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**ERP and fMRI correlates of retrieval cues in  
episodic memory**

**A Thesis submitted to University College London for the degree of  
Doctor of Philosophy in Psychology**

**Michael Hornberger  
Supervisor: Dr. Leun Otten  
2006**

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## **Abstract**

EEG event-related potentials (ERPs) and fMRI blood oxygenation level dependent (BOLD) new item contrasts were employed in six experiments to investigate the neural correlates of retrieval orientations – cognitive states or ‘sets’ that align cue processing with the demands of a particular retrieval goal. It is proposed that the neural correlates of different retrieval orientations can be investigated by comparing the activity elicited by the same class of retrieval cues when these were used to probe memory for different kinds of information (Rugg & Wilding, 2000), preferably with new items in memory tests, so as to minimize the confound between cue processing and processes associated with successful retrieval.

The reported results on new unstudied items replicate and extend recent findings (e.g. Robb & Rugg, 2002) by showing that retrieval orientation effects are robust ERP effects across different study and test materials and semantic encoding tasks. However, the occurrence of the same effect is sensitive to manipulations of the retrieval tasks employed, and further a one-to-one mapping of the reported scalp ERP effect onto the observed fMRI activations is difficult to make. In terms of a functional interpretation, the retrieval orientation effect seems to reflect differences in the need to constrain cue processing. Specifically, it is proposed that the more a cue representation must be constrained to the semantic/conceptual level, the more negative-going will be the associated ERPs.

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## **Foreword**

Experimental memory research was since the time of Ebbinghaus and Semon always concerned with the question of how encoded information is accessed in a retrieval attempt. More specifically, the interaction of a targeted memory and a given retrieval cue (named 'ecphory' by Richard Semon) was seen as the epitome of memory retrieval (see also Tulving, 1983). Studies such as Morris, Bransford & Franks (1977) and Tulving & Thomson (1973) investigated these retrieval cue/memory target interactions and embodied their findings in their transfer-appropriate processing and encoding specificity principles, respectively. The results of the Morris et al. (1977) and Tulving et al. (1973) studies suggested that tasks employed at study and test, as well as the format of study and test items, are crucial variables that determine the likelihood of successful retrieval. However, until today only a few studies have attempted to search for the neural correlates of retrieval cue/memory target interactions. One reason is that effects related to retrieval cue processing are assumed to be state and not item related, and hence should be tonically maintained across items. It follows that it is not easy to detect retrieval processes by behavioural means, which measure mainly item-related processing. However, the recent development of neuroimaging methods allows complementing and facilitating the research of retrieval cue processing. Another problem facing researchers investigating retrieval cue effects is to separate different types of retrieval-related processes. In this context most of the studies so far confounded retrieval cue processing with the neural correlates of successful retrieval (e.g. retrieval success). Nevertheless, a new framework, put forward by Rugg and Wildings in 2000, proposed to compare neural correlates of



correctly rejected new items only, and thus increasing the likelihood of a more pure neural correlate of retrieval cue effects. In this thesis I attempt to measure with ERP and fMRI correlates a specific retrieval cue process called retrieval orientation using the proposal of Rugg and Wilding. More explicitly, I investigated how manipulations of variables like study and test material, or different retrieval tasks, influence the ERP and fMRI correlates of this orientation effect.

The thesis consists of three main parts. First, a theoretical and methodological background to the present experiments will be provided. This will include a review of theoretical and experimental studies concerned with recognition memory and cue/target interactions, as well as a theoretical background of the experimental techniques (EEG & fMRI) applied in this thesis. Second, the results of each of 5 experiments will be presented. Third, I will attempt to discuss the findings of the experiments with regard to a broader background and their implications for further investigations of retrieval processes.

## **Chapter 1 - Retrieval cue/memory target interactions: empirical and theoretical perspectives**

### **Levels of processing**

Memory research in the 1950s was mainly focused on verbal learning under the umbrella of associationism. Associationism regarded memory as a matter of acquisition, retention, transfer, and interference of associations between stimuli and responses. However, at the end of the 1960s and especially the beginning of the 1970s a paradigm shift occurred in that memory research was no longer regarded as purely associative, instead retrieval operations were assumed to be distinct from encoding operations. Retrieval operations were now seen as processes completing the act of remembering that begins with encoding of information about an event into the memory store. Thus, remembering is regarded as a joint product of information stored in the past and information present at the time of remembering. Different research groups realized quickly that such a proposal leads to the question of the relation between effects of the past and present inputs (e.g. cues) and the interaction of the two (what Semon, 1904 called, 'ecphory'). Most notably Tulving and Thompson's (1973) encoding specificity principle and Craik and Lockhart's (1972) levels of processing framework provided some guidelines for investigations of retrieval cues specifically and encoding/retrieval processing in general.

Craik and Lockhart's paper from 1972 is one of the founding stones of the study of encoding and retrieