.32	0.039	19
Parahippocampal Gyrus	Right	5-15	37 -30 -26	166	8.82	0.047	36
Cingulate Gyrus	Left	25-35	-20 -23 39	120	6.64	0.008	31
Inferior Parietal Lobule	Left	25-35	-43 -71 39	33	6.20	0.039	
Precuneus	Left	25-35	-43 -74 35	33	6.20	0.031	39 / 7
Middle Occipital Gyrus	Right	5-15	51 -75 -12	1	5.96	0.047	19
		15-25	47 -68 -12	863	6.32	0.016	19
Anterior Lobe / Culmen	Right	5-15	30 -36 -30	166	8.82	0.008	

Table 5.11 Baseline activity (passive) versus 0 to 500 ms post stimulus onset activation (active) when correctly recognising previously seen words

Objects

During the first 500ms baseline comparison for the recognition of objects, statistically significant ERD was observed across all cortical regions, but with many areas showing hemispheric asymmetry (Table 5.12). In particular, whilst frontal ERD was completely right lateralised (middle, inferior and precentral frontal gyri), temporal activity was only observed within the left hemisphere (middle and superior temporal gyri). Bilateral ERD was observed in the limbic and parietal lobes, although different parietal regions were involved depending on the hemisphere (left precuneus and right superior parietal lobule). This hemispheric specialisation was also seen for occipital regions (left cuneus and right middle occipital gyrus), with ERD also in the left cerebellum.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Frontal Lobe	Left	25-35	-36 15 27	57	6.29	0.016	
Precentral Gyrus	Right	15-25	63 -6 30	25	8.07	0.031	44
Middle Frontal Gyrus	Right	15-25	51 12 42	79	7.17	0.016	6
Intermediate Frontal Gyrus	Right	25-35	51 12 42	79	7.17	0.016	8
Precuneus	Left	10-20	-30 -72 38	38	7.55	0.016	
		25-35	-18 -63 30	2412	14.26	0.016	
Superior Parietal Lobule	Right	20-30	33 -83 54	43	6.97	0.016	7
		25-35	33 -51 54	210	6.53	0.016	
Middle Temporal Gyrus	Left	25-35	-39 3 -33	337	6.97	0.016	21
Superior Temporal Gyrus	Left	15-25	-51 -27 6	18	7.43	0.031	
		25-35	-48 -18 0	38	6.28	0.016	
	Right	25-35	60 -57 12	4	5.86	0.031	
Middle Occipital Gyrus	Right	5-15	45 -81 0	1	5.66	0.047	19
		10-20	45 -75 6	3	6.09	0.047	
Cuneus	Left	15-25	-15 -81 9	167	8.36	0.016	17
Anterior Lobe	Left	25-35	0 -48 -9	2412	6.86	0.016	
Limbic Lobe	Left	25-35	-30 6 -33	337	6.93	0.016	
Cingulate Gyrus	Right	15-25	18 -12 42	1	6.80	0.047	

Table 5.12 Baseline activity (passive) versus 0 to 500 ms post stimulus onset activation (active) when correctly recognising previously seen objects

500-1000ms

Words

ERD during the second 500ms post-stimulus onset for the recognition of words was evident within frontal, temporal, limbic and parietal regions (Table 5.13). In particular, temporal and frontal ERD indicated that there was hemispheric specialisation in these cortical regions (left inferior and middle frontal and precentral gyri and right superior temporal gyrus, respectively). The insula was bilaterally activated, and whilst this was also evident for the parietal lobe, regions within this area also demonstrated hemispheric differences (bilateral inferior parietal lobule, left postcentral gyrus and right supramarginal gyrus).

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Inferior Frontal Gyrus	Left	15-25	-51 6 36	189	7.46	0.008	9
Middle Frontal Gyrus	Left	15-25	-47 10 36	189	7.46	0.008	9 / 6
Precentral Gyrus	Left	15-25	-46 -1 36	189	7.46	0.016	6
		25-35	-39 -21 39	6	5.59	0.047	4
Superior Temporal Gyrus	Right	25-35	44 -24 -7	42	5.88	0.039	
Insula	Right	25-35	41 -22 -8	42	5.88	0.047	22 / 13
Postcentral Gyrus	Left	15-25	-48 -24 42	1	5.67	0.047	
		20-30	-38 -27 42	9	6.76	0.031	2
		25-35	-47 -15 21	14	5.66	0.047	43
Inferior Parietal Lobule	Left	20-30	-39 -30 42	9	6.76	0.031	
	Right	25-35	62 -39 30	83	6.50	0.031	40
Supramarginal Gyrus	Right	25-35	57 -45 30	83	6.50	0.023	40
Precuneus	Left	25-35	-18 -54 35	68	6.38	0.023	

Table 5.13 Baseline activity (passive) versus 500 to 1000 ms post stimulus onset activation (active) when correctly recognising items previously seen words

Objects

Recognition of objects between 500 and 1000ms post-stimulus onset produced left lateralised frontal ERD (middle and inferior frontal and precentral gyri) (Table 5.14). Temporal activity was observed in both hemispheres but in different regions (left middle temporal gyrus, and right posterior transverse temporal gyrus). In addition the right corpus callosum and left lingual gyrus also showed ERD. Finally, parietal activation occurred in both hemispheres, but again different regions showed hemispheric asymmetry (left inferior and superior parietal lobules, left precuneus, right postcentral gyrus, right paracentral lobule, and bilateral supramarginal gyrus).

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Frontal	Right	15-25	15 24 21	35	7.05	0.016	
		25-35	9 54 24	1	6.13	0.047	
Precentral Gyrus	Left	15-25	-51 -3 30	106	8.25	0.016	6
Inferior Frontal Gyrus	Left	25-35	-42 3 33	499	7.54	0.016	44
Middle Frontal Gyrus	Left	25-35	-30 -9 63	499	9.56	0.016	
Postcentral Gyrus	Left	5-15	-36 -21 27	22	7.31	0.047	
		15-25	-30 -36 66	194	8.44	0.016	3
	Right	25-35	27 -33 63	8	6.09	0.047	
Supramarginal Gyrus	Left	10-20	-57 -48 30	18	7.87	0.031	
		15-25	-48 -48 30	1	6.37	0.047	
	Right	25-35	42 -51 33	259	7.17	0.016	
		30-40	60 -54 30	38	7.83	0.016	
Superior Parietal Lobule	Left	15-25	-36 -57 51	3	6.65	0.016	7
Inferior Parietal Lobule	Left	10-20	-30 -42 57	18	8.21	0.016	40
Paracentral Lobule	Right	25-35	9 -39 66	87	6.19	0.047	
Precuneus	Left	25-35	-18 -78 42	1777	7.83	0.016	
Middle Temporal Gyrus	Left	15-25	-33 -81 18	66	6.78	0.016	
Posterior Transverse Temporal	Right	25-35	60 -15 9	66	8.44	0.016	42
Occipito-temporal	Left	15-25	-54 -42 -21	274	7.99	0.016	37
Occipital	Left	15-25	-27 -75 9	66	7.48	0.016	
Lingual Gyrus	Left	5-15	-30 -75 -15	65	7.82	0.047	

Table 5.14 Baseline activity (passive) versus 500 to 1000 ms post stimulus onset activation (active) when correctly recognising items previously seen objects

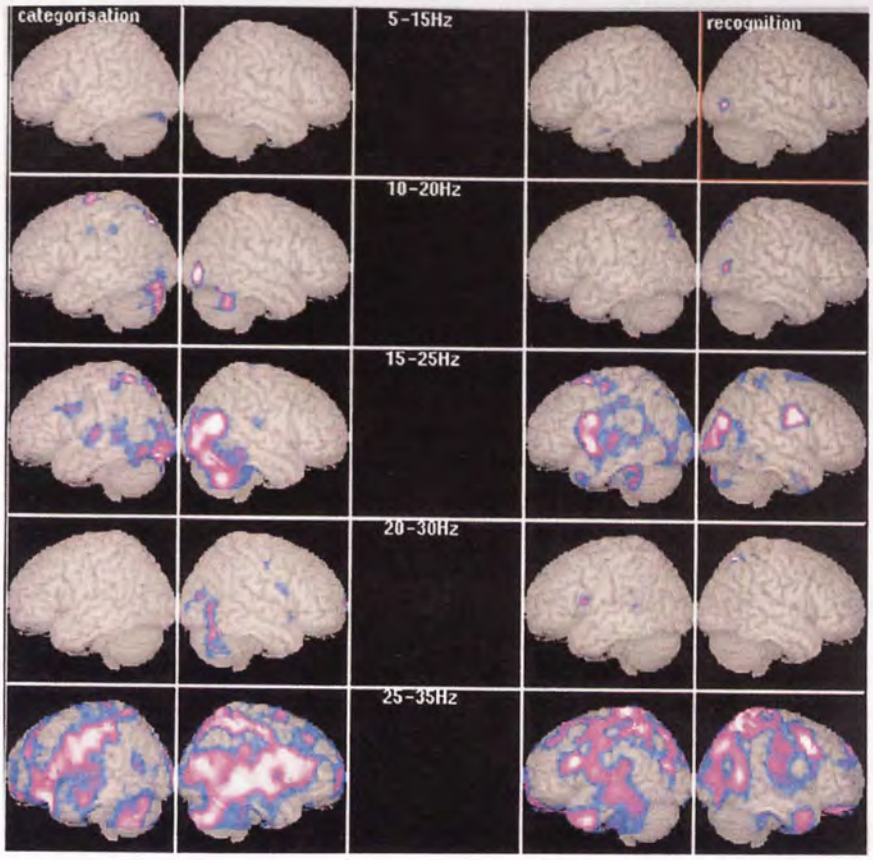
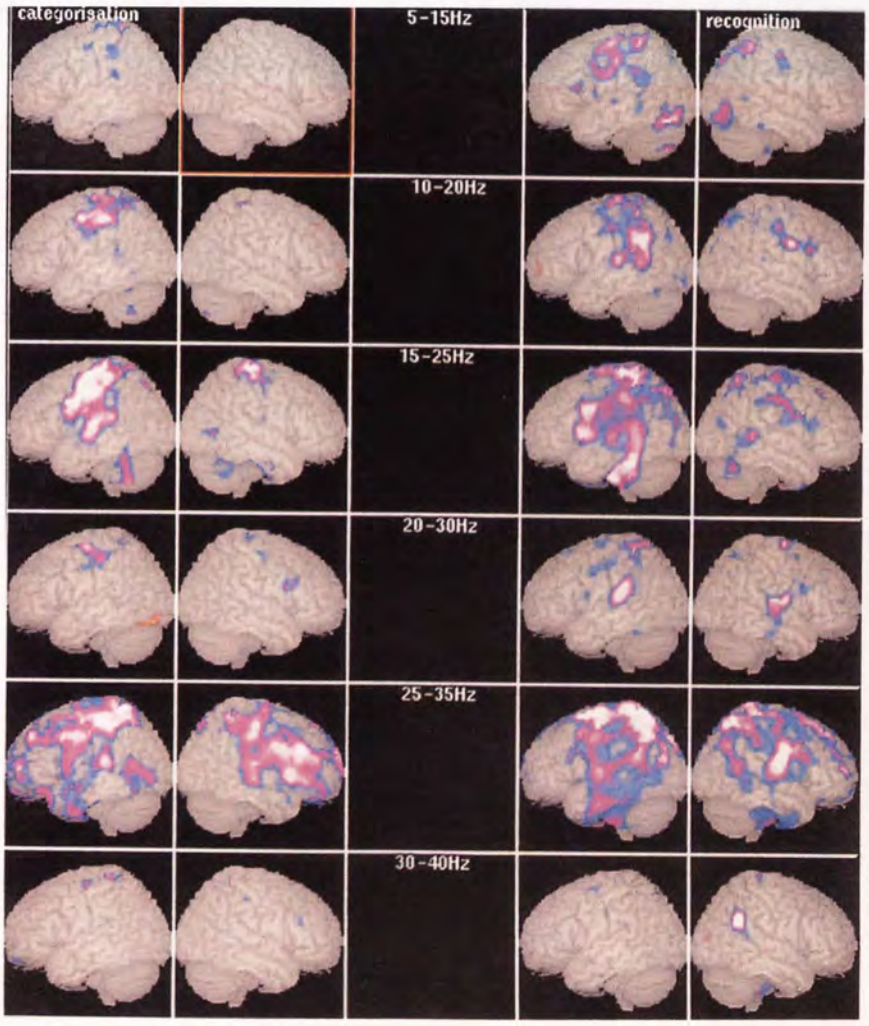


Figure 5.5: Left and right hemispheric ERD activity following a comparison of baseline activity (500ms pre-stimulus onset) with categorisation (left two columns) and recognition (right two columns) during the first 500ms post stimulus onset (0-500ms) for 5 frequency bands (rows – 5-15; 10-20; 15-25; 20-30; 25-35 Hz)

Figure 5.6 : Left and right hemispheric ERD activity following a comparison of baseline activity (500ms pre-stimulus onset) with categorisation (left two columns) and recognition (right two columns) during the second 500ms post stimulus onset (500-1000ms) for 6 frequency bands (rows – 5-15; 10-20; 15-25; 20-30; 25-35; 30-40 Hz)



5.4.2.4 Summary of Encoding versus Recognition

The direct SAM comparison between encoding and recognition for both objects and words showed more ERD during the recognition phase of the task. Across the entire trial (0-1500ms), ERD for words was only observed within the parietal and occipital lobes. For objects it was more widespread, and predominantly within the left hemisphere with only small localised areas of ERD in the right hemisphere. The two smaller timed comparisons (0-500ms and 500-1000ms post stimulus onset) produced much more widespread ERD across both hemispheres for both words and objects, particularly during the recognition phase of the task.

Table 5.15 summarises all left and right hemispheric, frontal, temporal and limbic regions that showed statistically significant ERD (at $p < 0.05$ significance level) over the entire trial. Tables 5.16 and 5.17 summarise all left and right hemispheric, frontal, temporal and limbic regions that showed statistically significant ERD (at $p < 0.05$ significance level) over the two 500ms time windows for both words and objects. As discussed previously, all observed activation was ERD, the baselines indicating this was due to increased ERD during recognition. For words, ERD was only observed during the two smaller time comparisons, not over the entire trial. For objects, more areas showed ERD during the smaller 500ms time comparisons.

Whole Trial (0-1500ms)	Objects	Words
Left Hemisphere	Middle Frontal Gyrus	
	Medial Frontal Gyrus*	
	Precentral Gyrus	
	Superior Temporal Gyrus*	
	Middle Temporal Gyrus (MTL)*	
Right Hemisphere	Prefrontal Cortex / Insula*	
	Middle Frontal Gyrus	
	Precentral Gyrus	

Table 5.15 Summary of statistically significant frontal, temporal and limbic ERD for encoding versus recognition, for both words and objects across the entire trial (0-1500ms). * Hemispheric-specific regions within stimulus modality

	Left Hemisphere	Right Hemisphere
0-500ms	Middle Frontal Gyrus Precentral Gyrus Superior Temporal Gyrus Middle Temporal Gyrus Fusiform Gyrus Insula	Superior Frontal Gyrus Inferior Frontal Gyrus Medial Frontal Gyrus Superior Temporal Gyrus Inferior Temporal Gyrus Parahippocampal Gyrus
500-100ms	Middle Frontal Gyrus Inferior Frontal Gyrus Precentral Gyrus Middle Temporal Gyrus Superior Temporal Gyrus Insula	Medial Frontal Gyrus Middle Temporal Gyrus Superior Temporal Gyrus Fusiform Gyrus Parahippocampal Gyrus Anterior Cingulate

Table 5.16 Summary of statistically significant ERD within the frontal temporal and limbic lobes for encoding versus recognition, produced by both words and objects in two 500ms time comparisons (0-500ms and 500-1000ms post-stimulus onset).

	Words	Objects
0-500ms		
Left Hemisphere	Inferior Frontal Gyrus Inferior Temporal Gyrus Posterior Cingulate	Superior Frontal Gyrus Medial Frontal Gyrus
Right Hemisphere	Middle Temporal Gyrus	Middle Frontal Gyrus Precentral Gyrus Fusiform Gyrus Insula Anterior Cingulate
500-100ms		
Left Hemisphere	Posterior Cingulate	Superior Frontal Gyrus Medial Frontal Gyrus
Right Hemisphere	Inferior Frontal Gyrus Inferior Temporal Gyrus	Middle Frontal Gyrus Superior Frontal Gyrus Precentral Gyrus Transverse Temporal Gyrus Insula Posterior Cingulate

Table 5.17 Summary of statistically significant modality-specific ERD within the frontal temporal and limbic lobes for encoding versus recognition, for both words and objects in two 500ms time comparisons (0-500ms and 500-1000ms post-stimulus onset).

A number of areas showed ERD for both objects and words within the same hemisphere (Table 5.16). During the initial 500ms post stimulus onset, the left middle frontal, precentral, superior and middle temporal, fusiform gyri and insula all showed ERD for both objects and words. Similarly, within the right hemisphere, the superior, inferior and medial frontal, superior and inferior temporal and parahippocampal gyri were also activated by both stimulus types. Similar ERD was observed during the later 500ms (500ms – 1000ms) time window with both objects and words activating the left middle and inferior frontal gyri, precentral gyrus and the insula. Within the right hemisphere, both objects and words produced ERD in the medial frontal, fusiform and parahippocampal gyri

and the anterior cingulate. In addition ERD was seen bilaterally in the middle and superior temporal gyri.

Within each of the hemispheres and modalities, regions specific to either objects or words, or the left and right hemispheres were observed. For objects, over the entire trial, a number of regions were activated within the left hemisphere only, specifically the medial frontal gyrus and the superior and middle temporal gyri. ERD for objects in the right hemisphere was seen in the prefrontal cortex / insula only.

Clear regional differences in ERD were seen between words and objects during the two 500ms time comparisons (Table 5.17). During the initial 500ms post stimulus onset, both the left and right hemispheres showed modality-specific ERD. In the left hemisphere, the superior and medial frontal gyri were only activated by the object stimuli, whilst the inferior frontal and temporal gyri and posterior cingulate only showed ERD for words. More regions showed object-specific ERD than word-specific within the right hemisphere. These included the middle frontal, precentral and fusiform gyri, the insula and the anterior cingulate. Word-specific ERD was only observed in the middle temporal gyrus and a small region of the limbic lobe (the uncus).

A similar pattern of modality-specific hemispheric ERD was also seen between 500ms and 1000ms post-stimulus onset. Within the left hemisphere, object-specific ERD was seen in the superior and medial frontal gyri and smaller regions of the limbic lobe, whilst words activated the inferior temporal gyrus and the posterior cingulate. Again more modality-specific ERD was observed in the right hemisphere for objects than for words. In particular, the middle, superior and precentral gyri, transverse temporal gyrus and insula all showed object-specific ERD. For words, the right inferior frontal and temporal gyri were specifically activated.

Whilst there were a number of task-specific regions there was specific hemispheric ERD that did depend on the modality of the stimulus. Specifically, the left posterior cingulate by words, compared to the right insula and right transverse temporal gyrus by objects.

It must also be noted, however, that the regions summarised in the preceding tables (Tables 5.1.6 and 5.17) were not necessarily single activations produced when comparing encoding with recognition. Rather the multiple areas reported were often large clusters that extended over several cortical regions. It is within these extensive activations that smaller

localised clusters are situated. The activation maps generated by SnPM visually indicated that there were several large areas of ERD, in which ten discrete cortical clusters (identified by their size) were located. Furthermore, some of these also contained smaller clusters. For example, the first region covering a size of 1099mm^3 comprised three smaller areas, identified by their Talairach co-ordinates. It was these smaller clusters that were reported here.

	Encoding		**Recognition**	
	Objects	Words	Objects	Words
0-500 ms				
Left Hemisphere	Inferior Frontal Gyrus Superior Parietal Lobule Postcentral Gyrus Lingual Gyrus Posterior Lobe – Declive		Middle Temporal Gyrus Superior Temporal Gyrus Limbic Lobe – Uncus Precuneus Cuneus Anterior Lobe – Culmen	Middle Frontal Gyrus Precuneus Inferior Parietal Lobule
Right Hemisphere	Inferior Frontal Gyrus Middle Temporal Gyrus Superior Temporal Gyrus Insula Cingulate Gyrus Inferior Parietal Lobule Middle Occipital Gyrus Lingual Gyrus Posterior Lobe - Declive	Inferior Parietal Lobule Supramarginal Gyrus Middle Occipital Gyrus Cuneus	Middle Frontal Gyrus Inferior Frontal Gyrus Precentral Gyrus Cingulate Gyrus Superior Parietal Lobule Middle Occipital Gyrus	Inferior Temporal Gyrus Fusiform Gyrus Parahippocampal Gyrus Precuneus Middle Occipital Gyrus Cerebellum
500-1000ms				
Left Hemisphere	Middle Frontal Gyrus Superior Frontal Gyrus Precentral Gyrus Postcentral Gyrus Inferior Occipital Lobe Posterior Lobe		Middle Frontal Gyrus Inferior Frontal Gyrus Precentral Gyrus Middle Temporal Gyrus Occipito-temporal Region Postcentral Gyrus Inferior Parietal Lobule Superior Parietal Lobule Precuneus Supramarginal Gyrus Lingual Gyrus	Middle Frontal Gyrus Inferior Frontal Gyrus Precentral Gyrus Limbic Lobe – Insula Inferior Parietal Lobule Precuneus Postcentral Gyrus
Right Hemisphere	Middle Frontal Gyrus Inferior Frontal Gyrus Medial Frontal Gyrus Precentral Gyrus Fusiform Gyrus Limbic Lobe – Cingulate Gyrus Supramarginal Gyrus		Transverse Temporal Gyrus Corpus Callosum Postcentral Gyrus Supramarginal Gyrus Paracentral Lobule	Superior Temporal Gyrus Insula – Claustrum Inferior Parietal Lobule Supramarginal Gyrus

Table 5.18 Summary of all baseline comparisons in the two 500ms time windows; recognition and encoding, objects and words.

5.4.3 'Old' versus 'New'

5.4.3.1 Comparison Across the Entire Trial (0-1500ms)

A direct comparison between the identification of 'new' stimuli (active) with 'old' stimuli (passive) across the entire trial (0 – 1500ms post stimulus onset) was conducted for both words and objects. Figures 9 and 10 show areas that are differentially activated between these two tasks for words and objects, respectively.

Words

No regions were found to be statistically significantly activated at either the level of $p < 0.05$ or $p < 0.1$.

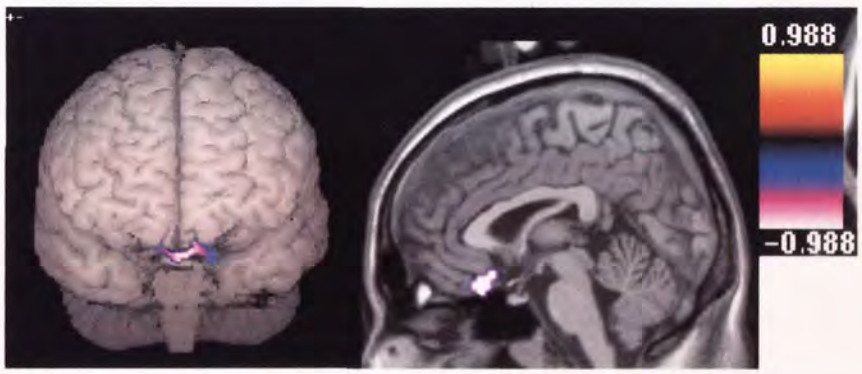


Figure 5.7: Regions showing statistically significant ERD ($p < 0.05$) between the recognition of 'old' and 'new' stimuli across the entire trial, for objects (30-40Hz)

Objects

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Prefrontal Cortex	Right	30-40	3 24 -21	42	7.60	0.047	11

Table 5.19 Regions showing statistically significant differences in activation ($p < 0.05$) between the recognition of 'old' and 'new' objects across the entire trial

The direct comparison between activation for 'old' and 'new' objects produced only one statistically significant cluster (see Table 5.19 and Figure 5.7), which was in the right PFC. The activation produced was ERD and again the baseline comparisons indicated that this was due to more ERD in the active phase, i.e. when identifying 'new' items compared

to recognising 'old' objects. Furthermore, the removal of eye movements data suggests that this may be true activation and not eye movement artefacts

5.4.3.2 Time Span Comparisons

Direct SAM comparisons between the recognition of 'old' (identification of 'new' (active) stimuli were also conducted for two 500m again to provide a measurement of the temporal resolution. The first (0-500m (500-1000ms) 500ms post stimulus onset blocks analysed for both objec showed very little statistically significant (at the level of $p < 0.05$) activation.

0-500ms

The comparison between items correctly recognised as 'old' (passi correctly identified as 'new' (active) during the initial 500ms post-stimulus (produce any statistically significant differences ($p < 0.05$) or trends ($p <$ words or objects.

500-1000ms

Words

The SAM comparison between 'old' and 'new' words during the following stimulus onset also failed to produce any statistically significant activation (again at neither of the two significance levels).

Objects

The second 500ms time comparison between 'old' and 'new' items for to produce any statistically significant clusters, although two clusters were the frontal lobe which had a trend towards significance ($p = 0.15$), sugge statistical power of the study may need to be increased. Specifically, the re statistically significant differences in ERD between 'old' and 'new' items medial and superior frontal gyri. The SAM analysis for the entire trial (see

baseline comparisons over the same time period, indicated that the differences were observed because there was greater ERD during the identification of 'new' items compared to the recognition of 'old' objects.

5.4.3.3 Baseline Comparisons

Detailed results are reported below for the baseline comparison of old and new objects and words. Table 5.28 (section 5.4.3.4) provides a summary of all significant activations. Figures 5.8 and 5.9 illustrate the significant regions in both 500ms time windows.

5.4.3.3.1 Baseline versus 'Old'

0-500ms

Words

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Middle Frontal Gyrus	Left	15-25	-47 9 41	7	5.77	0.047	8
Inferior Temporal Gyrus	Right	15-25	45 -71 -6	863	6.46	0.016	
Fusiform Gyrus	Right	5-15	37 -33 -23	166	8.82	0.016	37 / 20
		15-25	46 -69 -18	863	6.32	0.039	19
Parahippocampal Gyrus	Right	5-15	37 -30 -26	166	8.82	0.047	36
Cingulate Gyrus	Left	25-35	-20 -23 39	120	6.64	0.008	31
Inferior Parietal Lobule	Left	25-35	-43 -71 39	33	6.20	0.039	
Precuneus	Left	25-35	-43 -74 35	33	6.20	0.031	39 / 7
Middle Occipital Gyrus	Right	5-15	51 -75 -12	1	5.96	0.047	19
		15-25	47 -68 -12	863	6.32	0.016	19
Anterior Lobe / Culmen	Right	5-15	30 -36 -30	166	8.82	0.008	

Table 5.20 Baseline activity (passive) versus 0 to 500 ms post stimulus onset activation (active) when correctly recognising old words during the recognition phase

The baseline comparison for words during the first 500ms-recognition of 'old' items epoch showed ERD in all cortical regions, but also more hemispheric asymmetry. Frontal activity (middle frontal gyrus) was only observed in the left hemisphere, whilst all statistically significant temporal (inferior temporal and fusiform gyri) and limbic (parahippocampal gyrus) ERD was right-lateralised. Some bilateral parietal ERD was seen

(precuneus), in addition to the left inferior parietal lobule, right middle occipital gyrus and right cerebellum also being involved.

Objects

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Frontal Lobe	Left	25-35	-36 15 27	57	6.29	0.016	
Precentral Gyrus	Right	15-25	63 -6 30	25	8.07	0.031	44
Middle Frontal Gyrus	Right	15-25	51 12 42	79	7.17	0.016	6
Precuneus	Left	10-20	-30 -72 38	38	7.55	0.016	
		25-35	-18 -63 30	2412	14.26	0.016	
Superior Parietal Lobule	Right	20-30	33 -83 54	43	6.97	0.016	7
		25-35	33 -51 54	210	6.53	0.016	
Middle Temporal Gyrus	Left	25-35	-39 3 -33	337	6.97	0.016	21
Superior Temporal Gyrus	Left	15-25	-51 -27 6	18	7.43	0.031	
		25-35	-48 -18 0	38	6.28	0.016	
	Right	25-35	60 -57 12	4	5.86	0.031	
Middle Occipital Gyrus	Right	5-15	45 -81 0	1	5.66	0.047	19
		10-20	45 -75 6	3	6.09	0.047	
Cuneus	Left	15-25	-15 -81 9	167	8.36	0.016	17
Anterior Lobe	Left	25-35	0 -48 -9	2412	6.86	0.016	
Limbic Lobe	Left	25-35	-30 6 -33	337	6.93	0.016	
Cingulate Gyrus	Right	15-25	18 -12 42	1	6.80	0.047	

Table 5.21 Baseline activity (passive) versus 0 to 500 ms post stimulus onset activation (active) when correctly recognising old objects during the recognition phase

Statistically significant ERD was observed within all major cortical regions when recognising 'old' objects (0-500ms post stimulus onset). Furthermore there were distinct hemispheric differences, especially in the frontal and temporal regions (right middle and inferior frontal and left middle and superior temporal, respectively). Bilateral ERD was observed in the limbic lobes and also parietal (left precuneus, right superior parietal) and occipital (left cuneus, right middle occipital gyrus) regions. The left cerebellum also showed statistically significant ERD.

500-1000ms

Words

ERD during the second 500ms post-stimulus onset for the recognition of 'old' words was evident within frontal, temporal, limbic and parietal regions. In particular, temporal and frontal ERD showed hemispheric specialisation (left inferior and middle frontal and precentral gyri and right superior temporal gyrus, respectively). The insula was bilaterally activated, and whilst this was also evident for the parietal lobe, regions within this area also demonstrated hemispheric differences (bilateral inferior parietal lobule, left postcentral gyrus and right supramarginal gyrus).

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Inferior Frontal Gyrus	Left	15-25	-51 6 36	189	7.46	0.008	9
Middle Frontal Gyrus	Left	15-25	-47 10 36	189	7.46	0.008	9 / 6
Precentral Gyrus	Left	15-25	-46 -1 36	189	7.46	0.016	6
		25-35	-39 -21 39	6	5.59	0.047	4
Superior Temporal Gyrus	Right	25-35	44 -24 -7	42	5.88	0.039	
Insula	Right	25-35	41 -22 -8	42	5.88	0.047	22/ 13
Postcentral Gyrus	Left	15-25	-48 -24 42	1	5.67	0.047	
		20-30	-38 -27 42	9	6.76	0.031	2
		25-35	-47 -15 21	14	5.66	0.047	43
Inferior Parietal Lobule	Left	20-30	-39 -30 42	9	6.76	0.031	
	Right	25-35	62 -39 30	83	6.50	0.031	40
Supramarginal Gyrus	Right	25-35	57 -45 30	83	6.50	0.023	40
Precuneus	Left	25-35	-18 -54 35	68	6.38	0.023	

Table 5.22 Baseline activity (passive) versus 500 to 1000 ms post stimulus onset activation (active) when correctly recognising old words in the recognition phase

Objects

Recognition of 'old' objects between 500 and 1000ms post-stimulus onset produced left lateralised frontal ERD (middle, and inferior frontal and precentral gyri). Temporal activity was observed in both hemispheres but in different regions (left middle temporal gyrus, and right posterior transverse temporal gyrus). In addition, the right corpus callosum and left lingual gyrus also showed ERD. Finally, parietal activation occurred in both hemispheres, but again different regions showed hemispheric asymmetry (left inferior and superior parietal lobules, left precuneus, right postcentral gyrus, right paracentral lobule, and bilateral supramarginal gyrus).

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Frontal	Right	15-25	16 24 21	35	7.05	0.016	
		25-35	9 54 24	1	6.13	0.047	
Precentral Gyrus	Left	15-25	-51 -3 30	106	8.25	0.016	6
Inferior Frontal Gyrus	Left	25-35	-42 3 33	499	7.54	0.016	44
Middle Frontal Gyrus	Left	25-35	-30 -9 63	499	9.56	0.016	
Postcentral Gyrus	Left	5-15	-36 -21 27	22	7.31	0.047	
		15-25	-30 -36 66	194	8.44	0.016	3
	Right	25-35	27 -33 63	8	6.09	0.047	
Supramarginal Gyrus	Left	10-20	-57 -48 30	18	7.87	0.031	
		15-25	-48 -48 30	1	6.37	0.047	
	Right	25-35	43 -51 33	259	7.17	0.016	
		30-40	60 -54 30	38	7.83	0.016	
Superior Parietal Lobule	Left	15-25	-36 -57 51	3	6.65	0.016	7
Inferior Parietal Lobule	Left	10-20	-30 -42 57	18	8.21	0.016	40
Paracentral Lobule	Right	25-35	9 -39 66	87	6.19	0.047	
Precuneus	Left	25-35	-18 -78 42	1777	7.83	0.016	
Middle Temporal Gyrus	Left	15-25	-33 -81 18	66	6.78	0.016	
Transverse Temporal	Right	25-35	60 -15 9	66	8.44	0.016	42
Occipito-temporal	Left	15-25	-54 -42 -21	274	7.99	0.016	37
Occipital	Left	5-15	-30 -75 -15	65	7.82	0.047	
		15-25	-27 -75 9	66	7.48	0.016	
Corpus Callosum	Right	15-25	15 24 21	35	7.05	0.016	
Lingual Gyrus	Left	5-15	-30 -75 -15	65	7.82	0.047	

Table 5.23 Baseline activity (passive) versus 500 to 1000 ms post stimulus onset activation (active) when correctly recognising old objects in the recognition phase

5.4.3.3.2 Baseline versus 'New'

0-500ms

Words

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Middle Temporal Gyrus	Right	25-35	44 -84 17	23	6.23	0.047	19
Precuneus	Right	25-35	18 -51 33	11	5.76	0.039	31
Cerebellum	Right	25-35	51 -75 -39	22	6.29	0.031	

Table 5.24 Baseline activity (passive) versus 0 to 500 ms post stimulus onset activation (active) when seeing new words during the recognition phase

During the initial 500ms post-stimulus onset, identification of 'new' words resulted in right lateralised statistically significant ERD. Activation extended over the right middle temporal gyrus and right precuneus. The right cerebellum, specifically the posterior lobe also showed some statistically significant ERD.

Objects

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Frontal Lobe	Left Right	25-35 25-35	-21 -12 51 36 30 9	76 54	6.66 7.09	0.016 0.016	
Precentral Gyrus	Right	25-35	45 -15 30	156	6.93	0.016	4
Middle Frontal Gyrus	Left	25-35	-21 -12 51	76	6.66	0.016	
Superior Frontal Gyrus	Right	25-35	18 51 3	54	7.09	0.016	
Medial Frontal Gyrus	Left	25-35	-12 -48 9	23	6.56	0.016	10
Parietal Lobe	Left	25-35	-39 -33 45	67	6.98	0.016	
Occipital Lobe	Left Right	15-25 25-35	-24 -75 6 24 -72 27	19 256	6.92 9.84	0.031 0.016	
Temporal Lobe	Left	15-25	-42 -12 -12	51	7.16	0.031	21
Cerebellum	Left Right	25-35 15-25	-15 -72 -18 51 -66 -48	137 14	7.33 7.20	0.016 0.031	
Insula	Right	25-35	45 -21 18	156	6.32	0031	
Hippocampus	left	25-35	-33 -18 -18	16	6.71	0.016	

Table 5.25 Baseline activity (passive) versus 0 to 500 ms post stimulus onset activation (active) when seeing new objects during the recognition phase

Statistically significant frontal activity was observed bilaterally, although over different regions within the left hemisphere (middle and medial frontal gyri) than the right (superior frontal and precentral gyri). Similarly, this hemispheric difference was also evident within the limbic lobe (left parahippocampal gyrus and left hippocampus, right insula). ERD could also be seen within both the left and right cerebellum.

500-1000ms

Words

Very little statistically significant ERD was seen during the second 500ms epoch for the identification of 'new' words. This ERD was limited to the left hemisphere, extending over parietal (inferior parietal lobule and precuneus) and occipital regions (cuneus).

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Inferior Parietal Lobule	Left	25-35	-45 -66 48	34	6.55	0.016	40
Precuneus	Left	25-35	-17 -75 18	36	6.37	0.016	
Cuneus	Left	25-35	-15 -81 18	36	6.37	0.016	18

Table 5.26 Baseline activity (passive) versus 500 to 1000 ms post stimulus onset activation (active) when seeing new words during the recognition phase

Objects

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Precentral Gyrus	Left	20-30	-45 -15 57	4	6.91	0047	
		25-35	-42 -9 33	184	8.32	0.016	6
	Right	25-35	63 -3 27	4	6.35	0.047	6
Superior Frontal Gyrus	Left	25-35	-9 54 39	549	8.11	0.016	9
Middle Frontal Gyrus	Right	15-25	18 3 63	3	6.79	0.047	
Medial Frontal Gyrus	Right	25-35	9 57 15	549	10.29	0.016	
Postcentral Gyrus	Left	5-15	-39 -30 51	85	6.96	0.047	
		30-40	-48 -15 15	2	6.06	0.031	3
	Right	15-25	30 -48 66	49	7.69	0.016	
Precuneus	Left	15-25	-18 -72 33	5	6.85	0.047	
		25-35	24 -60 51	62	6.53	0.047	
Paracentral Lobule	Left	25-35	-3 -36 63	3	6.42	0.047	
Inferior Parietal Lobule	Right	25-35	45 -36 30	58	6.90	0.016	
Superior Temporal Gyrus	Right	25-35	48 -18 6	58	6.47	0.047	22
Middle Occipital Gyrus	Right	5-15	42 -66 0	12	6.71	0.047	37
Insula	Right	25-35	48 -27 18	58	6.38	0.047	

Table 5.27 Baseline activity (passive) versus 500 to 1000 ms post stimulus onset activation (active) when seeing new objects during the recognition phase

Identification of 'new' objects (500-1000ms post stimulus onset) produced statistically significant bilateral ERD in the frontal lobes, although specific local regions showed some hemispheric differences (left superior frontal, right middle and medial frontal gyri, and bilateral precentral gyri). Temporal (superior temporal gyrus) and limbic (insula) ERD was completely right lateralised. The bilateral parietal activity too demonstrated left and right hemispheric differences (left precuneus, left paracentral lobule, right inferior parietal lobule and bilateral postcentral gyrus). Finally ERD was also observed within the right middle occipital gyrus.

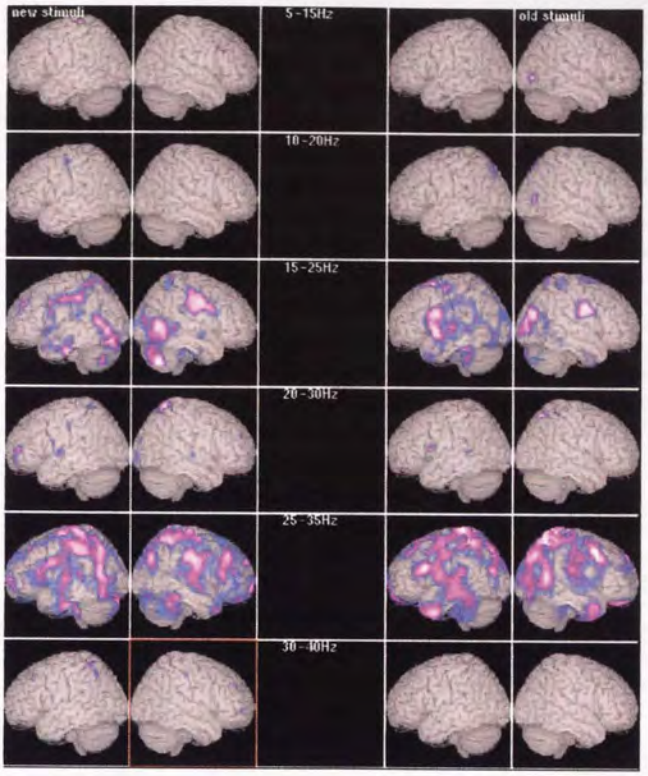
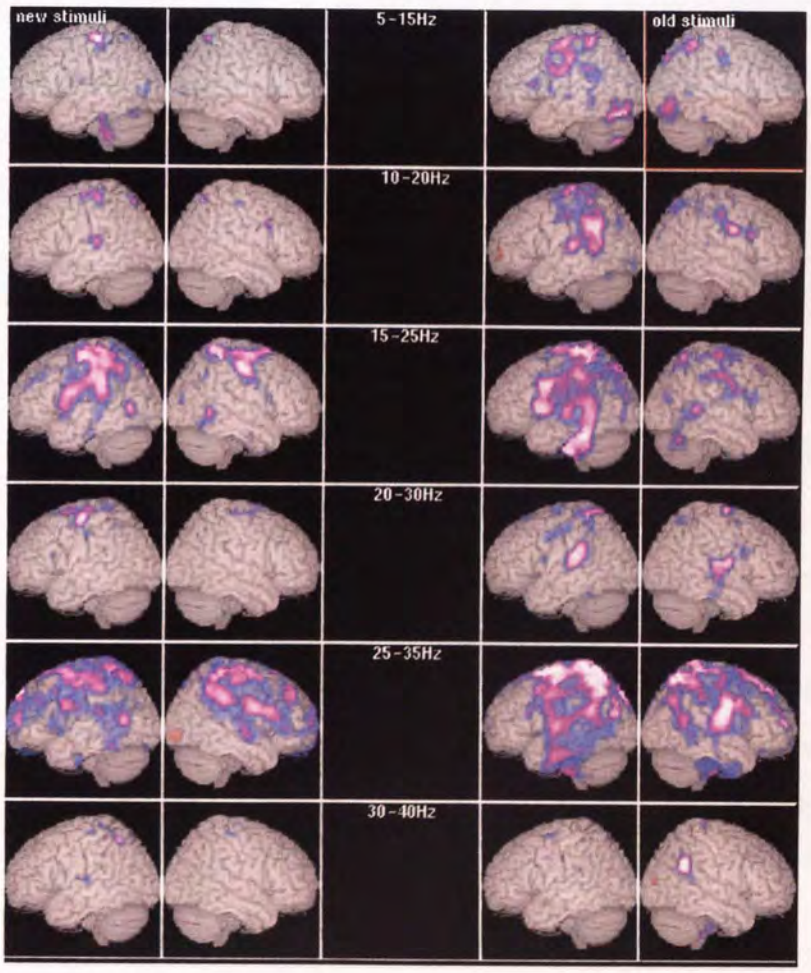


Figure 5.8: Left and right hemispheric ERD activity following a comparison of baseline activity (500ms pre-stimulus onset) with new stimuli (left two columns) and old stimuli (right two columns) during the first 500ms post stimulus onset (0-500ms) for 6 frequency bands (rows – 5-15; 10-20; 15-25; 20-30; 25-35; 30-40Hz), with the greatest activation seen the 15-25 and 25-35Hz bandwidths.

Figure 5.9 : Left and right hemispheric ERD activity following a comparison of baseline activity (500ms pre-stimulus onset) with new stimuli (left two columns) and old stimuli (right two columns) during the second 500ms post stimulus onset (500-1000ms) for 6 frequency bands (rows – 5-15; 10-20; 15-25; 20-30; 25-35; 30-40 Hz), with the greatest activation seen the 15-25 and 25-35Hz bandwidths.



5.4.3.4 Summary of 'Old' versus 'New'

	Old		New	
	Objects	Words	Objects	Words
0-500 ms				
Left Hemisphere	Middle Temporal Gyrus Superior Temporal Gyrus Limbic Lobe Precuneus Cuneus Anterior Lobe – Culmen	Middle Frontal Gyrus Precuneus Inferior Parietal Lobule	Middle Frontal Gyrus Medial Frontal Gyrus Parahippocampal Gyrus Hippocampus Cerebellum	
Right Hemisphere	Middle Frontal Gyrus Inferior Frontal Gyrus Precentral Gyrus Cingulate Gyrus Superior Parietal Lobule Middle Occipital Gyrus	Inferior Temporal Gyrus Fusiform Gyrus Parahippocampal Gyrus Precuneus Middle Occipital Gyrus Cerebellum	Superior Frontal Gyrus Precentral Gyrus Insula Cerebellum	Middle Temporal Gyrus Precuneus Cerebellum
500-1000ms				
Left Hemisphere	Middle Frontal Gyrus Inferior Frontal Gyrus Precentral Gyrus Middle Temporal Gyrus Occipito-temporal Region Postcentral Gyrus Inferior Parietal Lobule Superior Parietal Lobule Precuneus Supramarginal Gyrus Lingual Gyrus	Middle Frontal Gyrus Inferior Frontal Gyrus Precentral Gyrus Limbic Lobe – Insula Inferior Parietal Lobule Precuneus Postcentral Gyrus	Superior Frontal Gyrus Precentral Gyrus Postcentral Gyrus Precuneus Paracentral Lobule	Inferior Parietal Lobule Precuneus Cuneus
Right Hemisphere	Transverse Temporal Gyrus Corpus Callosum Postcentral Gyrus Supramarginal Gyrus Paracentral Lobule	Superior Temporal Gyrus Insula – Claustrum Inferior Parietal Lobule Supramarginal Gyrus	Middle Frontal Gyrus Medial Frontal Gyrus Precentral Gyrus Superior Temporal Gyrus Insula Inferior Parietal Lobule Postcentral Gyrus Middle Occipital Gyrus	

Table 5.28 Summary of all Baseline activity (passive) versus activation (active) when seeing old / new object / word stimuli

The direct SAM comparison between the recognition of previously seen items ('old') and the identification of novel stimuli ('new') across the entire trial failed to produce any statistically significantly different ERD for words, and only showed one cluster for objects (within the prefrontal gyrus). Separate, smaller timed comparisons (0-500ms and 500-1000ms post stimulus onset) also failed to produce any statistically significant ERD for words. Furthermore, for objects, only the right medial and superior frontal gyri showed statistically significant ERD for objects in the second timed comparison. Baseline comparisons revealed a number of statistically significant activations, and these are summarised Table 5.28.

5.5 Discussion

The main aims of this study were (1) to demonstrate the use of MEG as a tool for studying higher-order cognitive tasks, such as recognition memory, (2) to extend the research on recognition memory and (3) to assess the 'task-specific' and 'modality-specific' hypotheses of hemispheric specialisation during recognition memory tasks. The results obtained from the MEG recordings were analysed using Synthetic Aperture Magnetometry (SAM). Data presented were generated by SAM and showed statistically significant differences in ERD (at the $p < 0.05$ significance level). From the output generated, regions specifically activated during recognition memory tasks for both objects and words were identified. All activation was ERD and through the analysis of several baseline comparisons it was concluded that this was due to more ERD during the recognition task compared to the encoding / categorisation task. The high statistical significance (at the $p < 0.05$ significance level) of the ERD observed suggests that MEG is a successful neuroimaging tool for investigating higher-order cognitive tasks such as recognition memory. However, what can we conclude from these results and how do they compare to previous work? In the following sections, the findings are compared to previous functional imaging studies of recognition memory and the theoretical implications of the data discussed.

5.5.1 MEG Studies of Recognition Memory

In general, more widespread bilateral frontal and temporal ERD was observed for objects than for words. Frontal regions activated by both objects and words included the left, middle frontal, and precentral gyri and the right superior, inferior and medial frontal gyri during the initial 500ms, and during the second 500ms, the left middle and inferior frontal and right medial frontal gyri. Similar ERD for objects and words within temporal and limbic regions were also observed. In particular, both stimulus modalities produced ERD in the left hemispheric superior and middle temporal gyri, the fusiform gyrus and insula and right superior and inferior temporal and parahippocampal gyri during the first 500ms time window. Finally, between 500ms and 1000ms, ERD for both objects and words was found bilaterally in the middle and superior temporal gyri, and also in the left insula, right fusiform, right parahippocampal gyrus and right anterior cingulate.

Many of the previous functional imaging studies that used MEG primarily focused on sensory (Barnes et al, 2001), motor (Taniguchi et al, 2000) and language (Singh et al, 2002) tasks and to date there are only two other published MEG study of recognition memory (Tendolkar et al, 2000; Duzel et al, 2003). In their study, Tendolkar et al (2000) used dipole fitting to identify the brain regions involved in recognition memory of words. Dipoles were located within the right parahippocampal gyrus, right inferior frontal gyrus and left inferior parietal lobule. In this study, the SAM comparison between encoding and recognition showed concurrence, at least partially, with Tendolkar et al's findings. ERD was found within the right parahippocampal gyrus, not only for words but also for objects, which supports their findings of the MTL being involved in recognition processes. The involvement of the inferior frontal gyrus was not however, restricted to the right hemisphere as suggested by Tendolkar et al. For words, ERD was observed bilaterally within this area, and for objects within the right and then left hemispheres for the first and second 500ms time comparisons, respectively. The involvement of the left inferior parietal lobule in recognition memory, as suggested by Tendolkar et al, was not completely supported by these findings. In this study, ERD was only seen within this region during the initial 500ms for words, and was bilaterally activated for objects across the entire trial. This may have been due to differences in stimuli used; encoding task between the two studies, or more likely it is due to the use of different analysis techniques, Tendolkar et al using dipole modelling, in comparison to SAM analysis used in this study. In a previous study (chapter 4), the same dataset was analysed using these two different MEG analyses techniques and a number of differences in cortical activation revealed. Similarly in the current study, there were a considerable number of other brain regions identified by the SAM comparisons as being statistically significant that were not reported in Tendolkar et al's study.

5.5.2 Hemispheric Differences in Recognition Memory Tasks

As discussed in the Introduction, one of the major debates currently being investigated through neuroimaging studies is the role of the left and right hemispheres during encoding and recognition memory tasks for verbal and non-verbal stimuli. This study aimed to test both the 'task-specific' and 'modality-specific' hypotheses through comparisons of encoding versus recognition for both objects and words. It was predicted that if the left and right hemispheres were differentially activated by the encoding and

recognition phases, respectively, regardless of stimulus modality, this would be evidence in support of the 'task-specific' hypothesis. In contrast, the 'modality-specific' hypothesis predicts that, regardless of task, the left hemisphere should show more ERD for words, and the right hemisphere for objects.

A number of studies have observed bilateral prefrontal activation during episodic memory retrieval (Kohler et al, 2000; McDermott et al, 1999a) whilst many report right lateralised dominance (Grady, McIntosh, Beig & Craik, 2001; Buckner, Koustaal, Schacter, Wagner and Rosen, 1998; Cabeza and Nyberg, 1997). The results from this study were more consistent with those identifying bilateral prefrontal involvement in recognition memory. For both objects and words, the left and right prefrontal cortex showed ERD during the two smaller 500ms time comparisons. However, ERD within the PFC and insula was more right lateralised when the comparison was completed over the entire trial. This time-dependent difference in prefrontal ERD may reflect the hemispheric differences reported in previous neuroimaging studies. The advantage of MEG as a neuroimaging tool is its high temporal resolution, and with further analysis it may be possible to accurately identify the specific role of the PFC in recognition memory. However, there are also a number of studies which identify the involvement of the left PFC in semantic memory retrieval tasks (Kapur, Rose, Liddle, Zipursky, Brown, Stuss, Houle and Tulving, 1994; Buckner, Raichle and Petersen, 1995). The bilateral ERD observed in this study may be related to semantic processing during the recognition memory task. The semantic nature of the categorisation task during the encoding phase may have consequently resulted in semantic memory stores being accessed during the recognition task.

The widespread frontal ERD observed during the recognition phase of this study is consistent with earlier neuroimaging literature. A dipole has previously been identified in the right inferior frontal cortices, consistent with activation of this area being enhanced during successful retrieval (Fletcher et al, 1997). As described above, the MTL has also been shown through fMRI (Gabrieli et al, 1997) and some PET (Fletcher et al, 1997) studies to be involved in recognition memory tasks, this idea again supported by the findings here of increased ERD within the middle and superior temporal gyri. Furthermore it is known that the temporal area, and specifically the hippocampus, is involved in memory processes (Almkvist, 2000) but to date there are very few studies that have shown this using MEG.

As shown in the cortical activation images and table of activation values much of the parietal lobe activity is quite deep (medial) within the brain, extending over posterior cingulate. This area is referred to as the retrosplenial cortex and has been reported to be involved in memory functioning (Maddock, 1999) specifically, lesion studies have demonstrated that damage within this area can result in impaired episodic memory retrieval (Valenstein, Bowers, Verfaellie, Heilman, Day and Watson, 1987). Evidence from this study would also seem to indicate the involvement of the retrosplenial cortex in recognition memory tasks, although further analysis would be necessitated to identify regions of activation deep within the brain. It may then be possible to identify its role in both encoding and recognition tasks.

It is interesting to note that different areas were activated during the overall encoding versus recognition comparison (0-1500ms post-stimulus onset) compared to the two smaller 500ms time comparisons (0-500ms and 500-1000ms), for both objects and words. This suggests that the location of ERD may be time-dependent with a neuronal network for memory existing over the frontal and temporal cortices. Indeed, McIntosh (1999) has suggested that during episodic retrieval, there is evidence of connections between the right PFC and other fronto-temporal regions. Areas within the fronto-parietal region, have connections with some frontal areas, the occipital lobe and the temporal (specifically posterior temporal) lobe (Talairach & Tournoux, 1988). The baseline comparison performed here gave some support for this with different regions being activated within the two 500 ms time windows reported. The fact that not all of the areas are activated initially does suggest that information takes time to pass between cortical regions, leading the way forward for a cortical network to be mapped. This is further supported by evidence that the retrosplenial cortex, which has been shown to be involved in recognition memory, is believed to receive projections from a number of prefrontal, parietal, temporal and thalamic regions (Maddock, 1999). One of the advantages of MEG is the possibility of obtaining good temporal information from cognitive tasks such as this. Evidently the time windows used here may not have been small enough to identify the true temporal dynamics of memory processing, but a significant issue has been raised. Whilst complex cognitive tasks may produce too many dipoles to be fitted using the standard dipole-fitting procedure common to many MEG experiments, the development of SAM delivers the potential for new temporal analyses to be computed. The course temporal resolution used in this study provides some basic evidence of this and it should not therefore be long before it is

possible to identify a more detailed cortical network such as that described by McIntosh (1999).

The encoding versus recognition comparisons revealed greater ERD during recognition. Due to the nature of the active (recognition) versus active (encoding) comparison, if there had been regions specific to the encoding phase, this would have been indicated by statistically significant increases in power during these comparisons (and would have been illustrated as red on the SAM images), but none were observed. This would imply that all areas activated during encoding were subsequently activated during the recognition phase as well. However, it is unlikely that this is the case as the baseline comparisons indicated that different regions were activated during the two tasks. It is more probable that the course temporal resolution and the wide frequency bands, in particular, were responsible for the lack of ERS. For example, ERS is often observed within the theta frequency band, this band having a width of 4Hz (4-7Hz), in comparison to the 10Hz bandwidths used in this study.

The significance of frequency-specific activation is a topical issue in EEG research and a number of studies have shown that alpha and theta band activity may be related to memory processes (refer to section 1.3). Upper alpha desynchronisation (10-12 Hz) has been reported to be linked to semantic memory processing (Klimesch, Doppelmayr, Pachinger & Russegger, 1997) while synchronisation within the theta band (4-7 Hz) is linked to working memory (Klimesch, Schimke & Schwaiger, 1994) and the encoding of new information (Klimesch, Doppelmayr, Russegger & Pachinger, 1996; Klimesch, Doppelmayr, Schimke & Ripper, 1997).

However, the relatively arbitrary frequency bands used in this study do not exclusively correspond to either the theta or alpha bands, but spread across both (specifically, 5-15 Hz). Therefore, it is possible that because the 5-15 Hz band used in this study predominantly includes alpha waves (8-12 Hz), with much smaller amounts of theta (5-7 Hz), any potential ERS is blocked and consequently only ERD within the alpha is seen in the SAM images. The importance of narrow frequency bands is further demonstrated in a study by Krause et al (2000). Following a visual sequential letter task involving varying levels of memory load, the 4-6 Hz theta, 6-8 Hz and 8-10 Hz alpha frequency bands all showed ERS, whilst in the 10-12 Hz band there was only an increase in ERD. Furthermore, the temporal information obtained from Krause et al (2000) suggest that the 500ms epoch analyses conducted in this study may not be the most effective time

windows to use in order to show ERS. Krause et al showed that whilst ERD was long lasting in both the 8-10 Hz (~200 – 1500ms post stimulus onset) and the 10-12 Hz bands (~0 – 1500ms), ERS was seen during much smaller time windows (~500-600ms and ~100-300ms for 4-6 HZ and 6-8Hz bands, respectively). Therefore, taken together, the 10Hz frequency bands, and 500ms time windows used in this study may be too wide and long, respectively, to successfully show ERS.

In addition, many of the neuroimaging studies reported in the literature identify task-specific regions by comparing the individual task activation to a control task. For example, in a recent paper, Reber et al (2002) reported an fMRI study comparing categorization with recognition for dot-pattern stimuli. Whilst different task-specific regions were identified during separate task versus control comparisons, for both the categorisation (encoding) and recognition phases, the recognition versus categorisation comparison only produced recognition-specific activation. The authors concluded that the comparison of two active states (as opposed to an active versus control /passive) effectively produced a 'double subtraction' analysis. This reduced the power of the activation observed (Reber et al, 2002), but this should not be interpreted as being indicative of the encoding phase not producing a statistically significant activation. Other fMRI studies perform two analyses, subtracting condition one from condition two and then vice versa. Simons et al (2001) identified different regions for face and object recognition using this methodology. In future work, it may be necessary to include a more cognitively demanding baseline task (rather than fixating on a white square) to assess whether there are brain areas are selectively involved in encoding as well as in recognition.

One interesting finding was that there was more activity in the theta and alpha bandwidths during the first 500ms post stimulus onset for the encoding phase but the second 500ms time window for the recognition task. It might be that the frequency-specific memory activation reported previously (Klimesch, Vogt and Doppelmayr, 1999) may change over the course of the task, or be linked to particular components of memory tasks.

Nevertheless, despite this course frequency-specific activation, the current data show that both the right and left hemispheres were activated during the recognition phase of the task. During the first 500ms, objects activated the middle, medial and superior frontal gyri bilaterally and the right inferior frontal gyrus. Words activated the middle and inferior frontal gyrus. This data lends some support for the 'task-specific' hypothesis, because, although there was more bilateral frontal ERD during recognition compared to encoding,

there were additional areas activated in the right frontal cortex for words and for objects. The data are less consistent with the 'modality-specific' hypothesis, which predicts more left-lateralised activation during recognition of words.

During the second 500ms, objects activated the middle, superior and medial frontal gyri bilaterally and the left inferior frontal gyrus. Words activated the inferior frontal gyri bilaterally, the left middle frontal and the right medial frontal gyri. The data indicate that over time, activation in the frontal cortex has changed. In particular, for objects the activation in the inferior frontal cortex has changed from the right (0-500ms) to the left (500-1000ms) hemisphere. For words, the activation in the right superior frontal gyrus has disappeared.

The data from our MEG study are partially consistent with previous PET studies. For instance, Fletcher, Shallice, Frith, et al (1998) observed increased rCBF within the right DLPFC and the right ventral PFC in recognition memory tasks with words as stimuli. The word condition in the current study produced bilateral ERD within the ventral PFC. However, recognition of words in our MEG study activated the left DLPFC rather than the right as reported by Fletcher, Shallice, Frith, et al.

Although there was no clear hemispheric lateralisation for words and objects, it appears that more inferior cortical regions may be specifically involved with processing words, compared to the medial and superior regions for objects. A number of regions showed modality-specific activation. In particular, the left inferior frontal and bilateral inferior temporal gyri for words, and the bilateral superior frontal, left medial frontal and right middle temporal gyri for objects.

In the Introduction, a recent PET study conducted by Kohler et al (2002) was reviewed, in which hemispheric specialisation (for object and word recognition memory) within MTL structures was assessed. They reported increased bilateral rCBF during the recognition of objects in the inferior temporal gyrus and the MTL, although greater in the right hemisphere, and in the right anterior parahippocampal gyrus. Recognition of words produced greater rCBF in the left inferior parietal lobe and in the left cuneus. A number of areas also showed increased rCBF during recognition of both objects and words. These included bilateral middle and inferior frontal gyri and the left MTL. These results partially concur with Kohler et al's findings. During the second 500ms, ERD for the recognition of previously presented objects was observed bilaterally in MTL structures and in the right inferior temporal gyrus, and during the first 500ms in the left MTL. Word recognition

produced ERD in the cuneus bilaterally, and in the left inferior parietal lobe during the second 500ms. However, Kohler et al reported that MTL structures were not involved in recognition of words. The SAM analyses conducted in the current study showed that there was bilateral ERD in the MTL for objects during the second 500ms, and for words across both 500ms time spans. This suggests that the MTL may be involved in accessing semantic representations of all episodically encoded material (i.e. visual and verbal) and not just objects as proposed by Kohler et al. Furthermore, Kohler et al only reported greater rCBF in the right parahippocampal gyrus for objects. Again, in this study ERD was seen in this region for both stimulus modalities. Consequently, the right parahippocampal gyrus may have a role in accessing memory traces for all episodically encoded stimuli, not just pictorially represented material (as suggested by Kohler et al). The current study did not show any encoding-specific activation for both objects and words and so it is not possible to comment on whether MTL structures and the right parahippocampal gyrus are also involved in the establishment of these semantic representations and creation of memory traces, respectively. It is believed that in order for them to be successfully involved in recognition memory tasks, their contribution during episodic encoding should also be evident. In future analyses we propose to address this issue by identifying those regions specifically involved in the encoding of visual and verbal material.

The data from this MEG study do not appear to clearly replicate any of the findings from previous neuroimaging studies. However, it would seem that these too fail to explicitly replicate each other or to directly link each hemisphere with either stimulus modality or with task. Table 1.1 briefly summarised a number of these studies, including the ten most recently published experiments, and outlined the location of any activation within the prefrontal cortex that was reported by the authors. It can be seen that in addition to the utilisation of different neuroimaging techniques, there is also variation in the stimuli, the encoding conditions / tasks and the analysis comparisons used. Many of the studies focused on one modality, separate experiments conducted using different stimulus categories. Indeed, only nine of the twenty studies summarised used more than one stimulus modality. Furthermore, many of these did not either directly compare activations between stimulus modality or between task. Only five of the studies included in Table 1.1 directly compared activations between stimulus modalities, with only two studies providing results for both encoding and recognition phases (Idiaka et al, 2000; Kohler et al, 2000). Raye et al (2002) failed to find any statistically significant for either stimulus type in either task phase and the remaining studies only observed activation for either the

recognition phase (Simons et al, 2001) or the encoding phase (Grady et al, 1998). As Table 1.1 illustrates, the comparisons made are often task versus control or baseline (for example Reber et al 2002). Consequently, these experiments cannot distinguish between brain areas involved in general recognition memory, and those that are modality- or task-specific. Simons et al, (2001) compared rCBF in the retrieval phase for faces and objects and concluded that hemispheric specialisation was 'modality-specific'. There was increased rCBF for objects in the left anterior PFC and for faces in the right anterior PFC, as well as left DLPFC. Simons et al argued that the greater bilateral activation for objects and right-sided activation for faces supported the idea that hemispheres are specialised for modality of stimulus rather than task. However, they did not directly compare encoding and retrieval, as was compared in this study, and thus were unable to comment on a possible 'task-specific' hypothesis.

Perhaps a more accurate analysis of 'task-specific' or 'modality-specific' hemispheric dissociations during recognition memory could be achieved through direct task and modality comparisons. Whilst it is not uncommon for direct comparisons to fail to identify specific regions for both tasks (for example, Vaidya et al, 2002; Kohler et al, 2000; Lee et al, 2000; Ragland et al, 2000), this study has already suggested that this may be overcome through the use of a number of small time- and frequency-specific comparisons. The development of SAM will enable specific task and modality comparisons to be completed with the potential of identifying task and modality specific cortical areas over millisecond time resolution.

The results from different imaging studies using verbal stimuli (i.e. words) tend to consistently report greater prefrontal activation within the left hemisphere during encoding (for example, Otten et al, 2001; McDermott et al, 1999; Kelley et al, 1998). The variation in hemispheric activation during recognition (for example, Buckner et al, 2001, Grady et al, 2001, Ragland, 2000 report left-, bilateral and right-hemispheric PFC activations respectively) may be accounted for by the different encoding tasks, such as intentional learning, sentence generation and semantic categorisation. Previous neuroimaging literature has identified different regions of activation according to depth of encoding. For example, Grady et al (2001), using PET, identified different prefrontal areas that were involved in perceptual and semantic encoding tasks. As this study involved a deep encoding task, that of semantic categorisation, the subsequent brain areas identified may vary to those identified by previous literature which used a shallow encoding task. The involvement of semantics in recognition memory processes is an important issue and this

difference between a deep and shallow encoding task will be addressed in a follow-up study, presented later.

However the stimuli used to identify regions associated with non-verbal stimuli often vary between studies. The objects used in this MEG study, whilst only simple line drawings, may have evoked semantic associations or may have been encoded verbally. Many studies use faces as non-verbal stimuli (e.g. Simons et al, 2001; Kelley et al, 1998) as usually it is difficult to encode them verbally. However, they too may have semantic associations and these semantic links may also exist for words. It is possible, therefore, that there are semantic stores accessed during both encoding and recognition phases.

The concept of a semantic network may explain the widespread activation, and more specifically the large number of cortical areas similarly activated across different modalities in neuroimaging studies of recognition memory (as shown in Table 1.1). This may be particularly pertinent to this study, as the discrete cortical areas reported tended to be sub-regions of larger clusters of ERD, which were observed to extend over multiple cortical regions. Furthermore, although many previous studies focus their attention on a few discrete areas, multiple widespread regions of activation are often observed, but not necessarily discussed in detail. Therefore, areas identified may not be explicitly associated with encoding or recognition, but may reflect more general demands on semantics. The use of pure verbal and non-verbal stimuli, such as non-words and non-objects, may provide a more accurate account of recognition memory.

Nevertheless, the results from our MEG study, combined with those from previous neuroimaging studies, could be interpreted as indicating the existence of frontal and temporal regions specialised for encoding and recognition memory tasks, and that within these are specialised modality-specific regions. For example, the prefrontal and middle temporal gyri are consistently shown to be involved with episodic encoding. Although these have a tendency to show left and right hemispheric dominance, respectively, there are a large number of studies that show bilateral activation within these areas. Therefore, whilst 'modality-specific' regions may exist, they do not seem to be closely linked to one hemisphere or the other. Instead, the hemispheric differences often reported may simply be related to stimulus modality, or encoding strategy.

The results from this study do suggest, however, that there may be at least one region that shows complete hemispheric asymmetry depending on stimulus modality. ERD was seen within the posterior cingulate exclusively within the left and right hemisphere for

words and objects respectively. The apparent specialised involvement of this region is consistent with its location within the retrosplenial cortex. The retrosplenial cortex is an area situated within the medial region of the parietal lobe, extending over the posterior cingulate, which has been consistently shown to be involved in recognition memory tasks (Maddock, 1999). Indeed, lesion studies have demonstrated that damage within this area can result in impaired episodic memory retrieval (Valenstein, Bowers, Verfaellie, Heilman, Day & Watson, 1987).

5.5.3 Old versus New Effect

Comparing old versus new stimuli for both objects and words only produced statistically significant ERD for objects. All activation was ERD and from the baseline comparisons it was possible to conclude that this was due to increased ERD when identifying stimuli as new compared to old. All comparisons for the word stimuli failed to produce any statistically significant activation. For objects, across the entire trial, a small cluster was identified in the PFC, and only within the second 500ms time comparison (500-1000ms) did the right medial and superior frontal gyri show ERD. Tendolkar et al (2000) have previously reported an old/new effect using MEG. Between 400 and 1000 ms after stimulus onset a significant difference between the correctly recognised old and new words was observed. The magnetic evoked fields (MEFs) were larger to the old words over the left hemisphere and with time were more parietal in location. This is partially consistent with the findings of this experiment in which the frontal areas showing ERD for new objects were completely right lateralised.

In Tendolkar et al's study, the strongest fields generated by dipole fitting over the scalp for old words, was in the region of the MTL. This supports earlier findings (Gabrieli et al, 1997) that the MTL, while associated with both encoding and retrieval, responds more strongly to previously encountered stimuli. Although in this study no ERD was identified in the MTL through the direct comparisons, the baseline comparisons suggested that the MTL is involved in encoding and retrieval processes. The importance of this area in recognition memory has been further demonstrated through studies of patients in which the MTL is damaged. In these cases the old/new effect is significantly reduced (Rugg et al, 1991; Allan et al, 1998).

Many studies report this old/new effect. Ranganah and Paller (1999) report an EEG study in which the old/new effect was largest over the tempero-parietal regions, and was more predominant over the left hemisphere (see also Allan et al, 1998; Paller & Kutas, 1992). Why therefore, did this study fail to show such an old/new effect? As discussed previously, direct comparisons are not always effective in identifying cortical areas specific to both conditions. Furthermore, the importance of temporal dynamics has also been suggested, and the course resolution in this study may not have been sufficient to highlight such differences. It is plausible that initially, many of the regions involved in processing old and new stimuli are similar. Primarily it is a recognition task and the first regions involved will be concerned with processing or encoding the stimuli as it is presented. This input will then be compared to those previously encountered and a judgment made. It may therefore be at this judgement stage that differences in cortical activations are observed between old and new stimuli. MEG analyses could identify the time course of this process and so it is hypothesised that with a number of small time comparisons, an old/new effect might be observed.

Furthermore, the relative null result of an old / new comparison, as found in this experiment, has actually been reported on number of occasions in previous fMRI studies (McDermott et al, 1999b; Schacter, Buckner, Koustaal, Dale and Rosen, 1997; Buckner, Koustaal, Schacter, Dale, Rotte and Rosen, 1998b). Buckner et al (1998) suggested that the existence of the old/new effect was simply due to methodological constraints. Specifically, the use of a block design in which participants were able to identify clusters of old and clusters of new stimuli has been implicated (McDermott et al, 1999). Consequently, participants may utilise different strategies in recognising old and new stimuli (Wagner, Desmond, Glover and Gabrieli, 1998). Indeed, Tendolkar et al utilised such a block design for their recent MEG study. This study has also questioned the validity of a dipole approach for studying recognition memory.

5.6 Concluding Remarks

In conclusion, the first aim of this study was to extend the research on recognition memory using MEG. Using Synthetic Aperture Magnetometry (SAM) (Robinson & Vrba, 1999), rather than the standard dipole fitting of the evoked response it was hypothesised that the involvement of prefrontal and medial temporal structures in encoding and recognition tasks would be identified and furthermore that the MEG data could be used to

identify the additional cortical areas involved in recognition memory. In the current study, statistically significant areas of activation were identified within the prefrontal and medial temporal cortices during encoding and recognition .This data suggests that MEG can be used to study high-level cognitive tasks such as recognition memory and there was some consistency between the findings of this study and those from previous research, with activity. However, it was suggested that the variation already present in the current literature is due to the varying stimuli, neuroimaging techniques, tasks and analysis techniques.

Secondly, this study aimed to use MEG to assess the 'task-specific' and 'modality-specific' hypotheses of hemispheric specialisation in prefrontal regions during recognition memory tasks. Although there was some indication of hemispheric asymmetry, there was no left- or right-lateralised activation during encoding and recognition respectively, as predicted by the 'task-specific' hypothesis. In contrast, there was some evidence of modality-specific asymmetry, with increased left PFC activation during encoding and recognition of words, and right-lateralised for objects. However, the larger number of bilaterally activated regions, which did not demonstrate hemispheric asymmetry, suggests that the 'modality-specific' hypothesis can also not fully accommodate these findings.

It is therefore proposed that there is a more general network of cortical areas involved in encoding and recognition of words and objects, and if modality-specific region do exist, they are not lateralised. In particular, the diverse cortical activity observed may be due to influence of semantic processes, occurring in conjunction with the memory processes. Similarities are known to exist between semantic and encoding memory, and it is therefore suggested that through the use of a semantic encoding task, the subsequent recognition phase also involves semantic processing. It is necessary, therefore to assess the influence of these semantic associations on recognition memory, and the following study was designed to do just that. In a replication of this study, category-specific effects (between living and non-living stimuli) were assessed in both the encoding and recognition phases.

6 CATEGORY-SPECIFIC BRAIN REGIONS IN RECOGNITION MEMORY

6.1 Overview

In a previous study (chapter 5), it was suggested that the diverse cortical activity observed in studies of recognition memory may not be specifically due to memory processes, but to the additional involvement of semantic processing. This study was designed to assess the influence of these semantic associations on recognition memory. Similarities are known to exist between semantic and encoding memory, and it was hypothesised that when using a semantic encoding task the subsequent recognition phase will also involve semantic processing.

In a replication of the previous study, category-specific effects (between living and non-living stimuli) were assessed in both the encoding and recognition phases to determine whether different regions of the brain were activated in the encoding and recognition phases for living and non-living items., testing the hypothesis that there is category specificity during recognition memory tasks. As expected, and consistent with numerous previous studies, differences were observed between living and non-living items during the categorisation (encoding) task. Furthermore, differences were also observed between the two stimuli in the recognition phase, consistent with the experimental hypothesis that category specificity also exists during recognition memory tasks. This suggests that activation observed in recognition memory tasks may not specifically reflect memory processes but might be due to the involvement of a semantic network.

6.2 Introduction

Neuroimaging studies of recognition memory have demonstrated differential involvement of frontal, parietal and temporal regions in accurate encoding, retrieval and recognition. Across the large number of studies, however, multiple, widespread cortical regions have been linked to recognition memory processes (see for example Table 1.1). It has been suggested (chapter 5) that these identified areas may not be explicitly associated with encoding or recognition, but may reflect more general demands on semantics. The

concept of a semantic network, therefore, may help explain this diverse activation pattern. Specifically, the variation in hemispheric activation during recognition tasks (as illustrated in Table 1.1) may be accounted for by the different encoding tasks, such as semantic categorisation.

As there are a number of differences between episodic and semantic memory (Tulving, 1983), they are generally considered separately. The most obvious is that, whilst retrieval of semantic memory necessitates conscious awareness, episodic retrieval involves additional autonoetic (unconsciousness) awareness. Consequently, these two types of memory are usually considered separate. The interaction, however, between episodic and semantic memory is well documented, and so it is feasible that that in task of episodic recognition memory, semantic memory may also be involved.

Successful episodic encoding is believed to require the information to first be successfully processed in semantic memory (Tulving, 1995). In addition, Tulving (1972) argued that semantic memory could play a significant role in the processes occurring during episodic recollection. Furthermore, recognition is believed to be facilitated by the linking of components / features when an episode is meaningfully interpreted.

Neuroimaging literature has illustrated that some of the same cortical regions are activated in multiple memory systems. For example, (Kapur, Rose et al, 1994) reports that episodic, semantic and working memory all involve some of the same regions in the left inferior prefrontal cortex. The progress in this field of research suggests that our understanding of the interactions existing between different types of memory is continuing to develop. The current existence of studies to support these interactions substantiates the hypothesis that the existence of a semantic network and the use of a semantic categorisation encoding task may account for the variation in hemispheric activation during recognition memory reported previously (chapter 5).

A double dissociation in category-specific recognition and naming impairments for living and nonliving things has been widely reported in the neuropsychological literature for over 20 years (for a comprehensive review, see Humphreys & Forde, 2001). For example, in the first detailed report of category-specific recognition impairments, Warrington and Shallice (1984) reported a case study of a patient, JBR, who was only able to name a small percentage of living things but the majority of nonliving things. In addition, he was only able to provide definitions of 6% of living things compared to 90% nonliving things. He described a compass as "tools for telling direction you are going" and

a briefcase as "a small case used by students to carry papers", but when asked to describe a parrot he said "don't know" and he described a snail as "an insect animal". Warrington and Shallice (1984) suggested that impairments of category-specific recognition emerge following brain damage because different forms of knowledge are important for identifying living and nonliving things. They proposed that stored visual information, such as colour, shape and size, was important for differentiating between two living things (e.g. colour and size for differentiating between an orange and a grapefruit) but that information concerning the function of the object was more important for nonliving thing. They suggested that we have evolved separate semantic systems that store visual and functional knowledge and mediate recognition of living and nonliving things, respectively (the 'sensory-functional' hypothesis). According to this account, JBR had sustained damage to stored visual semantic knowledge, which led to his category-specific impairment for living things. Others have suggested that differences in recognising living and nonliving things can emerge at earlier, pre-semantic stages in object recognition. For instance, Humphreys, Riddoch & Quinlan (1988) suggested that disorders of category-specific recognition for living things could arise from impairment of the structural description system because living things tend to belong to categories with numerous structurally similar exemplars (the 'similarity' hypothesis). As a consequence, living things require greater perceptual differentiation than nonliving things to access knowledge concerning individual exemplars (Forde, Francis, Riddoch, Rumiati & Humphreys, 1997). Nonliving things tend to be structurally distinct from one another and require less differentiation to access the structural description system.

Several functional imaging studies have investigated whether there are category-specific brain regions by comparing the patterns of neuronal activity when normal participants are asked to name or make judgements about living and nonliving things. In a number of these studies, using both PET (Martin, Wiggs, Ungerleider & Haxby, 1996; Moore & Price, 1999) and fMRI (Chao, Haxby & Martin, 1999; Thompson-Schill, Aguire, D'Esposito & Farah, 1999), posterior occipito-temporal activation has been associated with recognition of living things, although there is a degree of variability in the findings (Price & Friston, 2002). Few studies have controlled for the visual complexity of stimuli (for an exception, see Moore & Price, 1999) and it is currently unclear whether this occipito-temporal activation reflects greater perceptual processing because (1) living things require prolonged access to stored visual knowledge (required to differentiate one structurally

similar exemplar from another, see Humphreys et al, 1988) or (2) they are more visually complex images.

The pattern of activation revealed in different functional neuroimaging studies on category-specificity is more consistent for nonliving things, which typically activate the left medial temporal and inferior frontal regions close to the areas activated when participants generate or observe actions (Martin, Wiggs et al, 1996; Martin, Haxby, Lalonde, Wiggs & Ungerleider, 1995). This supports the idea that recognition of nonliving things depends on access to stored function / action information in semantic memory (Warrington & Shallice, 1984). One problem, however, with all of the PET and fMRI studies is that the temporal resolution is too poor to determine whether differences between living and nonliving things arise at 'early' or 'late' (e.g. semantic) stages in object recognition. That is, whether differences occur during the initial visual object recognition processes occurring within the fist 100-200ms, or whether they are during the more cognitive processing of the category-specific attributes, occurring later (such as the cognitive P300 component).

To examine the time course of differences in processing living and nonliving things, Kiefer (2002) used event-related potentials (ERPs). Kiefer showed that when participants were asked to categorise pictures of living and nonliving things there were significant category-specific differences at 'early' and 'late' stages in the categorisation process. In particular, living things elicited a greater N1 ERP component (between 160-200ms after target onset) compared to nonliving things. This N1 component reflects visual perceptual processing and is enhanced when attention is paid to visual stimuli (Mangun & Hillyard, 1991). This is consistent with the idea that living things belong to structurally similar categories and require more fine-grained visual perceptual processing in recognition tasks (Humphreys et al, 1988; Forde et al, 1997). Importantly, living things were less visually complex than nonliving things; so the larger N1 component was not simply because these items were more visually complex. A later component (between 300-500ms after target onset), termed the N400 (or N4) component, was also modulated by semantic category. This was particularly interesting because the N400 component has consistently been shown to be associated with semantic processing in numerous studies (e.g. Kutas & Hillyard, 1980; Kutas & Van Petten, 1994). Living things modulated the N400 component in occipito-temporal regions (predominantly over the right hemisphere) and nonliving things modulated the N400 component over fronto-central regions (predominantly over the left hemisphere). The 'late' N400 component, but not the 'early' N1 component, was also

modulated by category when the experiment was repeated with words. These data demonstrate that category specific effects can be found at temporally distinct stages in the categorisation process. With words, category specific differences were confined to semantic processing, but with pictures there were also category specific differences in perceptual processing.

There are three popular models of category specificity, of which Kiefer et al's (2002) data are consistent with the first two. The first model suggests that living things belong to more perceptually similar categories (Humphreys et al, 1988). According to this model, the categories share the same processing system, but that differences arise due to the different demands they place on it. Consequently, living things necessitate more perceptual discrimination as they share more visual attributes than do non-living things. Furthermore, within this model, there should also be an effect of stimulus modality as when processing objects compared to words for example, object recognition processes could be involved with the former. Kiefer's (2002) data was also consistent with the idea that there are category-specific differences in accessing stored semantic knowledge (Warrington & Shallice, 1984). This model proposes that there are separate systems that are involved in the processing of perceptual and functional knowledge. More specifically, living object identification relies primarily on perceptual knowledge, in contrast to the functional information needed for non-living objects. The third most popular of the category-specificity models proposes that there are category-specific neuronal systems (Caramazza & Shelton, 1998), with the different biological salience of the categories reflected in the functional specialisation reported.

Assessment of category specificity by neuroimaging techniques provides a way of identifying the functionally integrated and segregated cortical regions involved. Identification of this semantic network can then be used in tasks of recognition memory in which semantic associations are believed to be influential, and possibly responsible for the diverse activation in the recognition memory neuroimaging literature. Curran (2001) reported an ERP study in which the mechanisms involved in categorisation and recognition were investigated. Although Curran suggested that categorical differences were not present at very late stages of the recognition process, amplitude differences were observed between categorisation and recognition in a P300-like component, occurring between 400-600ms post-stimulus onset.

6.2.1 Aims and Hypotheses

The aim of this study was to test the hypothesis that there is category-specificity during recognition memory tasks. A similar experiment to Kiefer (2002) was conducted to identify the brain areas involved in processing living and nonliving things at different stages in the categorisation process, and to determine whether different regions of the brain were activated in the encoding and recognition phases for living and non-living items. In the experiment, participants were asked to categorise a series of pictures as living or nonliving things. A recognition task followed the semantic categorisation task, in which participants performed a yes /no recognition judgement task. It was expected that in-line with previous studies, the MEG data would identify category-specific differences for living and non-living items during the encoding task. Due to the overlap between episodic and semantic memory, it was further predicted that these category-specific differences would also be evident during the recognition memory phase of the task. Therefore, it was hypothesised that different cortical regions would be involved in performing a 'yes / no' recognition judgement tasks for living items, compared to those for non-living stimuli. SAM analysis was used to analyse the data, previous findings (chapter 4) indicating that this may be more appropriate than the standard dipole fitting technique for MEG studies of 'higher level' cognitive processes, such as object recognition and categorisation.

6.3 Method

6.3.1 Participants

Six normal healthy right-handed participants (two male, four female, with a mean age of 35 ± 11 years) volunteered and gave consent to be involved in the study. Anatomical MRI scans had previously been taken for each of these individuals and were made available for the analysis.

6.3.2 Stimuli

All objects were obtained from the Snodgrass and Wanderwart set of line drawings (Snodgrass & Wanderwart, 1980). Equal numbers of living and non-living, high and low

frequency objects were split between the encoding and recognition stage. The stimuli for the two phases (encoding and retrieval) were pair-wise matched, for frequency and for category, and presentation was counterbalanced, to ensure consistency across all groups.

6.3.3 Presentation of Stimuli

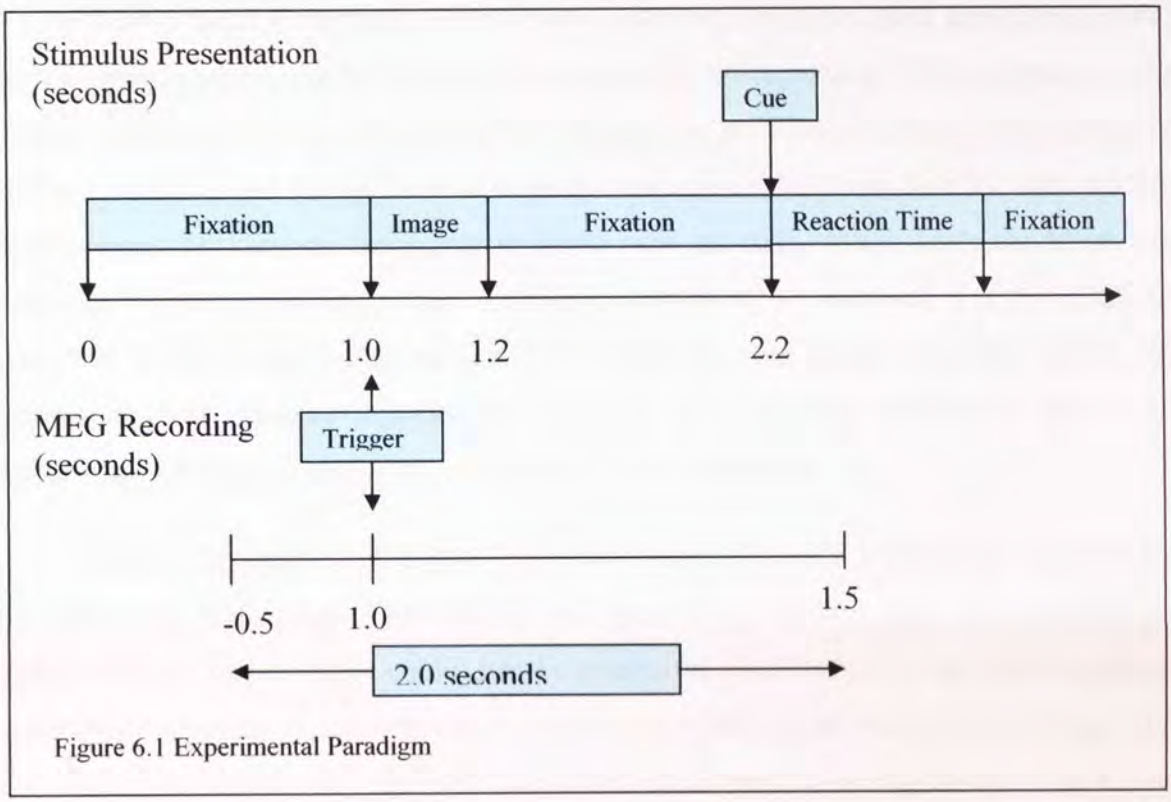


Figure 6.1 Experimental Paradigm

Participants were seated in a magnetically shielded room and viewed the stimuli, presented on an Eizo T662 monitor, through a mirror at a distance of two meters. In both the encoding and recognition phases of the experiment, the participants were required to fixate on a centrally presented small white square for a period of 1000 ms. A stimulus was then presented to the centre of the screen for 200 ms before the fixation point returned for another period of 1000 ms. The fixation point then changed from white to black, and this was the participants' cue to make a response with a button press using their dominant hand. In the encoding phase, participants were asked to categorise the stimulus as a living or non-living thing and, in the recognition phase, as an old or new item. Accuracy and reaction time responses were recorded. Participants had 2000 ms to respond before the fixation point turned white again. This marked the onset of the next trial. The timing is illustrated in Figure 6.1. Stimuli were presented in a different random order for each participant.

6.3.4 MEG Recording and Analysis

Recording of neural activity took place using a 151-channel CTF Omega MEG system (CTF Systems Inc, Canada.). Following MEG recording, a Polhemus Isotrak system was used to digitise the surface shape of the participant's head, this information then being used to co-register the MEG data with the participant's anatomical MRI.

Event-Related Potentials (ERPs) were analysed for living and non-living stimuli during categorisation and recognition. For a detailed description of ERP analysis, refer to section 3.3. The 151 channels of the MEG Scanner are positioned so that frontal, temporal, parietal, occipital and central cortical activity can be recorded from both the left and right hemispheres. To increase the signal to noise ratio all trials within each condition were averaged together, enabling peaks in cortical activity to be observed. For the ERP data presented in this study, the neural activity recorded by each group of sensors within each hemisphere was averaged together for each trial. This provided ERP traces for left and right, frontal, temporal, occipital, parietal and central channels.

The peak activation value (nA) was then obtained for each 100ms time period across the trial; that is 0-100ms, 100-200ms and then every 100ms until 900-1000ms post stimulus-onset. These values could then be compared across stimulus and task conditions, depending on the study; objects versus words; encoding versus recognition; living versus non-living; old versus new. The peak activation values were in the region of 1^{-14} to 1^{-13} nA, so for graphical illustration purposes, the peak activation values were each multiplied by 10^{13} so that small positive values greater than zero could be displayed.

Analysis of the cortical activation took place using SAM (Robinson & Vrba, 1999; Barnes et al, 2001), a method of producing a three-dimension map of cortical synchronous and desynchronous activation (see section 3.5). SAM Analysis compares one state (active) with another (passive). Positive t-statistics are produced when the active state shows and increase in power, negative when it shows a decrease. These are interpreted as event-related synchronisation (ERS) and event-related desynchronisation (ERD) respectively (Pfurtscheller & Lopes da Silva, 1999).

Several SAM comparisons were made on the raw, correctly categorised and recognised data. Firstly, a comparison between living and non-living categorisation (during the encoding stage) was conducted. Following this a living versus non-living comparison was made for correctly recognised 'old' items, i.e. those previously seen during the

encoding phase. Two baseline SAM comparisons were also computed (baseline (500ms before stimulus onset) versus 1st, and 2nd 500ms time spans following stimulus onset) for each of the stimulus types (living and non-living stimuli during encoding and recognition of old images). These time windows were selected as they corresponded roughly to the early and late components identified previously. All power changes were calculated in the same six overlapping frequency bands as in the previous study; 5-15Hz, 10-20Hz, 15-25Hz, 20-30Hz, 25-35Hz and 30-40Hz. Group SAM images were generated by spatially normalising each of the participant's SAM data using SPM99 (Friston et al, 1995) and mapping each of these onto a template brain. Statistically significant regions of activation were identified using statistical non-parametric mapping (SnPM). For further detail on all methods, please refer to Chapter 3.

6.4 Results

6.4.1 Behavioural Data

	1	2	3	4	5	6	**Mean**
Number of correctly categorised living items during encoding	26 (100%)	26 (100%)	26 (100%)	26 (100%)	26 (100%)	26 (100%)	**26 (100%)**
Number of correctly categorised non-living items during encoding	26 (100%)	25 (96.2%)	25 (96.2%)	25 (96.2%)	25 (96.2%)	22 (84.6%)	**24.67 (94.9%)**

Table 6.1 Raw behavioural data showing correctly categorised living and non-living items during encoding for each of the participants (1-6). *The percentages were calculated from the total number of possible correct responses (26 items)

The behavioural data retrieved from the MEG recordings demonstrated near perfect categorisation accuracy. All errors made by the participants were for non-living stimuli, and a non-parametric Wilcoxon signed ranks test revealed a statistically significant difference in accuracy for the two conditions ($z = -2.121$, $df = 5$, $p = 0.034$).

	1	2	3	4	5	6	**Mean**
Number of correctly recognised 'old' living items	22 (84.6%)	21 (80.8%)	18 (69.2%)	19 (73.1%)	26 (100%)	24 (92.3%)	**21.67 (83.3%)**
Number of correctly recognised 'old' non-living items	23 (88.5%)	26 (100%)	22 (84.6%)	23 (88.5%)	24 (92.3%)	17 (65.4%)	**22.50 (86.5%)**
Number of correctly identified 'new' living items	19 (73.1%)	23 (88.5%)	22 (84.6%)	22 (84.6%)	23 (88.5%)	20 (76.9%)	**21.50 (82.7%)**
Number of correctly identified 'new' non-living items	24 (92.3%)	22 (84.6%)	22 (84.6%)	22 (84.6%)	24 (92.3%)	22 (84.6%)	**22.67 (87.2%)**

Table 6.2 Raw behavioural data showing correctly recognised and identified old and new (respectively) items during the recognition memory phase for each of the participants (1-6). *The percentages were calculated from the total number of possible correct responses for each stimulus type (26 items)

The behavioural data obtained during the recognition memory phase of the experiment also indicated very high accuracy across all participants. There was a difference in the mean number of stimuli correctly recognised across category for both the old (21.67 and 22.50 respectively) and new (21.50 and 22.67 respectively), with higher accuracy for non-living stimuli throughout the recognition memory phase. However, neither of the living – non-living differences for old nor new objects were statistically significant ($z = -0.526$, $df = 5$, $p = 0.599$ and $z = -1.289$, $df = 5$, $p = 0.197$ respectively).

6.4.2 Evoked Response Data

6.4.2.1 Encoding: Living versus Non-Living

ERP analyses were conducted on the correctly categorised living and non-living stimuli. Each cortical region (central, frontal, temporal parietal and occipital) was considered separately, and ERPs reported for both left and right hemispheric activation. Figure 6.2 illustrates the ERPs, maximum activation (nA) plotted as a function of time (100ms time windows between 0 and 1000ms post stimulus onset) for each of the cortical regions (A-E).

Central

For the left central MEG channels, qualitatively no difference could be seen in the average maximum peak activations between living and non-living stimuli. For both stimulus types, there was an initial increase between 100-200ms followed by a small decrease between 200 and 300ms. No statistically significant differences were observed between these two groups. For the right central MEG sensors, however, this initial peak occurred slightly later (200-300ms) and was less strong (average maximum peak of about 10^{-11}, compared to 12^{-13} for MEG left sensors). Furthermore, for the living stimuli, this activation rapidly decreased but for the non-living stimuli the decrease was less steep. This was illustrated by the difference observed between 300-400ms showing trend level significance ($p = 0.120$). The pattern of activation for the two stimuli across these right central channels mirrored each other well, with the exception of the final 100ms analysed (900-1000ms) in which the only statistically significant difference was observed [$F(1,5) = 5.158$, $p < 0.05$]. A slight difference between living and non-living stimuli was also evident in the initial 0-100ms time frame although this failed to reach significance ($p = 0.104$).

Frontal

In the frontal MEG channels, there was evidence for category specificity. Across the left frontal channels, significant differences in average peak activation values were observed between 300-400ms [$F(1, 5) = 5.586$, $p < 0.05$] and 400-500 ms [$F(1, 5) = 7.55$, $p < 0.05$] with a difference also observed between 100-200ms, although this did not reach statistical significance ($p = 0.150$). The initial increase at the start of the trial occurred earlier for living things (100-200ms, compared to 200-300ms for non-living). Following this, there were significant differences between the two categories (described previously) until 500ms whereby the activation values resumed a similar pattern.

Across the right hemisphere, although the activations for the two categories followed the same pattern in the initial stages, activations for non-living things were greater with statistical differences being observed at 0-100ms [$F(1,5) = 6.286$, $p < 0.05$] and again at 100-200ms [$F(1,5) = 4.973$, $p < 0.05$]. This difference in strength continued for the next 500ms, although after 300ms post stimulus onset with the living items now showed greater activation than the non-living items. The large visual difference between 400-500ms was confirmed with this meeting statistical difference [$F(1, 5) = 10.652$, $p < 0.05$], but not for the differences also seen at 600-700ms or 900-1000ms.

Temporal

Across the temporal channels, a significant number of category specific differences could also be observed. Within the left sensors, although both categories produced an initial peak of activation at 100-200ms, the second peak produced by living things at 300-400ms was absent for the non-living stimuli. Consequently, this produced a statistically significant difference in the 300-400ms time frame [$F(1, 5) = 7.018$, $p < 0.05$]. Conversely, the small peak for non-living stimuli at 500-600ms was absent for living things. This difference was statistically significant [$F(1, 5) = 4.373$, $p < 0.05$]. The activation for both categories then appeared to remain relatively constant; although in the final 100ms (900-1000ms) there was an indication that, whilst for non-living stimuli the activity remained constant, there was a visual decrease in average maximum peak value for living items. This difference however, did not reach statistical significance ($p = 0.129$).

In the right temporal MEG sensors, there was an initial increase in activation for both stimulus types, but a difference was then observed between the 100-200ms and 200-300ms time windows. At this point, the activation for living stimuli continued to increase, whereas

for the non-living items activation showed a significant decrease. Consequently at 200-300ms, a significant trend towards statistical significance was observed [$F(1, 5) = 5.499$, $p < 0.1$]. This increase for living items was followed by a steep decrease in activation during the next time frame. Although there was a lesser steep decrease for the non-living stimuli, the activation values at 300-400ms were not significantly different between the two groups. Both the living and non-living stimuli followed a similar activation pattern across the next 500ms, characterised by an increase at 300-400ms followed by a gradual decline until 800-900ms. For the left sensors, at 900-1000ms there was a divergence in the activations of the two groups, although within the right sensors it was the living stimuli which showed an increase in activation, the non-living stimuli a decrease in activation. This difference, however, was not found to be statistically significant ($p = 0.126$).

Parietal

Across the parietal channels there was a considerable similarity in the activation values of the two groups. Across the left parietal MEG sensors, for both stimulus types, there was a very strong initial peak at 100-200ms, with a second smaller peak observed at 300-400ms. The decrease in activation that followed this peak was greater for the non-living stimuli and consequently, the difference in activation observed at 500-600ms showed a trend towards significance ($p = 0.123$). For the remaining 400ms, the activation of the two groups remained relatively constant, with a small peak of activation observed at 700-800ms.

For the right parietal MEG sensors, an initial peak was also observed between 100-200ms, although this was smaller in magnitude than that observed across the left hemisphere. Furthermore, it was significantly greater for the living items than for the non-living items [$F(1, 5) = 8.846$, $p < 0.041$]. For both the stimulus types, activation was then seen to show a gradual decrease across the remaining time frames.

Occipital

Across the left occipital sensors, the activation for living and non-living stimuli followed the same pattern with no significant differences observed. Both demonstrated an initial peak at 100-200ms, a second smaller peak at 300-400ms, which was followed by an obvious decrease at 400-500ms before the activation remained constant for the remaining 500ms.

Across the right sensors, there was considerably less similarity between the two groups. The initial activation (0-100ms) was significantly greater for living than non-living stimuli [$F(1, 5) = 17.471$, $p < 0.01$]. Both stimuli then showed a peak between 100-300ms before the living stimuli show a second peak at 400-500ms. The absence of a similar peak for the non-living stimuli produced a statistically significant difference in activation in this time window [$F(1, 5) = 23.744$, $p < 0.01$]. For the following 300ms, the two stimulus types followed a similar pattern but the greater activation observed for the living stimuli produced significant differences at both 600-700ms and 700-800ms [$F(1,5 = 24.040$, $p < 0.01$; and $F(1,5 = 4.292$, $p < 0.1$ respectively].

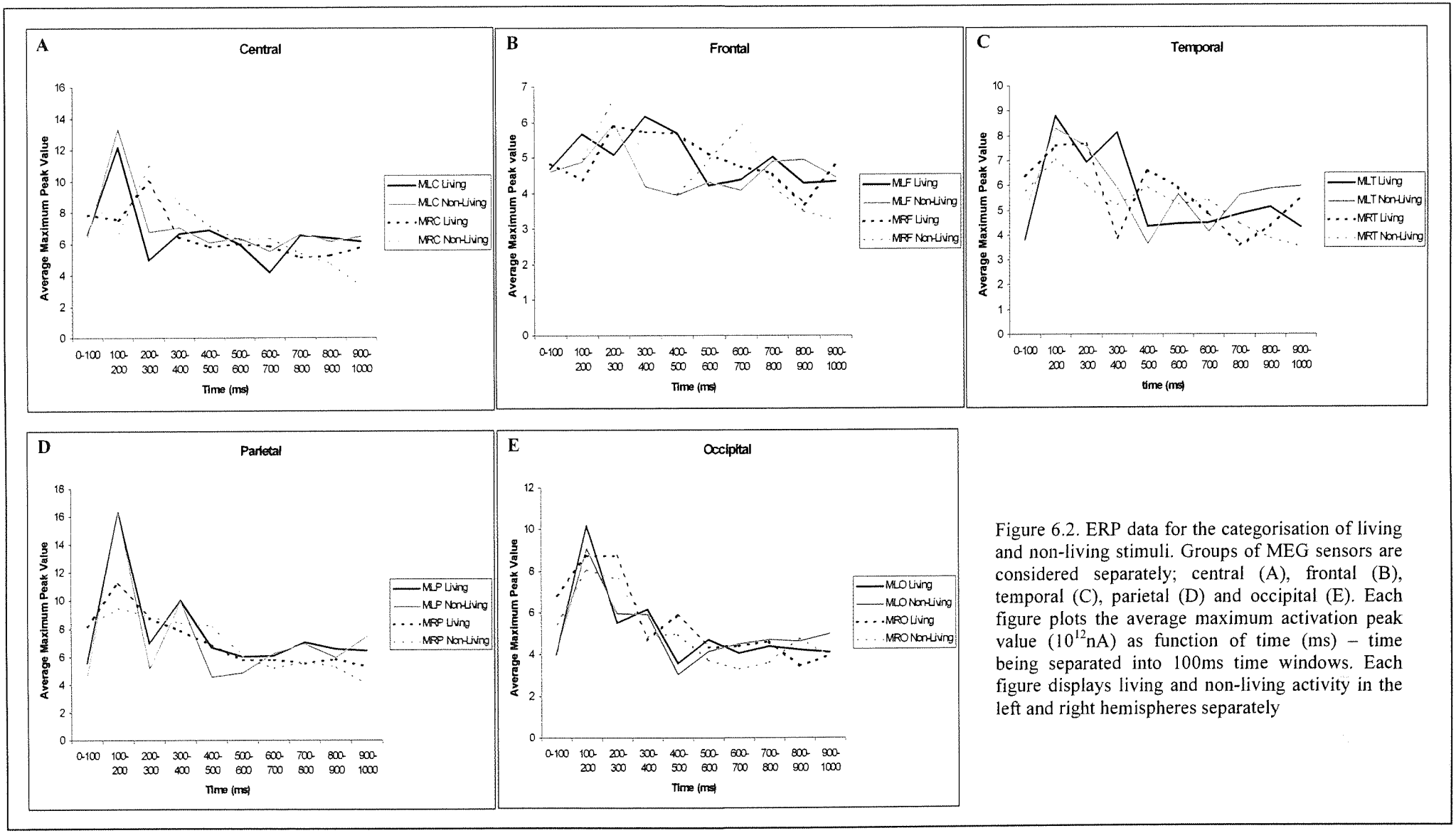


Figure 6.2. ERP data for the categorisation of living and non-living stimuli. Groups of MEG sensors are considered separately; central (A), frontal (B), temporal (C), parietal (D) and occipital (E). Each figure plots the average maximum activation peak value (10^{12}nA) as function of time (ms) – time being separated into 100ms time windows. Each figure displays living and non-living activity in the left and right hemispheres separately

6.4.2.2 Recognition: Living versus Non-Living

ERP analyses were conducted on the correctly recognised 'old' living and non-living stimuli. Each cortical region (central, frontal, temporal parietal and occipital) was considered separately, and ERPs reported for both left and right hemispheric activation. Figure 6.3 illustrates the ERPs, maximum activation (nA), averaged across subjects, plotted as a function of time (100ms time windows between 0 and 1000ms post stimulus onset) for each of the cortical regions (A-E).

Central

During the recognition phase, across the left central channels there was an observed peak of activation between 100-200ms. However, the increase in activation to this peak was steeper for the non-living items due to a statistically significant difference observed at 0-100ms [$F(1, 5) = 4.979$, $p < 0.05$]. Activation then turned to the baseline level for both stimulus types until 400-500ms when the non-living stimulus showed a significant reduction in activation compared to the sustained activation of the living stimuli. Consequently, this produced a statistically significant difference at 400-500ms [$F(1, 5) = 9.571$, $p < 0.05$]. Despite the visual difference at 500-600ms where the non-living stimuli showed an increase in activation (contrasting to the decrease for the living stimuli), both item types showed sustained activation for the reminder of the trial. For the right MEG central sensors there were two obvious peaks of increased activation for both stimulus types occurring at 200-300ms and again at 400-500ms. For both peaks, the living stimuli had greater activation values, but only that at 400-500ms produced a statistically significant difference between the living and non-living stimuli values [$F(1,5) = 8.332$, $p < 0.05$]. For the remaining time windows, the activation of both stimulus types remained constant.

Frontal

Across the left frontal MEG sensors, an initial peak could be seen at 100-200ms for both stimulus types. Although this increase in activation was sustained for the non-living items but not for the living stimuli, no significant difference was observed in the succeeding time window. At 400-500ms, however, activation detected by these sensors decreased significantly for the non-living stimuli compared to the living items, and consequently a significant difference was observed [$F(1,5) = 10.950$, $p < 0.05$]. Activation

remained constant for both stimuli until about 700ms when the activation for living stimuli began to increase. It was not until 800-900ms that a statistically significant difference was observed [$F(1,5) = 4.546$, $p < 0.1$]. At 900ms, while the activation for living items began to decrease, that for the non-living items increased, although the difference in the final time window (900-1000ms) did not reach statistical significance. No significant differences were observed across the right channels for any of the time windows. Both stimulus types showed a peak of activation qt 200-300ms and a larger one again at 400-500ms, before the activation remained constant.

Temporal

Across the left temporal channels, a peak of activation was observed for both stimuli at 100-200ms. However, the greater magnitude of the activation peak for living items compared to the non-living stimuli produced a statistically significant difference [$F(1, 5) = 7.938$, $p < 0.05$]. Because the values remained constant for the non-living items and there was a sharp decrease for the living stimuli, by 200-300ms, the activation patterns were quite similar. Both showed a decrease in activation at 400-500ms, which was greater for the non-living stimuli, but not sufficient to produce a statistically significant value, after which the values become constant for the remainder of the trial.

The only difference observed across the right temporal sensors occurred in the 200-300ms time window. The initial increase in activation (100-200ms) for both stimulus types continued for the living stimuli into the 200-300ms time window, whilst there was a decrease at the same time window for the non-living items. This difference, however, did not reach statistical significance ($p = 0.148$). For the rest of the trial, the activation for both stimulus types was similar, a decrease observed at 300-400ms, followed by a sustained increase (400-600ms) before remaining relatively constant at the end of the trial.

Parietal

Although the activation patterns for the two stimulus types were quite similar across the left parietal MEG sensors for the entire trial, the greater magnitude of the activation for the living stimuli illustrated a couple of differences. There was a large peak of activation at the start of the trial (100-200ms) for both stimuli, but the larger decrease observed for the non-living items resulted in a later difference observed at 300-400ms, which showed a trend towards significance [$F(1, 5) = 4.413$, $p < 0.1$]. In the succeeding time windows, the

activation values were very similar with only a small, non-significant difference observed in the penultimate time window (800-900ms, $p = 0.48$).

The initial peak observed in the same time window as that described previously for the left sensors, was smaller in magnitude for the right sensors. Activation for both stimulus types then appeared to show a small decrease before a smaller peak was observed at 400-500ms. The greater activation for the living stimuli at this point produced a statistical difference [$F(1, 5) = 7.658$, $p < 0.05$]. The decrease in activation for both stimulus types resulted in a final small peak at 700-800ms, the subsequent activation for the non-living stimuli remaining slightly greater than that for the living stimuli. Consequently, there was a notable difference in values between the stimulus types at 800-900ms, but again this did not reach statistical significance ($p = 0.133$).

Occipital

For all occipital sensors, left and right, an initial peak of activation for both stimulus types could be seen (100-200ms). It was greater in the left hemisphere, although, across the right sensors, the increase in activation to produce this peak was greater for the non-living stimuli. This was due to the difference observed at 0-100s [$F(1, 5) = 5.561$, $p < 0.01$]. After 200-300ms, activation for both living and non-living stimuli detected across all left and right occipital sensors was sustained at the same level.

6.4.3 Neuroimaging Data

6.4.3.1 Encoding: Living versus Non-Living

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Limbic Lobe – extending over inferior frontal gyrus	Left	15-25	-18 9 -21	9	6.80	0.031	34

Table 6.3 Regions showing statistically significant differences in activation ($p < 0.05$) between categorisation living and non-living objects.

A comparison of activity elicited when categorising living and non-living stimuli during the encoding phase produced cortical maps which differed between these two phases. There was consistency between activated areas across all participants and as such, group SAM data are presented with considerable confidence. The SAM analysis compared the active non-living objects with the passive living stimuli.

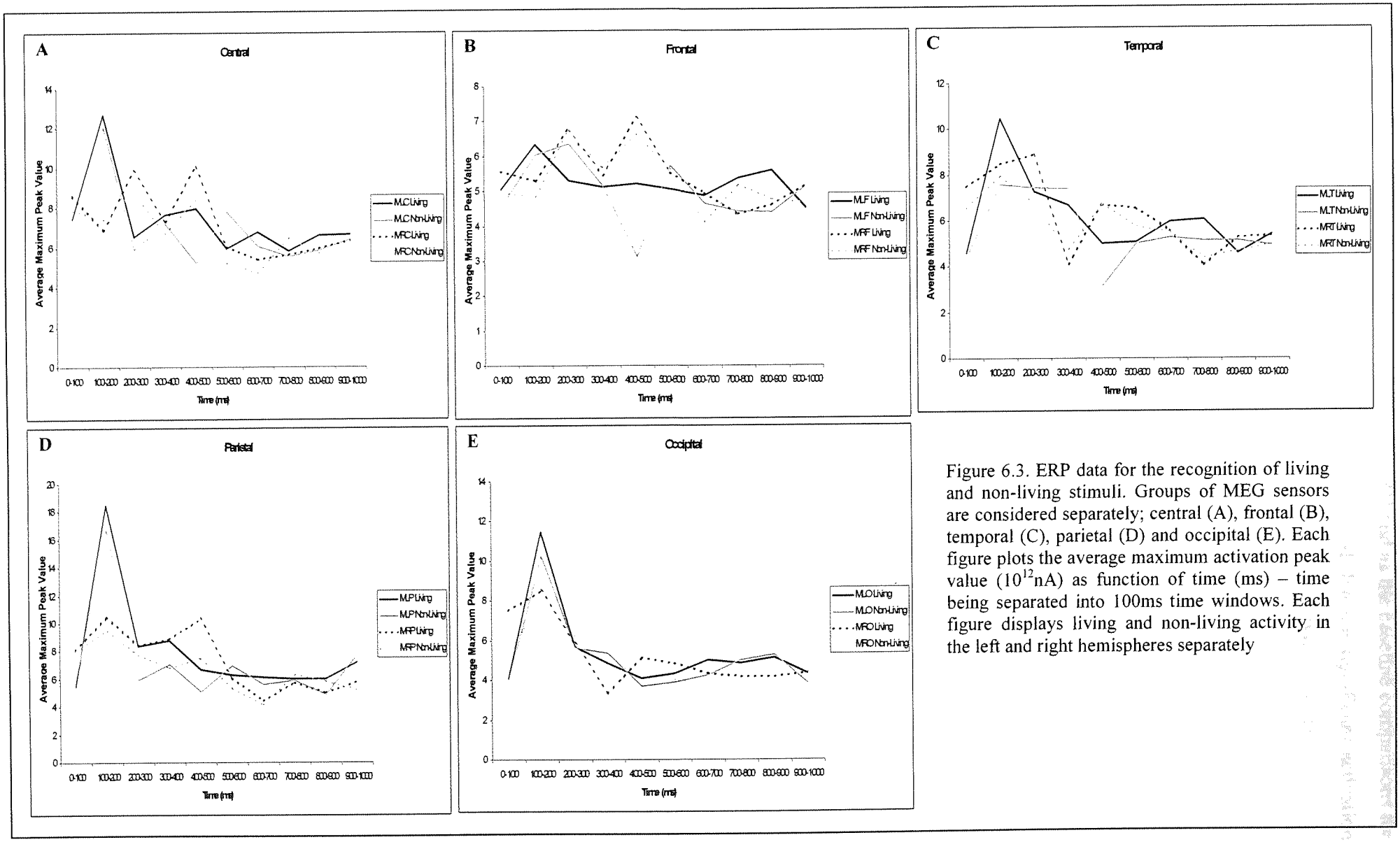


Figure 6.3. ERP data for the recognition of living and non-living stimuli. Groups of MEG sensors are considered separately; central (A), frontal (B), temporal (C), parietal (D) and occipital (E). Each figure plots the average maximum activation peak value (10^{12}nA) as function of time (ms) – time being separated into 100ms time windows. Each figure displays living and non-living activity in the left and right hemispheres separately

All activation produced was observed to be ERD and as the baseline comparisons for each stimulus type also produced ERD, it can be assumed that the significant activation observed, occurs from an increase in ERD when categorising non-living objects.

6.4.3.2 Living: Encoding versus Baseline

0 – 500 ms

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Fusiform Gyrus	Left	5-15	-27 -81 -18	157	8.43	0.016	
Cuneus	Left	15-25	-19 -93 3	102	8.50	0.016	
Superior Parietal Lobule	Left	5-15	-21 -63 48	4	6.06	0.031	7
Superior Frontal Gyrus	Right	20-30	15 60 12	1	6.19	0.047	
Cingulate Gyrus	Right	25-35	9 -27 39	699	9.74	0.016	31
Postcentral Gyrus	Right	25-35	51 -18 45	4	6.53	0.031	3
Precuneus	Left	25-35	-15 -54 57	3	6.53	0.031	

Table 6.4 Regions showing statistically significant activation ($p < 0.05$) when categorising living objects (compared to baseline) in the first 500ms post-stimulus onset.

Areas of the brain activated during the first 500 ms post living stimulus onset included areas of the occipital, parietal, frontal and limbic lobes, as reported in Table 6.4 and illustrated in Figure 6.4.A. Activation within the occipital lobe was seen to be left lateralised, extending over the fusiform gyrus and cuneus. Activation within the parietal lobe was also predominantly seen within the left hemisphere, specifically the superior parietal lobule and precuneus. However, activation was also seen within the right postcentral gyrus. Further ERD activation was centred around the right superior frontal gyrus and also within the right limbic lobe, encompassing the cingulate gyrus and corpus callosum.

500 – 1000 ms

In comparison to the initial time window, during the second 500ms post stimulus onset, activation did not appear to be as widespread. Only the temporal and frontal lobes showed activity, with a small amount of activation also observed within the cerebellum and limbic lobe. Table 6.5 and Figure 6.4.B illustrate regions of statistically significant activation. Cerebellar activation was restricted to the left declive whilst superior temporal gyrus ERD was also left lateralised. Right cingulate gyral activity, within the limbic lobe,

was also seen. Bilateral ERD activation of the frontal lobe was more widespread, extending over the right inferior and medial frontal gyri and bilaterally over the precentral gyrus.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Superior Temporal Gyrus	Left	5-15	-27 6 -27	126	8.26	0.016	
Cerebellum	Left	5-15	-27 -78 -30	7	6.77	0.031	
Precentral Gyrus	Left	10-20	-30 -33 57	25	7.28	0.016	4
		20-30	-36 -12 63	5	6.39	0.047	6
	Right	25-35	57 0 33	4	6.89	0.031	6
Cingulate Gyrus	Right	25-35	6 -21 36	109	7.64	0.016	24
Inferior Frontal Gyrus	Right	30-40	39 24 12	31	6.66	0.031	
Medial Frontal Gyrus	Right	30-40	51 30 24	1	5.92	0.047	46

Table 6.5 Regions showing statistically significant activation ($p < 0.05$) when categorising living objects (compared to baseline) in the second 500ms post-stimulus onset.

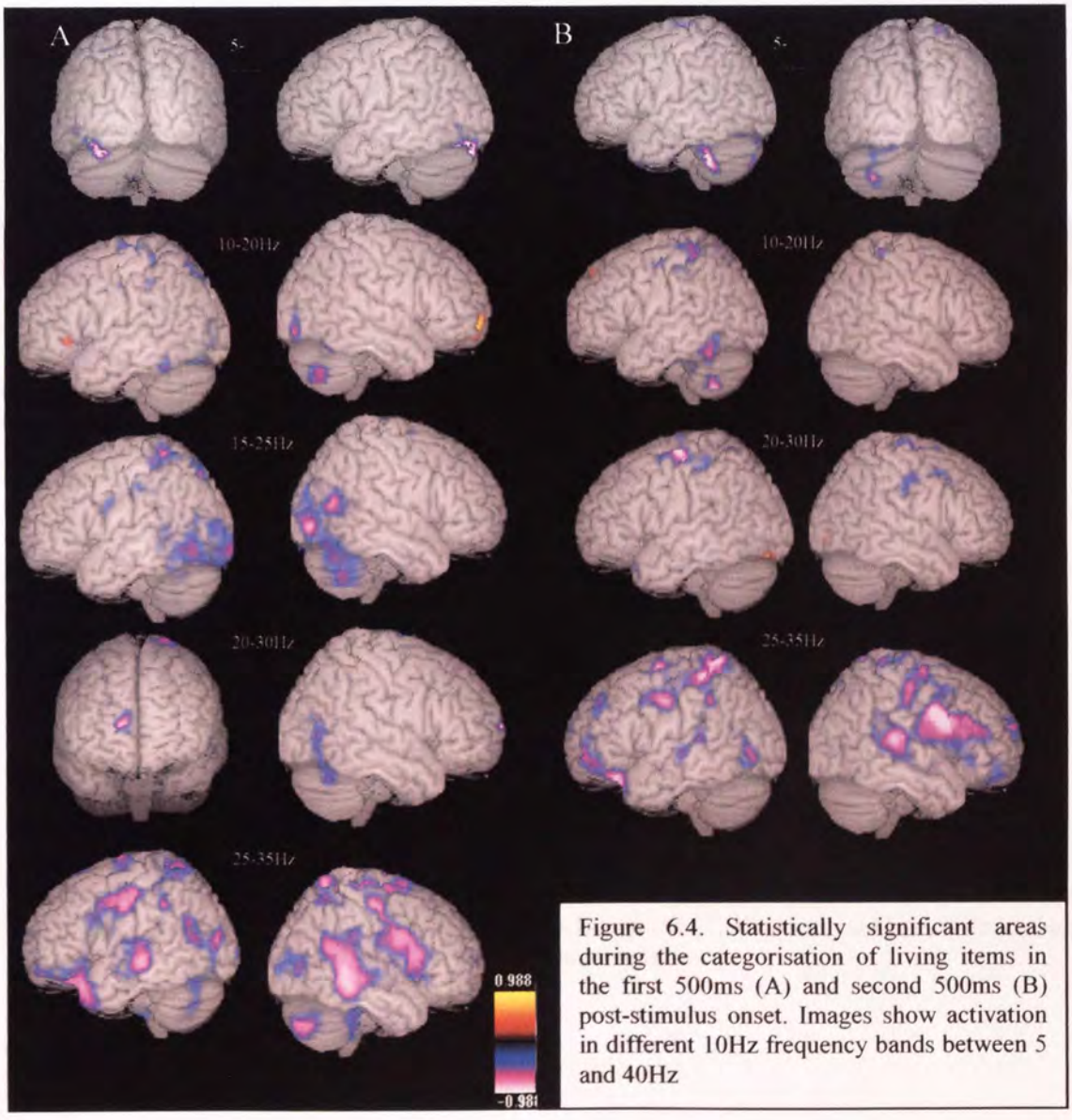


Figure 6.4. Statistically significant areas during the categorisation of living items in the first 500ms (A) and second 500ms (B) post-stimulus onset. Images show activation in different 10Hz frequency bands between 5 and 40Hz

6.4.3.2.1 Overall Baseline Activation for Categorising Living Objects

Summarising these baseline comparisons, during the initial presentation of stimulus (0-500ms) ERD was centred on the parietal and occipital lobes. As the t continued, the small amount of activation within the frontal lobe seen initially (0-500 increased. During the second, large areas of the right frontal lobe, specifically the infe and medial gyri were activated. Bilateral precentral gyrus activation was also obser The temporal lobes remained mostly inactivated with the exception of a relatively sr region of the superior temporal gyrus during the second time window. Consis activation across the entire trial could really only be seen within the limbic l specifically the cingulate gyrus.

6.4.3.3 Non-Living: Encoding versus Baseline

0 – 500 ms

Following the initial presentation of the stimulus, during the next 500ms activa was centred predominantly around the right occipital lobe, extending over the precu and middle occipital gyrus (Table 6.6, Figure 6.5.A). Left hemispheric activity restricted to the middle occipital gyrus, and the fusiform gyrus within the temporal l Cerebellar ERD was also present, specifically the left declive within the posterior lobe.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Occipital Lobe	Right	10-20	30 -72 -6	92	8.13	0.016	
Cerebellum	Left	10-20	–21 -66 -30	68	6.33	0.031	
Precuneus	Right	15-25	15 -66 21	861	7.54	0.016	
Middle Occipital Gyrus	Right	15-25	33 -72 6	861	7.32	0.016	
Cuneus	Left	15-25	-15 -90 18	20	6.88	0.016	18
Fusiform Gyrus	Left	30-40	-60 -12 -33	16	7.02	0.016	20

Table 6.6 Regions showing statistically significant activation ($p < 0.05$) when categorising non-living ob (compared to baseline) in the first 500ms post-stimulus onset.

500 – 1000 ms

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Precentral Gyrus	Left	10-20	-51 -6 45	75	7.03	0.016	6
		15-25	-54 -12 42	491	9.10	0.016	
	Right	15-25	3 -27 57	294	7.29	0.016	6
Postcentral Gyrus	Left	10-20	-51 21 48	75	6.91	0.016	1/2/3
		25-35	-51 -27 57	81	8.25	0.016	1
Cingulate Gyrus	Left	15-25	-9 -33 39	294	6.74	0.031	
Fusiform Gyrus	Left	15-25	-27 -66 -12	14	6.46	0.031	
		25-35	-39 -48 -18	64	7.23	0.047	
Inferior Parietal Lobule	Left	15-25	-60 -39 21	16	6.26	0.031	
Inferior Frontal Gyrus	Right	25-35	48 18 3	22	6.51	0.047	45
Superior Temporal Gyrus	Left	25-35	-51 6 -12	6	6.47	0.047	

Table 6.7 Regions showing statistically significant activation ($p < 0.05$) when categorising non-living objects (compared to baseline) in the second 500ms post-stimulus onset.

During the second 500ms baseline comparison it can be seen from Table 6.7 and Figure 6.5.B, that categorisation of non-living objects produced activation generally within the left hemisphere around the frontal and parietal lobes, with smaller regions of the occipital and temporal lobes also being activated. Frontal lobe ERD was bilateral within the precentral gyrus, extending over the right inferior frontal gyrus. Parietal activity was completely left lateralised, incorporating the postcentral gyrus and inferior parietal lobule. Further activation was found within a small region of the left superior temporal gyrus, and within both the temporal and occipital parts of the left fusiform gyrus. This left lateralised activation further extended to the limbic lobe where the cingulate gyrus also showed ERD activation.

6.4.3.3.1 Overall Baseline Activation for Categorising Non-Living Objects

Summarising this baseline activity, therefore, it can be seen that as the categorisation process for non-living objects continued, ERD activation shifted from being relatively restricted in location during the initial 500ms, to being more widespread during the later part of the trial. Specifically, activation progressed from being predominantly right occipital in location (only the cuneus and fusiform gyrus being activated within the left hemisphere), to covering the bilateral frontal lobes and left parietal and tempero-occipital regions during the second 500ms.

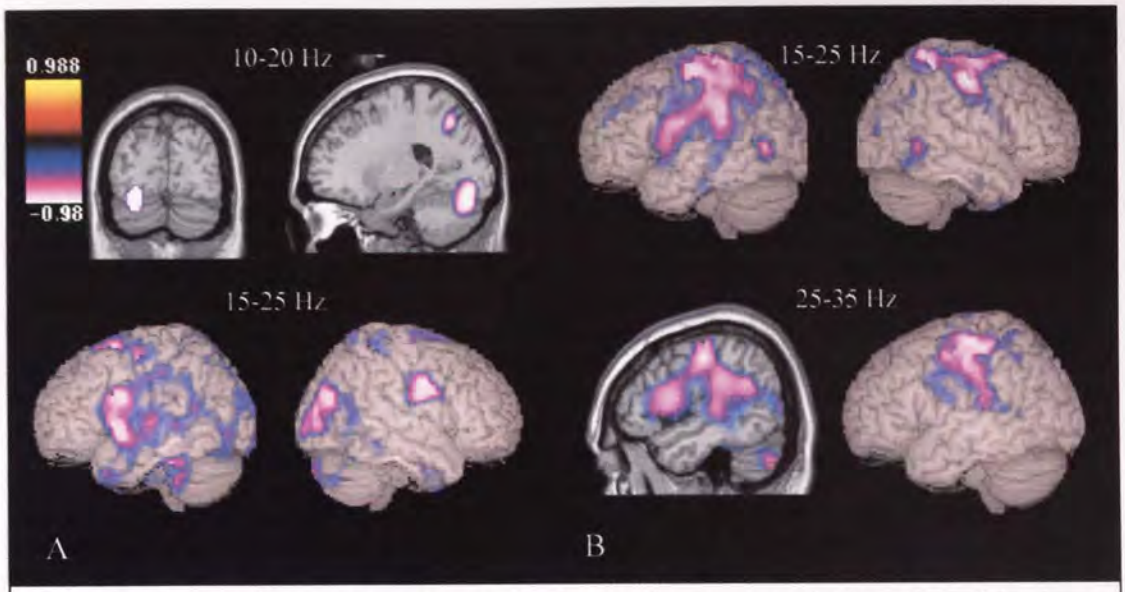


Figure 6.5. Statistically significant regions of activation for the categorisation of non-living items during the first (A) and second (B) 500ms post-stimulus onset. Activation is interpreted as ERD (blue) and occurred in different 10Hz frequency bands for the two time windows

6.4.3.4 Summary of Encoding versus Baseline

Whilst a direct comparison of living and non-living categorisation produced only one statistically significant region, the limbic lobe, it can be seen through the individual baseline comparisons that there were differences (Table 6.8). Firstly, there was no significant superior parietal lobe activation during the initial phase for the non-living stimuli and the precuneus appeared to show hemispheric category-specificity with the left precuneus activated for living items and the right for non-living categorisation. The right cingulate activation observed for living stimuli was absent for non-living items. Conversely, the left cerebellum and right middle occipital gyrus were activated only for the non-living stimuli. Two left-lateralised regions were identified as being involved in the categorisation of both living and non-living stimuli, the fusiform gyrus and the cuneus.

As the trial progressed (500-1000ms), frontal lobe activation increased for both stimulus types. Both stimulus types yielded bilateral activation of the precentral gyrus and right hemispheric inferior frontal ERD, with living items also activating the right medial frontal gyrus. Whilst the cingulate gyrus within the limbic lobe was activated for both stimulus types, it is interesting to observe that during this middle phase, it was right lateralised for living stimuli, left lateralised for non-living. Furthermore, the parietal activity observed for living stimuli in the initial phase no longer existed, but for non-living objects the inferior parietal lobule and postcentral gyrus were activated during this middle

500ms time span. Whilst left superior temporal ERD was present for both stimulus types, categorisation of non-living stimuli also activated the left fusiform gyrus. Two further regions in the left hemisphere were also activated according to category, the left cerebellum and left precentral gyrus for living and non-living stimuli respectively.

	Living	Non-Living
0-500ms	Right Superior Frontal Gyrus	
	Left Fusiform Gyrus	Left Fusiform Gyrus
	Right Cingulate Gyrus	
	Right postcentral Gyrus	
	Left Precuneus	Right Precuneus
	Left Superior Parietal Lobule	
	Left Cuneus	Right Cuneus
		Right Middle Occipital Gyrus
		Left Cerebellum
500-100ms	Right Inferior Frontal Gyrus	Right Inferior Frontal Gyrus
	Right Medial Frontal Gyrus	
	Bilateral Precentral Gyrus	Bilateral Precentral Gyrus
	Left Superior Temporal Gyrus	Left Superior Temporal Gyrus
	Right Cingulate Gyrus	Left Cingulate Gyrus
		Left Postcentral Gyrus
		Left Fusiform Gyrus
		Left Inferior Parietal Lobule
	Left Cerebellum	

Table 6.8 Summary of statistically significant ERD for categorisation of living and non-living stimuli (as identified through baseline comparisons) in two 500ms time comparisons

6.4.3.5 Recognition: Living versus Non-Living

A comparison between living items and non-living correctly recognised as 'old' yielded no statistically significant regions of activation.

6.4.3.6 Living: Recognition versus Baseline

0 – 500 ms

Within the first 500ms of recognising a previously seen object, ERD was observed in both hemispheres, although no cortical region showed significant bilateral activation (Table 6.9 and Figure 6.6.A). Within the right hemisphere, activity was found in the cerebellum, specifically the posterior lobe, and in the frontal lobe, specifically the middle frontal gyrus. Activity in the left hemisphere covered the temporal, limbic and parietal lobes, but with only the left precuneus being an identifiable sub-region of these cortical areas.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Posterior Lobe	Right	15-25	12 -72 -18	50	7.25	0.016	
Middle Frontal Gyrus	Right	15-25	27 -18 45	1	6.41	0.047	
Temporal Lobe	Left	25-35	-42 -3 -21	50	6.80	0.016	
Limbic Lobe	Left	25-35	-18 12 -36	46	6.48	0.016	
Precuneus	Left	25-35	-21 -72 48	26	6.25	0.016	7

Table 6.9 Regions showing statistically significant activation ($p < 0.05$) when recognising living objects (compared to baseline) in the first 500ms post-stimulus onset.

500 – 1000 ms

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Inferior Parietal Lobule	Left	10-20	-33 -42 57	4	6.70	0.047	40
Precentral Gyrus	Right	10-20	48 -15 33	12	6.66	0.047	
	Left	15-25	-33 –30 60	19	7.02	0.016	4
		25-35	-42 -12 57	90	7.43	0.016	
Cingulate Gyrus	Left	15-25	-3 -9 48	24	7.12	0.016	24
Inferior Frontal Gyrus	Left	15-25	-48 9 15	24	6.95	0.016	
Precuneus	Left	25-35	-9 -78 48	26	6.83	0.016	7

Table 6.10 Regions showing statistically significant activation ($p < 0.05$) when recognising living objects (compared to baseline) in the second 500ms post-stimulus onset.

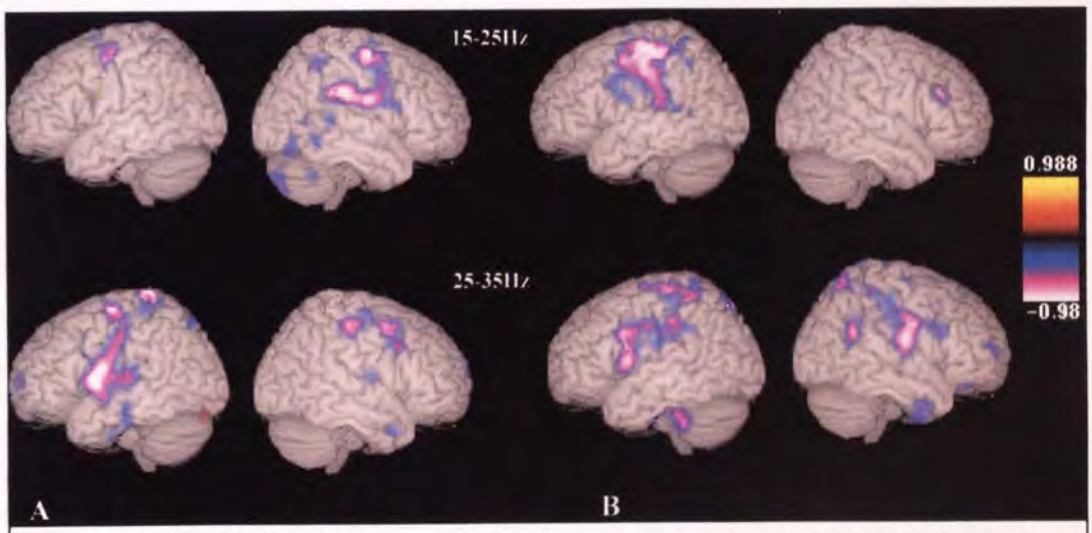


Figure 6.6. Statistically significant regions of activation for the recognition of living items during the first (A) and second (B) 500ms post-stimulus onset. Activation is interpreted as ERD (blue) and occurred predominantly in the 15-25 and 25-35Hz frequency bands

Between 500ms-1000ms post stimulus onset, ERD was observed predominantly in the left hemisphere (Table 6.10 and Figure 6.6.B) and in particular the inferior parietal lobule, cingulate gyrus, inferior frontal gyrus and precuneus. No unique right hemispheric activation was observed, although bilateral regions of the parietal lobe and precentral gyrus were activated.

6.4.3.7 Non-Living: Recognition versus Baseline

0 – 500 ms

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Precuneus	Left	10-20	-27 -69 42	35	6.66	0.016	
		15-25	-21 -81 24	183	7.09	0.031	31
	Right	25-35	18 -69 42	89	7.09	0.013	
Lingual Gyrus	Left	15-25	-18 -90 -3	183	6.36	0.031	
Middle Occipital Gyrus	Left	15-25	-24 -78 3	183	6.13	0.031	
Middle Temporal Gyrus	Right	15-25	51 -75 18	57	6.35	0.031	
		25-35	54 9 -33	46	6.99	0.013	
Postcentral Gyrus	left	25-35	-21 -33 57	41	6.88	0.013	3

Table 6.11 Regions showing statistically significant activation ($p < 0.05$) when recognising non-living objects (compared to baseline) in the first 500ms post-stimulus onset.

For non-living items, in the 0-500ms time window, left-lateralised activatio observed in the occipital lobe, in particular the lingual and middle occipital gyri, an in the postcentral gyrus (Table 6.11 and Figure 6.7.A). Right lateralised ERD was obs in the middle temporal gyrus whilst the precuneus was observed to be bilaterally activ

500 – 1000 ms

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T value	P Value	BA
Frontal Lobe	Left	5-15	-33 -12 33	16	6.54	0.016	
Precentral Gyrus	Left	10-20	-42 -6 54	2	6.03	0.047	
Superior Temporal Gyrus	Left	10-20	-66 -24 12	2	6.02	0.047	2
Superior Parietal Lobule	Left	25-35	-24 -54 63	256	9.70	0.016	7
Middle Frontal Gyrus	Left	25-35	-39 3 48	295	8.64	0.016	6

Table 6.12 Regions showing statistically significant activation ($p < 0.05$) when recognising non-living objects (compared to baseline) in the second 500ms post-stimulus onset.

Between 500-1000ms post stimulus onset, all observed significant ERD wa lateralised (Table 6.12 and Figure 6.7.B). Specific identifiable regions included the r frontal, precentral and superior temporal gyri, and also the superior parietal lobul significant activation was observed within the right hemisphere.

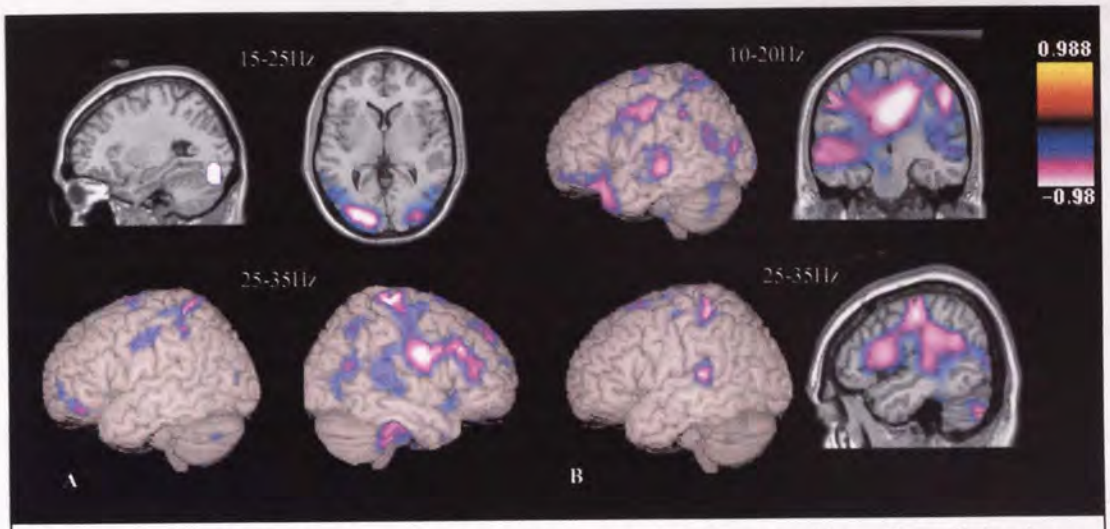


Figure 6.7. Statistically significant regions of activation for the recognition of non-living items during the first (A) and second (B) 500ms post-stimulus onset. Activation is interpreted as ERD (blue) and generally occurred in different frequency bands for the two stimuli

6.4.3.8 Summary of Recognition versus Baseline

	Living	Non-Living
0-500ms	Right Middle Frontal Gyrus	
	Left Temporal Lobe	
		Right Middle Temporal Gyrus
	Left Limbic Lobe	
	Left Precuneus	Bilateral precuneus
		Left Posterior Cingulate
		Left Middle Occipital Gyrus
		Left Lingual Gyrus
	Right Cerebellum – Posterior / Declive	
500-100ms	Left Inferior Frontal Gyrus	
		Left Middle Frontal Gyrus
	Bilateral precentral Gyrus	Left Precentral gyrus
		Left Superior Temporal Gyrus
	Left Cingulate Gyrus	
		Left Superior Parietal Lobule
	Left Inferior Parietal Lobule	
	Left Precuneus	

Table 6.13 Summary of statistically significant ERD for recognition of living and non-living stimuli (as identified through baseline comparisons) in two 500ms time comparisons.

For the recognition of living and non-living items, the direct comparison failed to reveal any statistically significant differences. Separate baseline analyses, however, revealed numerous differences. In the initial phase (0-500ms), there was very little similarity between the activated regions for living and non-living stimuli, with only the left precuneus being similarly activated for the two stimulus types. Furthermore, the right precuneus was additionally activated for non-living items, as too were the left postcentral, lingual and middle occipital gyri. Within the temporal lobe, non-identifiable regions within

the left hemisphere were identified for the living items, whilst the right middle temporal lobe showed ERD for the recognition memory of non-living stimuli. Living stimuli-specific regions during this initial phase included the left limbic lobe, the right cerebellum (specifically the declive region of the posterior lobe) and the right middle frontal gyrus.

Despite the fact that the observed ERD was predominantly left lateralised, this lack of similarity for the two conditions was also evident in the second 500ms time window. Although for both stimulus types the left frontal lobe was significantly activated, the identified sub-regions were not the same. The inferior frontal gyrus was involved with the recognition memory for living items, compared to the middle frontal gyrus for the non-living items. A similar pattern was also observed within the parietal lobe, the inferior parietal and superior parietal lobules being differentially activated for living and nonliving stimuli, respectively. Both stimulus types showed ERD within the precentral gyrus, but this region did show the only right hemispheric activity in this time window, the precentral gyrus being bilaterally activated for non-living stimuli. Additional category-specific regions were observed in the left cingulate gyrus and left precuneus for living items, and for non-living stimuli in the left superior parietal lobule.

6.5 Discussion

A visual object recognition memory task was performed, incorporating a living – non-living categorisation task during the encoding phase of the experiment. The aim was to identify the brain areas involved in processing living and non-living items at different stages in the categorisation process, and to determine whether different regions of the brain were activated for these two stimulus categories in both the encoding and recognition phases. By assessing whether there is category specificity during recognition memory tasks, it was hoped that this would enable a semantic network to be identified, which would be useful in tasks of recognition memory where semantic associations are believed to play an integral role.

6.5.1 Event Related Potentials

Previous studies have examined the time course of differences in processing living and non-living things. One such electroencephalography (EEG) study by Kiefer (2002)

reported significant category-specific differences at 'early' and 'late' stages in the categorisation process. Specifically, a greater N1 ERP component between 160-200ms after target onset was elicited by the living stimuli, compared to non-living things.

ERP analyses were used in this study to identify the temporal dynamics of categorisation and recognition processes. Figures 6.8 and 6.9 illustrate the average maximum activation values at different time windows across the trial for both living and non-living stimuli during the encoding and recognition tasks respectively. A significant peak of activation could be seen in the 100-200ms time window for both categories during both tasks. In addition, the magnitude of the activation was greater for the living stimuli compared to the non-living items. This was more evident during the recognition task but was still evident during the encoding task. This peak of activation is consistent with the N1 component reported previously which is thought to reflect visual perceptual processing, and which is enhanced by attentional mechanisms (Mangun & Hillyard, 1991). As detailed in the introduction to this chapter, living things are thought to belong to structurally similar categories and thus require additional perceptual processing compared to non-living things (Humphreys et al, 1988; Forde et al, 1997). It is this additional, fine-grained visual perpetual processing, and not stimulus complexity (Kiefer 2002) which could account for the greater activation observed for the living stimuli. The difference in this component is more obvious during the recognition stage and it is feasible that it is further enhanced due to the additional attentional demands of performing a recognition memory task. The similarity between the structural categories for the living things would necessitate additional processing to accurately determine which items had definitely been seen before, and eliminate those which were similar novel items.

Kiefer (2002) also reported a later N400 (N4) component, occurring between 300-500ms post stimulus onset, which showed category-specificity. No obvious N400-type component was evident in this study, although during the encoding phase there was a steeper decrease of activation for the non-living stimuli compared to the living items between 300-500ms. Also, in the recognition phase the living things showed a second peak of activity between 400-500ms. This demonstrates some support for the idea that category-specific effects can be found at temporally distinct stages in the categorisation process (Kiefer, 2002). It may be that in an experiment specifically designed to look at category-specificity, with no additional cognitive processing (such as memory as in this study) this temporal sequence of events will be more evident.

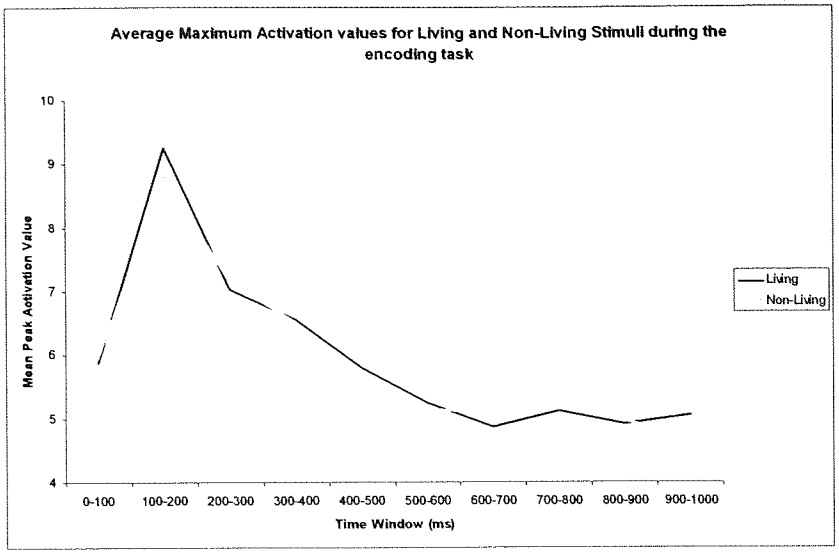


Figure 6.8. Average maximum Activation Values for the Living and Non-living stimuli during the encoding task (categorisation). Mean peak activation (nA) is plotted as a function of time (ten 100ms time windows)

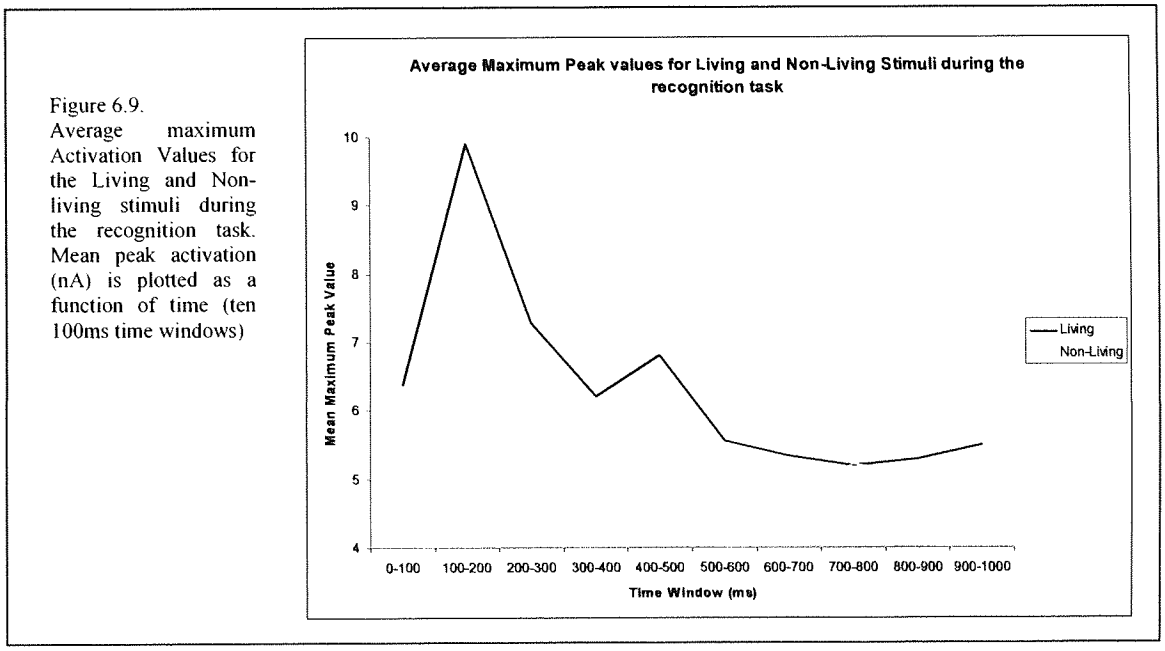


Figure 6.9. Average maximum Activation Values for the Living and Non-living stimuli during the recognition task. Mean peak activation (nA) is plotted as a function of time (ten 100ms time windows)

6.5.2 Category-Specific Effects during Encoding

In frontal regions, both living and non-living stimuli produced activation within the right inferior frontal (500-1000ms) and bilateral precentral (500-1000ms) gyri. The remaining activated frontal regions exhibited category-specific type effects with the right superior (0-500ms) and medial (500-1000ms) frontal gyri activated by only the living items.

Previous literature has identified the inferior frontal cortex as exhibiting category-specificity (Spitzer, Kischka, Guckel, Bellemann, Kammer, Seyyedi, Weisbrod, Schwartz, & Brix, 1998; Perani, Schnurt, Tettanmanti, Gorno-Tempini, Cappa & Fazio, 1999). Spitzer et al (1998) reported that for nine of their twelve participants, differences in

activation between named animals and named household items were observed in small regions of the middle and inferior frontal gyri. Furthermore the left inferior frontal gyrus has been reported to show greater activation for manmade tools compared to animals (Perani, Cappa, Bettinardi, Bressi, Gorno-Tempini, Matarrese & Fazio, 1995), and for tool naming compared to a baseline (Grabowski, Damasio & Damasio, 1998). The activation of the right inferior temporal cortex in this study, for both stimulus types, is not, therefore, consistent with the literature. However in the direct living versus non-living comparison, the only brain region to show a statistically significant difference in activation was the left limbic lobe, extending over the left inferior frontal gyrus.

Although one study (Grabowski et al, 1998) has suggested that the precentral gyrus region of the frontal lobe has category-specific properties (they reported greater activation within the left precentral gyrus for tools), category-specific activation within this region is not widely reported in the literature. This absence of reliably reported differences in the literature for this region is consistent with this study where both categories produced precentral gyral activation.

Analysis of the strength of activations for the living and non-living stimuli measured through the frontal MEG channels demonstrated greater activation of non-living items compared to living items in the right hemisphere (0-200ms) during the early stages. A switch then occurred with the living items showing greater for the remainder of the trial, the exception being a peak of non-living activation at 600-700ms. Across the left hemisphere, living items demonstrated greater activation for the majority of the trial, especially between 300-500ms. Assessment of the literature (summarised in Table 6.14) indicates that this should in fact be reversed, with a number of the studies reporting left hemispheric non-living specific activation in frontal regions (Perani et al, 1995; Grabowski et al, 1998). However, some studies simply report a difference between living and non-living items without specifying hemisphere (Spitzer et al, 1998) and furthermore, right-hemispheric activation is rarely reported. It is feasible, therefore, that non-living items do indeed show greater activation within the frontal regions of this hemisphere with the living items showing activation in these regions but to a lesser magnitude.

	LIVING	NON-LIVING
Perani et al (1995)	Occipital and temporal regions Left fusiform Left lingual gyrus	Occipital and temporal regions Left inferior frontal
Martin et al (1996)	Left lingual gyrus	Left posterior middle temporal region
Damasio et al (1996)	Ventral temporal cortex Medial inferior temporal cortex (non sig)	Ventral temporal cortex Left posterior middle temporal cortex
Mummery et al (1996)	Bilateral, medial anterior temporal cortices Right inferior parietal lobe	Left posterior middle temporal cortex
Mummery et al (1998)	Left middle frontal gyrus Right inferior parietal cortex	Left Posterior middle temporal cortex Left Parahippocampal gyrus
Cappa et al (1998)	Right middle frontal Right fusiform gyrus	Left posterior middle temporal area Left supramarginal gyrus Right superior temporal gyrus Right thalamus
Grabowski et al (1998)		Anterior bank of left precentral gyrus Left inferior and middle frontal gyrus
Spitzer et al (1998)	Difference between two observed in middle and inferior frontal, superior temporal and inferior parietal	
Perani et al (1999)	Thalamus Right superior parietal lobule	Left posterior middle temporal Left lingual Left cuneus Left precuneus
Moore & Price (1999)	Bilateral anterior temporal cortices Right posterior temporal Left anterior temporal	Left lingual gyrus
Gerlach et al (1999)	Right inferior and anterior fusiform gyri	
Thompson-Schill et al (1999)	Left fusiform (non sig)	
Chao et al (1999)	Bilateral medial and inferior occipital Bilateral ventral temporal Bilateral superior temporal	Medial fusiform gyrus Lateral middle posterior temporal gyrus
Gorno-Tempini et al (2000)	Medial extra-striate visual areas	Left posterior middle temporal

Table 6.14 Category-Specific Regions reported in previous neuroimaging studies

One temporal region is consistently reported as showing category-specific activation; the left posterior middle temporal cortex in favour of non-living items (Martin et al, 1996; Damasio, Grabowski, Tranel, Hitchwa & Damasio, 1996; Mummery, Patterson, Hodges & Price, 1998; Mummery, Patterson, Hodges & Wise, 1996; Cappa, Perani, Schnur, Tettamanti & Fazio, 1998; Perani et al, 1999). The only temporal activation found in this study was observed within the left superior temporal cortex for both stimulus modalities. However, significant differences were observed in the magnitude of the responses for the

two categories, as measured by the temporal MEG sensors. Specifically, two time windows were identified in which there was significantly greater activation for the non-living stimuli (500-600ms and 900-1000ms). In addition, for the living stimuli, which have been reported to show category-specificity in both hemispheres, there are time windows identified in this study which illustrate this (greater activation in the left hemisphere at 300-400ms and in the right at 200-300ms and 900-1000ms).

For the parietal lobes all activated regions demonstrated category-specific effects with no identical parietal area being activated by both stimulus types. Specifically, the living items showed activation within the left superior parietal gyrus (0-500ms), left precuneus (0-500ms) and right postcentral gyrus (0-500ms). In contrast, the right precuneus (0-500ms) and left postcentral gyrus (500-1000ms) were activated by the non-living stimuli with the left inferior parietal lobule (500-1000ms) also activated by this stimulus group. The magnitude of living and non-living categories measured by the parietal MEG sensors indicates that across the left hemisphere living items consistently produced greater activation. This was also the case for the majority of the trial across the right hemisphere, the only deviation being between 200-500ms where the non-living stimuli showed greater activation. Indeed, the majority of parietal lobe activation that is specific to living-stimuli, has been reported in the right hemisphere (right inferior parietal lobe (Mummery et al, 1996; 1998; Spitzer et al, 1998) right superior parietal gyrus (Perani et al, 1999).

Of the parietal regions activated by the living stimuli in this study, only one has been previously reported as showing category-specificity, the superior parietal gyrus (Perani et al, 1999). Perani et al (1999) however reported right superior parietal activation which contrasts with the left-hemispheric activity observed in this study.

Within the occipital gyri and visual association areas, a number of category-specific regions were observed. The fusiform gyrus was not one of these however, as it can be seen that during the first 500ms time window (0-500ms), both living and non-living stimuli produced activation within the left fusiform gyrus, with the non-living stimuli showing prolonged activation (until 1000ms) within this region. Although the fusiform gyrus is considered to demonstrate category-specific properties (Perani et al, 1995; Gerlach et al, 1999), there is not a great deal of consistency within the literature. Two studies have reported the left fusiform gyrus to show category-specificity in favour of living things (Perani et al, 1995; Thompson-Schill et al, 1999), two further studies reporting this

specificity in the right hemisphere (Cappa et al, 1998; Gerlach et al, 1999). Activation of the fusiform gyrus in this study was shown to be left-lateralised for both categories, so is only partially consistent with other literature. The study by Chao et al (1999), however also reported fusiform activity by the non-living stimuli (as in this study) so perhaps the fusiform is engaged in more general categorisation processes, which may be dependent on specific qualities of stimuli as opposed to more category-specific properties.

The cuneus showed hemispheric category specificity with the left hemisphere activated for living items (0-500ms) and the right hemisphere for non-living stimuli (0-500ms). Only one previous study has reported category-specific activation of the cuneus. Perani et al (1999) reported left hemispheric cuneus activation in response to non-living items. This is the only other study reporting activation within this region, and as no specific role for the cuneus in categorisation processes has been identified it is not of great concern that their study and this study are not comparable in their findings. Furthermore, the analysis of the magnitude of parietal activation for the two categories indicates that temporal information may play an important role, with both living and non-living stimuli showing greater activations at different time windows. Consistent with this, Spitzer et al (1998) reported that activation and deactivation occurs in a rhythmic manner during presentation of living and then non-living items.

Not-surprisingly, the right middle occipital gyrus was also seen to be activated. This was however, only for the non-living items whilst previous literature (Perani et al, 1995) indicates that occipital regions are activated by both living and non-living items.

Two further cortical regions also showed hemispheric category specificity during the encoding phase, the cingulate gyrus and the cerebellum, neither of which have been reported in the literature. Whilst the right cingulate gyrus was activated throughout the entire trial (0-1000ms) for the living stimuli, the left cingulate gyrus showed activation for non-living items (500-1000ms). Similarly the left cerebellum was activated (0-500ms) for these non-living items, in contrast to the right cerebellum (500-1000ms) for living stimuli.

it may be that the temporal resolution, which has not been studied in detail in the previous literature, is an important factor in the category-specific response. One study in the literature used ERPs to examine the time course of differences in processing living and nonliving things (Kiefer, 2002). As detailed in the Introduction, Kiefer showed that when participants were asked to categorise pictures of living and nonliving things there were significant category-specific differences at 'early' and 'late' stages in the categorisation

process. In particular, living things elicited a greater N1 ERP component (between 160-200ms after target onset) compared to nonliving things, which is thought to reflect visual perceptual processing and is enhanced when attention is paid to visual stimuli (Mangun & Hillyard, 1991). A later component (between 300-500ms after target onset), termed the N400 (or N4) component, was also modulated by semantic category. This was particularly interesting because the N400 component has consistently been shown to be associated with semantic processing in numerous studies (e.g. Kutas & Hillyard, 1980; Kutas & Van Petten, 1994). These data demonstrate that category specific effects can be found at temporally distinct stages in the categorisation process.

6.5.3 Category-Specificity during Recognition Memory

Different regions with the frontal lobes were significantly activated, by the living and non-living categories. There were category-specific hemispheric differences in the middle frontal gyri, right lateralised activation observed for the living stimuli, left for the non-living category. Furthermore, this difference was also reflected by a difference in temporal information, activity in this region occurring in the initial 0-500ms for the living stimuli, and between 500-1000ms for the non-living stimuli. Comparing these findings to those reported in previous studies of category-specificity, the similarities are encouraging. Grabowski et al (1998) reported left inferior frontal gyrus activation for non-living items, Cappa et al (1998) reporting right-lateralised category-specific activity in favour of the living stimuli. Spitzer et al (1998) also reported differences between the two categories in this same region. Additional left-lateralised activation was observed in the precentral gyrus for the non-living items (consistent with Grabowski et al, 1998) although this was mirrored with bilateral activity in this region for the living stimuli. The left inferior frontal activation, however, seen in this study for the living items, is in contrast to the predominantly left-lateralised non-living category-specific activity reported previously (Perani et al, 1995; Grabowski et al, 1998). In the ERP analysis of the magnitude of the response measured by the frontal MEG sensors, a large decrease could be seen in the left hemisphere for the non-living stimuli (400-500ms) which may reflect the predominantly left-lateralised non-living specific frontal activity reported in the literature.

The one region consistently reported in previous studies as exhibiting category-specific properties is the left posterior middle temporal gyrus. No such category-specific activity was observed in this region in this study. Furthermore, the analysis indicated that

the living stimuli produced the greatest responses. This is perhaps not surprising as the participants were no longer explicitly performing a categorisation task. Instead it was a task of recognition memory which may be influenced by semantic processing.

Activation within parietal regions is believed to represent attentional processing (Crossman & Neary, 2000). Consequently, the absence of any obvious category-specific activation within parietal regions would be anticipated. As predicted, all observed parietal activation was present in the left hemisphere, irrespective of modality. Specific parietal regions did, however, show differences. For instance, living items activated the left inferior parietal lobule, in contrast to previous studies reporting right hemispheric category-specific activity in this area (Mummery et al, 1996, 1998). Non-living items activated the left superior region of the parietal lobe. This dissociation, however, does reflect a difference in category processing which may be similar to the difference reported by Spitzer et al (1998). In addition, all activation of the precuneus was left-lateralised for the living items, bilateral for the items in the non-living category, partially replicating the left precuneus activity reported by Perani et al (1999) for non-living items. The greater magnitude of activity observed across the parietal sensors for the living stimuli may indeed reflect greater attentional processes, the relative similarity of the living items to each other necessitating more focused attention than the diverse range of non-living stimuli used.

Within the occipital and related visual association areas, activation of the left lingual gyrus for non-living stimuli was consistent with a number of previous findings (Perani et al, 1999; Moore & Price, 1999). It must, however, be noted that other different studies have also reported category–specific activity in the left lingual gyrus for living items (Perani et al, 1995; Martin et al, 1996). Also, the middle occipital gyrus demonstrated category-specific properties with greater activation also seen in this region for the non-living stimuli. This may reflect the greater complexity of the non-living items.

6.5.4 General Discussion

Whilst some category-specific activation was observed to be consistent with previous findings, generalising all the stimuli into one of two categories (i.e. living versus non-living) is not thought to be a sufficient method of categorisation objects for a number of reasons.

Firstly, different brain regions have been shown to be activated for musical instruments, for tools, furniture, transport etc. (Martin et al, 1996). Secondly, related to this is the association of activity within the left posterior middle temporal cortex with action retrieval (Martin et al, 1995). In particular, it has been suggested that this is greater still for pictures of body parts (Gorno-Tempini, Cippolotti & Price, 2000). The stimuli used in this study incorporated body parts such as 'leg' and 'hand', which were categorised by many of the individuals as living due to their association with a living human or animal. It is therefore probable that the relatively small amount of consistency with previously reported findings for this region is a direct consequence of the ambiguity of categorising body parts as living or non-living.

In addition, Moore & Price (1999) demonstrated differences between animals and fruits, particularly in the lingual gyrus, and suggested that the visual complexity of the stimuli was a more significant component in the processing of the stimuli, rather than its semantic category. In this study, animals were grouped together with fruits and vegetables to create the 'living' category and thus this may have been another factor involved in the production of the results.

In the introduction, the similarities between episodic and semantic encoding were highlighted, with the one region, the inferior prefrontal cortex being highlighted as involved in both semantic and working memory processes. This study offers some further support for this overlap with the right inferior frontal gyrus being activated by both categories during the encoding phase, possibly reflecting working memory storage processing, and the left inferior frontal cortex being activated by only the living stimuli in the recognition phase, possibly reflecting some difference in semantic processing for the two categories.

As discussed previously, the data from this study indicate that living things require greater perceptual processing than non-living things. In their category-specificity model, Humphreys et al (1988) suggested that all categories share the same processing systems but place different demands on it. In accordance with this model, it could be argued that the living and non-living items in this study are processed through the same system, which would account for the activation of similar cortical regions, such as the left fusiform and superior temporal gyri, right inferior frontal gyrus, and bilateral precentral gyrus during the encoding phase and the left precuneus, precentral gyrus and parietal regions during the recognition phase. The additional perceptual processing required by the living stimuli (as

described by Humphreys et al, 1988) might therefore be performed within cortical structures, such as the right superior and medial frontal gyri, which in this study were only activated by the living stimuli, and not for the non-living things.

Similarly, there are regions which are activated only by the non-living stimuli, such as right middle occipital gyrus, and left cingulate gyrus. An explanation for this is offered by another popular cognitive model of category-specificity. Warrington & Shallice (1984) suggest that accessing stored semantic knowledge can produce category-specific differences, primarily due to the different cortical regions involved in processing perceptual and functional knowledge. Living object identification primarily involves perceptual processing, in contrast to the focus of functional knowledge processing for non-living stimuli. It may be therefore, that these differentially activated cortical regions are responsible for these different processes.

Following on from this therefore, it is plausible that in tasks of recognition memory perceptual and functional knowledge about the encoded items are also stored and later used to facilitate accurate recognition. The regions described above which were activated by both categories during the recognition phase may be responsible for performing the processes required in tasks of recognition memory, and the additional regions activated by only one of the categories may be processing the additional semantic (e.g. perceptual or functional) knowledge about the item. Indeed as discussed in the introduction, not only is it believed that for successful episodic encoding to occur, the information must first be successfully processed in semantic memory (Tulving, 1995), but also it is argued that semantic memory could play a significant role in the processes occurring during episodic recollection (Tulving, 1972).

6.6 Concluding Remarks

The aim of this study was to test the hypothesis that there is category-specificity during recognition memory tasks. The experiment was conducted to identify the brain areas involved in processing living and nonliving things at different stages in the categorisation process, and to determine whether different regions of the brain were activated in the encoding and recognition phases for living and non-living items. As predicted, this MEG study identified a number of cortical regions that showed category-specific differences for living and non-living items during the encoding task, which can be supported by the literature on category-specificity. However, although the participants were required to perform a categorisation task on the stimuli, pure category-specific effects might not have been shown due to contamination from active rehearsal processes as the participants knew they would subsequently be required to remember the encoded items. Nevertheless, it makes sense that there will be differences between living and non-living things when retrieving stored semantic information about them, as in the categorisation task.

Due to the overlap between episodic and semantic memory, it was further predicted that these category-specific differences would also be evident during the recognition memory phase of the task and it was hypothesised that different cortical regions would be involved in performing a 'yes / no' recognition judgement tasks for living items, compared to those for non-living stimuli. Although the findings from this study did not fully replicate the findings from other neuroimaging studies in terms of identifying cortical regions which demonstrate category-specific properties, the fact that any category-specific effect exists has important implications for research into recognition memory. It would not necessarily be expected that the same differences reported in a living / non-living categorisation tasks as would be observed in a simple yes / no recognition task. Yet, differences between living and non-living things were seen in the different cortical regions activated during the recognition memory component of the task.

This substantiates the proposal that a semantic network exists which is used in other cognitive processes not explicitly focussing on semantics. Consequently, this semantic network, or at least parts of it, may be responsible for the diverse activation in the recognition memory neuroimaging literature. To identify the specific neural correlates of recognition memory it is therefore important to attempt to omit semantics from the process. This was the aim of the following recognition memory study. By selecting a shallow

encoding task, which did not require any semantic processing, it was proposed that the subsequent recognition memory tasks should not involve semantic processing. By doing this those cortical areas which are necessary for successful recognition memory and not those non-essential regions which are additionally activated, may be identified, which has implications for clinical memory research.

7 NEURAL CORRELATES OF RECOGNITION MEMORY FOLLOWING A SHALLOW ENCODING TASK

7.1 Overview

In the previous MEG study, hemispheric asymmetry in recognition memory was investigated. The data did not clearly replicate any of the findings from previous neuroimaging literature and a review of this literature suggested that these too showed significant differences in reported activation. It was suggested that this lack of consistency was due to the different stimuli, tasks and techniques used in acquiring and analysing the data. This highlighted the need for a direct replication of a study to determine the reliability of the findings. This was thought to be especially pertinent for MEG research because to date only a couple of MEG studies of recognition memory exist. This study, therefore, was designed as a replication to that presented previously (chapter 5). The experimental parameters were the same as for the previous study with the exception of the use of a shallow encoding task (as opposed to a deep categorisation task). An investigation of the semantic processes during encoding and recognition tasks suggested that a semantic network may account for the diverse activation often reported in recognition memory studies. Removing the semantic component from the encoding task was believed to facilitate the identification of true memory processes in the subsequent recognition phase. The results suggested that MEG can provide reliable data in tasks of higher order cognitive functioning and that the use of EEG-defined frequency bands enables comparison with the EEG literature.

7.2 Introduction

In a previous study (chapter 5), the neural correlates of object and word recognition memory were investigated using magnetoencephalography. In particular, hemispheric differences between encoding and recognition and between objects and words were investigated. The data from the MEG study, however, did not appear to clearly replicate any of the findings from previous neuroimaging studies. In a review of some of the most

recent neuroimaging literature associated with recognition memory, it was illustrated that these too also failed to explicitly replicate each other or to directly link each hemisphere with either stimulus modality or with task (Table 1.1).

In this review it was suggested that the lack of consistency in the literature was due to a number of factors. Firstly, different neuroimaging techniques were utilised in the different studies, these included PET, fMRI, TMS and MEG, each of which have different advantages and disadvantages. Secondly, there was also variation in the stimuli, some using words, other using objects and faces. Thirdly, the encoding conditions / tasks and the analysis comparisons used also differed. Finally, many of the studies focused on one modality, separate experiments conducted using different stimulus categories. Indeed, only nine of the twenty studies summarised used more than one stimulus modality. It seems, therefore, that any recognition memory experiment needs to be repeated with similar experimental parameters, thus enabling the replicability of the results to be investigated.

Furthermore, many of the previous neuroimaging studies (detailed in Table 1.1) did not either directly compare activations between stimulus modality or between tasks. Only five of the studies included in Table 1.1 directly compared activations between stimulus modalities, with only two studies providing results for both encoding and recognition phases (Idiaka et al, 2000; Kohler et al, 2000). Raye et al (2002) failed to find any statistically significant differences for either stimulus type in either task phase and the remaining studies only observed activation for either the recognition phase (Simons et al, 2001) or the encoding phase (Grady et al, 1998).

The comparisons made were often task versus control or baseline (for example Reber et al. 2002). Consequently, these experiments could not distinguish between brain areas involved in general recognition memory, and those that are modality- or task-specific. Simons et al., (2001) compared rCBF in the retrieval phase for faces and pictures and concluded that hemispheric specialisation was 'modality-specific'. There was increased rCBF for pictures in the left anterior PFC and for faces in the right anterior PFC, as well as left DLPFC. Simons et al. argued that the greater bilateral activation for pictures and right-sided activation for faces supported the idea that hemispheres are specialised for modality of stimulus rather than task. However, they did not directly compare encoding and retrieval, as was compared in the study previously detailed in chapter 5, and thus did not comment on a possible 'task-specific' hypothesis.

This leads to the suggestion that in addition to a direct replication of a recognition memory task using similar experimental parameters, perhaps a more accurate analysis of 'task-specific' or 'modality-specific' hemispheric dissociations during recognition memory would be achieved through direct task and modality comparisons. Although it is not uncommon for direct comparisons to fail to identify specific regions for both tasks (for example, Vaidya et al, 2002; Kohler et al, 2000; Lee et al, 2000; Ragland et al., 2000), this may be overcome through the use of a number of small time- and frequency-specific comparisons. The use of MEG and development of SAM enables specific comparisons to be completed with the potential of identifying task and modality specific cortical areas over millisecond time resolution.

Previous neuroimaging literature has identified different regions of activation according to depth of encoding. For example, Grady et al. (2001), using PET, identified different prefrontal areas that were involved in perceptual and semantic encoding tasks. The previous MEG study (chapter 5) involved a deep encoding task, that of semantic categorisation, and it may be that the subsequent brain areas identified as being involved in recognition memory processes might have been contaminated with semantic processing. Consequently, those brain regions identified in recognition memory following deep encoding tasks may vary to those identified by previous literature which used a shallow encoding task.

The preliminary results from the previous MEG study, combined with those from earlier neuroimaging studies, suggested the existence of frontal and temporal regions specialised for encoding and recognition memory tasks, and that within these are specialised modality-specific regions. For example, the prefrontal and middle temporal gyri are consistently shown to be involved with episodic encoding. Although these have a tendency to show left and right hemispheric dominance, respectively, there are a large number of studies that show bilateral activation within these areas. Therefore, whilst 'modality-specific' regions may exist, they do not seem to be closely linked to one hemisphere or the other. Instead, the hemispheric differences often reported may simply be related to stimulus modality, or encoding strategy, and it is these variables which now need to be investigated.

One further issue that was discussed in light of the findings from the previous experiment was the frequency specific ERD observed in the data. The significance of frequency-specific activation is a topical issue in EEG research and previous EEG studies

have shown that during memory processes, cortical synchronisation is evident in the narrow theta frequency band (4-7 Hz) (Klimesch, Doppelmayr, Schimke & Ripper, 1997) and desynchronisation within the alpha (8-12 Hz) range (Klimesch, Doppelmayr, Pachinger & Russegger, 1997). Some EEG studies have focused on the alpha and theta bands in particular, identifying these in memory processes (Burgess & Gruzelier, 1997; 2000). Upper alpha desynchronisation (10-12 Hz) has been reported to be linked to semantic memory processing (Klimesch, Doppelmayr, Pachinger & Russegger, 1997) while synchronisation within the theta band (4-7 Hz) is linked to working memory (Klimesch, Schimke & Schwaiger, 1994) and the encoding of new information (Burgess & Gruzelier, 2000; Klimesch, Doppelmayr, Russegger & Pachinger, 1996; Klimesch, Doppelmayr, Schimke & Ripper, 1997).

The comparisons in the overlapping 10Hz frequency bands conducted in the previous MEG study did not exclusively correspond to either the theta or alpha bands, but spread across both (specifically, 5-15 Hz). Therefore, it is possible that because the 5-15 Hz band used in the study predominantly included alpha waves (8-12 Hz), with much smaller amounts of theta (5-7 Hz), any potential ERS was not shown and consequently only ERD within the alpha was seen in the SAM images. The importance of narrow frequency bands was further demonstrated in a study by Krause et al (2000). Following a visual sequential letter task involving varying levels of memory load, the 4-6 Hz theta, 6-8 Hz and 8-10 Hz alpha frequency bands all showed ERS, whilst in the 10-12 Hz band there was only an increase in ERD.

Differences were also observed in the previous MEG study between the frequency bands in reference to the time course of the brain activation, leading to the suggestion that the frequency-specific memory activation reported previously (Klimesch, Vogt and Doppelmayr, 1999) might change over the course of the task, or be linked to particular components of memory tasks.

7.2.1 Aims and Hypotheses

This experiment was therefore conducted to answer several of those questions generated following the results from the previous experiment (chapter 5). Primarily, it was performed to investigate the reproducibility of the results obtained from the previous study. The study presented previously was the first to use SAM to analyse recognition memory

MEG data. As suggested above, it was necessary to ensure that the experimental paradigm remained similar to that of the previous study. Therefore, this MEG study also comprised an encoding task immediately succeeded by a recognition memory task involving yes/no recognition judgements, enabling direct comparisons of these two processes. However, following this it was decided that a direct comparison of objects and words might also provide additional information regarding the cortical differences between these modalities. Consequently, encoding and recognition tasks were conducted for objects and words sequentially, within one recording session.

In order to answer some of the other questions highlighted following the previous study a number of small manipulations were made to the experimental paradigm. It was hypothesised that much of the widespread activation and variability in the neuroimaging literature of recognition memory may be due to the involvement of semantic processing (chapter 5). An investigation of category-specific effects during recognition memory following a categorisation encoding task (chapter 6), concluded that the semantic processes used in the encoding tasks were also evident during the subsequent recognition memory task. It was therefore hypothesised that reducing the involvement of semantics in the encoding task will minimise the level of semantic processing used in the succeeding recognition task. Furthermore, it was anticipated that this would reduce the number of cortical regions activated in the recognition phase. The experimental paradigm was therefore altered to incorporate a simple shallow encoding task, which was anticipated to reduce the amount of semantic processing which might contaminate the memory-specific processes. Differences in the encoding–related activation were therefore expected for this study, compared to that detailed previously (chapter 5).

In an attempt to determine whether the difference in results from the previous study, compared to that from previous literature, was due to cortical oscillatory frequency, the data were analysed using two groups of frequency bands. The first was the identical bandwidths to those used in previous studies: 10Hz bandwidths (5-15Hz, 10-20Hz, 15-25HZ, 20-30Hz and 25-35Hz). The sixth bandwidth of 30-40Hz was not analysed as very little activity was shown to occur in this frequency band in the previous study. Secondly, the data were re-analysed using standard EEG frequency bandwidths corresponding to delta (0-4Hz), theta (4-7Hz), alpha (8-13), alpha and theta combined (3-13Hz), beta (14-20Hz) and finally a large broad bandwidth (0-40Hz). The importance of the alpha and theta frequency bands in memory processes is well documented (see Klimesch et al). It was therefore hypothesised that the alpha and theta frequency bands would be particularly

important in the memory processes and regions showing activation within these areas would correspond most closely to those identified in the 10Hz bandwidth analyses.

7.3 Method

7.3.1 Participants

Eight healthy right-handed participants (five females and three males, age range 22-51 years) volunteered to participate in the study. Anatomical MRI scans had previously been taken for each of these individuals and were made available for the analysis.

7.3.2 Stimuli

The pictures of objects presented to the participants during the study taken from the Snodgrass and Vanderwart (1980) set of line drawings. In the encoding phase, there were 44 pictures, 22 living and 22 non-living matched for frequency (Kučera and Francis, 1967). In the recognition phase, participants were presented with the same 44 stimuli and 44 new pictures. The new items were 22 living and 22 non-living, matched for frequency to the stimuli presented in the encoding phase. For the word stimuli, the participants were presented with the corresponding names of the pictures as words.

7.3.3 Encoding Task

For this study, a shallow encoding task was used. This involved a spatial location task, during which participants were presented with a series of stimuli and were required to identify the location of a red dot placed either above or below the horizontal plane of fixation (see Figure 7.1). A button-press was then used to indicate the participant's response. The use of the red dot enabled the stimuli to be presented to central fixation. This was decided to be the best way of presenting the stimuli following a pilot run during which the stimuli themselves were presented above or below the central line of fixation. This failed to produce significant recognition memory responses, with the two participants involved only scoring at chance levels (48% and 53% accuracy respectively) in this trial.

They both reported inability to consciously see the presented stimulus, instead only being aware of a dark image above or below their horizontal plane of fixation.

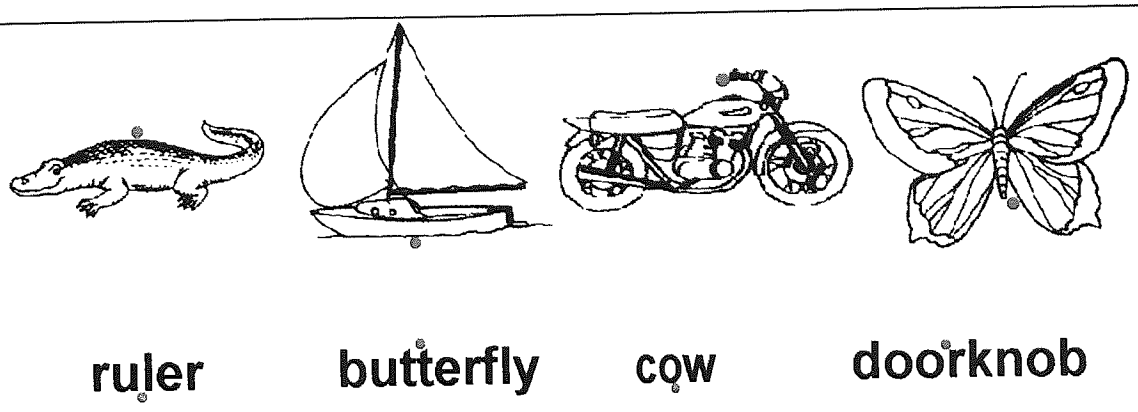


Figure 7.1. Examples of object and word stimuli used in the encoding and recognition phases. The position of the red dot was used as the spatial location task (participants required to judge whether it was above or below the horizontal plane of fixation) during the shallow encoding task

7.3.4 Presentation of Stimuli

Before, commencement of the study, participants were randomly assigned to one of two experimental groups. The first group performed the object recognition memory task first, followed by the recognition memory tasks for words. In contrast, the second group performed the word recognition memory tasks first, followed by that for objects (see Figure 7.2). Within each group, the location of the red dot (above or below) was randomised amongst the stimuli and the stimuli themselves were randomly presented.

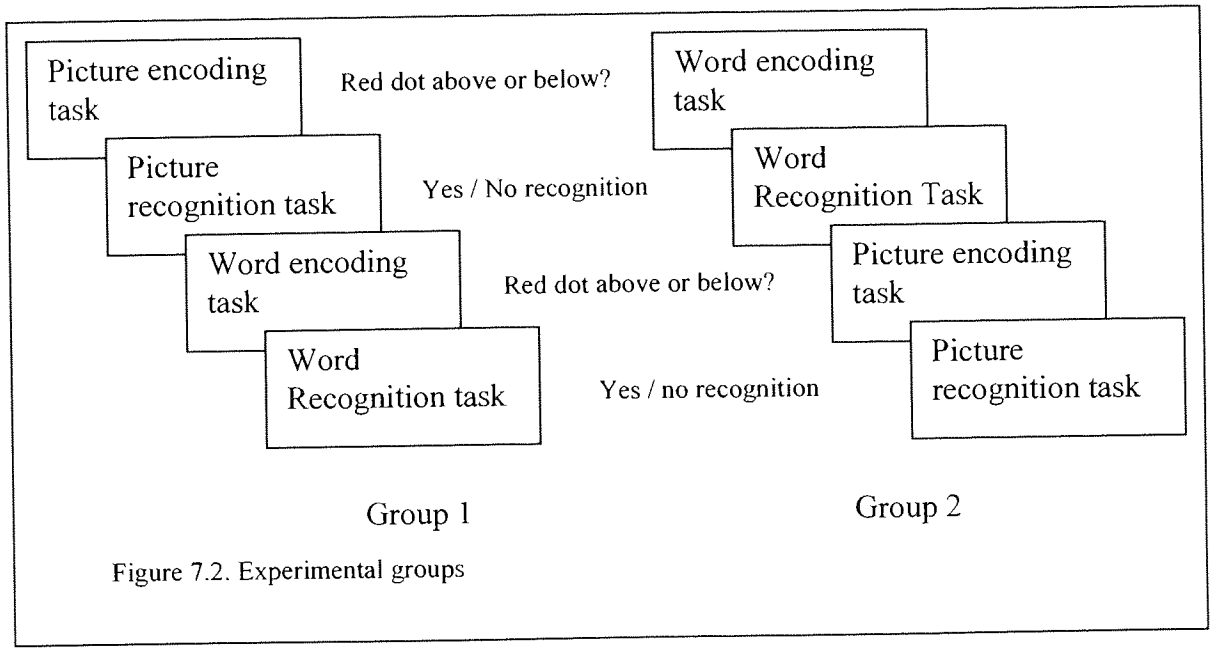


Figure 7.2. Experimental groups

Participants were seated in a magnetically shielded room and viewed the stimuli, presented on an Eizo T662 monitor, through a mirror at a distance of two meters. In both the encoding and recognition phases of the experiment, the participants were required to fixate on a centrally presented small white square for a period of 1500 ms. A stimulus was then presented to the centre of the screen for 500 ms before the fixation point returned for another period of 1000 ms. The fixation point then changed from white to black, and this was the participant's cue to make a response with a button press using their dominant hand. In the encoding phase, participants were asked to make a judgment about whether the red dot was located above or below their horizontal plane of fixation (above / below spatial judgement task) and, in the recognition phase, as an old or new item. Accuracy and reaction time responses were recorded. Participants had 2000 ms to respond before the fixation point turned white again. This marked the onset of the next trial. The timing is illustrated in Figure 7.3. Stimuli were presented in a different random order for each participant. The same procedure was followed for words and pictures.

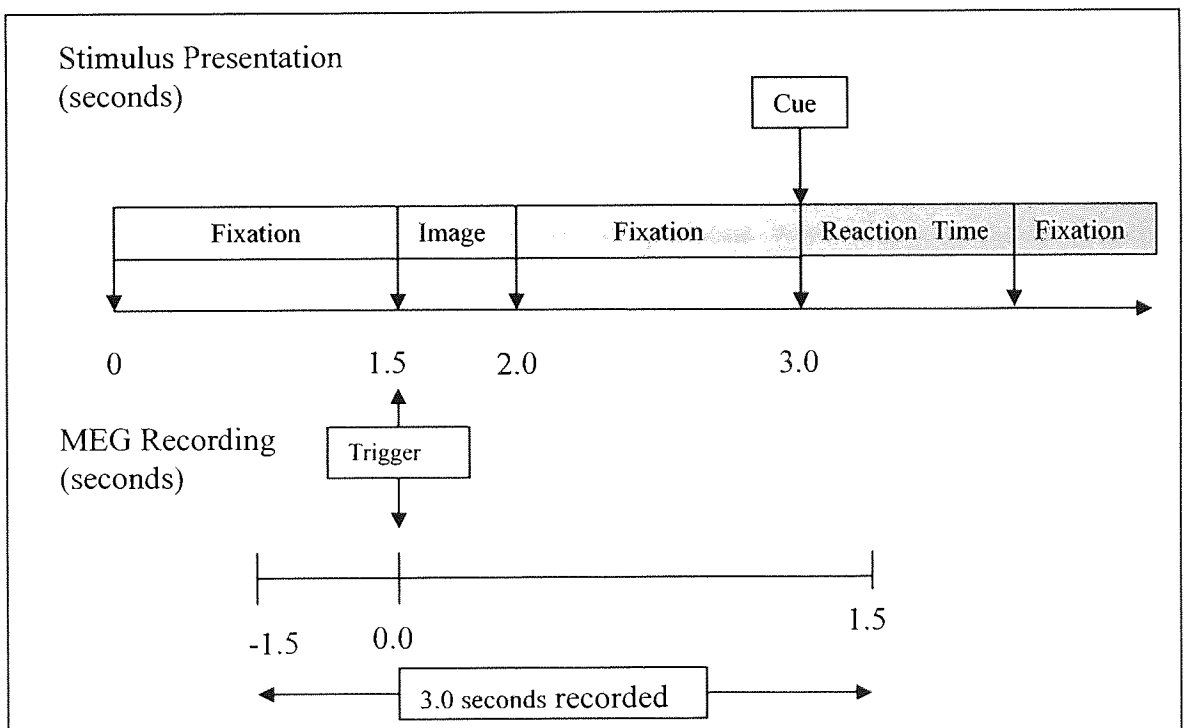


Figure 7.3. Experimental paradigm

The 500ms-stimulus presentation was determined following a two-participant pilot run in which the stimuli were only presented for 200ms. This short time-length resulted in chance responding in the subsequent recognition memory phase for both participants. An increase to 500ms then yielded recognition memory responses (76% and 81% accuracy) which were found to be statistically significantly greater then chance responding.

7.3.5 MEG Recording and Analysis

Recording of neural activity took place using a 151-channel CTF Omega MEG system (CTF Systems Inc, Canada.). Following MEG recording, a Polhemus Isotrak system was used to digitise the surface shape of the participant's head, this information then being used to co-register the MEG data with the participant's anatomical MRI.

Analysis of the cortical activation took place using SAM (Synthetic Aperture Magnetometry) (Robinson & Vrba, 1998; Barnes et al, 2001), a method of producing a three-dimension map of cortical synchronous and desynchronous activation. SAM Analysis compares one state (active) with another (passive). Positive t-statistics are produced when the active state shows and increase in power, negative when it shows a decrease. These are interpreted as event-related synchronisation (ERS) and event-related desynchronisation (ERD) respectively (Pfurtscheller & Lopes da Silva, 1999).

Several SAM comparisons were made on the raw, correctly encoded and recognised data. Firstly, comparisons were made between encoding and recognition for the objects and words separately. Following this pictures and words were directly compared. SAM comparisons directly compared pictures and words for both the encoding phase and for the recognition phase. Several baseline SAM comparisons were also computed (baseline (500ms before stimulus onset) versus 1st, and 2nd 500ms time spans following stimulus onset) for each of the stimulus types, words and pictures, during encoding and recognition of old images. The third possible 500ms was not analysed for a couple of reasons. Firstly, a button-press response was performed at 1000ms post-stimulus onset and it was expected that this would contaminate any data in the final 500ms time span. Secondly, previous neuroimaging research suggested that cognitive processing is probably finished by 1000ms post stimulus onset. The list of analyses is shown below.

Encoding and Recognition

1. Encoding versus recognition during the first and second 500 ms post-stimulus onset for pictures

2. Encoding versus recognition during the first and second 500 ms post-stimulus onset for words

3. Four baseline comparisons of encoding / recognition during first / second 500 ms compared to 500ms fixation (baseline) for pictures

4. Four baseline comparisons of encoding / recognition during first / second 500 ms compared to 500ms fixation (baseline) for words

Pictures and Words

5. Direct comparison of pictures versus words during the first and second 500ms compared of encoding

6. Direct comparison of pictures versus words during the first and second 500ms compared of recognition of old items

All power changes were calculated in two groups of frequency bands. The first group corresponded to those used in the previous MEG study (chapter 5); 5-15Hz, 10-20Hz, 15-25Hz, 20-30Hz, and 25-35Hz. The second group corresponded to standard EEG frequency bandwidths; corresponding to delta (0-4Hz), theta (4-7Hz), alpha (8-13), alpha and theta combined (3-13Hz), beta (14-20Hz) and finally a large broad bandwidth (0-40Hz).

Group SAM images were generated by spatially normalising each of the participant's SAM data using SPM99 (Friston et al, 1995) and mapping these onto a template brain. Statistically significant regions of activation were identified using statistical non-parametric mapping (SnPM).

7.4 Results

There were three main aims of this study. The first was to replicate the findings from the previous MEG study detailed in chapter 5. Secondly a direct comparison of objects and words in both encoding and recognition phases was conducted to determine modality differences. Finally a comparison of 10Hz frequency bands with standard EEG frequency bands was performed to provide additional frequency-specific information about recognition memory processing.

Accordingly, the results are detailed in three such sections. The first describes the results of this replication experiment using the same analysis parameters as in the previous study. The second provides a direct comparison of objects and words, in both encoding and

recognition. The third part details the results of analyses using EEG frequency bandwidths, which are subsequently compared to those of the original analysis in the discussion.

7.4.1 Behavioural Data

Behavioural data was collected from the eight participants. Trials on which participants responded before the cue, had reaction times greater than 2000ms, or made an incorrect response, were removed from the analysis. Participants were highly accurate on both the encoding tasks for objects and words (95/1% and 95.8%, respectively). Although accuracy was not as high during the recognition test (80.4% for objects and 79.7% for words), a chi-square analysis showed this level of accuracy to be above chance for both objects (χ^2 (df1) = 26.58; $p < 0.001$) and for words ($\chi 2$ (df1) = 25.38; $p < 0.001$).

7.4.2 SAM Analysis using 10Hz Frequency Bandwidths

7.4.2.1 Direct Comparison of Recognition versus Encoding

0-500ms

Objects and Words

No statistically significant differences were found between the encoding and recognition phases for either the objects or the words during the first 500ms post-stimulus onset in any of the 10Hz frequency bandwidths analysed.

500-1000ms

Objects

In the second 500ms post-stimulus onset, three statistically significant regions were identified as being differentially activated for the encoding and recognition phases (Table 7.1). This difference could either be interpreted as greater ERS in these regions in the encoding phase compared to the recognition phase, or as greater ERD in the recognition

phase. The regions which showed this differential activation were all located in the right hemisphere, specifically in the middle frontal, precentral and cingulate gyri.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Frontal Gyrus	Right	25-35	23 18 58	253	6.88*	0.039	6
Precentral Gyrus	Right	25-35	24 21 60	253	5.71*	0.023	
Cingulate Gyrus	Right	25-35	18 18 39	253	6.88*	0.008	24

Table 7.1Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and recognition memory phases for objects, 500-1000ms post stimulus onset. *indicates ERD.

Words

As for the initial time period, no statistically significant differences were found between the encoding and recognition phases for the words in any of the 10Hz frequency bandwidths analysed.

7.4.2.2 Baseline Comparisons for Encoding and Recognition

7.4.2.2.1 Encoding versus Baseline

0-500ms

Objects

In the initial half of the trial, several regions were activated by objects during the encoding phase (Table 7.2; Figure 7.4.A). These were identified using cluster analysis, as opposed to a voxel-wise analysis. Consequently, statistically significant clusters, not voxels are reported. These included bilateral inferior frontal and superior temporal gyri, left middle frontal and middle temporal gyri and right precuneus and inferior occipital gyri. Interestingly, activation was only seen in two frequency bands. All left hemispheric activity was observed in the 5-15Hz range. In the right hemisphere, however, those regions which showed lateralised activity produced activity in this 5-15Hz frequency band, compared to the activity in the right hemisphere of bilaterally activated regions which was in the 25-35Hz range.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Frontal Gyrus	Left	5-15 c	48 45 9	5153	4.02^	0.082	
Inferior Frontal Gyrus	Left	5-15 c	-51 42 3	5.53	4.67^	0.082	44
	Right	25-35 c	60 21 -7	7568	3.89^	0.059	
Middle Temporal Gyrus	Left	5-15 c	-60 -33 -3	5153	4.76^	0.082	21
Superior Temporal Gyrus	Left	5-15 c	-59 -26 -3	5153	4.23^	0.082	22
	Right	25-35 c	18 69 18	1853	3.56^	0.094	10
Precuneus	Right	5-15 c	6 76 55	4661	4.03^	0.090	
Inferior Occipital Gyrus	Right	5-15 c	24 -101 -15	4661	4.18^	0.090	

Table 7.2 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and baseline phases for objects, 0-500ms post stimulus onset. ^ indicates ERS; c indicates regions identified through cluster analysis.

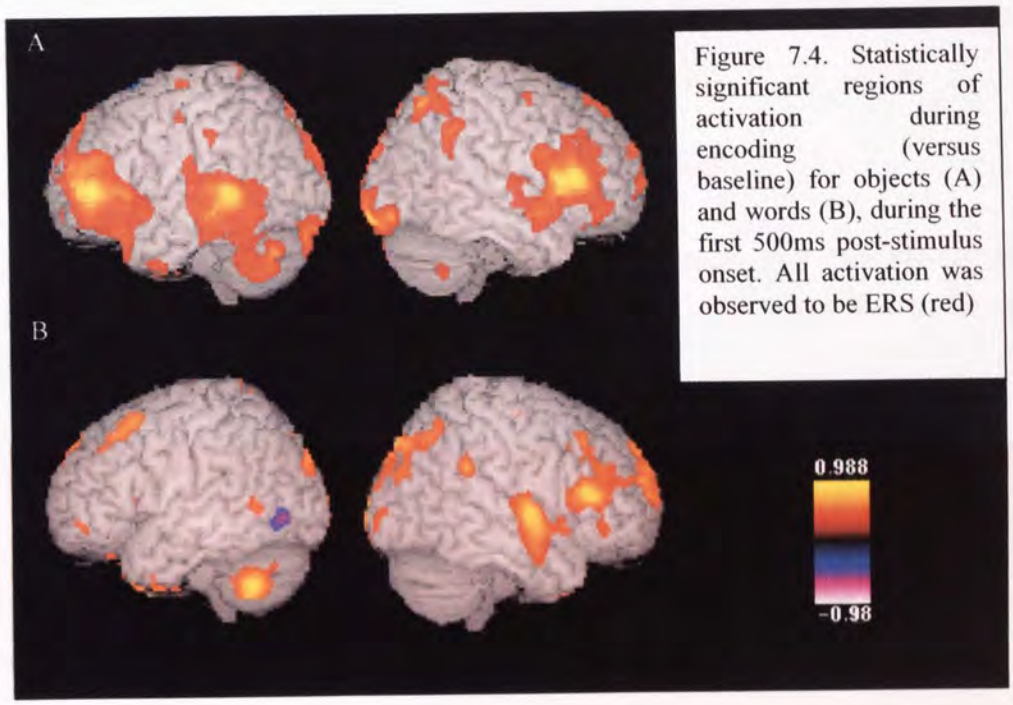


Figure 7.4. Statistically significant regions of activation during encoding (versus baseline) for objects (A) and words (B), during the first 500ms post-stimulus onset. All activation was observed to be ERS (red)

Words

As for the objects, all statistically significant regions were identified using a cluster analysis as a voxel-wise analysis did not reveal and statistically significant activity (Table 7.3.; Figure 7.4.B). All activation was lateralised with no region showing bilateral activity. Left lateralised activity was observed within the limbic region, specifically the parahippocampal gyrus and amygdala. Right lateralised ERS was seen in the medial and superior frontal gyri, middle and superior temporal gyri and the anterior cingulate. The left hemispheric activity and the right temporal activations were all seen in the 5-15Hz range, with the remaining right lateralised activity observed within the 10-20Hz range.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Medial Frontal Gyrus	Right	10-20 c	6 45 21	135	4.87^	0.059	9
Superior Frontal Gyrus	Right	10-20 c	30 39 36	135	4.84^	0.059	
Middle Temporal Gyrus	Right	5-15 c	65 -3 -5	1961	3.32^	0.070	21
Superior Temporal Gyrus	Right	5-15 c	48 0 -6	1961	3.94^	0.070	22
Parahippocampal Gyrus	Left	5-15 c	-24 -5 -27	1961	3.41^	0.070	
Amygdala	Left	5-15 c	-24 -5 -27	1961	3.41^	0.070	
Anterior Cingulate	Right	10-20 c	6 38 21	135	4.14^	0.059	32

Table 7.3 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and baseline phases for words, 0-500ms post stimulus onset. ^ indicates ERS; c indicates regions identified through cluster analysis.

500-1000ms

Objects

Neither the voxel-wise nor cluster analyses revealed any statistically significant activations for the encoding of objects (500-1000ms) within the five 10Hz frequency bandwidths during either.

Words

Three left lateralised regions were observed to be statistically significantly activated (ERS) during the encoding of words (500-1000ms). These were the superior and medial frontal gyri in the 15-25Hz bandwidth and the middle occipital gyrus in the 10-20Hz frequency range (Table 7.4, Figure 7.5).

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Superior Frontal Gyrus	Left	15-25	-7 58 26	57	6.51^	0.039	
Medial Frontal Gyrus	Left	15-25	-9 48 18	57	6.51^	0.012	10
Middle Occipital Gyrus	Left	10-20	-15 -102 15	1	5.27^	0.086	18

Table 7.4 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and baseline phases for words, 500-1000ms post stimulus onset. ^ indicates ERS;

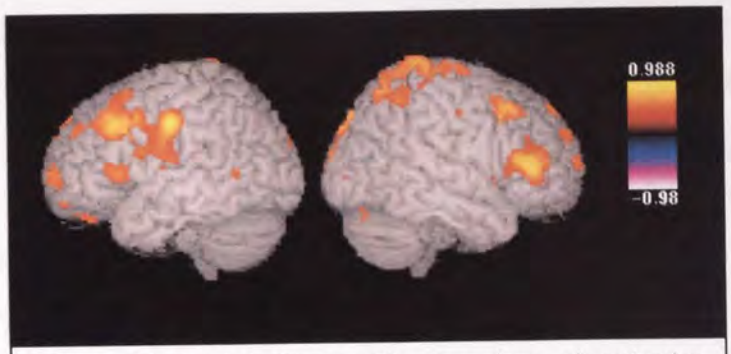


Figure 7.5. Statistically significant regions of activation during encoding (versus baseline) for words during the second 500ms post-stimulus onset. All activation was observed to be ERS (red)

7.4.2.2.2 Recognition versus Baseline

0-500ms

Objects

No significant voxels were shown to be activated, although a significant left-lateralised ERS cluster was identified within the frontal and temporal gyri during the recognition of objects (0-500ms) produced activation (Table 7.5, Figure 7.6.A). Specifically the significant cluster extended over the inferior, middle, superior and medial frontal gyri and over the superior and middle temporal gyri. Activation was specific to the 5-15Hz frequency band.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Inferior Frontal Gyrus	Left	5-15 c	-46 48 2	3385	3.33^	0.059	
Middle Frontal Gyrus	Left	5-15 c	-24 48 15	3385	3.05^	0.059	
Superior Frontal Gyrus	Left	5-15 c	-22 48 4	3385	3.79^	0.059	
Medial Frontal Gyrus	Left	5-15 c	-20 48 11	3385	3.53^	0.059	
Superior Temporal Gyrus	Left	5-15 c	-51 -24 -3	3385	4.30^	0.059	22
Middle Temporal Gyrus	Left	5-15 c	-97 -30 -18	3385	3.77^	0.059	21

Table 7.5 Regions showing statistically significant differences in activation ($p < 0.05$) between the recognition and baseline phases for objects, 0-500ms post stimulus onset. ^ indicates ERS; c indicates regions identified through cluster analysis.

Words

The significantly activated right-lateralised regions during the recognition of words (0-500ms) were predominantly only identified by a cluster analysis (Table 7.6, Figure 7.6B). Specifically, this cluster extended over the temporal lobe, comprising the parahippocampal gyrus, and more specifically the hippocampus, and also extended to the fusiform gyrus. A small region within the right cerebellum was shown to be statistically significantly activated at the voxel level. All significant neural activity occurred within the 20-30Hz frequency band.

Region	Hemisphere	Frequency bands	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Temporal Lobe	Right	20-30 c	42 -27 -15	1648	4.31	0.051	
Fusiform Gyrus	Right	20-30 c	45 -27 -36	1648	3.65	0.051	20
Parahippocampal Gyrus	Right	20-30 c	35 -25 -16	1648	3.95	0.051	36/20
Hippocampus	Right	20-30 c	33 -24 -11	1648	3.95	0.051	
Cerebellum	Right	20-30	36 -54 -39	49	5.10	0.055	

Table 7.6 Regions showing statistically significant differences in activation ($p < 0.05$) between the recognition and baseline phases for words, 0-500ms post stimulus onset. * indicates ERD; c indicates regions identified through cluster analysis, other regions were identified through a voxel-wise analysis.

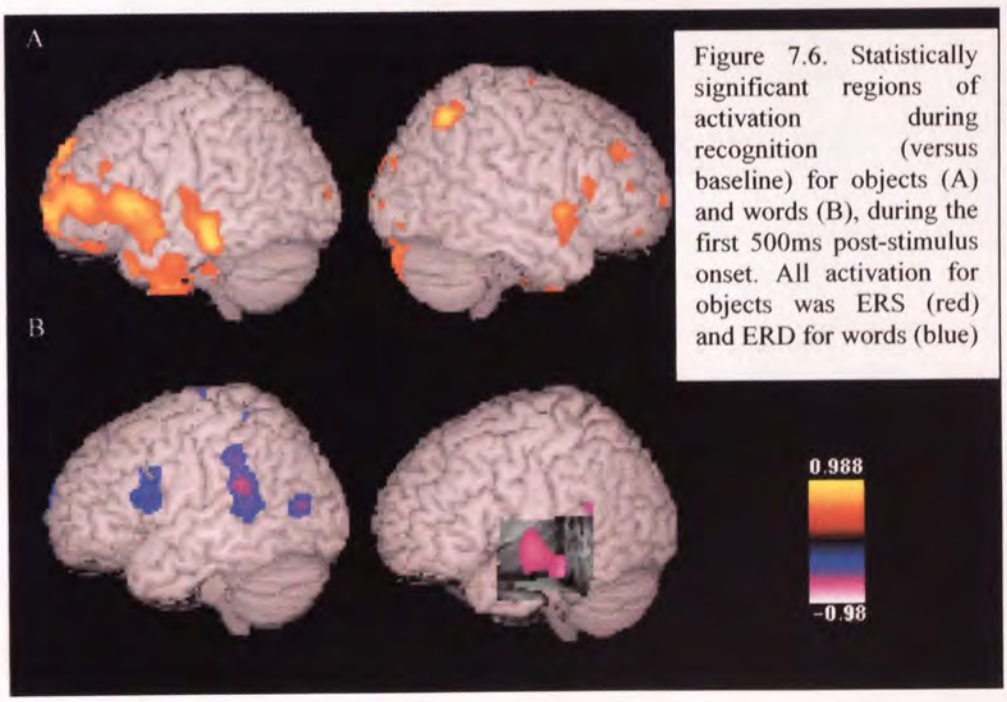


Figure 7.6. Statistically significant regions of activation during recognition (versus baseline) for objects (A) and words (B), during the first 500ms post-stimulus onset. All activation for objects was ERS (red) and ERD for words (blue)

500-1000ms

Objects

During the second 500ms time – comparison of the recognition of previously seen objects (compared to baseline fixation), no statistically significant neural activity was observed.

Words

Predominantly right-lateralised activity was observed for the recognition of words during the second 500ms time–comparison (Table 7.7, Figure 7.7). Within the 20-30 Hz frequency band, significant ERD was observed within the middle and inferior temporal gyri. Significant voxels were also observed in the precentral gyrus and within two visual processing regions, the middle occipital gyrus and the lingual gyrus. A small region within the left cerebellum was also activated.

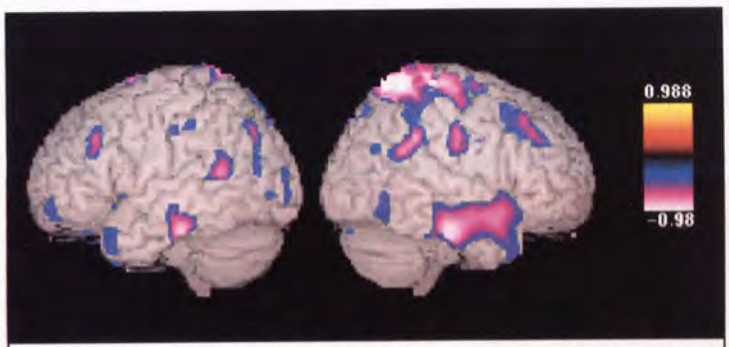


Figure 7.7. Statistically significant regions of activation during recognition (versus baseline) for words during the second 500ms post-stimulus onset. All activation was observed to be ERD (blue)

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Temporal Gyrus	Right	10-20	42 -62 3	67	5.52*	0.047	37
Inferior Temporal Gyrus	Right	10-20	47 -66 -5	67	5.52*	0.078	
Precentral Gyrus	Right	15-25	36 -10 40	389	6.55*	0.051	
Middle Occipital Gyrus	Right	5-15	42 -69 -9	14	5.09*	0.066	
Lingual Gyrus	Right	10-20	-24 -77 -16	389	6.37*	0.051	18
Cerebellum	Left	15-25	-24 -78 -21	69	6.15*	0.020	

Table 7.7 Regions showing statistically significant differences in activation ($p < 0.05$) between the recognition and baseline phases for words, 500-1000ms post stimulus onset. * indicates ERD.

7.4.2.3 Quantification Analysis

The percentage of activation within each of the left and right frontal, temporal, parietal, occipital and limbic lobes was calculated for the encoding and recognition of objects and words. This quantification analysis calculated the number of activated voxels within a given region and converted this to a percentage of the total number of voxels within that region. These are illustrated in the Figures 7.8 and 7.9.

Chi-square analyses were performed on the raw quantification analysis data to determine whether hemispheric asymmetry was present during the encoding or recognition phases for either objects or words. The data for all frequency bands were combined together to improve the degrees of freedom of the statistical analysis. For each cortical region the number of participants showing left- and right-lateralised dominance was calculated.

Objects

Figure 7.8 (A and B) shows the activations for the encoding and recognition of objects. It can be seen that there is predominantly increased activity during the recognition phase of the task. In the 5-15Hz frequency band, the left hemisphere shows greater activity in both the encoding and recognition phases for the majority of cortical lobes, across both time windows. This is not the case, however, for the parietal lobes (0-500ms), which show greater left hemispheric activity during the encoding phase, and increased activity within the right lobe during the recognition phase, or for the temporal lobe (500-1000ms) which shows greater activity in the right lobe during both task phases.

In the 10-20Hz range, the percentage of activation within the lobes across the two hemispheres for both phases mirrors each other reasonably well, again either with predominant left-hemispheric activity or equal amounts across the two hemispheres. Only the temporal lobe during the second time window (500-1000ms) differs, with greater right hemispheric activity during the encoding phase.

The percentage of activation observed within the 15-25Hz frequency band, is similar for the two phases within the first 500ms, and greater for recognition during the second. In the initial 500ms, only the parietal lobes demonstrated hemispheric differences between the two phases (greater activity in the right during encoding, left during recognition). The frontal, temporal and limbic lobes all showed greater activity in the left, compared to the right, the converse being true for the occipital lobes. The pattern of left-right activation

during the second 500ms, is similar with both phases showing the same hemispheric dominant activation (e.g. greater left hemispheric in the frontal, temporal and limbic lobes, equal activation in the parietal lobes and greater right hemispheric activation in the occipital lobes).

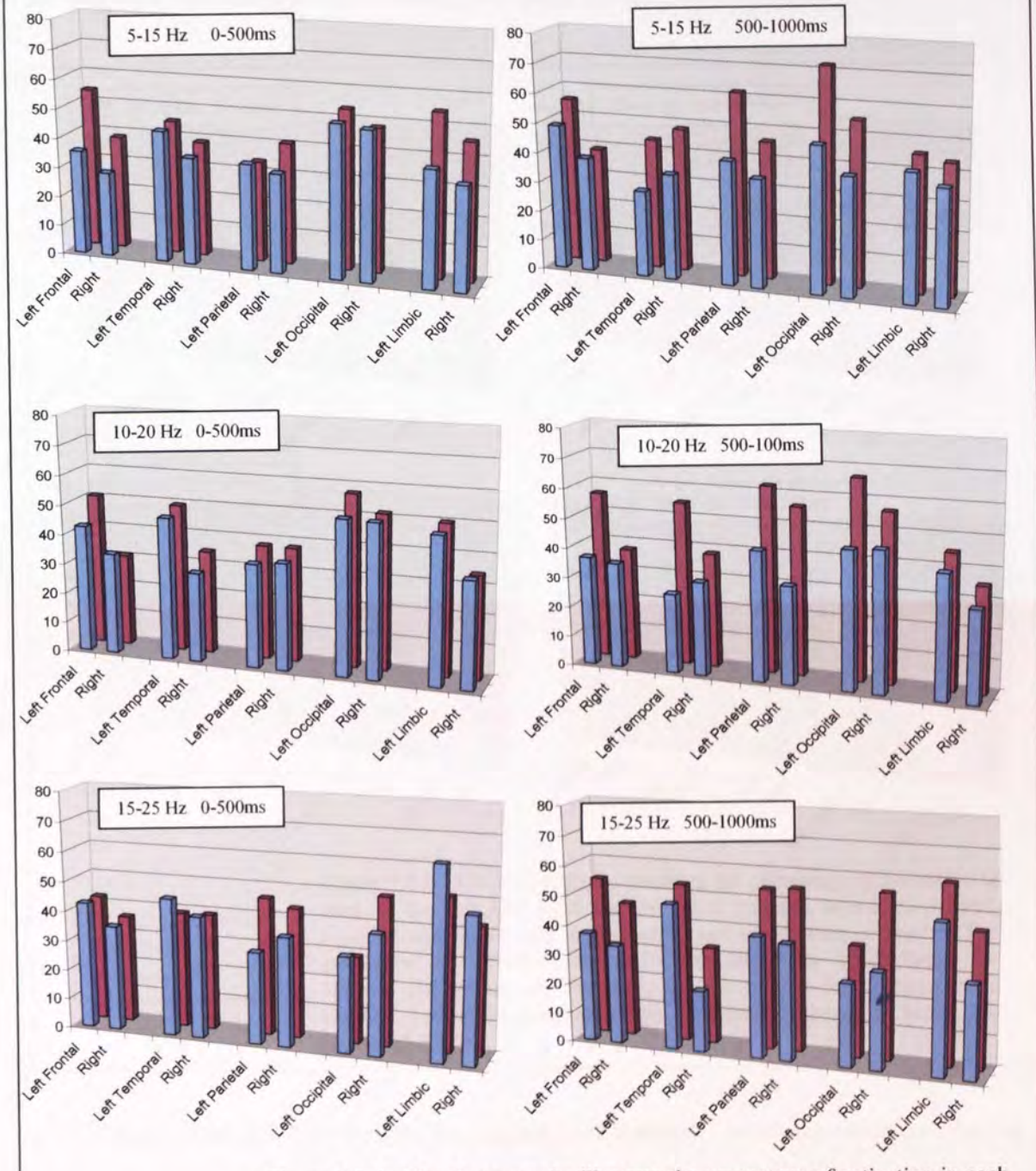


Figure 7.8 A. The above graphs illustrate the percentage of activation in each of the left and right cortical lobes (frontal, temporal, parietal, occipital and limbic) for the encoding and recognition of objects. The graphs on the left show the activation during the initial 500ms (0-500ms), the graphs on the right for the second 500-1000ms, time window. Activation is separated into each of the following frequency bands (one per line), 5-15, 10-20, and 15-25 (Frequency bands 20-30 and 25-35Hz are illustrated in Figure B below)

The amount of activity for both encoding and recognition in the 20-30Hz range is very similar. In the encoding phase, greater activation in the left is observed for the frontal and temporal lobes (0-100ms) and for the limbic lobe (500-1000ms). In contrast, greater right-hemispheric activity was observed in the parietal and occipital region (0-1000ms) and in the limbic lobe (0-500ms). For recognition, however, the reverse patterns were observed in the temporal and occipital lobes during the initial 500ms.

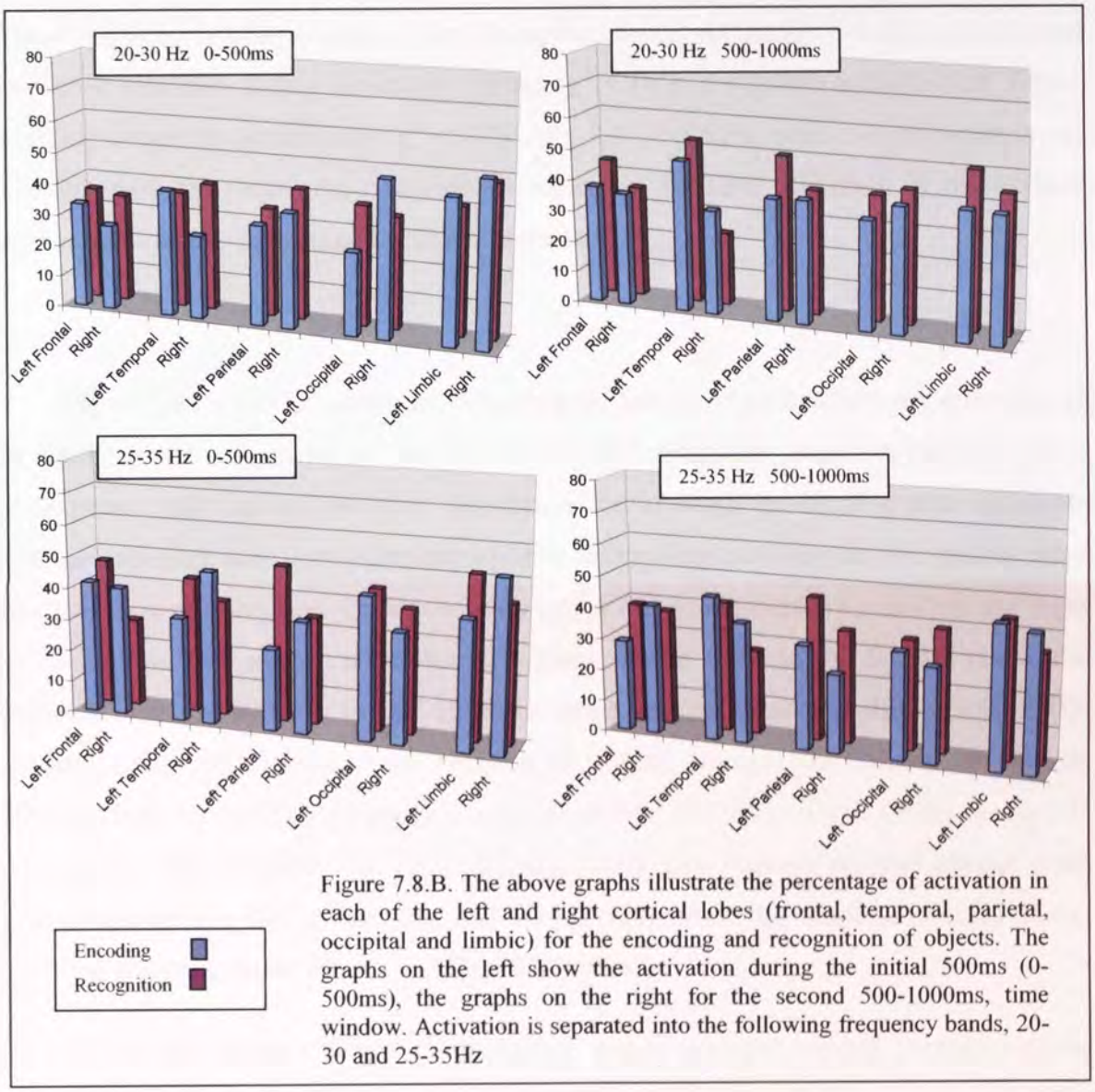


Figure 7.8.B. The above graphs illustrate the percentage of activation in each of the left and right cortical lobes (frontal, temporal, parietal, occipital and limbic) for the encoding and recognition of objects. The graphs on the left show the activation during the initial 500ms (0-500ms), the graphs on the right for the second 500-1000ms, time window. Activation is separated into the following frequency bands, 20-30 and 25-35Hz

Finally, in the 25-35Hz range, hemispheric differences were also observed. In the encoding phase, the left hemisphere showed greater activity in most regions, with the right hemisphere only showing dominant activity in the temporal and limbic regions in the initial 500ms, and in the frontal lobe in the second 500ms. For recognition, all regions in the initial 500ms showed greater activity in the left. This was the same for the second 500ms, with the exception of greater activity in the occipital lobe.

Chi-square analysis across all frequency bands revealed several cortical regions which showed significantly greater activation within the left hemisphere, compared to the right. During the first 500ms of object encoding, only the frontal lobe showed a trend for hemispheric asymmetry ($\chi^2 = 3.756$, $p < 0.1$), whilst in the second 500ms, the limbic region showed left-hemispheric dominance ($\chi^2 = 5.0$, $p < 0.05$). Object recognition revealed several more cortical regions with left-lateralised dominance. These were the frontal lobes ($\chi^2 = 11.756$, $p < 0.001$ and $\chi^2 = 13.889$, $p < 0.001$ for the first and second 500ms respectively), the temporal lobe during the second 500ms ($\chi^2 = 8.02$, $p < 0.01$) and the limbic lobe also during the second 500ms ($\chi^2 = 16.2$, $p < 0.001$) with the first 500ms revealing a trend to significance ($\chi^2 = 3.756$, $p < 0.1$). No right-lateralised dominance was revealed, with the remaining comparisons indicating bilateral activation of the cortical regions, particularly parietal and occipital regions.

Words

Figure 7.9 (A and B) shows the percentage of left and right hemispheric activation in the encoding and recognition of words. Across both hemispheres, in all regions and across all frequency and time comparisons, the recognition of words produced greater activation than the encoding task. Left-right hemispheric differences between the two phases were observed in several regions. Greater activity in the left hemisphere for encoding and right for recognition was seen in a number of regions. These were, in the 5-15Hz range, the temporal lobe (0-1000ms), in the 10-20Hz range the occipital and limbic lobe (500-1000ms), in the 15-25Hz range, the occipital (0-500ms), frontal (500-1000ms and parietal (500-1000ms), in the 20-30hz range the occipital lobe (0-1000ms) and finally in the 25-35Hz range, the occipital lobe (500-1000ms). Only two regions showed greater right hemispheric activity during encoding, and left for recognition; the temporal lobe (15-25Hz, 0-500ms) and the parietal lobe (25-35Hz, 500-1000ms).

Chi-square analysis across all frequency bands revealed several cortical regions which showed significantly greater activation within the left hemisphere, compared to the right. During the first 500ms of word encoding, only the parietal lobe showed significant hemispheric asymmetry ($\chi^2 = 11.756$, $p < 0.001$), whilst in the second 500ms, the frontal, temporal and limbic regions all showed this left-hemispheric dominance ($\chi^2 = 5.0$, $p < 0.05$, $\chi^2 = 6.42$, $p < 0.05$ $\chi^2 = 11.756$, $p < 0.001$, respectively). Word recognition revealed left-lateralised dominance within the frontal lobe during the first 500ms ($\chi^2 = 8.022$, $p < 0.01$) and trend towards significance within the parietal lobe during the second 500ms ($\chi^2 =$

3.756, $p < 0.1$). As with the objects, no right-lateralised dominance was revealed, with the remaining comparisons indicating bilateral activation of the cortical regions.

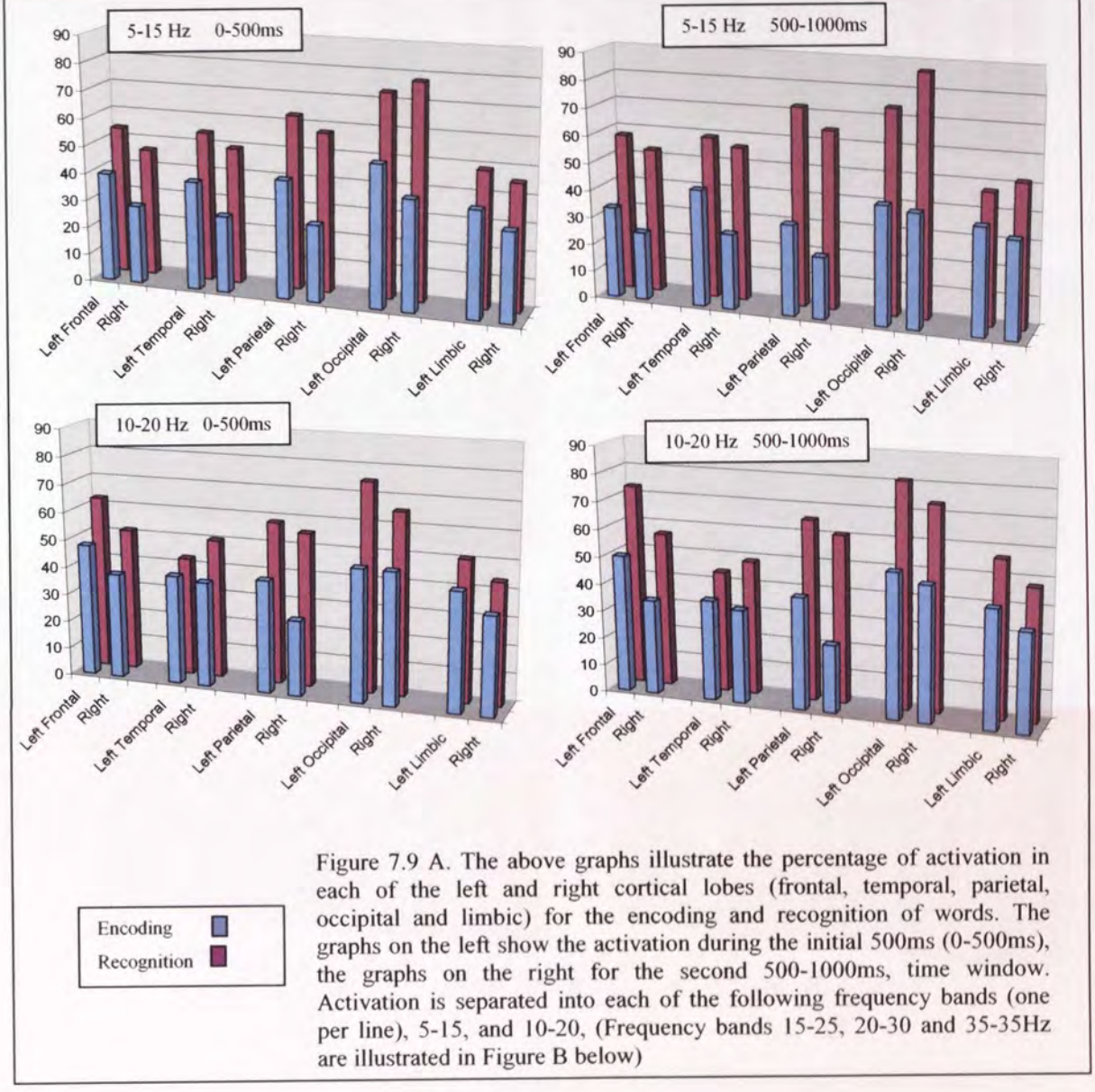


Figure 7.9 A. The above graphs illustrate the percentage of activation in each of the left and right cortical lobes (frontal, temporal, parietal, occipital and limbic) for the encoding and recognition of words. The graphs on the left show the activation during the initial 500ms (0-500ms), the graphs on the right for the second 500-1000ms, time window. Activation is separated into each of the following frequency bands (one per line), 5-15, and 10-20, (Frequency bands 15-25, 20-30 and 35-35Hz are illustrated in Figure B below)

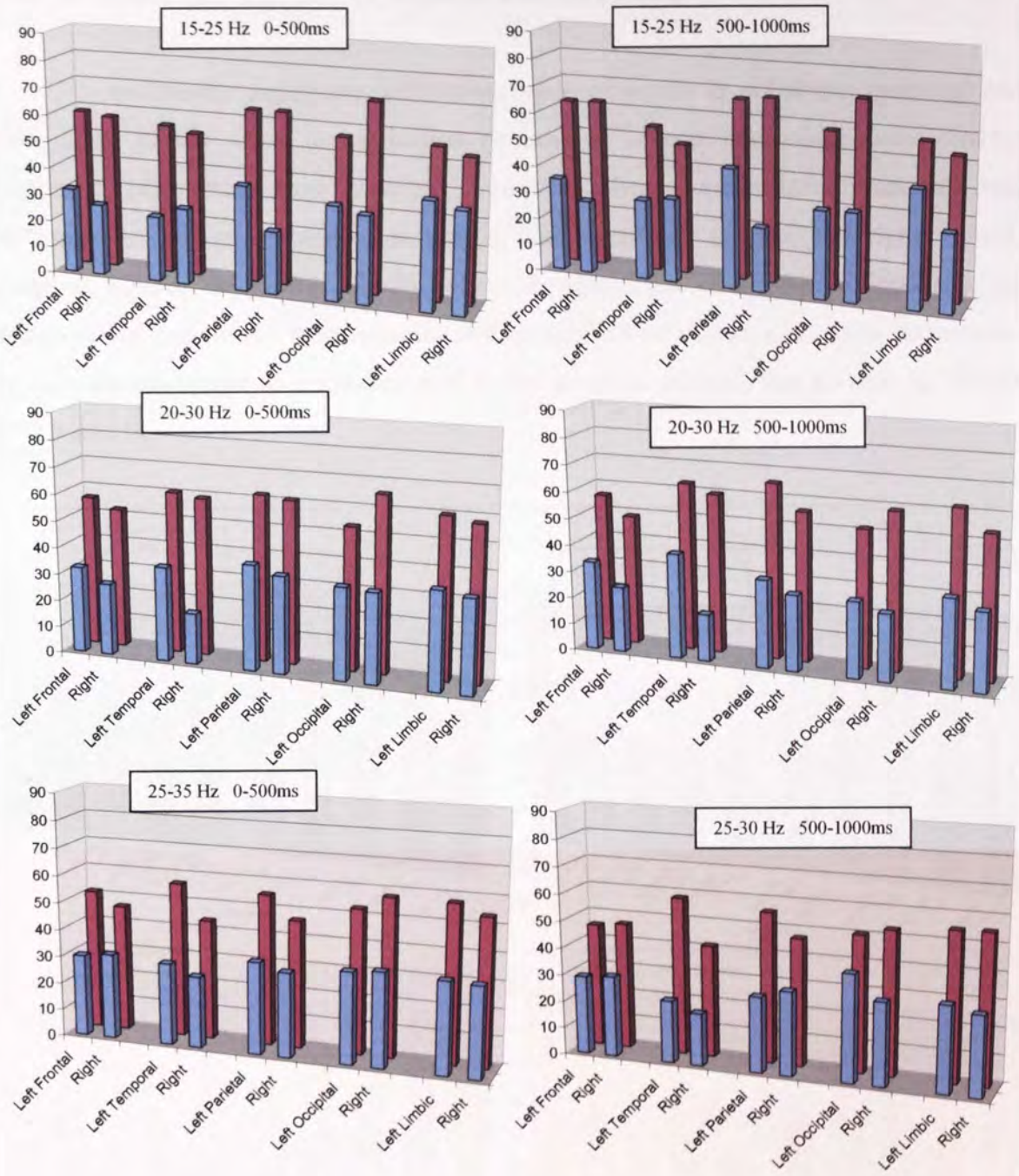


Figure 7.9 B. These graphs illustrate the percentage of activation in each of the left and right cortical lobes (frontal, temporal, parietal, occipital and limbic) for the encoding and recognition of words. The graphs on the left show the activation during the initial 500ms (0-500ms), the graphs on the right for the second 500-1000ms, time window. Activation is separated into each of the following frequency bands (one per line), 15-25, 20-30 and 35-35Hz

7.4.2.4 *Direct Comparison of Objects versus Words*

No statistically significant differences were observed in either the encoding and recognition phases when the activation patterns of objects and words were directly compared. Differences were observed, however, when a quantification analysis was performed on the percentage of activation within each of the left and right, frontal, temporal, parietal, occipital and limbic lobes. The significant left-lateralised dominance for many cortical regions for both encoding and recognition of objects and words, as revealed through the chi-square analysis (reported in the previous section), can be seen in Figures 7.10 A and B.

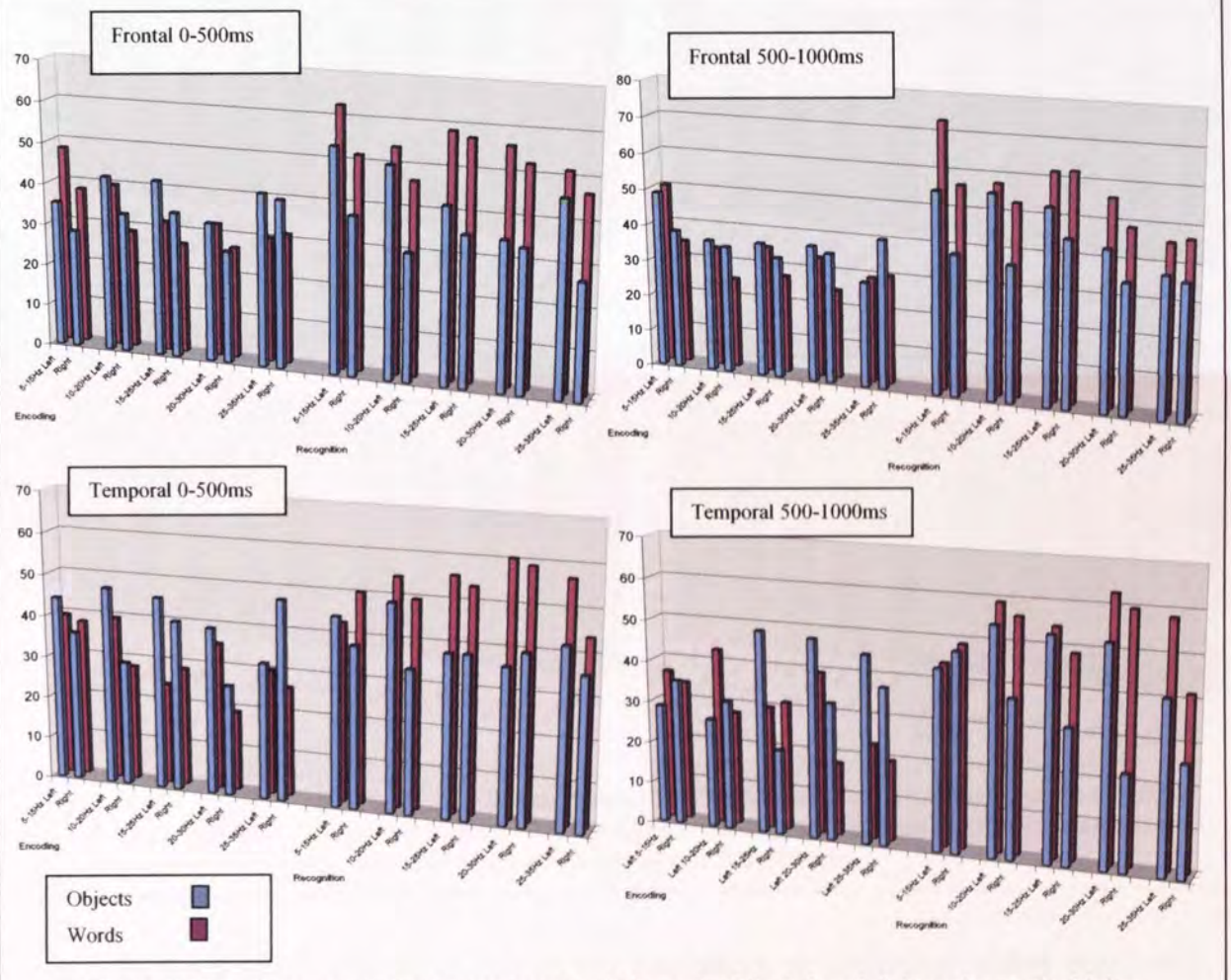


Figure 7.10 A. Percentage of activated voxels within each of the left and right major cortical lobes during the encoding and recognition of objects and words in two time windows (0-500ms and 500-1000ms. Continued in Figure 7.10 B below

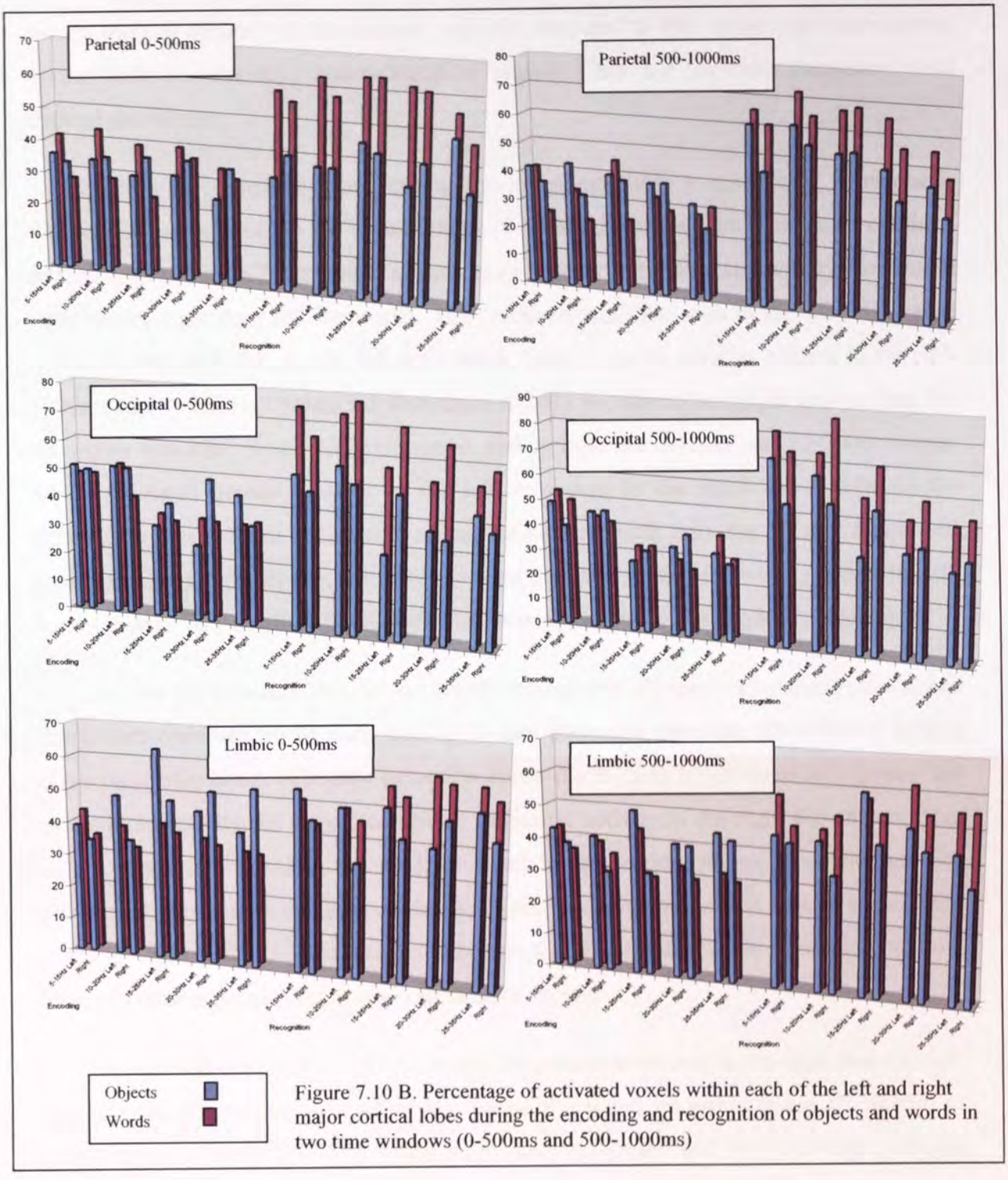


Figure 7.10 B. Percentage of activated voxels within each of the left and right major cortical lobes during the encoding and recognition of objects and words in two time windows (0-500ms and 500-1000ms)

Figure 7.10 (A and B) illustrates the percentage of activation within the frontal, temporal, parietal, occipital and limbic regions sequentially. If we first consider all of the regions, there is evidence that during the recognition phase there is greater activation for words that for objects across all regions and hemispheres, compared to a slightly greater amount of activation for objects during the encoding phase.

The percentage of activation within the frontal lobes shows that for both objects and words, there is greater left hemispheric activity compared to that in the right hemisphere, during both the encoding and recognition phases. Only the 25-35Hz frequency band showed the reverse.

Within the temporal lobes, during the encoding phase a number of hemispheric differences can be seen. In the initial 500ms (0-500ms), two frequency bands reveal these differences; in the 15-25Hz range, objects show greater left than right activity, contrasted with greater right than left for words. The converse was then seen in the 25-35Hz range (greater in the right for objects, left for words). Similar results are also evident in the 500-1000ms time window. Greater left than right activity for objects and right greater than left for words was seen in the 15-25Hz range, and in both the 5-15Hz and 10-20Hz ranges, words produced greater activity in the left compared to the right for objects. In the recognition phase, these differences are not as evident, with only the 5-15Hz range (left greater than right for objects, compared to right greater than left for words) and in the 20-30Hz range (a very small difference with left dominance for words, right for objects).

Across the parietal lobes, a number of hemispheric differences between objects and words were observed, particularly during the first 500ms of encoding. Specifically, in four of the frequency bands (the only exception being the 5-15Hz band) there was greater left hemispheric activity for words, compared to greater activity in the right for objects. This pattern was also evident in the 25-35Hz band in the second 500ms time window. For recognition, this pattern was also evident to a smaller degree in the first 500ms, specifically in the 5-15Hz and 20-30Hz bands, although the magnitude of the activation in both hemispheres was greater for words compared to objects.

In occipital regions there is a tendency for greater activation in the right than the left. Hemispheric differences were observed during the initial encoding phase (0-500ms) in three frequency bands; 15-25Hz where words showed greater activity in the right, objects in the left; 20-30Hz and 25-35Hz where the activation was similar in the two hemispheres for words, which highlighted the greater activity in right hemisphere (20-30Hz) and he left (25-35Hz) for words. Greater right hemispheric activation for words was further evident during the recognition phase, specifically in the 10-20Hz and 20-30Hz bandwidths during the initial 500ms, and in the 10-20Hz band during the 500-1000ms time window.

Finally, in the limbic lobes, hemispheric differences in encoding were seen in the initial 500ms in the 20-30Hz and 25-35Hz frequency bands, both illustrating greater right

than left activity for objects. In the recognition phases, however, it was the word stimuli which showed this greater right – hemispheric activation, specifically in the 20-30Hz (0-500ms) and 10-20Hz (500-1000ms range).

7.4.3 Analysis Using EEG Frequency Bandwidths

7.4.3.1 Direct Comparison of Recognition versus Encoding

0-500ms

Objects

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Superior Frontal Gyrus	Right	0-4	27 57 39	1	5.50^	0.023	

Table 7.8 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and recognition memory phases for objects, 0-500ms post stimulus onset. ^ indicates ERS

A direct comparison between the recognition and encoding phase for objects only revealed a very small cluster of ERS activation in the 0-4Hz frequency range (Table 7.8). It was identified within the right superior frontal gyrus.

Words

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Temporal Lobe	Left	3-13	-29 -36 9	1	5.54*	0.047	
Fusiform Gyrus	Right	0-40	61 -51 -24	1	5.45*	0.047	37

Table 7.9 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and recognition memory phases for words, 0-500ms post stimulus onset. * indicates ERD

Similarly, for the encoding of words during the first 500ms-time window, only two small regions were identified (Table 7.9). These were seen as ERD in the left temporal lobe in the theta-alpha (3-13Hz) bandwidth, and in the right fusiform gyrus in the general 0-40Hz bandwidth.

500-1000ms

Objects

In the second 500ms time span, no significant regions were identified as being differentially activated between the encoding and recognition phases for objects.

Words

As for the first time window, activity in the second 500-ms time window was only seen in the wide 0-40Hz frequency band (Table 7.11). The direct comparison between the encoding and recognition phases for words produced a significant cluster of ERD within the left frontal lobe.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Frontal Lobe	Left	0-40	-20 13 22	94	6.24	0.008*	

Table 7.10 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and recognition memory phases for words, 500-1000ms post stimulus onset. * indicates ERD

7.4.3.2 Baseline Comparisons for Encoding and Recognition

7.4.3.2.1 Encoding versus Baseline

0-500ms

Objects

During the first 500ms of the shallow encoding of objects, statistically significant regions of ERS activation were observed within the alpha and theta frequency bandwidths, although only within the theta range were these regions identified by voxel-wise analysis (Table 7.12). Within the frontal lobes, ERS was observed in the theta range in bilateral middle frontal gyri and right inferior frontal gyrus. The cluster analysis also revealed ERS in the alpha range in the right medial and inferior frontal gyri. Activation within the temporal gyri was predominantly left-lateralised, with significant ERS voxels found in the middle, inferior and superior temporal gyri. The cluster analysis further revealed activity in the alpha range in the left middle and right superior temporal gyri. Other activated voxel

clusters were observed in bilateral precentral gyri (theta), left postcentral gyrus (theta), right inferior occipital gyrus (theta and alpha) and bilateral cerebella (alpha and theta). A significant cluster of ERS was also found in the left anterior cingulate (alpha).

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Frontal Gyrus	Left	4-7	-45 39 18	162	4.18^	0.016	46
	Right	4-7	51 51 -18	179	4.91^	0.016	7/11
Inferior Frontal Gyrus	Right	4-7	51 48 -12	179	4.91^	0.016	47 / 9
		8-13 c	60 27 15	7168	4.39^	0.035	45/44
Medial Frontal Gyrus	Right	8-13 c	9 9 -21	7168	3.49^	0.035	
Rectal Gyrus	Right	8-13 c	9 13 -21	7168	3.49^	0.035	21
Middle Temporal Gyrus	Left	4-7	-60 -9 -6	613	4.03^	0.031	21
		8-13 c	-48 -48 3	1976	4.37^	0.035	21
Superior Temporal Gyrus	Left	4-7	-63 -48 18	613	4.44^	0.016	22/13
	Right	8-13 c	-36 -40 3	1976	4.70^	0.094	10
Inferior Temporal Gyrus	Left	4-7	-51 -77 -6	36	4.35^	0.062	
		8-13 c	-60 -58 -9	1976	3.68^	0.094	
Anterior Cingulate	Left	8-13 c	-3 16 -5	7168	3.55^	0.035	25
Precentral Gyrus	Left	4-7	-57 -9 45	184	4.35^	0.016	4/6
	Right	4-7	43 -10 66	3319	4.88^	0.063	6
Postcentral Gyrus	Left	4-7	-66 -9 15	613	4.13^	0.031	43
Inferior Occipital Gyrus	Right	4-7	30 -90 -18	335	3.89^	0.031	18
		3-13	30 -99 -15	2	5.16^	0.094	
Posterior Lobe	Left	3-13	-51 -51 -42	49	6.06^	0.020	
	Right	4-7	42 -83 -33	335	4.82^	0.031	

Table 7.11 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and baseline phases for objects, 0-500ms post stimulus onset.^ indicates ERS; c indicates regions identified through cluster analysis, other regions were identified through a voxel-wise analysis.

Words

During the first 500ms of the encoding of words, significant clusters of ERS were also revealed in the alpha and theta frequency bands (Table 7.13). Specifically, right-lateralised frontal theta activity was observed through voxel analysis in the medial and superior frontal gyri, with activation in the inferior frontal gyri being in the left hemisphere in the theta band, and in the right hemisphere in the alpha band. Bilateral middle frontal gyri activity was only observed with a cluster analysis. One other area within the right hemisphere, the inferior parietal lobule showed significant ERS (theta), with all remaining voxels being left-lateralised. These included regions in the limbic lobe, fusiform gyrus, cerebellum and post- and precentral gyri.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Medial Frontal Gyrus	Right	4-7	12 39 42	201	4.72^	0.016	
Superior Frontal Gyrus	Right	4-7	18 45 45	201	4.69^	0.016	8
Inferior Frontal Gyrus	Left	4-7	-45 36 12	1948	4.65^	0.016	46
	Right	8-13	60 36 9	16	5.08^	0.075	46
Middle Temporal Gyrus	Left	4-7	-60 -3 -9	1948	4.60^	0.016	
Middle Frontal Gyrus	Right	3-13 c	21 55 24	41	4.09^	0.094	10
	Left	8-13 c	-51 21 39	7057	4.17^	0.031	9
Inferior Parietal Lobule	Right	4-7	45 -45 57	397	4.19^	0.016	40
Limbic Lobe / Uncus	Left	3-13	-13 -3 -43	22	5.46^	0.098	
Fusiform Gyrus	Left	4-7	-48 -57 -12	671	3.79^	0.047	37
Posterior Lobe / Tuber	Left	4-7	-54 -63 -27	671	4.30^	0.016	
Precentral Gyrus	Left	8-13	-57 -15 39	26	4.92^	0.070	4
Postcentral Gyrus	Left	8-13	-52 -16 39	26	4.92^	0.086	

Table 7.12 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and baseline phases for words, 0-500ms post stimulus onset. ^ indicates ERS; c indicates regions identified through cluster analysis, other regions were identified through a voxel-wise analysis.

500-1000ms

Objects

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Medial Frontal Gyrus	Right	4-7	3 63 6	29	4.39^	0.055	10
Middle Frontal Gyrus	Left	4-7	-27 45 36	38	4.52^	0.047	9
Superior Frontal Gyrus	Right	4-7	18 45 36	31	4.12^	0.086	
Inferior Frontal Gyrus	Left	8-13 c	-15 18 6	1623	3.17^	0.098	45
Precuneus	Right	0-40 c	39 -63 36	426	4.38*	0.086	39
Thalamus	Right	4-7	12 -3 6	99	4.26^	0.078	
Lentiform Nucleus	Right	4-7	24 3 9	99	4.30^	0.062	
Occipital Lobe	Left	0-40 c	-30 -66 -3	464	4.08*	0.082	
Anterior Lobe	Left	0-40 c	-21 -45 -30	464	4.52*	0.082	
Anterior Lobe	Right	4-7	24 -39 -21	4	5.27^	0.008	

Table 7.13 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and baseline phases for objects, 500-1000ms post stimulus onset * indicates ERD ^ indicates ERS; c indicates regions identified through cluster analysis, other regions were identified through a voxel-wise analysis.

For 500-1000ms post stimulus onset, activation was predominantly ERS within the theta band (Table 7.14). In the frontal lobes, activated voxel clusters were seen in the right

medial and superior gyri, and in the left middle and inferior gyri, this latter cluster being restricted to the alpha frequency band. Additional regions showing ERS were in the right limbic lobe and cerebellum. Several small regions of ERD were seen when activation was analysed across all frequencies between 0 and 40Hz (using a cluster analysis). These included areas in the left occipital lobe, extending into the left cerebellum and also in the right precuneus.

Words

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Inferior Temporal Gyrus	Left	4-7	-51 -69 -3	158	4.98^	0.016	19/37
Superior Frontal Gyrus	Right	0-4	15 48 33	1	5.36*	0,047	
		3-13	24 48 36	1	5.3^	0.090	9
Middle Temporal Gyrus	Right	4-7	34 -74 18	219	3.88^	0.045	
	Left	4-7	-57 -70 6	158	4.5^	0.078	37
Precentral Gyrus	Right	4-7	41 -24 69	112	4.26^	0.032	4
Middle Occipital Gyrus	Left	4-7	-21 -99 3	56	4.39^	0.016	18/37
Precuneus	Right	4-7	25 -83 24	219	4.64^	0.016	
Superior Parietal Lobule	Right	4-7	15 -75 55	88	4.5^	0.016	7
Fusiform Gyrus	Left	4-7	-27 -93 -18	237	4.57^	0.045	18/19
Inferior Occipital Gyrus	Left	4-7	-24 -97 -18	237	4.57^	0.032	17/18
	Right	14-20	39 -92 -12	8	5.62^	0.075	18
Posterior Lobe	Left	4-7	-21 -90 -30	237	3.86^	0.031	
Cuneus	Right	4-7	15 -84 15	219	4.01^	0.016	19/18
	Left	4-7	-12 -102 7	56	3.88^	0.094	18

Table 7.14 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and baseline phases for words, 500-1000ms post stimulus onset. * indicates ERD ^ indicates ERS;

For words in the 500-1000ms time window, again predominantly ERS was seen in the theta bandwidth (Table 7.15). These activated voxels were found in the left inferior and right superior frontal gyri, and in bilateral middle temporal gyri. Additionally significant clusters of voxels were also found in the right precentral gyrus, precuneus, and superior parietal lobule, in the left middle occipital and fusiform gyri and cerebellum, and bilaterally in the inferior occipital gyri and cuneus.

7.4.3.2.2 Recognition versus Baseline

0-500ms

Objects

Recognition of previously seen objects (0-500ms post-stimulus onset) produced ERS, predominantly within alpha and theta frequency bands (Table 7.16). Voxel-wise analysis revealed significant activation in the theta band in the right middle frontal gyrus, left inferior temporal and precentral gyri, right postcentral gyrus, right inferior parietal lobule and left superior parietal lobule. Activity within the right superior temporal gyrus was in the frequency band that combined alpha and theta activity. Other regions identified through cluster analysis included the left inferior frontal gyrus (alpha), left middle frontal gyrus (alpha), bilateral superior frontal gyrus (0-40Hz in the left and 8-13Hz in the right), left medial frontal gyrus (0-40Hz), left anterior cingulate (0-40Hz), left limbic lobe (alpha-theta) and left cuneus.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Inferior Frontal Gyrus	Left	8-13 c	-48 49 8	6729	4.23^	0.082	46
	Right	0-40	54 18 -3	83	6.03^	0.012	47
Middle Frontal Gyrus	Left	8-13 c	-48 54 9	6729	4.23^	0.082	46
	Right	4-7	35 12 60	37	3.78^	0.047	
Superior Frontal Gyrus	Left	0-40 c	-30 57 -9	1511	3.74^	0.023	11
	Right	8-13 c	15 69 15	6729	3.91^	0.082	10
Medial Frontal Gyrus	Left	0-40 c	-12 41 16	1511	4.30^	0.023	10
Superior Temporal Gyrus	Right	3-13	21 10 -47	15	5.03^	0.098	38
Inferior Temporal Gyrus	Left	4-7	-51 -33 -24	415	4.43^	0.016	20/37
Anterior Cingulate	Left	0-40 c	-12 45 12	1511	4.71^	0.023	32
Limbic Lobe / Uncus	Left	3-13 c	-24 2 -39	9699	3.18^	0.027	36
Precentral Gyrus	Left	4-7	-18 -36 75	54	4.28^	0.016	4
Postcentral Gyrus	Right	4-7	15 -51 69	47	4.42^	0.016	3
Inferior Parietal Lobule	Right	4-7	60 -33 41	174	4.22^	0.047	40
Superior Parietal Lobule	Left	4-7	-21 -68 66	44	3.73^	0.047	7
Cuneus	Left	8-13 c	-6 -93 9	6729	3.90^	0.082	18

Table 7.15 Regions showing statistically significant differences in activation ($p < 0.05$) between the recognition and baseline phases for objects, 0-500ms post stimulus onset. ^ indicates ERS; c indicates regions identified through cluster analysis, other regions were identified through a voxel-wise analysis.

Words

No significant regions of activity were identified during the initial 500ms of visual word recognition.

500-1000ms

Objects

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Superior Frontal Gyrus	Right	4-7	24 -6 66	56	3.99^	0.016	6
Superior temporal Gyrus	Right	4-7	42 9 -30	231	4.27^	0.016	38
Middle Occipital Gyrus	Left	0-40 c	-24 -90 12	34	4.67*	0.090	
Angular Gyrus	Right	0-40	39 -60 33	49	5.52*	0.059	
Cingulate gyrus	Left	0-40	-18 -33 33	88	5.44*	0.066	
Insula	Left	0-40	-30 -24 15	88	5.40*	0.066	13
Inferior Occipital Gyrus	Left	0-40 c	-33 -75 -3	34	4.72*	0.090	
Posterior Lobe /	Left	0-40	-21 -48 -36	18	5.24*	0.074	
Cuneus	Right	4-7	21 -93 36	18	4.28 ^	0.016	19

Table 7.16 Regions showing statistically significant differences in activation ($p < 0.05$) between the recognition and baseline phases for objects, 500-1000ms post stimulus onset* indicates ERD ^ indicates ERS; c indicates regions identified through cluster analysis, other regions were identified through a voxel-wise analysis.

In the second 500ms after stimulus onset (500-1000ms) of visual object recognition, ERS was observed in the theta range in the right hemisphere, specifically voxels in the superior frontal and temporal gyri and in the cuneus (Table 7.17). ERD was only observed when the entire frequency range was analysed (0-40Hz). Significant voxels in this analysis were revealed in the right angular gyrus, left cingulate gyrus, insula, and cerebellum. The significant ERD in the left inferior and middle occipital gyri were only seen right an analysis of cluster size.

Words

ERD was observed during the recognition of words (500-1000ms), although in frequency bands which were not EEG frequency specific, i.e. in the band which combined alpha and theta activity (3-13Hz) and in the band that combined all analysed frequencies (0-40Hz) (Table 7.18). Activated voxels were observed entirely in the right hemisphere,

especially in the middle and inferior temporal gyri, pre- and postcentral gyri, middle occipital and lingual gyri and cerebellum.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Temporal Gyrus	Right	0-40	39 -63 18	610	5.27	0.051	37
		3-13	45 -72 6	20	5.24	0.078	
Inferior Temporal Gyrus	Right	0-40	54 -69 -3	610	7.98	0.004	37/19
Precentral Gyrus	Right	3-13	68 -10 35	42	6.54	0.031	
Middle Occipital Gyrus	Right	3-13	45 -75 -15	10	5.27	0.078	
		0-40	54 -65 -8	610	7.98	0.004	37/19
Lingual Gyrus	Right	0-40	12 -81 -12	8	5.06	0.074	
Posterior Lobe / Declive	Right	0-40	3 -78 -21	122	5.75	0.023	
Postcentral Gyrus	Right	3-13	68 -15 35	42	6.54	0.016	

Table 7.17 Regions showing statistically significant differences in activation ($p < 0.05$) between the recognition and baseline phases for words, 500-1000ms post stimulus onset* indicates ERD

7.4.3.2.3 Direct Comparison of Objects versus Words

The direct comparison of objects and words failed to reveal any statistically significant differences in activation for either the encoding or the recognition phases.

7.5 Discussion

Cortical activation during recognition memory tasks of objects and words were assessed using MEG. A shallow encoding task was used to reduce the amount of semantic related activity that occurred concurrently. The findings are summarised in the Table 7.19.

During the encoding phase, bilateral regions of the temporal lobe were activated by both pictures and words, although it is interesting to note that the majority of processing appeared to have been completed during the initial 500ms, and that all activation was due to an increase in synchronous neural activity (i.e. ERS). It has been suggested that this synchronous activity may be due to the simple nature of the task, very little in-depth processing being necessary for a simple spatial location task. This may also be the case for the subsequent recognition memory task for objects, which again produced only statistically significant regions of cortical synchrony, in contrast to the words which produced desynchronous activity.

In the recognition phase however, there is a distinct hemispheric difference with objects only activating regions within the left hemisphere, words in the right. Furthermore, the recognition of objects appears to be a much faster process with no statistically significant regions seen to be activated after 500ms post-stimulus onset. Perhaps this may be attributed to the necessity to decode the information prior to accessing the lexical information, in contrast to the recognition of objects which are quickly identifiable leading to an almost immediate recognition memory response. An assessment of recognition memory reaction times may enable this supposition to be quantified. Analysis of reaction times in this study however, was not possible due to the cued nature of the response. This was a deliberate design consideration of the study to ensure that any motor-related cortical activation would not interfere with activation associated explicitly with the recognition memory processes. It does, mean, however, that they cannot be used to determine whether objects are processed more quickly than words in recognition tasks. Similar cortical regions were identified as being significantly activated during the recognition phase, specifically the inferior and middle regions of the temporal lobe, areas which are consistently shown to be involved in recognition memory processes. Only the objects produced prefrontal activation, this covering the majority of this lobe.

	Encoding		**Recognition**	
	Pictures	Words	Pictures	Words
0-500 ms				
Left Hemisphere	Middle Frontal Gyrus^ Inferior Frontal Gyrus^ Middle Temporal Gyrus^ Superior Temporal Gyrus^	Parahippocampal Gyrus^ Middle Temporal Gyrus^ Amygdala^	Inferior Frontal Gyrus^ Middle Frontal Gyrus^ Superior Frontal Gyrus^ Medial Frontal Gyrus^ Superior Temporal Gyrus^ Middle Temporal Gyrus^	
Right Hemisphere	Inferior Frontal Gyrus^ Superior Temporal Gyrus^ Precuneus^ Inferior Occipital Gyrus^	Superior Frontal Gyrus^ Middle Temporal Gyrus^ Medial Frontal Gyrus^ Anterior Cingulate^		Temporal Lobe* Parahippocampal Gyrus* Hippocampus* Cerebellum*
500-1000ms				
Left Hemisphere		Superior Frontal Gyrus^ Medial Frontal Gyrus^ Middle Occipital Gyrus^		
Right Hemisphere				Middle Temporal Gyrus* Inferior Temporal Gyrus* Precentral Gyrus* Middle Occipital Gyrus* Lingual Gyrus* Cerebellum*

Table 7.18 Summary of Baseline activations for objects and words. * indicates ERD; ^ indicates ERS.

Both stimulus modalities also activated regions within the limbic lobe during the recognition phase, although the specific locations differed slightly; anterior cingulate and

amygdala for the objects, parahippocampal gyrus and hippocampus for the words. It is interesting to note that the hippocampus was significantly activated during a task of recognition memory. It is widely considered to be one of the most crucial brain regions for successful recognition memory but is actually rarely identified through functional imaging due to it being a region located deep within the brain. Much of the evidence associated with this area to date has been reported through patient and animal lesion studies. This is a very positive finding for MEG research, as too is the identification of amygdala activation, as one of the possible limitations of using MEG is its relatively poor ability to show activation in deep sources. It may be that SAM analysis is a tool which can overcome this problem, and with experiments specifically designed to produce activations within these deep structures, their specific role in cognitive tasks such as emotional and memory related tasks.

7.5.1 Comparison with Previous Research

One of the main aims of this study was to determine the replicability of MEG recognition memory results. A large number of regions were identified in a previous MEG study (chapter 5). These data, however, did not appear to clearly replicate any of the findings from previous neuroimaging studies. In a review of some of the most recent neuroimaging literature associated with recognition memory, however, it was illustrated that these too fail to explicitly replicate each other or to directly link each hemisphere with either stimulus modality or with task. This current experiment was designed to assess the replicability / reproducibility of the previous MEG findings by conducting a follow-up study which maintained many of the same experimental parameters.

Table 7.20 details the findings from the two studies for encoding and recognition, with the hemispheric locations for each significantly activated region reported. During the encoding phase for objects, both studies revealed activation within the bilateral inferior frontal gyrus and right medial frontal gyrus. Activation was also observed in both studies in the middle temporal gyrus, precentral gyrus and superior parietal lobule. The hemispheric location of these, however, did differ between studies. Activity was seen in the right middle temporal activity in the first, left in the second, and left precentral and superior parietal activation in the left for first and right and bilateral respectively in the second. This may be due to individual differences with different participants being involved in this study, compared to that previously, to ensure naivety to the stimuli.

The right precentral gyrus was activated in the 0-500ms time window in the second study, was also seen in the 500-1000ms time window in the second. Similarly, the left middle frontal gyrus was activated in the initial time window in the second study, and bilaterally in the second 500ms in the first study. The decrease in semantic processing in the second study may account for this. During the encoding process in the first study, participants had to perform a semantic categorisation task and encode the stimuli to memory. This process may have taken longer, and thus the encoding processes occurred within the second 500ms, compared to the simple visual spatial location task occurring in the first, which may take less time meaning the encoding processes can occur sooner.

	Encoding								*Recognition*							
	0-500ms				500-1000ms				0-500				500-1000ms			
	Objects		Words		Objects		Words		Objects		Words		Objects		Words	
	1	2	1	2	1	2	1	2	1	2	1	2	1	2	1	2
Amygdala				L												
Anterior Cingulate				R												
Cerebellum	B				L				L		R	R				R
Cingulate Gyrus	R				R				R							
Cuneus			R						L							
Fusiform Gyrus					R						R					
Hippocampus												R				
Inferior Frontal Gyrus	B	B			R				R	L			L		L	
Inferior Occipital Gyrus		R			L											
Inferior Parietal Lobule	R		R								L		L		B	
Inferior Temporal Gyrus											R					R
Insula	R														B	
Limbic Lobe									L							
Lingual Gyrus	B												L			R
Medial Frontal Gyrus				R	R			L		L						
Middle Frontal Gyrus		L			B				R	L	L		L		L	
Middle Occipital Gyrus	R		R					L	R		R					R
Middle Temporal Gyrus	R	L		B					L	L			L			R
Parahippocampal Gyrus				L							R	R				
Postcentral Gyrus					L								B		L	
Posterior Cingulate																R
Precentral Gyrus	L	R			R				R				L		L	
Precuneus				R				L	L	L	B		L		L	
Superior Frontal Gyrus					L											
Superior Parietal Lobule	L	B							R	L		R	L			
Superior Temporal Gyrus	R								L						R	
Supramarginal Gyrus			R		R								B		R	
Thalamus																

Table 7.19 Summary of statistically significant activations from both MEG studies (Chapter 5 and Chapter 7)
L = left lateralised; R = right lateralised; B = bilateral

There was no similarity between the two studies for the encoding of words, but again this may reflect the absence of any explicit encoding or rehearsal strategies due to the nature of the tasks.

For the recognition of objects, both studies revealed significant activation in the left middle temporal gyrus and precuneus during the initial 500ms. This activation also extended into the second 500ms in the first study, which may reflect the longer recognition memory processes needed to compensate for the additional semantic-related activation initiated following the semantic nature of the encoding task. As in the encoding phase, a number of regions were similarly activated between the two studies, but the specific hemispheric location was different. These included the inferior frontal gyrus, middle frontal gyrus and superior parietal lobule (all right and left for studies one and two respectively). Again, interestingly, in the first study, these three regions demonstrated left hemispheric activation in the second 500ms time window, possibly reflected a more prolonged process due to semantic influences.

For word recognition, the right cerebellum and right parahippocampal gyrus were activated during the initial 500ms in both studies. Only two other regions were activated in this time window during the second study (hippocampus and superior parietal lobule), compared to an additional six regions in the first. The additional regions in the first study, such as the cuneus and superior temporal gyrus, might reflect the large clusters of activation extending from the regions associated with recognition memory over those semantically associated areas. The right inferior temporal and middle occipital gyri were also activated in both studies, although in the first and second 500ms time windows for studies one and two respectively.

Activation was also seen to continue into the second 500ms time window, indicating that recognition memory processes for words may take longer than for objects possibly due to the language component necessitated to complete the task. Interestingly, this was restricted to right hemisphere in the second study, compared to left, right and bilateral activations in the first. These may reflect attention and language related activations, initiated by reading of a word on the screen.

It is encouraging to see some reproducibility in these MEG findings. The activation of the left middle temporal gyrus in recognition memory for objects is probably one of the only consistent findings in the recognition memory neuroimaging literature. EEG studies of recognition memory have demonstrated that event-related potentials (ERPs) for old words are more positive than for new words (Ranganah et al, 1999). This 'old/new' effect is largest over the temporo-parietal regions, and is more predominant over the left hemisphere. This is thought to be indicative of episodic memory retrieval (Allan et al,

1998; Paller & Kutas, 1992), and evidence from PET studies would certainly seem to substantiate this.

A previous study using MEG has replicated the ERP findings demonstrating an MEF old/new effect (Tendolkar et al, 2000). Between 400 and 1000 ms after stimulus onset a significant difference between the correctly recognised old and new words was observed. As with the ERPs, the MEFs were larger to the old words over the left hemisphere and with time were more parietal in location. Similarly stronger fields were generated by dipole fitting over the scalp for old words, the strongest being in the region of the medial temporal lobe (MTL). This supports earlier findings (Gabrieli et al, 1997) that the MTL, while associated with both encoding and retrieval, responds more strongly to previously encountered stimuli.

The left middle temporal lobe was not significantly activated during word recognition, only when objects were used. Interestingly, activation of this and connecting temporal structures were seen in the right hemisphere during word recognition. It might be argued that it is not solely the left hemisphere that is involved in recognition processes, but that the hemispheric activation of this structure might depend upon stimulus modality, underlying semantic, language and attentional processes and ultimately the individual participants involved in the study.

7.5.2 Frequency-Specific Activation

One further issue that was highlighted following the findings from the previous experiment was the frequency specific activation observed in the data. EEG studies have shown that during memory processes, cortical synchronisation is evident in the narrow theta frequency band (4-7 Hz) (Klimesch, Doppelmayr, Schimke & Ripper, 1997) and desynchronisation within the alpha (8-12 Hz) range (Klimesch, Doppelmayr, Pachinger & Russegger, 1997). Upper alpha desynchronisation (10-12 Hz) has been reported to be linked to semantic memory processing (Klimesch, Doppelmayr, Pachinger & Russegger, 1997) while synchronisation within the theta band (4-7 Hz) is linked to working memory (Klimesch, Schimke & Schwaiger, 1994) and the encoding of new information (Klimesch, Doppelmayr, Russegger & Pachinger, 1996; Klimesch, Doppelmayr, Schimke & Ripper, 1997).

The comparisons in the overlapping 10Hz frequency bands conducted in the previous MEG study did not exclusively correspond to either the theta or alpha bands, but spread across both (specifically, 5-15 Hz). Therefore, it is possible that because the 5-15 Hz band used in the study includes alpha waves (8-12 Hz), and some theta (5-7 Hz), any potential ERS was blocked and consequently only ERD within the alpha was seen in the SAM images. Differences were also observed in the previous MEG study between the frequency bands in reference to the time course of the brain activation, leading to the suggestion that the frequency-specific memory activation reported previously (Klimesch, Vogt and Doppelmayr, 1999) might change over the course of the task, or be linked to particular components of memory tasks.

Consequently, the analysis of this MEG study involved both the 10Hz frequency band used previously, and also standard EEG frequencies. Comparisons of the regions activated within these frequency bands may help to determine which bandwidths are most useful in memory research and may enable more realistic comparisons with previous neuroimaging research.

Table 7.21 details the hemispheric location of regional activations during encoding and recognition for objects and words. Initial observations indicate that different regions were highlighted as statistically significant by the different frequency analyses, even for bands with overlapping frequencies. It would therefore seem that the frequency bandwidth selected for analysis is an important consideration.

A number of regions were revealed as being activated during encoding and / or recognition by both frequency analyses. For example, during the encoding of objects, the right inferior occipital gyrus, left middle temporal gyrus and bilateral superior temporal gyrus were activated in both the 10Hz and the EEG analyses. For word encoding, these similarly activated regions included the right medial and superior frontal gyri. Regions only identified in the EEG bandwidths were the bilateral cerebellum and right medial frontal gyrus for objects, and the left fusiform, bilateral inferior frontal and precentral gyri for words. Furthermore, other activations only seen in the initial 500ms with the 10Hz bandwidths remained activated in the second 500ms time window when the EEG bandwidths are used (for example, the left inferior and middle frontal gyri for objects; bilateral middle temporal and right superior frontal gyri for objects).

In the first 500ms of object recognition, the 10Hz bandwidths and EEG bands identified the same activated regions, with the exception of the left middle temporal gyrus

which was only seen in the 10Hz analysis. Furthermore, the EEG analyses revealed ma more activated regions in both 500ms time windows, particularly in the second 500ms which time the 10Hz analyses suggested all recognition memory activation for objects l finished. Conversely, no activations were seen in the initial 500ms, for word recognit (compared to the four right hemispheric regions identified by the 10Hz bandwidths). In second 500ms time window, however, the EEG and 10HZ analyses showed absol concurrence in the identified activated regions.

	Encoding								***Recognition***							
	0-500ms				**500-1000ms**				**0-500**				**500-1000ms**			
	Objects		**Words**		**Objects**		**Words**		**Objects**		**Words**		**Objects**		**Words**	
	10Hz	EEG	10Hz	EEG	10Hz	EEG	10Hz	EEG	10Hz	EEG	10Hz	EEG	10Hz	EEG	10Hz	EEG
Amygdala			L													
Anterior Cingulate		L	R							L						
Cerebellum		B		L		B					R			L	R	
Cingulate Gyrus														L		
Cuneus								B		L				R		
Fusiform Gyrus				L				L								
Hippocampus											R					
Inferior Frontal Gyrus	B	R		B		L		B	L	B						
Inferior Occipital Gyrus	R	R						B						L		
Inferior Parietal Lobule				R						B						
Inferior Temporal Gyrus		L						L		L					R	
Insula														L		
Limbic Lobe				L		R				L						
Lingual Gyrus															R	
Medial Frontal Gyrus		R	R	R		R	L		L	L						
Middle Frontal Gyrus	L	B		B		L			L	B						
Middle Occipital Gyrus						L	L	L						L	R	
Middle Temporal Gyrus	L	L	B					B	L						R	
Parahippocampal Gyrus			L								R					
Posterior Cingulate		L		L						R						
Precentral Gyrus		B		L				R		L					R	
Precuneus	R					R		R								
Superior Frontal Gyrus			R	R		R	L	R	L	B				R		
Superior Parietal Lobule								R		L						
Superior Temporal Gyrus	B	B							L	R	R			R		
Thalamus						R										

Table 7.20 Summary of statistically significant activations from both the 10Hz and EEG frequency bandwidths; L = left lateralised; R = right lateralised; B = bilateral

This consistency between the 10Hz and EEG frequency bandwidths is encoura as it suggested that the findings from the previous MEG study those from this study ca reliably compared to those from previous EEG studies. For example, it has been sugge that alpha activity may relate to inhibitory networks (Klimesch et al, 2000) and changes in attention (Cooper et al, 2002), and thus the widespread activation seen in t

recognition memory studies may indeed show this additional activity. Furthermore, the EEG – 10Hz comparison suggests that, it might be more pertinent to use the EEG bandwidths in future studies, to ensure that no activation is omitted, particularly in later time windows.

7.6 Concluding Remarks

This experiment was conducted to investigate the reproducibility of the results obtained from the previous study. The results indicate that MEG can be reliably used as tool for studying recognition memory, with reasonable consistency shown between the findings of two separate MEG studies. Although this consistency is encouraging, there were still a number of regions differentially activated by the studies, the specific role of which still needs to be determined.

It was hypothesised that reducing the involvement of semantics in the encoding task would minimise the level of semantic processing used in the succeeding recognition task. Furthermore, it was anticipated that this would reduce the number of cortical regions activated in the recognition phase. The differences observed between the two studies suggest that it is possible to manipulate the involvement of semantics in recognition memory tasks. However, widespread activation was still observed in this study and the hemispheric asymmetry observed was not consistent. It may be that the hemispheric activation of this structure might depend upon stimulus modality, underlying semantic, language and attentional processes and ultimately the individual participants involved in the study.

Comparing activation across studies for the same individuals and the removal of further semantic processes, through the use of non-objects (e.g. random shapes) or non-words may enable some of these variables to be constrained. The final study aims to do just this and reveal further details about the specific regions and hemispheric asymmetry involved in recognition memory processes.

Observation of activated deep structures, such as the hippocampus and amygdala in this study is also a very positive finding for MEG research. SAM appears to overcome the inherent problem of MEG of imaging deep sources and as stated previously, with experiments specifically designed to produce activations within these deep structures, their

specific role in cognitive tasks such as emotional and memory related tasks may be identified.

It must be noted however, that the EEG frequency bandwidths failed to reveal activity within these deep structures. However, the 10Hz – EEG comparison suggests the suitability of using these EEG frequencies in future research. Similar findings were observed for the EEG and 10Hz bandwidths, and using the EEG frequencies in MEG studies will enable more reliable comparisons between previously published EEG studies and current data to be made. Furthermore, the EEG bands appear to reveal more prolonged activation. This prolonged activation is probably not surprising as previous research has shown that the most effective time windows are dependent on the width of the frequency band and vice versa. Consequently, therefore, careful design of experimental paradigms and analysis parameters may enable the roles of these deep structures to be identified in cognitive research.

8 NEURAL CORRELATES OF RECOGNITION MEMORY FOR NON-OBJECTS AND NON-WORDS USING A SHALLOW ENCODING TASK

8.1 Overview

In previous studies, MEG has been shown to yield relatively consistent results for recognition memory processes. The presence of semantic processes during recognition memory tasks has been highlighted and it was suggested that the semantic nature of encoding tasks may be partially responsible. In a recent study (chapter 7), however, where the encoding task did not involve a semantic task, diverse cortical activity was still observed. It is possible that semantic activations may still have been present due to the nature of the objects and words used. These were all very familiar items which have multiple semantic associations which may still have been influencing subsequent recognition memory. To identify the true correlates of recognition memory, non-objects and non-words were presented in a replication of the previous MEG study. The results supported previous findings in the neuroimaging literature which identified regions such as the PFC and MTL in recognition memory processes. The predominantly bilateral nature of these activations was discussed with respect to the task-specific and modality-specific hypotheses.

8.2 Introduction

Previously detailed neuroimaging studies of recognition memory have demonstrated differential involvement of frontal, parietal and temporal regions in accurate encoding, retrieval and recognition. Across the large number of studies, multiple widespread cortical regions have been linked to recognition memory processes (Table 1.1, chapter 1) and there was a lack of consistency within the findings. It was suggested that the variation might be due to the different imaging techniques themselves, the different stimuli used or the different analysis comparisons undertaken. In an attempt to show consistency between studies of recognition memory in separate experiments (chapters 5 and 7), the neural correlates of recognition memory were studied using magnetoencephalography. By

maintaining similar protocols and analysis parameters, it was demonstrated that MEG can be reliably used as a tool for studying recognition memory and that reasonable consistency can also be shown in the findings.

In an earlier study, it was suggested (chapter 5) that these identified areas may not be explicitly associated with encoding or recognition, but may reflect more general demands of semantics. This is especially appropriate as a separate study had highlighted differences between the brain processing of living and non-living items not only during the encoding (categorisation) task, but also in the subsequent recognition memory task. Consequently, the MEG study (chapter 7) was designed to eliminate the semantic component from the encoding phase by using a shallow spatial location task, thus reducing the semantic processing that may contaminate the memory-specific processes.

Yet, despite the encouraging nature of these MEG findings, and its reproducibility, a number of regions still showed differential activation. It may be that through the use of objects and words for which semantic association can be generated. These semantic processes are still evident during the subsequent recognition phase. Generating such semantic associations may actually be used by some individuals to facilitate recognition. Accessing stored semantic knowledge can produce category-specific differences due to the different cortical regions involved in processing perceptual and functional knowledge (Warrington & Shallice, 1984). Living object identification primarily involves perceptual processing, in contrast to the focus of functional knowledge processing for non-living stimuli. These different processes, therefore, may require the involvement of different cortical regions, or that semantic associations produce different demands on the same system (Humphreys et al, 1988) and through that the involvement of multiple regions.

8.2.1 Aims and Hypotheses

What is needed is the complete removal of explicit semantic associations throughout the entire encoding and recognition phases. A MEG study was conducted which involved the encoding and recognition of non-objects and non-words. It was hypothesised that using random shapes (non-objects) and non-words is an appropriate way of removing semantic associations from a recognition memory task. They do not possess any explicit semantic associations, but are similar enough to true objects and words to enable comparisons to be drawn from any of the findings to those detailed previously (chapter 7) and reported in the

neuroimaging literature. It was anticipated that removal of this semantic network may enable the true neural correlates of recognition memory to be identified, and to determine whether there are indeed any hemispheric differences between modalities or between recognition and encoding tasks.

8.3 Method

8.3.1 Participants

Eight healthy right-handed participants (six females and two males, age range 22-51 years) volunteered to participate in the study. Anatomical MRI scans had previously been taken for each of these individuals and were made available for the analysis.

8.3.2 Stimuli

The pictures of non-objects presented to the participants during the study taken from the Kroll and Potter (1984) set of line drawings. All images in this series were created from true objects and manipulated to produce a set of non-objects. In the original study (Kroll & Potter, 1984), ratings of 'similarity to real true objects' were provided for each of the non-objects. These values were used so that the images in the encoding phase matched those on 'similarity' to those presented in the subsequent recognition phase. In the encoding phase, there were 44 non-objects, and in the recognition phase participants were presented with the same 44 stimuli and 44 new non-objects.

For the word stimuli, a set of non-words was obtained from the Psycholinguistic Assessments of Language Processing in Aphasia (PALPA, Kay, Lesser & Coltheart, 1992). These were created from true words but were manipulated by changing some of the letters to create pronounceable non-words. 88 non-words were used in the study; the 44 used in the encoding phase were matched for number of letters and number of syllables to the 44 new non-words presented in the recognition phase.

8.3.3 Encoding Task

As in the previous study, a shallow encoding task was used. This involved the same spatial location task, during which participants were presented with a series of stimuli and were required to identify the location of a red dot placed either above or below the horizontal plane of fixation (see Figure 8.1). A button-press was then used to indicate the participant's response. The use of red dot enabled the stimuli to be presented to central fixation.

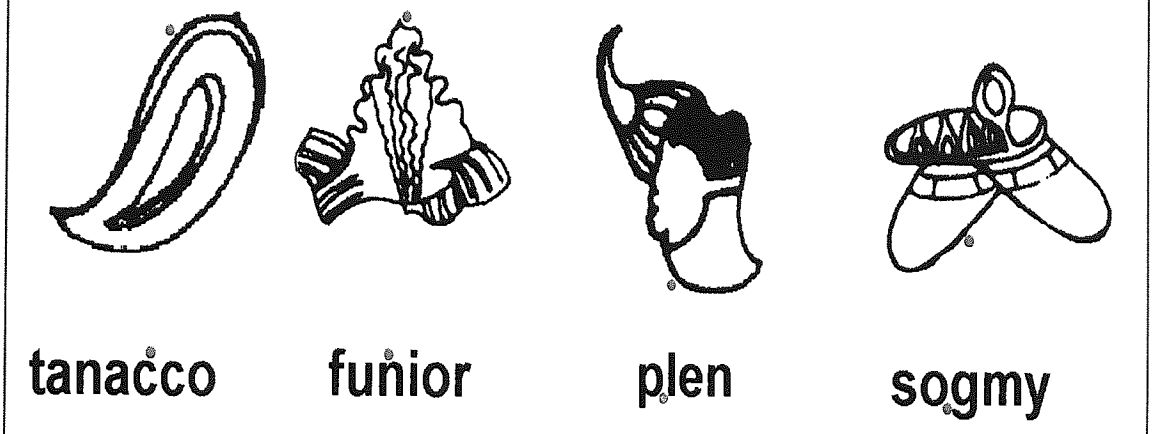


Figure 8.1. Examples of non-object and non-word stimuli used in the encoding and recognition phases. The position of the red dot was used as the spatial location task (participants required to judge whether it was above or below the horizontal plane of fixation) during the shallow encoding task

8.3.4 Presentation of Stimuli

Before commencement of the study, participants were randomly assigned to one of two experimental groups. The first group performed the non-object recognition memory task, followed by the recognition memory tasks for non-words. The second group performed the non-word recognition memory tasks first, followed by the non-objects (see Figure 8.2). Within each group, the location of the red (above or below) was randomised amongst the stimuli and the stimuli themselves were randomly presented.

Participants were seated in a magnetically shielded room and viewed the stimuli, presented on an Eizo T662 monitor, through a mirror at a distance of two meters. In both the encoding and recognition phases of the experiment, the participants were required to fixate on a centrally presented small white square for a period of 1500 ms. A stimulus was

then presented to the centre of the screen for 500 ms before the fixation point returned for another period of 1000 ms. The fixation point then changed from white to black, and this was the participants' cue to make a response with a button press using their dominant hand. In the encoding phase, participants were asked to make a judgment about whether the red dot was located above or below their horizontal plane of fixation (above / below spatial judgement task) and, in the recognition phase, as an old or new item. Accuracy and reaction time responses were recorded. Participants had 2000 ms to respond before the fixation point turned white again. This marked the onset of the next trial. The timing is illustrated in Figure 8.3. Stimuli were presented in a different random order for each participant. The same procedure was followed for non-words and non-objects.

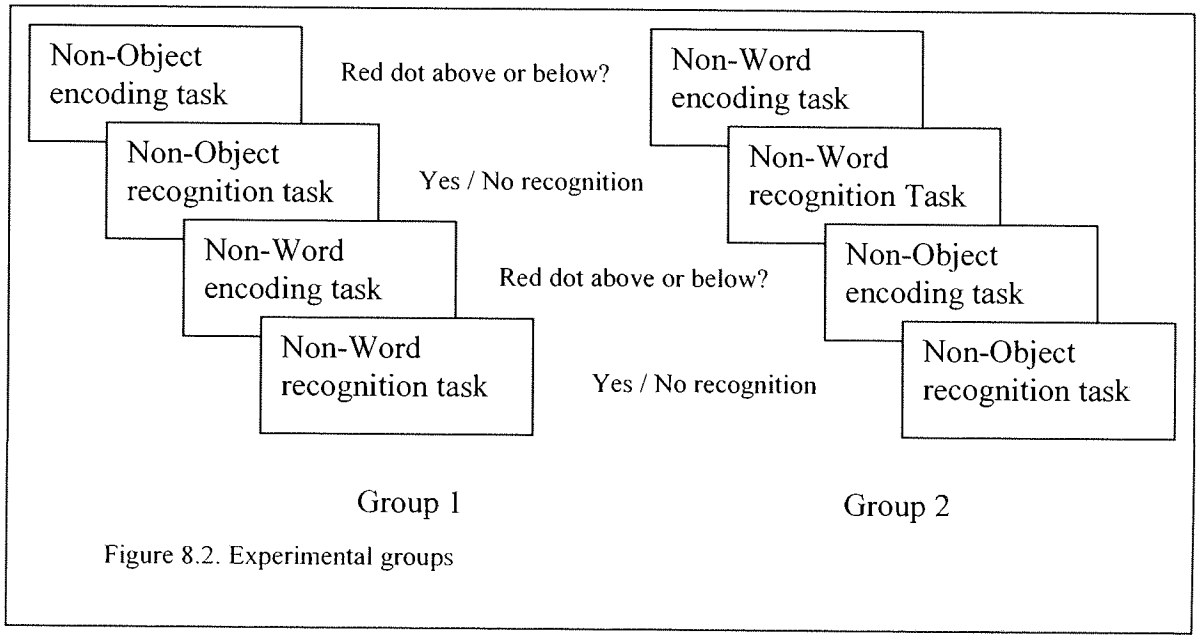


Figure 8.2. Experimental groups

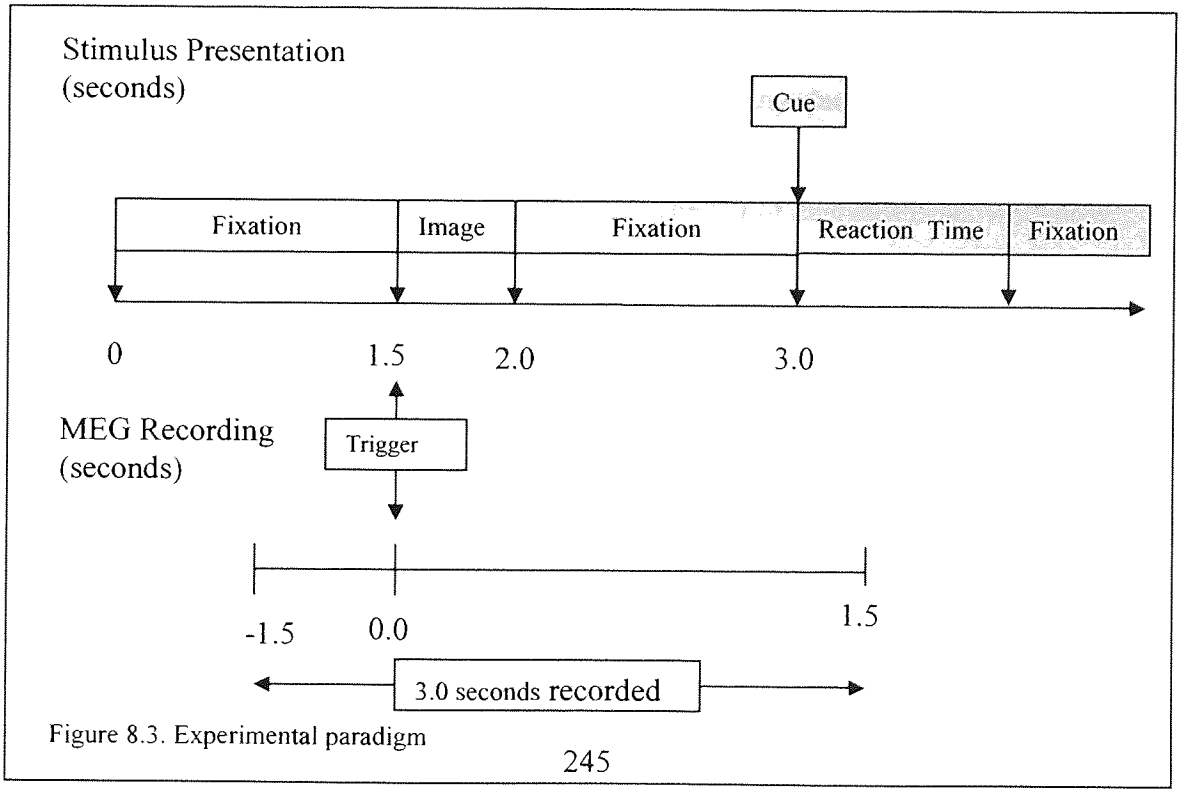


Figure 8.3. Experimental paradigm

8.3.5 MEG Recording and Analysis

Recording of neural activity used a 151-channel CTF Omega MEG system (CTF Systems Inc, Canada.). Following MEG recording, a Polhemus Isotrak system was used to digitise the surface shape of the participant's head, this information then being used to co-register the MEG data with the participant's anatomical MRI.

Cortical activation was analysed using SAM (Synthetic Aperture Magnetometry) (Robinson & Vrba, 1998; Barnes et al, 2001), a method of producing a three-dimension map of cortical synchronous and desynchronous activation. SAM Analysis compares one state (active) with another (passive). Positive t-statistics are produced when the active state shows and increase in power, negative when it shows a decrease. These are interpreted as event-related synchronisation (ERS) and event-related desynchronisation (ERD) respectively (Pfurtscheller & Lopes da Silva, 1999).

Several SAM comparisons were made on the raw, correctly encoded and recognised data. Firstly, comparisons were made between encoding and recognition for the non-objects and non-words separately. Then non-objects and non-words were directly compared. SAM comparisons compared non-objects and non-words for both the encoding phase and for the recognition phase. Several baseline SAM comparisons were also computed (baseline (500ms before stimulus onset) versus first, and second 500ms time spans following stimulus onset) for each of the stimulus types, non-words and non-objects, during encoding and recognition of old images. The third possible 500ms was not analysed for two main reasons: a button-press response was performed at 1000ms post-stimulus onset and it was expected that this would contaminate any data in the final 500ms time span; and previous neuroimaging research has suggested that cognitive processing is probably finished by 1000ms post stimulus onset. The list of analyses is shown below.

Encoding and Recognition

1. Encoding versus recognition during the first and second 500 ms post-stimulus onset for non-objects

2. Encoding versus recognition during the first and second 500 ms post-stimulus onset for non-words

3. Four baseline comparisons of encoding / recognition during first / second 500 ms compared to 500ms fixation (baseline) for non-objects

4. Four baseline comparisons of encoding / recognition during first / second 500 ms compared to 500ms fixation (baseline) for non-words

Non-Objects and Non-Words

5. Direct comparison of non-objects versus non-words during the first and second 500ms compared of encoding

6. Direct comparison of non-objects versus non-words during the first and second 500ms compared of recognition of old items

All power changes were calculated in the standard EEG frequency bandwidths; corresponding to delta (0-4Hz), theta (4-7Hz), alpha (8-13Hz), alpha and theta combined (3-13Hz), beta (14-20Hz) and finally a large broad bandwidth (0-40Hz).

Group SAM images were generated by spatially normalising each of the participant's SAM data using SPM99 (Friston et al, 1995) and mapping each of these onto a template brain. Statistically significant regions of activation were identified using statistical non-parametric mapping (SnPM).

8.4 Results

Several SAM analyses were conducted on the raw, unaveraged data. These were direct non-object versus non-word comparisons in both the encoding and recognition phases, direct encoding versus recognition comparison for both non-objects and non-words, and finally each stimulus modality at during each task versus baseline (fixation). Due to the low level of statistical power in the analyses, a significance level of $p<0.1$ was used in some of the comparisons to identify potential clusters of activation and trends in the data.

8.4.1 Behavioural Data

Behavioural data was collected from the eight participants. Trials on which participants responded before the cue, had reaction times greater than 2000ms, or made an incorrect response, were removed from the analysis. Participants were highly accurate on both the encoding tasks for non-objects and non-words (90.9% and 89.7%, respectively). Although accuracy was not as high during the recognition test (69.7% for non-objects and 63.5% for non-words), a chi-square analysis showed this level of accuracy to be above chance for both non-objects (χ^2 (df1) = 13.72; $p < 0.001$) and for non-words ($\chi 2$ (df1) = 6.41; $p < 0.02$).

8.4.2 Direct Stimulus Comparisons

The first analysis involved a direct comparison of non-objects versus non-words during both encoding and recognition phases. No statistically significant regions of activation were identified during these comparisons.

8.4.2.1 Direct Comparison of Recognition versus Encoding

Neural activation during recognition was directly compared to that for encoding. All statistically significant activation was ERD As this was also the case for the baseline comparisons, this is indicative of greater desynchronous activation for recognition, therefore suggesting that any significantly activated regions were in the recognition phase, and not during the encoding.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Frontal Gyrus	Left	3-13	-39 18 36	122	7.62	0.008	9
		14-20	-48 30 30	10	6.13	0.016	46 / 9
	Right	3-13	30 33 27	12	6.28	0.012	
Superior Frontal Gyrus	Left	3-13	-30 23 60	66	7.26	0.027	8
		14-20	-24 36 33	317	6.24	0.023	
Precentral Gyrus	Left	3-13	-43 15 38	122	7.62	0.012	9
Medial Frontal Gyrus	Right	14-20	10 25 34	87	7.31	0.012	9
Anterior Cingulate	Right	14-20	6 24 27	87	7.31	0.008	24/32
Parahippocampal Gyrus	Left	14-20	-33 -30 -21	77	6.31	0.012	36
Middle Occipital Gyrus	Left	3-13	-18 -102 10	5	6.06	0.043	18
		14-20	-36 -78 -15	23	6.14	0.016	
	Right	8-13	24 -90 30	28	5.95	0.027	18
Lingual Gyrus	Left	14-20	-24 -87 9	9	5.83	0.043	
Precuneus	Left	14-20	-3 -68 60	28	6.98	0.043	7/31/
		3-13	-3 -63 57	19	6.19	0.016	9
Superior Parietal Lobule	Left	14-20	-3 -69 58	28	6.98	0.043	7
Angular Gyrus	Right	8-13	45 -78 33	19	6.17	0.020	
Inferior Parietal Lobule	Left	14-20	-50 -68 39	22	6.54	0.020	39
Fusiform Gyrus	Left	14-20	-30 -36 -35	77	6.36	0.016	20/19
Inferior Occipital Gyrus	Left	14-20	-35 -74 -12	23	6.14	0.047	
Anterior Lobe / Culmen	Left	14-20	-27 -39 -30	77	6.36	0.008	
Posterior Lobe / Tuber	Left	14-20	-54 -63 -37	7	5.93	0.043	
Cuneus	Left	0-40	-9 -87 21	239	8.22	0.008	19/18
	Right	0-40	24 -78 33	115	6.80	0.016	
		3-13	18 -87 36	4	5.66	0.043	19
		8-13	12 -84 33	25	5.95	0.027	
Supramarginal Gyrus	Left	3-13	-54 -39 33	29	6.37	0.008	
Postcentral Gyrus	Left	14-20	-21 -42 63	140	5.80	0.031	

Table 8.1 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and recognition memory phases for non-objects, 0-500ms post stimulus onset

0-500ms

Non-Objects

In the initial 500ms post-stimulus onset, a decrease in oscillatory synchrony was seen in a number of regions for non-object recognition, when compared to encoding (Table 8.1). All activations were seen in the alpha (8-13Hz), beta (14-20Hz) and a broad alpha-theta bandwidth (3-13Hz). Bilaterally activated regions included the middle frontal gyrus, middle occipital gyrus and cuneus. Left-lateralised desynchronisation was observed in

superior frontal, precentral, parahippocampal, lingual, fusiform, inferior occipital and postcentral gyri, precuneus, superior and inferior parietal lobule and the cerebellum. Right-lateralised regions activated through non-object recognition included the medial frontal and angular gyrus and the anterior cingulate.

Non-Words

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Temporal Lobe	Left	3-13	-29 -36 9	1	5.54	0.047	
Fusiform Gyrus	Right	0-40	61 -51 -24	1	5.45	0.047	37

Table 8.2 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and recognition memory phases for non-words, 0-500ms post stimulus onset

Only two small regions were seen to be differentially activated by non-word recognition compared to encoding (0-500ms) (Table 8.2). These were in the left temporal lobe in the alpha-theta band (3-13Hz) and in the fusiform gyrus in the broad 0-40Hz bandwidth.

500-1000ms

In the 500-1000ms time window, a large number of regions showed greater activation during non-object recognition compared to encoding (Table 8.3). Again these were in the alpha, beta and theta-alpha bandwidths, and also in the broad 0-40Hz bandwidth. There was an increase in right hemispheric activity in comparison to the initial 500ms time window. Bilateral activations were observed in the medial frontal and orbital gyri, the cuneus and the insula. Left-lateralised was restricted to the anterior cingulate, middle occipital and lingual gyri. All other activated regions were within the right hemisphere.

Non-Objects

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Temporal Gyrus	Right	0-40	39 -75 21	18	5.91	0.031	
		8-13	-36 -54 21	40	5.64	0.023	22
		14-20	48 -39 12	992	7.43	0.004	
Superior Frontal Gyrus	Right	3-13	15 21 51	162	6.07	0.039	6
Orbital Gyrus	Left	3-13	-12 48 -27	114	6.98	0.027	11
	Right	0-40	9 36 -30	264	7.6	0.016	11
Medial Frontal Gyrus	Right	14-20	15 45 18	2	5.74	0.039	
	Left	14-20	-9 33 30	90	6.89	0.023	
Cingulate Gyrus	Right	3-13	3 18 42	162	6.82	0.027	32
		0-40	18 3 45	56	6.54	0.031	
Anterior Cingulate	Left	3 -13	-3 27 21	162	7.30	0.020	24
		0-40	0 24 -9	264	6.12	0.043	
Parahippocampal Gyrus	Right	8-13	30 -30 -12	201	7.16	0.008	
Middle Occipital Gyrus	Left	0-40	-21 -99 6	171	8.23	0.004	18
Insula	Left	14-20	-45 -12 9	272	6.70	0.012	
	Right	0-40	33 -18 15	330	5.72	0.047	
Lingual Gyrus	Left	0-40	-9 -84 -9	64	6.67	0.027	
Precuneus	Right	0-40	6 -69 39	328	6.33	0.016	7
		8-13	30 -78 39	107	5.87	0.023	19
Angular Gyrus	Right	8-13	51 -63 30	102	6.56	0.027	39
Posterior Cingulate	Left	14-20	-12 -54 15	244	6.70	0.008	
Posterior Lobe / Tuber	Right	14-20	33 -87 -27	231	6.21	0.035	
Cuneus	Left	8-13	-9 -66 9	223	6.64	0.012	
	Right	14-20	18 -90 21	194	5.71	0.035	18
Paracentral Lobule	Right	14-20	15 -36 48	992	7.43	0.004	5
Postcentral Gyrus	Right	14-20	42 -18 30	992	5.45	0.043	

Table 8.3 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and recognition memory phases for non-objects, 500-1000ms post stimulus onset

Non-Words

Only one cluster within the frontal lobe (0-40Hz) was seen to show greater activity for non-word recognition than non-word encoding during the 500-1000ms time-window (Table 8.4).

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Frontal Lobe	Left	0-40	-20 13 22	94	6.24	0.008	

Table 8.4 Regions showing statistically significant differences in activation ($p < 0.05$) between the encoding and recognition memory phases for non-words, 500-1000ms post stimulus onset

8.4.2.2 Encoding versus Baseline

0-500ms

Non-Objects

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Frontal Gyrus	Right	14-20	23 36 -1	3	5.83	0.090	
	Left	0-40 c	-51 9 60	8242	4.17	0.074	6
Limbic Lobe	Right	14-20	18 37 4	3	5.83	0.083	
Inferior Frontal Gyrus	Right	14-20 c	33 35 -10	97	4.07	0.031	
Precentral Gyrus	Left	14-20 c	-39 -6 63	9	4.89	0.078	
Parahippocampal Gyrus	Left	0-40 c	-33 -12 -27	8242	4.13	0.074	
Postcentral Gyrus	Left	0-40 c	-30 -18 30	8242	4.22	0.074	
Cerebellum	Left	0-40 c	-26 -13 -21	8242	4.13	0.074	

Table 8.5 Regions showing statistically significant differences in activation ($p < 0.1$) between the encoding and baseline phases for non-objects, 0-500ms post stimulus onset. c indicates regions identified through cluster analysis, other regions were identified through a voxel-wise analysis

When the neural activity of non-object encoding was compared to a baseline measure (fixation) (Table 8.5, Figure 8.4.A), desynchronous activity in the beta bandwidth was seen in the right middle and inferior frontal gyri, the right limbic lobe and the left precentral gyrus. Other regions showed left-lateralised desynchronisation when analysed using the 0-40Hz frequency band. These included the middle frontal, parahippocampal and postcentral gyri and the cerebellum.

Non-Words

Significant changes in beta activity were also seen during the initial 500ms of non-word encoding (Table 8.6, Figure 8.4.B). Activated regions were localised predominantly within the left hemisphere, specifically the middle and inferior temporal, parahippocampal, fusiform and supramarginal gyri, amygdala and cerebellum. The left thalamus was also activated in the 0-40Hz bandwidth. Right hemispheric activation was restricted to the middle temporal gyrus and the superior parietal lobule, the latter only seen in the broad 0-40Hz bandwidth.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Temporal Gyrus	Right	14-20	54 -42 -12	171	6.61	0.020	21
		0-40	54 -36 -15	7	5.20	0.074	
	Left	14-20	-42 3 -36	210	5.10	0.078	
Inferior Temporal Gyrus	Left	14-20	-42 9 -18	210	4.95	0.086	20
Parahippocampal Gyrus	Left	14-20	-24 0 -15	210	5.40	0.062	
Thalamus	Left	0-40	-12 -19 13	201	6.42	0.047	
Amygdala	Left	14-20	-25 -2 -16	210	5.40	0.67	
Superior Parietal Lobule	Right	0-40	27 -60 63	4	4.93	0.086	
Fusiform Gyrus	Left	14-20	-36 -54 -14	138	5.68	0.055	
Anterior Lobe	Left	14-20	-30 -54 -24	138	5.68	0.055	
Supramarginal Gyrus	Left	14-20	-45 -45 33	10 5.01	0.082		

Table 8.6 Regions showing statistically significant differences in activation ($p < 0.1$) between the encoding and baseline phases for non-words, 0-500ms post stimulus onset

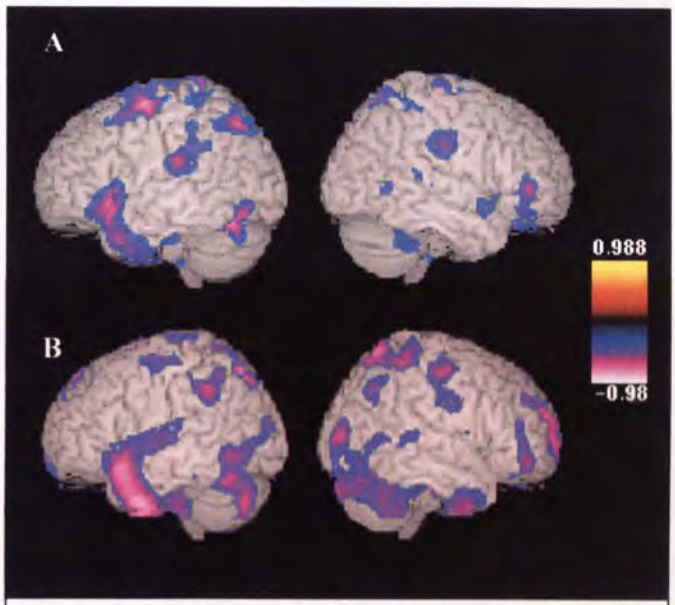


Figure 8.4. Statistically significant regions of activation for the encoding of non-objects (A) and non-words (B) during the first 500ms (0-500ms). Activation maps are group images, averaged across frequency. All significant activation was observed as ERD (blue)

500-1000ms

Non-Objects

No significant activations were seen for the encoding of non-objects in the second 500ms (500-1000ms) time window.

Non-Words

In the second 500ms time-window, desynchronous activity was again predominantly seen in the beta range (Table 8.7, Figure 8.5). Activated regions included the left superior and right middle temporal gyri, right parahippocampal, lingual and fusiform gyri, left insula and precuneus and the right cerebellum.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Superior Temporal Gyrus	Left	14-20	-35 6 -14	120	6.34	0.043	
Middle Temporal Gyrus	Right	14-20	68 -39 -22	22	5.65	0.094	
Parahippocampal Gyrus	Right	14-20	33 -48 -9	165	5.90	0.043	19/37
Insula	Left	14-20	-39 -21 0	120	5.69	0.055	
Lingual Gyrus	Right	14-20	17 -53 -3	165	5.90	0.082	
Precuneus	Left	8-13	-3 -45 45	9	5.65	0.059	
Fusiform Gyrus	Right	14-20	27 -51 -15	165	5.93	0.039	
		3-13	51 -63 -22	7	5.38	0.074	
Posterior Lobe / Declive	Right	3-13	51 -66 -24	7	5.38	0.070	
		14-20	27 -53 -17	165	5.93	0.043	

Table 8.7 Regions showing statistically significant differences in activation ($p < 0.1$) between the encoding and baseline phases for non-words, 500-1000ms post stimulus onset

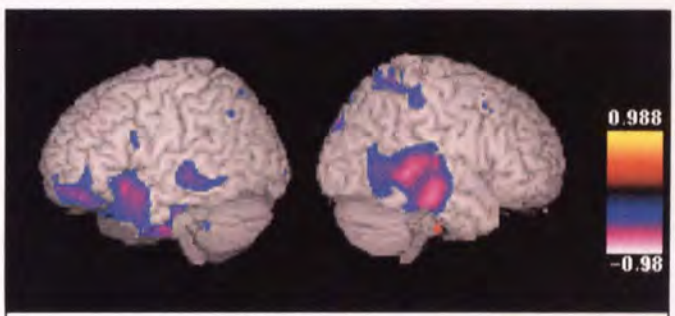


Figure 8.5. Statistically significant regions of activation for the encoding of non-words during the second 500ms (0-500ms). Activation maps are group images, averaged across frequency. All significant activation was observed as ERD (blue)

8.4.2.3 Recognition versus Baseline

0-500ms

Non-Objects

Initial stages of non-object recognition activated the left middle frontal gyrus in the broad 0-40Hz bandwidth, and the left middle temporal gyrus, left lingual gyrus, right fusiform gyrus and right cerebellum, all in the beta range (Table 8.8, Figure 8.6.A).

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Frontal Gyrus	Left	0-40	-30 36 30	9	5.56	0.094	9
Middle Temporal Gyrus	Left	14-20	-50 -75 26	6	4.17	0.062	39
Lingual Gyrus	Left	14-20	-9 0 -18	1	5.11	0.098	18/17
Fusiform Gyrus	Right	14-20	24 -89 -24	20	5.36	0.090	
Posterior Lobe	Right	14-20	22 -90 -29	20	5.36	0.090	

Table 8.8 Regions showing statistically significant differences in activation ($p < 0.05$) between the recognition and baseline phases for non-objects, 0-500ms post stimulus onset

Non-Words

Some desynchronous activity observed in the initial 500ms of non-word recognition was also within the beta range, specifically the right superior parietal lobule and postcentral gyrus (Table 8.9, Figure 8.6.B). The remaining activations were only observed in the broad bandwidth (0-40Hz), and were located in the middle temporal gyrus and precuneus in the left hemisphere, and in the inferior occipital gyrus and cuneus on the right.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Temporal Gyrus	Left	0-40	-68 -45 -18	34	5.28	0.082	
Lingual Gyrus	Right	0-40	33 -102 -9	576	7.32	0.008	18
Precuneus	Left	0-40	-33 -69 39	3	4.89	0.098	19
Superior Parietal Lobule	Right	14-20	36 -54 69	108	4.90	0.078	7
Inferior Occipital Gyrus	Right	0-40	33 -102 -9	576	7.32	0.008	18
Cuneus	Right	0-40	6 -75 6	24	5.19	0.082	
Postcentral Gyrus	Right	14-20	30 -33 66	7	4.32	0.090	7

Table 8.9 Regions showing statistically significant differences in activation ($p < 0.05$) between the recognition and baseline phases for non-words, 0-500ms post stimulus onset

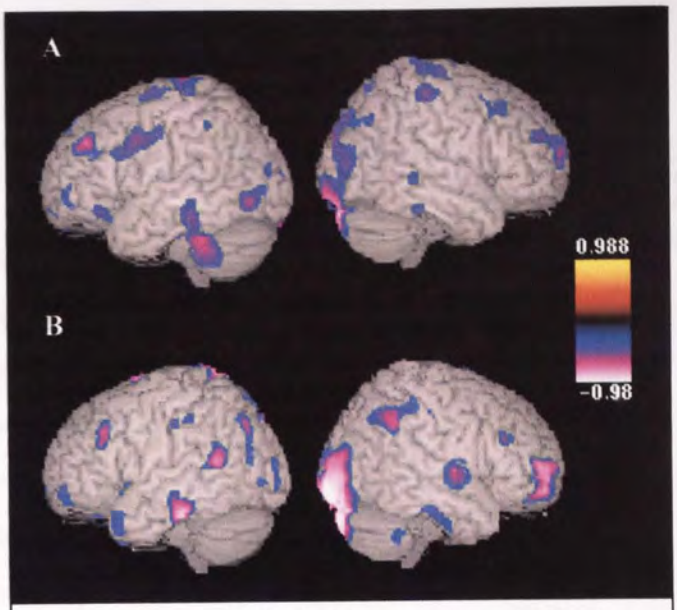


Figure 8.6. Statistically significant regions of activation for the recognition of non-objects (A) and non-words (B) during the first 500ms (0-500ms). Activation maps are group images, averaged across frequency. All significant activation was observed as ERD (blue)

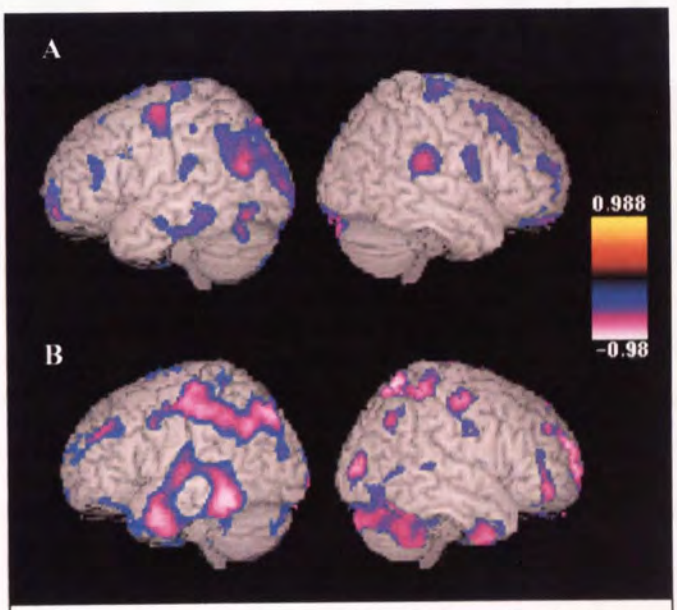


Figure 8.7. Statistically significant regions of activation for the recognition of non-objects (A) and non-words (B) during the second 500ms (0-500ms). Activation maps are group images, averaged across frequency. All significant activation was observed as ERD (blue)

500-1000ms

Non-Objects

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Middle Frontal Gyrus	Left	14-20	-33 -3 54	108	5.89	0.039	6
Superior Temporal Gyrus	Right	14-20	48 -39 3	46	5.70	0.051	
Inferior Temporal Gyrus	Right	14-20	56 -51 -18	246	7.06	0.066	
Middle Temporal Gyrus	Right	14-20	47 -40 -2	46	5.70	0.086	
Precentral Gyrus	Left	14-20	-39 -6 -61	108	5.89	0.070	
Middle Occipital Gyrus	Left	14-20	-36 -66 2	992	8.47	0.012	
Lingual Gyrus	Left	14-20	-9 -95 -4	42	5.83	0.062	17
Precuneus	Right	0-40	9 -78 33	199	6.06	0.012	7/31/
		3-13	24 -72 42	1	5.16	0.098	19
Superior Parietal Lobule	Right	8-13	27 -72 45	5	5.38	0.082	
Inferior Parietal Lobule	Left	14-20	-51 -42 42	2	5.13	0.094	40
Fusiform Gyrus	Right	3-13	48 -60 -21	28	5.46	0.098	37
		14-20	50 -60 -22	246	7.06	0.039	37
Posterior Lobe / Declive	Right	3-13	51 -60 -36	28	5.70	0.086	
		14-20	51 -63 -30	246	7.06	0.012	
Cuneus	Left	14-20	-9 -93 -3	42	5.83	0.059	17
	Right	14-20	3 -95 12	13	5.83	0.086	18
		0-40	9 -70 32	199	6.06	0.055	7/18
Postcentral Gyrus	Left	3-13	-51 -27 57	24	5.74	0.074	1

Table 8.10 Regions showing statistically significant differences in activation ($p < 0.1$) between the recognition and baseline phases for non-objects, 500-1000ms post stimulus onset

During the second 500ms time window, recognition of non-objects revealed beta activation within the left middle frontal gyrus, in the right middle, superior and inferior temporal gyri and in the left middle occipital and lingual gyri (Table 8.10, Figure 8.7.A). Right lateralised activation was also seen in the precuneus (alpha-theta and 0-40Hz bandwidths), superior parietal lobule (alpha), fusiform gyrus and cerebellum (both in alpha-theta and beta bands). Two additional regions showed left-lateralised desynchronisation: postcentral gyrus (alpha-theta) and inferior parietal lobule (beta); and the cuneus showed bilateral activation in the beta and broad 0-40Hz bandwidths.

Non-Words

Bilateral regions of the frontal lobe (superior, inferior and medial gyri) were activated with the right showing beta activity, the left only being visible in the 0-40Hz bandwidth (Table 8.11, Figure 8.7.B). In a similar way, the bilateral activations within the

temporal lobes showed differences in frequency; the left inferior, superior and temporal gyrus only being activated in the theta-alpha (3-13Hz) band, compared to right hemispheric activation in the theta-alpha, beta or broad 0-40Hz band.

Region	Hemisphere	Frequency bands (Hz)	Talairach co-ordinates (x y z)	Cluster size (mm3)	T-value	P Value	BA
Inferior Temporal Gyrus	Left	3-13	-53 -51 -18	1084	8.13	0.043	
	Right	14-20	63 -24 -30	10	4.19	0.090	20
Superior Temporal Gyrus	Left	0-40	-54 -12 0	502	5.10	0.078	22/13
Superior Frontal Gyrus	Left	14-20	-6 -9 75	19	4.41	0.086	6
Middle Temporal Gyrus	Right	0-40	45 -63 -3	46	5.33	0.051	37
		3-13	51 -81 21	78	5.97	0.031	39/19
		8-13	57 -78 12	27	5.40	0.066	19
	Left	5-15	-54 -36 -15	265	6.59	0.055	21
		3-13	-60 -30 -15	1084	5.50	0.047	21/20
Precentral Gyrus	Right	3-13	30 -18 75	9	4.98	0.086	
		14-20	36 -27 66	251	5.17	0.047	4
Hippocampus	Left	3-13	-33 -33 -17	1084	6.31	0.035	36
Middle Occipital Gyrus	Left	3-13	-21 -102 9	634	5.56	0.047	19
Transverse Temporal Gyrus	Left	0-40	-39 -27 9	502	6.56	0.004	14
Lingual Gyrus	Left	3-13	-18 -81 0	634	6.74	0.012	18
		14-20	-12 -71 1	25	4.32	0.090	
Superior Occipital Gyrus	Left	14-20	-33 -87 30	66	5.44	0.081	19
Precuneus	Left	0-40	-3 -9 69	9	5.07	0.078	7
		14-20	-27 -54 51	48	4.38	0.086	7
	Right	0-40	9 -75 24	426	6.37	0.008	31
		3-13	33 -80 46	70	5.59	0.074	19
Superior Parietal Lobule	Left	14-20	-18 -69 54	1	4.04	0.098	
	Right	3-13	33 -80 46	70	5.59	0.051	7
Inferior Parietal Lobule	Left	3-13	-59 -46 39	93	6.44	0.090	40
		14-20	-33 -60 48	48	4.26	0.090	
Fusiform Gyrus	Left	3-13	-42 -45 -21	1084	8.13	0.004	36/37
Insula	Left	0-40	-39 -23 -2	502	6.56	0.039	13
		3-13	-39 -9 0	6	4.91	0.090	
Anterior Lobe / Culmen	Left	0-40	-36 -38 -35	163	5.95	0.039	
Posterior Lobe / Declive	Right	0-40	13 -92 -33	76	5.93	0.094	
		8-13	24 -75 -45	32	5.43	0.088	
		14-20	33 -63 -33	210	4.70	0.066	
	Left	0-40	-36 -39 -42	163	5.95	0.031	
Cuneus	Right	0-40	13 -80 24	426	6.37	0.008	19/18
		3-13	9 -81 33	634	6.28	0.023	/7
	Left	0-40	-1 -76 24	426	6.37	0.035	
		14-20	-9 -78 3	25	4.32	0.086	
Postcentral Gyrus	Right	14-20	45 -27 63	251	5.15	0.051	3

Table 8.11 Regions showing statistically significant differences in activation ($p < 0.1$) between the recognition and baseline phases for non-words, 500-1000ms post stimulus onset

Occipital gyri (middle and superior) were only activated in the left hemisphere, while the visual association areas of the lingual and fusiform gyri were bilaterally activated. Parietal regions, such as the superior and inferior parietal and paracentral lobules were also bilaterally activated, covering most frequency bandwidths. This was also the case for both the cuneus and precuneus.

Limbic structures were more hemispheric lateralised in their activations with desynchronisation seen in the left insula, parahippocampal gyrus and hippocampus, and in the right cingulate gyrus. Additionally activated regions included bilateral postcentral gyrus (predominantly in the beta band) and the right precentral gyrus (predominantly alpha). The bilateral cerebellum also showed activation in all frequency bands.

8.4.2.4 Summary of Baseline

Table 8.12 illustrates significantly activated regions for non-objects and non-words during encoding and recognition in each of the two 500ms time windows. Several of these regions, in particular frontal and temporal regions, which have been identified in previous neuroimaging studies, were subjected to a further quantification analysis (Figure 8.8). The percentage activation (activated number of voxels expressed as a percentage) of each structure was calculated for both modalities and during both the encoding and recognition tasks. Chi-square analyses were also performed on the raw quantification analysis data to determine whether hemispheric asymmetry was present during the encoding or recognition phases for either non-objects or non-words. The data for all frequency bands were combined together to improve the degrees of freedom of the statistical analysis. For each cortical region the number of participants showing left- and right-lateralised dominance was calculated.

Three regions appeared to be either encoding specific or recognition specific. These were the parahippocampal gyrus showing encoding specific attributes; the cuneus and inferior parietal lobule showing recognition-specific activation. The parahippocampal gyrus showed non-significant left-hemispheric activation for the initial encoding of non-objects ($p=0.2$) and non-words ($p>0.2$), and significant right hemispheric dominant activation during the latter stages of non-word encoding ($\chi^2 = 6.125$, $p < 0.02$). When the amount of activation within the structure was quantified, the left hemispheric dominance can be seen during the initial encoding phase (although this was non-significant, $p > 0.2$),

and then greater in the right during the later encoding of non-words ($p < 0.02$). There were also comparable amounts of activation during the recognition phase, but no significant hemispheric asymmetry was revealed. This indicates that during the recognition phase the parahippocampal gyrus was also activated, but possibly not at a significant enough level to be identified, or not within the time frames that were used.

	Encoding				Recognition			
	0-500ms		500-1000ms		0-500ms		500-1000ms	
	Non-Objects	Non-Words	Non-Objects	Non-Words	Non-Objects	Non-Words	Non-Objects	Non-Words
Amygdala		L						
Cerebellum	L	L		R	R		R	B
Cuneus						R	B	B
Fusiform gyrus		L		R	R		R	L
hippocampus								L
Inferior Frontal Gyrus	R							
Inferior Occipital Gyrus						R		
Inferior parietal lobule							L	L
Inferior Temporal Gyrus		L					R	B
Insula				L				L
lingual gyrus				R	B	R	L	L
Middle Frontal Gyrus	B				L		L	
Middle Occipital Gyrus							L	L
Middle Temporal Gyrus		B		R	L	L	R	B
Paracentral Lobule								R
Parahippocampal Gyrus	L	L		R				
Postcentral Gyrus	L					R		R
Precentral Gyrus	L						L	R
Precuneus				L		L	B	B
Superior Frontal Gyrus								L
Superior Occipital Gyrus								L
Superior parietal lobule		R				R	R	B
Superior Temporal Gyrus				L			R	L
Supramarginal gyrus		L						R
Thalamus		L						

Table 8.12 Significantly activated regions for non-objects and non-words during encoding and recognition in each of the two 500ms time windows; L = left lateralised, R = right lateralised, B = Bilateral

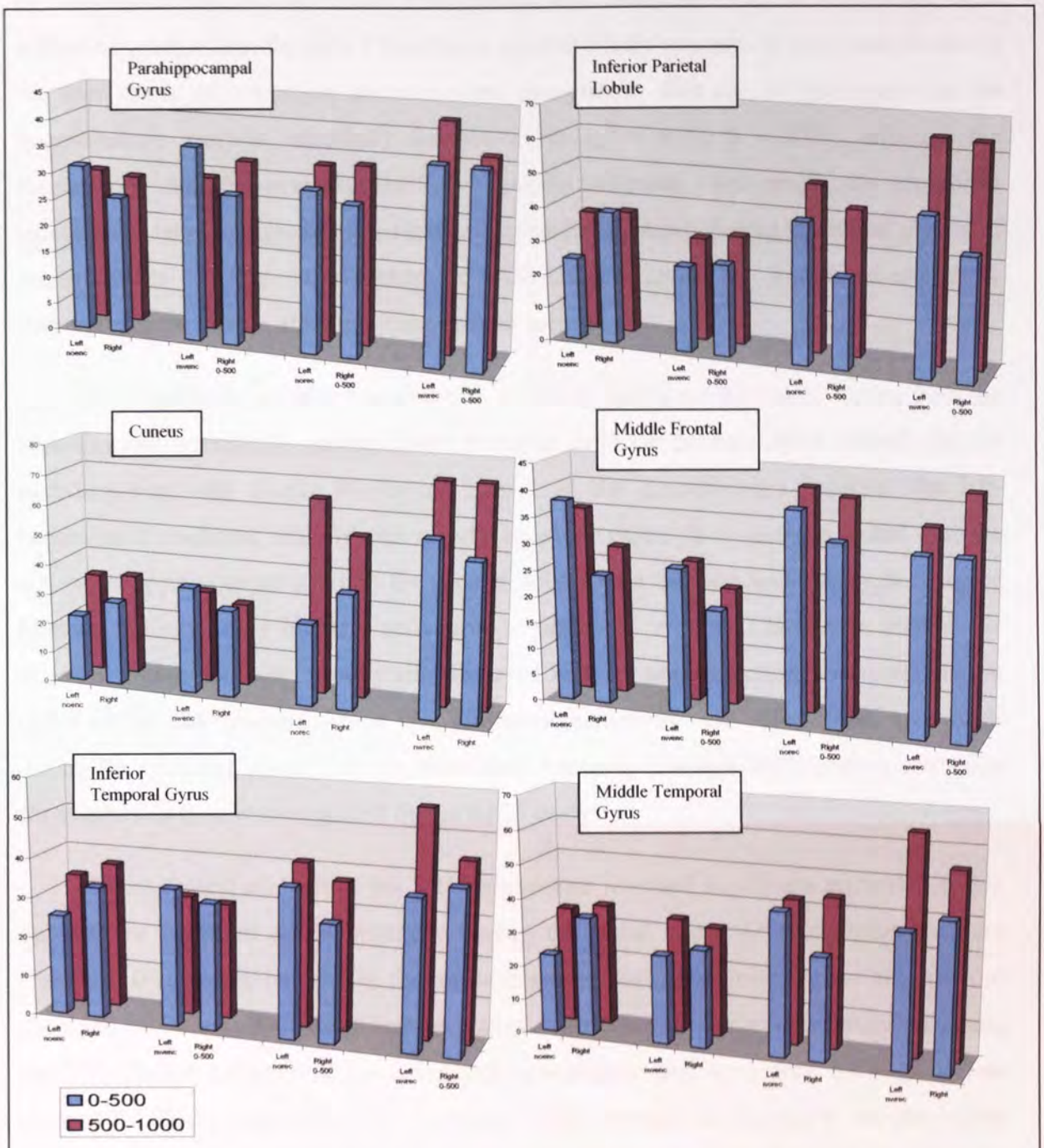


Figure 8.8: Quantification analysis for regions of interest. Percentage of activated voxels is plotted for non-objects and non-words during encoding (noenc and nwenc, respectively) and non-objects and non-words during recognition (norec, nwrec, respectively). Activation is illustrated for the left and right hemispheres in the two 500ms time windows.

The cuneus showed significant activation only during the recognition phase, specifically bilaterally in the latter stages. In the quantification analysis, there was little evidence of significant activation within the cuneus during the encoding phase, and the no-significant chi-square analysis supported this. There did appear to be bilateral activation during the recognition phase for both non-objects and non-words, although the recognition

of non-objects revealed significant hemispheric asymmetry ($\chi^2 = 4.5$, $p < 0.05$ with right activation greater than the left). The inferior parietal lobule was seen to only be activated in the later stages of non-object and non-word recognition. This can be clearly seen in the quantification analysis, especially for non-words ($\chi^2 = 6.25$, $p < 0.02$), although the activation is more bilateral than the SAM analysis indicated. Furthermore, for non-object recognition, there is a greater left-right hemispheric difference during the initial phases of recognition ($\chi^2 = 9.0$, $p < 0.01$) when the SAM failed to reveal any significant activation, than in the later 500ms, although it can still be seen.

One region, the middle frontal gyrus, revealed significant activation during both the encoding and recognition phases. It was however, only for the non-object stimuli, and for encoding was only during the initial 500ms. In the quantification analysis, the left-hemispheric encoding activity can clearly be seen, although it must be noted that the activation appears to persist into the second 500ms, and that the SAM analysis revealed bilateral activity. This bilateral activation is supported through Chi-Square analysis in which no hemispheric asymmetry was observed with the non-objects or non-words during either of the task phases. There was greater activation for non-objects than non-words during the encoding phase over the entire time window, although there is more activation for non-words than was suggested by the SAM analysis.

The statistical analysis of the SAM activations revealed significant activation within the inferior temporal gyrus primarily during the latter stages of recognition memory (bilateral, 0-1000ms), but also in the left hemisphere during the initial phase of non-word encoding (0-500ms). The quantification analysis demonstrates the greater activation during the 500-1000ms recognition phase for both non-objects and non-words, although is less obvious for the non-objects and is not greater within the right hemisphere as indicated from the SAM analysis. Furthermore, only significant asymmetry was observed for the non-words ($\chi^2 = 4.0$, $p < 0.05$).

The middle temporal gyrus revealed activation within the encoding for non-words only and for both stimulus modalities during recognition. From the quantification analysis, only non-word recognition (500-1000ms) showed significantly increased activations, and just a trend towards significant hemispheric asymmetry ($\chi^2 = 3.125$, $p = 0.1$) although it is evident that there is increased activation for recognition compared to encoding.

8.5 Discussion

A MEG study was conducted which involved the encoding and recognition of non-objects and non-words. Through the use of stimuli for which no semantic associations were readily available, it was anticipated that any semantic network which might otherwise be involved in the recognition memory process would be eliminated. It was proposed that this would enable the neural correlates of recognition memory to be identified, and determine whether there are any hemispheric differences between modalities, or between recognition and encoding tasks.

Analysis was performed using standard EEG frequencies. Activation was primarily observed within the alpha (8-13Hz) and beta (14-20Hz) frequency bandwidths, with some activations observed in a combined theta-alpha bandwidth (3-13Hz) and also in a more general (0-40Hz) broad band. No theta-specific activations were observed during either the encoding or recognition phases.

Theta synchronisation has been linked to working memory processes (Klimesch et al, 1997), so it is surprising that it is absent here. It might be, however, that this theta synchronisation is specifically linked to some part of the working memory system and not to it as a whole. For example, the necessity for a phonological component within a memory model has been demonstrated numerous times, particularly through the use of semantic paradigms (e.g. Baddeley, 1966; Kintsch and Buschke, 1969). As much as possible, all semantic components were omitted from this task, so it could be that the theta synchronisation often observed stems from parts of the working memory model, such as the phonological loop, and therefore in the absence of such processes is not necessitated. Theta synchronisation has also been linked to the encoding of new information (Klimesch et al, 1996, 1997), so in the absence of any active encoding task it may explain why theta activations were not observed.

The alpha and beta activations are consistent with previous findings from EEG literature which report alpha desynchronisation during recognition memory processes (Klimesch et al, 1997). A considerable amount of activation was observed in the broad 0-40Hz band. This might reflect one of two things: it could be gamma activity, which occurs at over 30 cycles per second; or it could simply account for any activity that was not consistent within one of the predefined frequency bandwidths for the entire time window. As time windows of 500ms were used, it is likely that the latter scenario is a more valid

explanation since the most effective frequency band is dependent upon the time window and vice versa.

It has also been suggested that synchronisation and desynchronisation may sometimes reflect task difficulty (Klimesch et al, 1999), with synchronisation often being observed when tasks require very little neural processing. Perhaps therefore, the absence of any semantic associations in this study resulted in an increase in task difficulty. Indeed, recognition accuracy scores, whilst not significantly different from previous studies, were lower than in the previous MEG studies (chapters 5 and 7). Recognition performance, however, was still significantly greater than chance responding.

For the regions that showed significant activations, it can be seen that fewer regions were active during the shallow encoding task than for the recognition task, which given task complexity was expected. All non-object encoding occurred within the first 500ms time window, while for non-words several regions were activated between 500 and 1000ms. This difference in processing time may reflect on the nature of the stimuli. The non-objects were completely unrecognisable so the spatial location task could begin as soon as the non-object had been seen. For the non-words, however, they were not just letter strings, but were actually pronounceable non-words. Upon presentation it is likely that the participants performed two tasks, completion of the spatial location task itself and an additional process involved in reading, decoding or verbalising the presented non-word. This additional process might account for some of the differences in the location and latency of cortical activity.

Regions of the temporal lobe, specifically the middle temporal lobe, have consistently been shown to be activated in both the encoding and recognition phases of recognition memory (Tendolkar et al, 2000). Both the SAM and quantification analysis substantiate this. SAM revealed middle temporal activation within the encoding for non-words only and for both stimulus modalities during recognition. The quantification analysis suggests that it is probably bilateral regions of this structure that are involved in encoding and recognition, with additional processing being completed in other nearby temporal regions such as the superior and inferior temporal gyri and the parahippocampal gyri. Furthermore, the fact that it is only a relatively small percentage of the regions that are involved may suggest why there is a lack of consistency in the neuroimaging literature.

It may be that the parahippocampal gyrus oscillates at a specific frequency within a specific time window, which was not identified during the SAM analysis. Interestingly, the

left hippocampus itself, a deeper structure within the parahippocampal gyrus did show significant activation during the recognition phase, although only for the recognition of non-words and in the later 500ms time window.

Other regions, such as the inferior parietal lobule and cuneus were only activated during the recognition phases and predominantly in the final 500ms. This suggests that these regions might be specifically involved in the recognition memory process itself, although its activation at the latter stages of the task could be related to attentional processes, such as waiting for the respond cue to appear.

	Encoding								Recognition							
	0-500ms				500-1000ms				0-500ms				500-1000ms			
	Objects		Words		Objects		Words		Objects		Words		Objects		Words	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
Amygdala				L												
Anterior Cingulate	L								L							
Cerebellum	B	L	L	L	B			R		R	R		L	R	R	B
Cingulate Gyrus													L			
Cuneus							B		L			R	R	B		B
Fusiform gyrus			L	L			L	R		R				R		L
hippocampus											R					
Inferior Frontal Gyrus	R	R	B		L		B		B							
Inferior Occipital Gyrus	R						B					R	L			
Inferior parietal lobule			R						B					L		L
Inferior Temporal Gyrus	L			L			L		L					R	R	B
Insula								L					L			L
Limbic lobe			L		R				L							
lingual gyrus								R		B		R		L	R	L
Medial Frontal Gyrus	R		R		R				L							
Middle Frontal Gyrus	B	B	B		L				B	L				L		
Middle Occipital Gyrus					L		L						L	L	R	L
Middle Temporal Gyrus	L			B			B	R		L		L		R	R	B
Paracentral Lobule																R
Parahippocampal Gyrus		L		L				R			R					L
Postcentral Gyrus		L										R				R
Posterior Cingulate	L		L						R							
Precentral Gyrus	B	L	L				R		L					L	R	R
Precuneus					R		R	L				L		B		B
Superior Frontal Gyrus			R		R		R		B				R			L
Superior Occipital Gyrus																L
Superior parietal lobule				R			R		L			R		R		B
Superior Temporal Gyrus	B							L	R		R		R	R		L
Supramarginal gyrus				L												R
Thalamus				L	R											

Table 8.13 Significantly activated regions in the current study (B – non-objects and non-words) and those for the previous MEG study (A – objects and words). I.e. A comparison between objects vs. non-objects and words vs. non-words.

It is easy to see why hemispheric differences between task (encoding and recognition) and modality (objects, words, faces etc) have often been reported in the literature. Within this study there is some evidence to suggest that there is greater left hemispheric activation during encoding and right during recognition. Significant activation within the cerebellum, for example, follows this pattern, but the quantification analysis indicated that the activations are more bilateral, with only a small number of chi-square analyses revealing significant hemispheric asymmetry. Furthermore, small differences were observed between the two 500ms time windows. Similarly, if the time windows are ignored, other regions show left lateralised activation for non-words, and right lateralised for non-objects. For example, in this study the fusiform gyrus showed this during the recognition phase, but not for the recognition phase.

Whilst the findings of the research which has suggested these modality-specific (McDermott, Buckner, Peterson, Kelley and Sanders, 1999a; Lee, Robbins, Pickard and Owen, 2000) or task-specific (Dolan and Fletcher, 1997; Fletcher et al., 1997; Nyberg, Cabeza and Tulving, 1996; Tulving, Kapur, Craik, Moscovitch and Houle, 1994) hypotheses are not disputed, it is unlikely that either hypothesis is in fact true. There are so many variables in the studies reported (e.g. differences in imaging technique, analysis methods, analysis comparisons etc), that even when as many variables are controlled as possible, as in this study, it is not possible to find convincing support for either hypothesis.

Table 8.13 illustrates the significantly activated areas in the current study (study B) and for those in the previous MEG study (study A) which involved object and word recognition memory following a shallow encoding task. Even from these two almost identical studies there are still a considerable number of diversely activated cortical regions. It is not possible to identify those which are uniquely involved in encoding and those that are uniquely involved in recognition, nor those unique to objects or words. There are regions which appear to perform a more active role in some tasks (e.g. inferior frontal gyrus in encoding, lingual gyrus in recognition), but it is not exclusive and cannot be used as conclusive evidence of unique involvement in specific processes.

8.6 Concluding Remarks

A MEG study was conducted which involved the encoding and recognition of non-objects and non-words. It was hypothesised that using random shapes (non-objects) and non-words was an appropriate way of removing semantic associations from encoding and recognition phases, and that this would reduce the amount of cortical activation observed in previous studies (chapters 5 and 7). For the regions that showed significant activations, it can be seen that fewer regions were active during the shallow encoding task than for the recognition task, which given task complexity was expected. Furthermore, activations during the recognition phases were less widespread than previous studies had reported, suggesting that the study was successful in removing semantic associations from the encoding and recognition phases.

It was anticipated that removal of this semantic network may enable the true neural correlates of recognition memory to be identified, and to determine whether there are indeed any hemispheric differences between modalities or between recognition and encoding tasks. Although several occasions of hemispheric asymmetry were reported, the data as a whole suggests that activation is more bilateral than suggested by either the task- or modality-specific hypotheses. It may be that task complexity, the involvement of semantic associations and individual variability are some of the main factors in producing the hemispheric asymmetry often reported in the neuroimaging literature.

There is sufficient evidence from these studies and those in the previous literature to identify regions of the cortex that are involved in recognition memory processes, such as the prefrontal cortex and middle temporal lobe. Furthermore, the data suggests that activation should be assumed to be bilateral and that any asymmetry may be due to other non task- or modality-specific variables. Therefore, instead of trying to allocate each hemisphere or region a unique role in recognition memory, perhaps what is now needed is more in-depth region of interest analysis which can be used to identify the specific qualities of each of these structures, such as oscillatory frequency and temporal resolution. Such information will enable more detailed understanding of each of these structures which can in turn be used to determine their precise role in recognition memory processes.

9 CONCLUSIONS

9.1 Aims of Research

There has been much research into memory and its neural correlates. Through the use of neuroimaging techniques it is possible to identify some of the regions associated with recognition memory. The neuroimaging literature has consistently identified several regions involved in encoding and recognition memory processes (e.g. Cabeza & Nyberg, 1997, Fletcher et al, 1997; Schacter & Wagner, 1999; Rugg et al, 1996; Fletcher, Frith, Grasby et al, 1995; Markowitsch, 1997). These include the prefrontal cortex and medial temporal lobe in particular. The extent to which each of these is activated appears to be quite dependent upon the task or procedure involved (refer to table 1.1). Differences have been recorded between encoding and retrieval procedures and also as a function of the accuracy of recall, with greater activation shown for correctly recalled items (Fletcher et al, 1997, 1995; Buckner et al, 1998).

One of the main differences between studies of recognition memory is the different neuroimaging techniques used. EEG, PET and fMRI have all been used to identify the cortical regions involved. MEG is a relatively new neuroimaging technique, and it is believed that this non-invasive, real-time imaging methodology can provide more detailed information about the processes involved. The first aim of this thesis was therefore to perform several studies using the same neuroimaging technique, analysis parameters and experimental paradigms, thus producing reliable and replicated data about recognition memory. This is important for MEG research as to date there are only two MEG studies of recognition memory in the literature (Tendolkar et al, 2000; Duzel et al, 2003), and as such the use of MEG as a suitable technique to study higher order cognitive tasks, such as recognition memory, needed to be investigated further. In addition, SAM analysis has been developed as an analysis tool for MEG data, and a direct comparison between this methodology and that of the frequently used dipole fitting technique was first needed to determine its suitability for use with cognitive data.

Previous research has shown that prefrontal and medial temporal structures are significantly activated during the encoding and recognition phases and many have also reported that additional cortical areas are involved in memory processing. There has also been a considerable debate in the literature concerned with whether there is hemispheric

asymmetry in recognition memory. There are two main hypotheses: the first suggesting hemispheric specialisation is a task specific effect (Tulving, Kapur, Craik, et al, 1994; Dolan & Fletcher, 1997; Fletcher et al, 1997; Nyberg, Cabeza & Tulving, 1996); the second that this specificity is determined by stimulus modality (McDermott, Buckner, et al, 1999; Lee, et al, 2000). The research on this, however, was unclear and lacked a significant amount of consistency and reliability across studies. Table 1.1 highlighted the widespread activation reported in the literature and it is suggested that this variability may be due to factors such as differences in the neuroimaging technique, analysis procedures, the specific tasks and stimuli used.

A series of experiments was therefore completed with two main aims: to determine whether there is evidence of any hemispheric specialisation for recognition memory; and to produce consistent and complementary recognition memory data with MEG. Specifically, conducting studies which involved encoding and recognition of objects and words enabled assessment of the 'task-specific' and 'modality-specific' hypotheses of hemispheric specialisation in prefrontal regions during recognition memory tasks. It was predicted that if the 'task-specific' hypothesis was true, objects and words would both activate the left and the right PFC during encoding and recognition, respectively. In contrast, if the 'modality-specific' hypothesis was accurate words would activate the left PFC during both encoding and recognition, whereas objects would produce activation within the right hemisphere for both tasks.

Within this series of experiments, one other issue was identified, that of the possible existence of a semantic network within the recognition memory process. A further series of experiments was designed to determine whether such a network exists and whether it is possible to eliminate such processing from recognition memory tasks. Through this, it was then hypothesised that the neural correlates necessary for recognition memory could be identified.

9.2 Research Findings

9.2.1 Use of MEG and SAM for Higher Order Cognitive Tasks

9.2.1.1 Analysis Tools

Many electromagnetic studies use various dipole fitting methods as a method of localising sources of activation, one of the most popular being the equivalent current dipole model (ECD). With this technique, however, many *a priori* assumptions are necessary and whilst it has proven to be very successful in localising visual and somatosensory cortical activity, only a few studies have used MEG and the ECD model to investigate memory processing. A relatively new technique, Synthetic Aperture Magnetometry (SAM), has been developed as a method to overcome these inherent problems and offers a novel way of analysing cognitive neural activation. To date, however, no study had directly compared the effectiveness of the two techniques for analysing recognition memory processes.

The first aim of this thesis was to identify the best tool for analysing MEG data from a recognition memory experiment. In chapter 4, the same data was analysed using the traditional MEG dipole fit tool and with SAM. The results suggested that because higher order cognitive tasks, such as recognition memory, generally do not elicit a strong evoked-type response, dipole fit is not the most appropriate analysis tool.

Dipoles were fitted for nine peaks across the recognition memory data. Stability of these dipole sources was assessed in a number of ways. Firstly, for each peak, the dipole was placed at different starting locations for five consecutive fits, and the end dipole location (co-ordinates) of each fit recorded. All peaks produced stable dipoles, with the same location being recorded for each on at least three of the five fits. χ^2 error volumes were generated for each of the dipoles, and for all dipoles an ideal value was obtained. Initially, therefore, dipole fitting appeared to have reliably identified cortical regions involved in recognition memory processes.

One final analysis, however, using Monte-Carlo (MC) volumes, tested this stability further and the results indicated that only some of the dipoles identified were reliable sources of activation. MC analysis generates an error volume, within which a reliable stable dipole solution can be found. Very small volumes do not permit much variation in the dipole source location and thus the MC volume can be used as a measure of solution

stability. For four of the peaks the MC volume indicated that stable dipole locations had been identified. These corresponded to early task processing, which was believed to indicate initial visual processing of the presented stimuli, and to processing occurring at the end of the task, hypothesised to be associated with the production of a response. For the remaining peaks, which were believed to correspond to the cognitive memory processes, very large MC volumes were obtained. This suggested that the dipole solutions identified were not necessarily accurate neural sources of memory processing. It was concluded, therefore, that for evoked-type responses, dipole fitting is a reliable method of identifying neuronal sources, but for cognitive processes results are less accurate, suggesting that a different method of analysis might need to be implemented.

This different method was hypothesised to be SAM as it offers a way of identifying multiple activated cortical regions on a millisecond time-scale. This is essential for the development of our understanding of recognition memory processes, with the ultimate aim of determining a cortical network for this complex process. The large number of SAM peaks identified, which extended over different regions of the cortex, suggested that because of the complexity of the task, the activity is widespread. Consequently, a successful dipole fit analysis would have to enable a large number of overlapping dipoles to be located. SAM provides an alternative way of identifying closely located and temporally overlapping sources. Multiple, closely located regions can be identified on a millisecond time-scale. Although the strength of the peaks varies, some not reaching significance, a large number of peaks with pseudo-t values greater than 1.5 were identified and could be analysed further.

One point to note is the usefulness of determining the temporal dynamics of the SAM activations. They are able to show the activation of the specific cortical region, as identified from the co-ordinates, in any time window and frequency band. This is a clear advantage of SAM, compared to dipole fitting, as the pattern of activation of any one area can be mapped over time. It is possible to see the temporal resolution of this activation as it 'switches' on and off and determine the length of activation over time. This may enable more detailed cortical networks to be identified, which would be especially useful in cognitive paradigms.

9.2.2 MEG and Recognition Memory

The main aims of these studies were: (1) to demonstrate the use of MEG as a tool for studying higher-order cognitive tasks, such as recognition memory, and show reproducibility in the findings; (2) to extend the research on recognition memory and to assess the 'task-specific' and 'modality-specific' hypotheses of hemispheric specialisation during recognition memory tasks. Within these studies, two additional concepts were also discussed. These were (3) the frequency-specific activation observed during recognition memory processes and (4) the involvement of a semantic network within studies of recognition memory.

Experiment 1 (chapter 5) investigated the neural correlates of hemispheric asymmetry in recognition memory using MEG. It involved a deep (semantic categorisation) encoding task and recognition memory processes were investigated for objects and words separately. The results indicated the necessity for the study to be replicated, to determine the reliability of the MEG data. Furthermore, the presence of a semantic network within the memory processes was discussed. Experiment 2 (chapter 6) was designed to assess this semantic activation. The activations of living and non-living stimuli were compared during encoding and recognition to determine whether there is category-specificity in recognition memory. These results are discussed in detail in section 9.2.2.4.

A replication of the first experiment was performed in Experiment 3 (chapter 7, part a) to determine the replicability of MEG recognition memory data. Experimental parameters were kept constant with the exception of the involvement of a shallow encoding task, implemented to remove the influence of semantic associations in the encoding and recognition phases. Objects and words were investigated separately, but recorded. For the direct comparison with Experiment 1, initial analysis of activated regions was performed within 10Hz frequency bandwidths. Results from the first two studies suggested the importance of frequency-specific activation in recognition memory. Consequently, the SAM data from the third experiment were re-analysed using EEG-defined frequency bandwidths. This study, hereafter referred to as Experiment 4 (chapter 7, part b), enabled more accurate comparisons to be made with the previous EEG literature. In a replication of Experiment 3, Experiment 5 (detailed in chapter 8) involved a recognition memory task of non-objects and words. Use of such stimuli was designed to eliminate the presence semantic associations within memory processes. Furthermore,

analysis using EEG-defined frequency bands enabled a direct comparison to be made with the results form the Experiment 4. Table 9.1 summarises the significantly activated regions during encoding and recognition processes across four of the experiments, (1, 3, 4 and 5) for both object and word stimuli.

9.2.2.1 Reliability of MEG for Studying Recognition Memory

Many of the previous functional imaging studies that use MEG primarily focused on sensory (Barnes et al, 2001), motor (Taniguchi et al, 2000) and language (Singh et al, 2002) tasks. The majority of published neuroimaging recognition memory experiments utilise techniques such as PET and fMRI and to date there are only two other published MEG studies of recognition memory (Tendolkar et al, 2000; Duzel et al, 2003). Despite the large number of published studies, a review of some of the most recent neuroimaging literature associated with recognition memory suggested that there is not a significant amount of consistency between the studies (Table 1.1).

Consequently, one of the main aims of this study was to determine the reliability and replicability of MEG recognition memory results. Thus a series of recognition memory experiments were conducted in which the experimental protocol remained relatively consistent across all studies. As can be seen in Table 9.1, there is a reasonable amount of consistency in terms of significant regions of activation observed. A number were consistently activated for the same stimulus modality, i.e. for objects or words, and in the same time window in all four experimental analyses. For the initial encoding of objects these were the inferior frontal gyrus and the precentral gyrus. This is consistent with previous literature, which has shown the PFC to be involved in episodic encoding (Kapur, Craik et al, 1994; Fletcher, Frith, Grasby et al, 1995; McDermott, Buckner et al, 1999); and with the lateralised activation reported in the left and right hemispheres for visual (Fletcher, Frith, Grasby et al, 1995) and verbal (McDermott, Buckner et al, 1999) encoding respectively. In the MEG studies, however, the hemisphere activated within these regions was not consistent. The quantification analyses performed for Experiments 3 and 4 revealed predominantly bilateral activation within the prefrontal lobes and may suggest that the semantic nature of the visually presented stimuli initiated both visual and verbal encoding strategies, and thus bilateral activation was observed. Furthermore, it may be that because SAM enables the temporal dynamics of processing to be investigated in more

detail, activations during recognition memory are bilateral in nature and are simply not revealed by the other techniques with less detailed temporal resolution.

The middle frontal gyrus was seen to be activated during the initial recognition process for objects. Several studies have reported activation within prefrontal structures (Cabeza & Nyberg, 1997; Buckner, 1996; Fletcher, Frith, Grasby et al, 1995). These studies suggested greater activation within the right hemisphere, whereas in the current MEG studies, activation was predominantly bilateral. As with encoding, it is suggested that this bilateral activation is accounted for by the nature of the stimuli and tasks. Cabeza et al (1997) and Nolde et al (1998) reported that various frontal regions were differentially activated by item and source memory processes. In the MEG study, there was no control over the processes used by the participants to facilitate recognition, and thus both item and source components may have been utilised.

A larger number of regions were shown to be activated in 75% of the MEG experiments. In the encoding phase, these were the middle frontal and temporal gyri during the initial 500ms for objects and the precuneus during the later 500ms for words. Activation of middle frontal and temporal regions during encoding has been reported by several previous studies (Kapur, Craik et al, (1994) and Montaldi et al, (1998) for frontal and temporal regions respectively). Squire and Kandel (1999) have suggested that during encoding, the role of the PFC is to co-ordinate sensory and contextual information. This is particularly relevant to this study, which involved visually presented stimuli with semantic associations.

The involvement of the precuneus in episodic encoding further demonstrates the reliability of MEG neuroimaging data and the consistency with other published studies. For example, Fletcher, Frith, Baker et al (1995) detailed the involvement of this region in encoding processes and its role has been linked to the encoding to the associations between encoded stimuli and their semantic representations (Mayes & Roberts, 2001). As such, its activation in a task involving semantic categorisation, such as that seen in the experiments reported in chapters 5 and 6, is fully supported.

Activation of the MTL during the recognition of objects and words is consistent with previous neuroimaging literature (Fletcher et al, 1997; Buckner et al, 1998). Importantly, a previous MEG study also reported activation of this region during recognition (Tendolkar et al, 2000). Superior parietal and occipital lobe activations observed in these MEG studies are believed to reflect attentional and visual processes respectively. The cerebellum has

also been implicated in recognition memory processes (Buckner, 1996; Bucker et al, 1998). Parahippocampal gyrus activation was also observed in these MEG studies. It has been suggested that it is this and other MTL regions which generate the familiarity feeling for recognised stimuli (Milner, 1999). Activation of this structure suggests that there may indeed be a dual-process of recognition (such as that suggested by Mandler, 1980), one involving familiarity, co-ordinated in the MTL regions, and the other in specific recognition processes, possibly controlled by PFC activation.

A significant number of other regions were activated in at least two of the studies, suggesting that MEG can provide replicable data associated with recognition processes. However, there is evidence of involvement of other variables as consistency was not seen across all studies. Although the studies were designed so that that many of the same experimental parameters were maintained, some of the differences in the activations may be accounted for by the differences in the experimental protocols. In particular Experiment 1 utilised a different encoding task and deeper encoding processing may activate other regions than those involved following shallow processing. For example, the cingulate gyrus was activated during the deep encoding task in Experiment 1, but was absence from encoding-related activation for the subsequent studies involving shallow encoding. Experiments 4 and 5 were analysed using standard EEG frequencies, compared to arbitrary 10Hz bandwidths, which may account for some of the differences (this frequency-specific activation is further discussed in section 9.2.2.3). Finally, Experiment 5 involved non-objects and non-words, stimuli which were used in an attempt to eliminate the involvement of any semantic processing during the recognition memory processes.

9.2.2.2 Hemispheric Differences in Recognition Memory

One of the major debates currently being investigated through neuroimaging studies is the role of the left and right hemispheres during encoding and recognition memory tasks for verbal and non-verbal stimuli. Tulving et al (1994) developed the Hemispheric Encoding / Retrieval Asymmetry (HERA) model to account for observations of prefrontal activation seen in PET studies. This model suggested that the left prefrontal regions were specialised for encoding, the right for retrieval processes. All of these PET studies (for example, Kapur et al, 1994; Petersen et al, 1988, 1990; Frith et al, 1991; Buckner et al, 1993; Tulving et al, 1994; Squire et al, 1992) involved the use of words as stimuli and consequently later studies utilised other stimulus modalities. These suggested that the HERA model might not necessarily be an accurate account of activation patterns.

	Encoding																Recognition													
	0-500ms								500-1000ms								0-500ms								500-1000ms					
	Objects				Words				Objects				Words				Objects				Words				Objects				Words			
	1	3	4	5	1	3	4	5	1	3	4	5	1	3	4	5	1	3	4	5	1	3	4	5	1	3	4	5	1	3	4	5
Amygdala						L		L																								
Anterior Cingulate			L			R													L													
Cerebellum	B		B	L			L	L	L		B					R	L			R	R	R	R				L	R		R	R	B
Cingulate Gyrus	R								R								R										L	R				
Cuneus					R										B		L		L					R			R	B				B
Fusiform Gyrus							L	L	R						L	R				R	R											L
Hippocampus																						R	R				L					
Inferior Frontal Gyrus	B	B	R	R			B		R		L				B		R	L	B						L			L				
Inferior Occipital Gyrus		R	R						L						B									R			L	B	R	B	L	
Inferior Parietal Lobule	R				R		R									L			B		L				L							
Inferior Temporal Gyrus			L					L							L				L													
Insula	R																															
Limbic Lobe							L				R						L		L													
Lingual Gyrus	B																															
Medial Frontal Gyrus			R			R	R		R		R			L				L	L													
Middle Frontal Gyrus		L	B	B			B		B		L						R	L	B	L	L											
Middle Occipital Gyrus	R				R						L		L	L			R				R											
Middle Temporal Gyrus	R	L	L			B		B							B	R	L	L		L												
Paracentral Lobule				L		L		L								R					R	R	R									
Parahippocampal Gyrus				L																												
Postcentral Gyrus			L				L		L										R													
Posterior Cingulate			B	L			L		R						R		R	L														
Precentral Gyrus	L	R				R					R			L	B	L	B															
Precuneus							R		L		R								B													
Superior Frontal Gyrus																																
Superior Occipital Gyrus								R																								
Superior Parietal Lobule	L	B																														
Superior Temporal Gyrus	R		B																													
Supramarginal Gyrus					R				R																							
Thalamus																																

Table 9.1 Summary of the statistically significant ($p < 0.1$) cortical regions in four recognition memory studies. L = left lateralised activation, R = Right lateralised activation. B = Bilateral activation.

Some recent studies support the HERA model suggesting that the left and right hemispheres are specialised for encoding and retrieval, respectively (Dolan & Fletcher, 1997; Fletcher et al, 1997; Nyberg Cabeza & Tulving, 1996; Tulving et al, 1994). This is referred to as the 'task-specific' hypothesis. Even with a recent revision, however (Habib et al, 2003), its ability to fully account for the activations reported in the literature is questioned (Owen, 2003). In contrast, other recent studies have suggested that the left and right hemispheres are specialised for verbal and visual material, respectively; the 'modality-specific' hypothesis (McDermott et al, 1999a; Lee et al, 2000).

This series of MEG studies aimed to test both the 'task-specific' and 'modality-specific' hypotheses through comparisons of encoding versus recognition for both objects and words. A number of studies have observed bilateral prefrontal activation during episodic memory retrieval (Kohler et al, 2000); McDermott et al, 1999a) whilst many report right lateralised dominance (Grady, McIntosh, Beig and Craik, 2001; Buckner, Koustaal, Schacter, Wagner and Rosen, 1998; Cabeza & Nyberg, 1997). The results from these studies were more consistent with those identifying bilateral prefrontal involvement in recognition memory.

It was predicted that if the left and right hemispheres were differentially activated by the encoding and recognition phases respectively, regardless of stimulus modality, this would be evidence to support the 'task-specific' hypothesis. For words there is some evidence to support this hypothesis. In at least two of the studies, left lateralised activations were seen during the encoding phase in the amygdala, cerebellum, fusiform gyrus, parahippocampal gyrus and middle occipital gyrus, and right lateralised activations during the recognition phase within the cerebellum, hippocampus, parahippocampal gyrus, superior parietal lobule and supramarginal gyrus. For objects only the right lateralised activation in the superior temporal gyrus during recognition is consistent with the task-specific hypothesis. None of these activations however, were in the prefrontal cortex. Furthermore, if the prefrontal regions are considered separately, for both objects and words during encoding and recognition, observations across the studies indicate bilateral activation. The only hemispheric lateralised frontal activations were seen in the right medial frontal gyrus for both modalities during encoding, and in the left medial and middle frontal gyri for object recognition. This lateralised activity is in fact the complete opposite to what would be predicted by the task-specific hypothesis. It would therefore seem that there is not sufficient evidence to support this task-specific hypothesis or the HERA model.

The 'modality-specific' hypothesis predicts that regardless of task, the left hemisphere should show more ERD for words and the right hemisphere for objects. As described above, some left-lateralised activity was seen during word encoding, although none of this activation was in prefrontal regions. Furthermore, during word recognition there was no consistent left-lateralised activity in any region. Activations for object encoding and recognition offer little support for the modality-specific hypothesis with only right-lateralised activations seen in inferior occipital gyrus and medial frontal gyrus during encoding and in the superior temporal gyrus during recognition. Furthermore, a number of regions showed left-lateralised activations during object recognition, including regions in the prefrontal cortex, specifically, the medial and middle frontal gyri.

Considering the different studies separately, it is possible to see how evidence for both hypotheses can be gained. The lack of consistency, however, suggests that it may be other factors within the tasks that have led previous research to inaccurately propose such hypotheses. A number of studies identify the involvement of the left PFC in semantic memory retrieval tasks (Kapur, Rose et al, 1994; Buckner, Raichle & Petersen, 1995). The concept of a semantic network may explain the widespread activation, and more specifically the large number of cortical areas similarly activated, across different modalities in published neuroimaging studies of recognition memory and in the studies detailed here. This may be particularly pertinent to these studies, as the discrete cortical areas reported tended to be sub-regions of larger clusters of activation, which were observed extending over multiple cortical regions. Furthermore, although many previous studies focus their attention on single areas within prefrontal and medial temporal regions, other diverse activations are often present. Therefore, areas identified may not be explicitly associated with encoding or recognition, but may reflect more general demands on semantics. It is suggested, therefore, that is the presence of semantics during these published recognition memory studies that confounds the hemispheric asymmetry data.

It is feasible that in studies illustrating lateralised activity that these may in fact be evidence of semantic processing and not necessarily specific to the recognition memory processes. Indeed, these studies have indicated that semantic processes are often involved during a recognition memory task and this is discussed further in section 9.2.2.4.

Pure verbal and non-verbal stimuli, such as non-words and non-objects, were used to provide a more accurate account of hemispheric asymmetry on recognition memory

(Experiment 4). This study also failed to demonstrate support for either the task- or modality-specific hypotheses, providing evidence that activation is predominantly bilateral.

In conclusion, it is suggested that recognition memory produces predominantly bilateral activation of cortical regions and that any lateralised activations are due to other factors. These may be individual variation across the participants, activations produced by other processes such as attention, or it may be that some regions were oscillating bilaterally but that only one hemisphere showed it at a magnitude or frequency which was significant, the other hemispheres not identified as it failed to reach significance. It may be that these bilateral activations are closely related to retrieval effort and retrieval success processes (Rugg et al, 1996; Buckner et al, 1998). Differences between the studies in the specific site and hemisphere of activation may reflect the varying the levels of effort and success within the processing system. Furthermore, it may be that the possibility of tracking the temporal dynamics with SAM has identified this bilateral activation which was hitherto not picked up by techniques with less detailed temporal resolution.

9.2.2.3 Frequency and Temporal-Specific Activation

In MEG research, SAM analysis provides one way of investigating the location of internal sources of externally recorded activation. When using SAM, activations are analysed across pre-defined frequency bands. In the first MEG study, comparisons were made using arbitrary 10Hz frequency bands. Although some degree of consistency was seen between the first and second studies using these 10Hz bandwidths, it was believed that as the frequency bands did not exclusively correspond specifically to the theta, alpha or beta bands, but spread across them (e.g., 5-15 Hz), some frequency-specific activations may have been missed.

Previous EEG studies have shown that during memory processes, cortical synchronisation is evident in the narrow theta frequency band (4-7 Hz) (Klimesch, Doppelmayr, Schimke & Ripper, 1997) and desynchronisation within the alpha (8-12 Hz) range (Klimesch, Doppelmayr, Pachinger & Russegger, 1997). Upper alpha desynchronisation (10-12 Hz) has been reported to be linked to semantic memory processing (Klimesch, Doppelmayr, Pachinger & Russegger, 1997) while synchronisation within the theta band (4-7 Hz) is linked to working memory (Klimesch, Schimke & Schwaiger, 1994) and the encoding of new information (Klimesch, Doppelmayr,

Russegger & Pachinger, 1996; Klimesch, Doppelmayr, Schimke & Ripper, 1997; Burgess & Gruzelier, 2000).

It is possible that because the 5-15 Hz band used in the first study predominantly included alpha waves (8-12 Hz), with much smaller amounts of theta (5-7 Hz), any potential ERS could not be measured and consequently only ERD within the alpha was seen in the SAM images. Consequently, the analysis of the second MEG study involved both the arbitrary 10Hz frequency band used previously (Experiment 2), and also standard EEG frequencies (Experiment 3). Comparisons of the regions activated within these frequency bands were completed to help in determining the most useful bandwidths in memory research and to enable more realistic comparisons with previous neuroimaging research.

The results from the two analyses indicated that a number of different regions were statistically significant by both frequency analyses. It would therefore seem that the frequency bandwidth selected for analysis is an important consideration. A number of regions were revealed as being activated during encoding and / or recognition by both frequency analyses and it may be that in these regions the activity occurs over several frequency bandwidths. Importantly these were in regions previously reported as being involved in recognition memory processes, such as the left middle temporal gyrus and regions within the prefrontal cortex.

This consistency between the 10Hz and EEG frequency bandwidths is encouraging as it suggested that the findings from the previous MEG study those from this study can be reliably compared to those from previous EEG studies. For example, it has been suggested that alpha activity may relate to inhibitory networks (Klimesch et al, 2000) and / or changes in attention (Cooper et al, 2002), and thus the widespread activation seen in these recognition memory studies may indeed show this additional activity. Nevertheless, the EEG – 10Hz comparison suggests that, it might be more pertinent to use the EEG bandwidths in future studies, to ensure that no activation is omitted, particularly in later time windows.

In Experiment 1, it was suggested that the absence of synchronous activation might be due to the wide frequency bands which were not alpha or theta specific. The importance of narrow frequency bands was demonstrated in a study by Krause et al (2000). Following a visual sequential letter task involving varying levels of memory load, the 4-6 Hz theta, 6-

8 Hz and 8-10 Hz alpha frequency bands all showed ERS, whilst in the 10-12 Hz band there was only an increase in ERD.

Although synchronous activation was observed in the EEG frequency analysis in Experiment 3, with a considerable amount of theta and alpha activation, some synchronous activation was actually observed in the 10Hz analysis. This suggests that it may not necessarily have been the absence of theta or alpha-specific frequency bands that was responsible for the absence of synchronous activity. Furthermore, in the final experiment (Experiment 4), there was no synchronous activation either, despite the analysis being conducted with the EEG bandwidths.

Theta synchronisation has been linked to working memory processes (Klimesch et al, 1997), so it is perhaps a little surprising that it was absent here (Experiment 4). However, it might be that this theta synchronisation is specifically linked to some part of the working memory system and not to it as a whole. For example, the necessity for a phonological component within a memory model has been demonstrated numerous times, particularly through the use of semantic paradigms (for examples, see Baddeley, 1966; Kintsch & Buschke, 1969). As any semantic component was omitted from the task in Experiment 4, it could be that the theta synchronisation often observed, stems from parts of the working memory model, such as the phonological loop, and therefore in the absence of such processes is not necessitated. Theta synchronisation has also been linked to the encoding of new information (Klimesch et al, 1996, 1997), so in the absence of any active encoding task perhaps it is not so surprising that theta activations were not observed. The absence of theta activation in the experiments when semantics were engaged (chapter 5) may be due to the large time windows, thus highlighting the importance of the temporal dynamics in recognition memory.

One obvious difference between these studies and those reporting theta synchronisation (Burgess & Gruzelier, 2000) is the difference in analyses. These MEG studies compared encoding and recognition, while the EEG studies conducted a new versus old comparison. It may be that this theta synchronisation is involved in the recognition process when new images are presented, and not specifically to the encoding processes of any recognition study. This idea, however, would not fully account for the inconsistent synchronous activation in earlier studies. It has been suggested that synchronisation and desynchronisation may sometimes reflect task difficulty (Klimesch et al, 1999), with synchronisation often being observed when tasks require very little neural processing. This

inhibition theory (Buckner & Tulving, 1995; Nyberg, 1999; Fletcher, Frith, Grasby et al, 1995) has been associated with the bilateral temporal cortices (Nyberg et al, 1995) and PFC (Nyberg et al, 1996), and thus may be implicated in the hemispheric asymmetry debate. Variations in activation and inhibition may be responsible for the variation in the reported literature. With reference to these studies, it could be postulated therefore, that the deep encoding task in the first study necessitated more complex neural processing to perform at the same high level of accuracy seen by all participants across the studies, and thus resulted in only desynchronous activations. In Experiments 2 and 3, only the frequency analysis differed and the fact that both produced synchronous activations when a simpler task (spatial location) with familiar stimuli was completed offers support for this. Furthermore, in Experiment 4, the absence of any semantic associations in this study may have resulted in an increase in task difficulty. Indeed, recognition accuracy scores, whilst not significantly different from previous studies, were lower than in those studies. Recognition performance, however, was still significantly greater than chance responding.

Nevertheless, the alpha and beta activations are generally consistent, with previous findings from EEG literature which report alpha desynchronisation during recognition memory processes (Klimesch et al, 1997, Burgess & Gruzelier, 2000). Quite a considerable amount of activation was also observed in the broad 0-40Hz band in the final study. This might reflect one of two things. First it could be gamma activity, which occurs at over 30 cycles per second, or it could simply account for any oscillation that was not consistently within one of the predefined frequency bandwidths for the entire time window. As time windows of 500ms were used, it is likely that the latter scenario is a more effective explanation as it is known that the most effective frequency band is dependent upon the time window and vice versa.

This in itself, however, suggests that future analyses might require varying time-window lengths to be investigated. Indeed Krause et al showed that whilst ERD was long lasting in both the 8-10 Hz (~200–1500ms post stimulus onset) and the 10-12 Hz bands (~0–1500ms), ERS was seen during much smaller time windows (~500-600ms and ~100-300ms for 4-6 HZ and 6-8Hz bands, respectively).

One final point to note is that differences were also observed in the MEG studies between the frequency bands in reference to the time course of the brain activation (i.e. differences between the first second 500ms, post-stimulus onset), leading to the suggestion that the frequency-specific memory activation reported previously (Klimesch, Vogt and

Doppelmayr, 1999) might change over the course of the task, or be linked to particular components of memory tasks.

9.2.2.4 Semantic Network and Recognition Memory

In Experiment 1, a deep encoding task was used which required participants to perform a living versus non-living categorisation task. It was suggested that the diverse activation observed may not be explicitly associated with encoding or recognition, but may reflect more general demands on semantics. A follow-up study was therefore completed in which differences between two semantic categories (living and non-living stimuli) were investigated during both encoding and recognition phases.

Similarities between episodic and semantic memory have already been highlighted (Tulving, 1995, 1972). It was probably not that surprising; therefore, that activations reported in this study indicated cortical regions, such as the inferior prefrontal cortex, might be involved in both episodic and semantic processes. Specifically, the right inferior frontal gyrus was activated by both categories during the encoding phase, possibly reflecting working memory storage processing, and the left inferior frontal cortex was activated only by the living stimuli in the recognition phase, possibly reflecting some difference in semantic processing for the two categories.

Although this research did not fully replicate the findings from other neuroimaging studies in terms of identifying cortical regions which demonstrate category-specific properties, the fact that any category-specific effect exists at all has important implications for research into recognition memory. It makes sense that there will be differences between living and non-living things when retrieving stored semantic information about them, as in the categorisation task, as they will evoke different associations. Indeed, a number of cortical regions were identified which can be supported by the literature on category-specificity.

It would not necessarily be expected, however, that the same differences would be observed in a simple yes/no recognition task. Yet, differences between living and non-living things were seen in the different cortical regions activated during the recognition memory component of the task. This substantiates the proposal that a semantic network exists which is used in other cognitive processes not explicitly designed to interrogate

semantics. Consequently, this semantic network, or at least parts of it, may be responsible for the diverse activation in the recognition memory neuroimaging literature.

To identify the specific neural correlates of recognition memory it was important to attempt to control semantics from the process. By doing this, those cortical areas which are necessary for successful recognition memory and not those non-essential regions which are additionally activated, could potentially be identified and used in clinical memory research to identify the early stages of memory impairments, such as in neurodegenerative disorders.

Experiment 3 attempted to do just this, omitting the semantic categorisation task from the encoding phase. It was believed that this would reduce the amount of semantic processing occurring during the succeeding recognition task. The results from the study were very encouraging and showed some consistency with previous research. In particular, the activation of the left middle temporal gyrus in recognition memory for objects, which is probably one of the only consistent findings in the recognition memory neuroimaging literature. (Ranganah et al, 1999) and is thought to be indicative of episodic memory retrieval (Allan et al, 1998; Paller & Kutas, 1992).

The observations of activated deep structures such as the hippocampus, was a very positive finding for MEG research. However, a number of regions were still differentially activated, and it was believed that the semantic associations which exist for familiar objects and words, whether explicitly activated or not, may have been responsible.

Consequently, Experiment 4 used non-objects (random shapes) and non-words (pronounceable non-words) as stimuli, thus potentially removing these semantic associations. In this study, some regions were differentially activated from the previous study. This alone suggests that the semantic component of the stimuli must have had an influential role in the activations reported. Nevertheless, there was still quite diverse activation, which suggests one of two things. Firstly, it is possible that the cortical representation of recognition memory does indeed utilise all of these regions and that we have illustrated those regions necessary for successful recognition memory. However, it is also plausible that even when using stimuli which are not familiar and which do not have any previous semantic associations, cortical regions are activated which are not directly involved in the recognition process. Moreover, they may reflect a language component for the non-words, produced due to the similarity of the words to true words in the English language, or for non-objects an internal description of the objects, associating it with

similar previously experience items. Nevertheless, the use of non-objects and non-words, however, would still seem to be appropriate stimuli for future studies of recognition memory.

9.3 Limitations of Research

The series of experiments presented in this thesis have yielded important information in the development of our understanding of recognition memory processes. It is however, also important to address a few of the limitations and caveats of these studies.

One issue common to most neuroimaging and experimental studies is that of statistical power. The statistical power of an experiment is determined by four criteria; the significance level used, the variability in the data, the size of the difference in the population the test is required to detect and the size of the samples. A good experiment will have high statistical power. For neuroimaging studies, the reduced sample size is a significant constraint in producing a study with high statistical power. Furthermore, the inter-individual variability, particularly pertinent to group imaging studies where individual data is normalised to enable group averages to be generated, is an additional consideration. As such, although the significance level of $p < 0.05$, which was used in the experimental studies presented in this thesis, will have increased the statistical power of the experiment, it may have reduced the number of statistically significant activations. The use of a $p < 0.1$ level of significance in several of the comparisons, particularly those in chapter 8, enabled additional regions to be considered and discussed with respect to their role in recognition memory. It is hypothesised that repeating the studies and increasing the number of participants, which would improve the statistical power, would identify these regions using a significance level of $p < 0.05$. It is important at this point, however, to acknowledge that in group imaging studies, increasing the number of participants will introduce more variability into the data and it has been shown that significant activations can be lost when the number of participants is too large, as well as too small (Singh, unpublished data)

The inherent problem of individual differences is a limitation of any experimental study. These MEG studies are no exception, and it is probable that this factor alone accommodates a significant proportion of the variation reported in the data. Due to the necessity to utilise the same stimuli in all experiments, different participants were involved

in the various studies to ensure there were no repetition effects. This, however, adds a further variable into the comparisons made between the studies, and perhaps it is not surprising, therefore, that identical activations were not revealed between studies. This does not, however, mean that group imaging is not a reliable tool for investigating memory processes. Rather, it should be used as the initial analysis tool to identify the main cortical regions involved in a specific task, and then these regions can be subjected to more detailed individual region of interest analyses. There is a large field of psychological research dedicated to the study of individual differences, and through this two phase approach, neuroimaging should be a useful tool in identifying phenotypic activation patterns which can be used in the clinical environment. It may be that in the recognition memory literature, individual differences may be involved in the hemispheric asymmetry reported by a number of studies, with some participants showing task-specific left or right-lateralised hemispheric dominance.

In these studies, modality-specific differences were investigated using objects and words, believed to involve visual and verbal encoding strategies, respectively. It is this visual versus verbal dichotomy that forms the basis of the modality-specific hypothesis. However the use of objects and words as stimuli may not have actually involved the separate visual and verbal processes they were designed to. In the first studies (chapters 5 and 7), although objects were presented visually on the screen, no control was made for verbal encoding strategies which may have been used by the participants during the categorisation or spatial location task. Specifically, participants may have sub-vocalised the name of the object to aid the subsequent recognition processes. The use of non-objects in the final study (chapter 8) will have reduced the amount of verbal processing that could have been used, but whether it was eliminated completely is unclear. Although the participants could not name the objects, some reported creating associations between the non-objects and a true everyday object to facilitate their recognition memory. For the word stimuli, it is less likely that the verbal processes will have been contaminated with visual cues, although as words were visually presented on the screen this cannot be completely satisfied.

In order to maintain experimental control, therefore, of visual and verbal encoding processes in recognition memory studies, other stimuli and methods of presentation may be beneficial. In particular, faces are believed to be good visual stimuli as they cannot easily be verbalised. A comparison between visual and auditory word presentation may also be useful for the verbal component.

One of the advantages of MEG as a neuroimaging tool for investigating recognition memory processes is the millisecond time resolution that can be generated. For these studies, however, only course temporal dynamics were investigated. It is important that this temporal information is investigated further in order to advance the research into recognition memory. Completing such a process would provide more information about the functioning of the brain, especially when it has been suggested that there is a network of connections within the brain.

9.4 Implications of Research and Future Work

9.4.1 Research on Recognition Memory

There is sufficient evidence from these studies and those in the previous literature to identify regions of the cortex that are involved in recognition memory processes, such as the prefrontal cortex, middle temporal lobe, parahippocampal gyrus and surrounding structures. Instead of trying to allocate each region a unique role in recognition memory, perhaps what is now needed is more in-depth region of interest analyses which can be used to identify the specific characteristics of the activation of each of these structures, such as oscillatory frequency and temporal dynamics. Such information will enable more detailed understanding of the functional involvement of each of these structures which can in turn be used to determine their precise role in recognition memory processes.

9.4.2 Combined MEG Studies and Neuropsychology

Through neuropsychological work, involving patients with memory disorders such as amnesia, it may be possible to identify those regions necessary and sufficient for recognition memory. The ability to recognise pictures, objects and words is an important skill in everyday life and the overall aim of this research is to understand what parts of the human brain are required for these tasks. Previous studies have shown that the frontal and temporal lobes in the brain are particularly important for recognising and remembering objects and words. Furthermore, some patients with frontal and temporal lobe damage (e.g. following stroke or head injury) have difficulties on these tasks. Interestingly, however, others do not. Consequently, it is important to investigate in more detail which parts of the

frontal and temporal lobes are crucially important for successfully performing picture and word recognition tasks.

In a recent paper, Price, Mummery et al (1999) have argued that functional brain imaging and neuropsychology can provide a way of delineating the brain areas that are necessary for a particular task. Their point is best illustrated with an example: functional imaging studies have consistently shown that normal participants activate left temporal, parietal and inferior frontal cortex in tasks that require judgements about the semantic similarity of items. Consistent with these data, patients with brain damage to temporal and parietal regions perform poorly on similar tasks. However, patients with inferior frontal cortex damage tend to perform within the normal range. This suggests that, although inferior frontal cortex is consistently activated in functional imaging studies with normal participants, it not necessary for successfully performing the task. It is possible, however, that patients with lesions to inferior frontal cortex can perform the task because: (1) there is some functional reorganisation involving the spared hemisphere or (2) there is peri-infarct activity around damaged tissue. Thus, it is important to scan patients performing the same tasks as normals to discount these two possibilities. If these alternatives can be ruled out, then patient data can be used to systematically determine the areas that are and are not necessary for performing a particular task.

By comparing the brain areas activated in the recognition phase for these patients (i.e. those with lesions who perform within the normal range) with normative data from healthy controls, and combining these findings with those from behavioural studies, it is suggested that the areas activated by controls, but not activated by patients, are not necessary for recognition memory (see Price et al, 1999).

9.5 Concluding Remarks

In conclusion, therefore, the research presented in this thesis has extended previous findings due to the power of SAM in tracking the spatio-temporal dynamics of such complex processes as recognition memory. Furthermore, it is suggested that the apparent lateralisation findings reported in the literature (i.e. task- and modality-specific hypotheses) may be due to the 'coarse' temporal analysis available with earlier imaging techniques, which 'over-simplified' the networks reported by being unable to discover the early complex processes associated with semantic processing which studies in this thesis have been able to identify.

These findings can now be used to begin the process of identifying the specific characteristics, such as oscillatory frequency and temporal dynamics, of the brain structures involved in recognition memory. Such information will enable more detailed understanding of the functional involvement of each of these structures which can in turn be used to determine their precise role in the network of recognition memory processes.

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11 APPENDICES

11.1 Technical Appendix

11.1.1 Techniques for Assessing Brain Function

11.1.1.1 Lesion Studies

Lesion studies involve the destruction of part of the brain. This may have occurred due to injury, accident or disease, as in the case of brain-damaged patients, or as in many animal lesion studies through specific removal of parts of the brain by a researcher. For all lesion studies the rationale is the same. It is assumed that the if there is a behaviour which can no longer be performed following a lesion, then the function of the damaged brain area can be inferred.

Brain-Damaged Patients

It is very common for individuals who have suffered some form of brain trauma or damage to report deficits in stimulus processing. Although the damaged areas can be used to determine where particular stimuli would normally be processed, the deficits demonstrated by any one individual are rarely specific. Usually, a number of deficits occur coincidentally and as there may be more than one brain region exhibiting some form of damage, it is not possible to exclusively link one particular brain area to its specific function. Furthermore, as the deficits are monitored after any damage has occurred, it is not known how the individuals performed prior to the damage, and therefore how much specific loss of stimulus processing has occurred.

Animal Lesion Studies

In lesion studies in which an experimenter/researcher damages/lesions a part of the animals brain it is possible to record behaviour before and after the lesion. Therefore, unlike when assessing brain-damaged humans, the specific amount of loss in stimulus processing can be recorded directly in an experimental setting.

It is, however, difficult to produce a lesion which is restricted to one area and which does not damage any other systems that may be linked to the lesioned site. The other major disadvantage is that many of the deficits have to be presumed rather than measured. If following lesion an animal consistently fails to run through a maze (a task at which it consistently performed well at before lesioning), does this mean that it is blind, that it has lost motor co-ordination or that it has lost motivation? Can it therefore be concluded that the lesioned brain region is involved in visual processing, in motor control, or in motivating processes? This issue is further complicated by the fact that all brain regions are interconnected and that no one brain region is solely responsible for a particular function. In fact each brain region performs a function which combined with other functions produces a specific behaviour. It is possible therefore that a function may be disrupted not because the lesioned site is responsible for that function, but because it is involved a neural circuit which produces the function or behaviour. Therefore, although lesion studies can provide important information, on its own it does not provide substantial enough evidence.

11.1.1.2 Transcranial Magnetic Stimulation (TMS)

Transcranial Magnetic Stimulation (TMS) is a method by which the normal functioning of a brain region can be disrupted. In this way it is similar to lesion studies, as although no part of the brain is lesioned, through stimulation using a magnetic field, it is possible to disrupt the functioning of a brain region, effectively simulating a lesion at the desired location. TMS involves placing an electromagnetic coil against an individual's skull and then passing an alternating current through it. The magnetic field produced temporarily disrupts the normal functioning of the brain region or neural network located directly beneath the coil.

However, as with lesioning studies, there are a number of disadvantages. Again it is difficult to accurately identify the specific structures that have been affected by the stimulation and to determine their specific function. Furthermore, the effectiveness of this technique is also determined by the intensity of the stimulation. Ideally it should be as close as possible to the spontaneously occurring activity within the cortex.

11.1.1.3 *Single-Cell Recording*

Single-cell recording, in which microelectrodes are surgically implanted into the brain of an animal and the electrical activity of a single neurone is measured, has been very useful in a number of psychological studies especially in vision research. Through this method it is possible to identify specific cells, and therefore networks, which are involved in the processing of a specific stimulus.

11.1.2 Structural Imaging Techniques

11.1.2.1 *Computerised Axial Tomography (CAT / CT)*

Computerised Tomography (CT) essentially produces an X-ray of the human head. A beam of radiation passes from a source, through the patient's head and is reflected off a surface underneath the head. Due to the fact that different structures in the brain are of varying density, they absorb and reflect this radiation at varying levels. Consequently, only a proportion of the radiation actually passes straight through the head and reaches the detector plate underneath. The radiation absorbed by the detector plate is translated using computer technology into a two-dimensional image. The beam scans the patient's head from numerous angles and finally a two-dimensional image is computer for every slice of the brain, showing the skull and brain structures.

This neuroradiological technique is not necessarily as detailed as other methods of functional imaging, such as MRI, PET; especially as generally the images from a CT scan are often only constructed in the horizontal plane, while MRI scans can also produce frontal and sagittal slices. It is, however, still considered to be the most appropriate procedure, at least in clinical terms when the patients comfort and well-being is paramount. Whilst useful diagnostically, in terms of ruling our other psychiatric disorders, there have been numerous reports demonstrating a significant correlation between cortical abnormalities, specifically atrophy, and cognitive impairment in AD patients (Drayer, Heyman, Wilkinson, et al 1985). Indeed cognitive functioning of AD patients has been shown to negatively correlated with both cortical atrophy and ventricular size (Burns, Jacoby, Philpot & Levy, 1991).

11.1.2.2 Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging (MRI) is similar to CT as it produces a detailed image of the structure of the skull and brain structures. Instead of using x-rays, however, it predominantly involves the study of the magnetic field gradients produced by the various parts of the brain, using the interaction between radio waves and a strong magnetic field. Due to the molecular structure of the human body, when a magnetic field is passed over the head, the hydrogen molecules found within the brain spin in a particular orientation. Passing a radio frequency wave through the brain causes these molecules to emit radio waves of their own. It is this radiation which is measured in the MRI scanner. As the different structures in the brain are of varying density (the same principle used in CT scanning) the concentration of the hydrogen molecules also varies. Therefore, it is possible to produce a detailed image of the brain, and as sequential slices are taken in different planes, the images produced are more detailed than those generated through CT scanning.

The distinct advantage of MRI over both PET and SPECT is the absence of any radiation, enabling frequent repeat measurements. Also, the length of time required to generate an image in considerably shorter, enhancing its cost-effectiveness. As with CT scanning, it is particularly useful in identifying cortical changes, such as atrophy etc, in the brain. However, the downfall of this structural imaging technique is the necessity for the head to remain in exactly the same position across testing, movement often being a prominent artefact.

Nevertheless, the clear advantage of MRI techniques over other methods is the non-invasive component and has been shown to very useful in patient studies. While consent from patients may be a little difficult to obtain, with some individuals requiring sedation, as in the study by Prasher, Barber, West and Glenholmes (1996), the same study indicates that despite this, useful and accurate images can still be produced. This study also demonstrates the usefulness of MRI as a diagnostic tool. They report a case study of a 74-year-old man with DS who developed dementia like symptoms during the last five years of his life and was clinically diagnosed with dementia of AD six months before the patient deceased. A MRI was used to assess the extent of the cerebral changes that had occurred. The images produced clearly indicated a severe degree of atrophy, which was observed symmetrically, and which focused greatly on the mesial temporal regions. Dilation of the ventricles could also be seen. While there was no earlier MRI scan to compare the

anatomical changes with, although comparisons with an earlier EEG were encouraging, the distinct pattern of atrophy does appear to correlate with that of AD.

11.1.3 Functional Imaging Techniques

Structural imaging techniques, such as CT and MRI are excellent tools for producing structural images or x-rays of the brain. However, as they produce static images, functional activity cannot be identified using these methods. There are however other neuroimaging tools and methods which enable functional information to be obtained. Specifically, these are PET, SPECT, fMRI, EEG and MEG.

11.1.3.1 Positron Emission Tomography (PET)

Positron Emission Tomography (PET) is a functional neuroimaging technique that provides information about the body's chemistry and therefore body function. It records information about the metabolic activity of specific brain regions, and by correlating this with task-performance, it is possible to investigate the specific function of many brain regions. The concept behind PET is that when part of the brain is being utilised, for example during a task, the tissue's in that region will require more energy and the blood flow to that region will increase. Therefore, by creating a method through which it is possible to track the movement of the metabolic activity, it is possible to identify the specific brain regions that are involved in a particular task. PET was developed as a method of doing this, and although is the probably the most expensive if the functional imaging techniques, it is highly sensitive and can the chemical selectivity enables specific functions of the brain to be targeted.

As PET is associated with the brain's metabolic activity, it uses radioactive isotopes of chemicals readily found in the body, such as oxygen (O), carbon (C), nitrogen (N) and Fluorine (F). As the name PET implies, the procedure involves a process of positron emission, and it is the isotopes of these biologically relevant elements that are the positron emitters. Essentially, the isotopes are identical to the stable element in terms of their chemical properties, but differ in their atomic mass, each having an odd number of protons. Because of this they are referred to as radioactive isotopes, or radioisotopes. Their similarity to the biologically occurring elements ensures that they are actively incorporated

into compounds found within the body, such as blood or glucose, and behave naturally. PET is a method by which the elements with an odd number of protons can be detected, so therefore by tracing these isotopes, it is possible to determine where the normal, stable elements are used in the brain, and thus the brain regions can be related to task-performance.

In PET, a radioisotope is intravenously injected into the patient. Depending on what is to be measured, different radioisotopes are used. For example, the blood contains high amounts of oxygen, so in order to monitor blood flow a radioisotope of oxygen, oxygen-15 ($^{15}0$), is used. Alternatively, for directly monitoring the metabolic processes occurring within the brain, a radioisotope of fluorine, fluroine-18, is combined with glucose. This radioactive glucose is the only metabolic fuel found in the brain and when part of the brain is being utilised, for example during a task, its tissue will utilise more energy, this energy being obtained from glucose. Whichever radioisotope is used, the procedure for recording from the PET scan is the same.

Once injected into the patient, the radioactive molecule begins to decay. It is during this process that a positron is released. This positron travels a few millimetres away from the compound and collides with an electron already present within the tissue. Due to the unstable nature of the radioisotope, its extra positron will be emitted. This collision causes an "annihilation reaction" in which high-energy radiation is produced in the form of two gamma rays at 180° to each other (two photons with equivalent energy travelling in opposite directions). These coincident photons can penetrate the brain and skull, they can be detected externally and thus the PET scanner is designed to detect any emissions that are 180° to each other. Consequently, three-dimensional images of the radioisotope distribution are produced and therefore, cortical activity.

The temporal resolution of PET scanning is determined by the decay (due to the collision and release of photons) of the radioactive particles, ^{15}O for example having a half-life of about 60 seconds. This therefore means that the temporal resolution is rarely less than about 1 minute. Furthermore, the anatomical and spatial resolution is quite limited, usually about 1cm. While the short half-lives of the isotopes is advantageous as it means the patients only receive low dosage radiation, the fact that radiation is involved is itself a disadvantage, time between repeat scans having to be quite long to account of this. There are also cost and timing issues, one scan taking anywhere from a couple of minutes to a couple of hours. (Sawle, 1995).

11.1.3.2 Single Photon Emission Computed Tomography (SPECT)

Single Photon Emission Computed Tomography (SPECT) incorporates an almost identical methodology to PET imaging, with the differences being the longer half-lives of the molecule used. Comparatively, cost is therefore reduced and the time constraints do not necessarily need to be as rigorous. However, as only single photons are involved, information about spatial resolution cannot be generated, unlike in PET scanning (Sawle, 1995). The length of time taken to produce an image is similar to that of PET and the use of radiation obviously has the same disadvantages. Nevertheless, the reduced cost makes SPECT more preferred in clinical environments.

11.1.3.3 Functional Magnetic Resonance Imaging (fMRI)

Functional Magnetic Resonance Imaging (fMRI) is a comparatively newer technique for studying the brain, (compared to PET and SPECT), involving the basic methodology of MRI scans and is primarily used to look specifically at brain function. It enables regional metabolism to be measured and it has proved to be a very useful tool in the study of various components of the brain, much attention being centred on the hippocampus and its' sub-regions (Gabrieli et al, 1997).

The principle of fMRI is that a series of images are taken in quick succession, enabling the visualisation of changes in the chemical composition of brain areas or the flow of fluid, such as blood, over time. Unfortunately, one of the disadvantages of fMRI is that this time-span is rarely less than about two seconds and so can provide little information about the temporal sequence of events.

Probably the most common fMRI technique is the blood oxygen dependent (BOLD) method (Ogawa, Tank, Menon, Ellermann, Kim, Merkle & Ugurbil, 1992), in which changes in oxygen levels within the brain are measured. As oxygen is one of the main components found within the blood, measuring the oxygen level can be used as indicator of blood flow. Furthermore, as it is assumed that an activated brain region will require more oxygen, the blood flow to this region will increase and thus cortical activity can be inferred.

The basic methodology of the BOLD response in fMRI is concerned with the natural magnetic field generated by molecules found within the brain. The blood travelling around

the body and through the brain has magnetic properties. These properties are dependent upon the amount of oxygen in the blood as it too has its own magnetic properties. Consequently, oxygenated and deoxygenated blood (or haemoglobin, which is the main component of blood) have different magnetic properties. When an individual is placed in a scanner, the magnetic fields of these molecules differ, oxygenated haemoglobin showing up better on MRI images than deoxygenated haemoglobin. As increase in blood flow is assumed to be correlated with an increase in brain activity, this BOLD method of fMRI infers that the visible oxygenated haemoglobin shows the location of brain activity.

Other methods involve the movement of hydrogen molecules. When placed in a scanner, the magnetic field causes the natural spin of some nuclei present in molecules found within the brain to align with it. One such molecule and the basis behind the BOLD fMRI method is the nuclei of the hydrogen molecules found in the water in the body. A radio frequency (RF) pulse emitted by the scanner temporarily disturbs this alignment. As the nuclei re-align, a detectable signal is emitted. Deoxygenated haemoglobin (Hg) distorts the magnetic field and thus the signal is lost. Any activity in the brain can therefore be measured as there will be an increase in the oxy : deoxy ratio.

FMRI does provide excellent spatial resolution. However, in addition to its poor temporal resolution, it is also expensive and not widely available. Care must also be taken to ensure that the patient's head remains still as any movement can often produce spurious results.

11.1.3.4 Electroencephalography (EEG)

Electroencephalography (EEG) is a functional imaging technique in which the electrical activity of the brain is measured by a number of electrodes placed on the scalp. The electrical activity is generated by the neurones in the brain as a signal is transmitted (more detail is provided in section 2.3.2). The electrodes placed on the surface of the scalp detect this activity and the information is amplified onto either a computer or onto a moving paper. The spatial location of brain activity is determined by the position of the electrodes, for example, those at the front could be used for detecting electrical activity in the frontal lobe, those at the back for measuring occipital or visual activity. The changes in the electrical activity detected by any one electrode over time results in the generation of a brain wave.

These waves can vary across time and is termed the frequency of the wave. It is measured in cycles per second, a unit referred to as hertz (Hz), and is defined as the number of complete cycles of repetitive waves in one second. In EEG research, the brain waves recorded are categorised into a number of different bands, according to their frequency. The most common are delta, theta, alpha and beta. Delta waves are the slowest waves, with a frequency of less than 4Hz, followed by theta which covers waves with frequencies between 4 and 8Hz. Alpha waves are probably the most common as they are usually observed during sleep or relaxation when the eyes are closed. Consequently, they are most common within the occipital brain regions. The average frequency in adults is about 10Hz, with the range being from 8 to 12Hz. Sometimes this band is itself split into two frequency bands, lower alpha between 8 and 10Hz, upper alpha between 10 and 12 Hz. Similarly whilst beta waves are categorised between 12 and 30 Hz, they too are often split into beta 1 (14 to 22 Hz) and beta 2 (22 to 30 Hz).

The amplitude (i.e. height) of these brain waves also varies and this provides information about the voltage or strength of the wave, the higher the amplitude, the larger the voltage (measured in microvolts (μV)).

Due to the nature of EEG and its information about frequency, it provides excellent temporal resolution. Furthermore it is relatively in expensive and does not involve any health risks. However, it can be quite time consuming to attach the desired number of electrodes, although electrode caps are becoming increasingly more common. In addition the spatial resolution tends to be inaccurate, it only being determined by the location outside the skull of the electrode picking up the electrical signal, and often conduction through the scalp has negative consequences.

11.1.3.5 Magnetoencephalography (MEG)

MEG is a very similar technique to Electroencephalography (EEG), the major difference being that the latter measures electrical activity in the brain. As discussed above, this electrical activity is the result of ionic movement within neural tissue and it is the potential difference of this activity that is recorded by EEG. This electrical activity produces a magnetic field and it is this 'neuromagnetic field' that is measured and recorded by MEG. Cohen (1968, 1972), who observed alpha frequency magnetic fields during EEG assessments, reported the first evidence of these recordings. Essentially the magnetic fields

arise due ionic movement, associated with electrical activity, within the neurones of the brain, i.e. an intra-neuronal ionic current flow. There are literally millions of neurones within the brain and it is thought that simultaneous activity of about 50,000 neurones will produce a magnetic-field that can be detected by conventional MEG methods (Okada, 1993).

MEG is a non-invasive technique, which also enables co-registration between MEG data and MRI scans. This co-registration overcomes many of the problems associated with MEG of lack of spatial resolution, and with its similarity to EEG, it can provide excellent temporal resolution.

11.2 Published Abstracts

Worthen, S.F., Forde, E.M.E., Singh, K.D. & Holliday, I.E. (2003). A magnetoencephalographic (MEG) study of hemispheric specialisation during recognition memory tasks with pictures and words. *Journal of Psychophysiology*; **17**: 110.

Neuroimaging literature indicates that there is some controversy over the roles of the left and right hemispheres in recognition memory tasks. Some authors suggest that the left and right hemispheres (particularly in the frontal and temporal lobes) are specialised for encoding and retrieval, respectively (the 'task-specific' hypothesis). Others suggest that the left and right hemispheres are involved in recognition memory for words and pictures, respectively (the 'modality-specific' hypothesis). A magnetoencephalographic (MEG) study was conducted to test these hypotheses. Pictures and the corresponding names were presented separately as stimuli in two recognition memory experiments. In each experiment, a fixation point was presented for 1000ms, followed by the stimulus for 200ms, the fixation point for a further 1000ms, and finally a cue indicating that participants should respond. The responses were living/non-living categorisation and old/new identification in the encoding and recognition phases, respectively. Synthetic Aperture Magnetometry (SAM) Analysis was used to identify the brain regions involved in encoding and recognition of pictures and words. During encoding, event-related desynchronisation (ERD) was observed for pictures over bilateral frontal and left-lateralised temporal regions. There was no significant ERD for words in frontal or

temporal regions. ERD during recognition was bilateral in both frontal and temporal areas for pictures, and was left-lateralised in the frontal lobes and right-lateralised in the temporal lobe for words. We suggest that neither the 'task-specific' nor the 'modality-specific' hypothesis can account fully for the hemispheric differences observed in recognition memory tasks. The data also indicate that MEG can be used to identify brain regions involved in 'high-level' cognitive tasks, such as recognition memory.

Worthen, S.F., Forde, E.M.E., Singh, K.D. & Holliday, I.E. (2003). A magnetoencephalographic (MEG) investigation of hemispheric specialisation during recognition memory tasks with verbal and non-verbal pictures and words. *NeuroImage*; **19**: S27, 238.

Neuroimaging literature indicates that there is some controversy over the roles of the left and right hemispheres in recognition memory. Some authors suggest that the left and right hemispheres (particularly in the frontal and temporal lobes) are specialised for encoding and retrieval, respectively (the 'task-specific' hypothesis). Others suggest that the left and right hemispheres are involved in recognition memory for words and pictures, respectively (the 'modality-specific' hypothesis). A magnetoencephalographic (MEG) study was conducted to test these hypotheses. Verbal and non-verbal pictures and words were presented as stimuli in four recognition memory experiments. Pictures and the corresponding names were presented separately in the first two studies. In these, a fixation point was presented for 1000ms, followed by the stimulus for 200ms, the fixation point for a further 1000ms and finally a cue indicating that participants should respond. The responses were living / non-living categorisation and old / new identification in the encoding and recognition phases, respectively. In a part-replication of the initial studies, the third experiment also involved the presentation of pictures and their corresponding names. However, these were presented consecutively within the same experimental paradigm to permit direct comparisons of pictures and words, and each image was presented for 500ms. Furthermore, the encoding task was a spatial discrimination task of a red circle placed either above or below the horizontal plane of fixation. For experiment four, study three was replicated using pure non-verbal stimuli, i.e. non-objects and non-words. Synthetic Aperture Magnetometry (SAM) Analysis was used to identify the brain regions involved in encoding and recognition of verbal and non-verbal pictures and words.

In the first two experiments, direct comparisons between encoding and recognition only showed event-related desynchronisation (ERD) during the recognition phase. Hemispheric and regional differences were observed within this phase for both the 0-500ms and 500-1000ms time windows. In the 15-25Hz and 25-35Hz frequency bands, for pictures, ERD was observed in the frontal gyri bilaterally and the right precentral and fusiform gyri. For words, ERD was seen in the left frontal gyrus and in the temporal gyri bilaterally. However, ERD was also observed in identical cortical regions for both stimulus modalities. In addition, statistical analyses were performed on the extent of activation observed within each of the four left and right hemispheric cerebral lobes. Preliminary analysis of study three indicates that these results are partially replicable, with some differences highlighted in the direct picture versus word comparisons. A similar pattern of activation, although less widespread, is also suggested for the non-verbal stimuli. We suggest that neither the 'task-specific' nor the 'modality-specific' hypotheses can account fully for the hemispheric differences observed in recognition memory tasks of pictures and words. Some of the widespread activation may reflect semantic processing, suggesting that these regions may not all be necessary for successful recognition memory. Semantic processing and different analysis comparisons may account in part for the diverse results reported in the literature. The data also indicate that MEG can be used to identify brain regions involved in 'high-level' cognitive tasks, such as recognition memory.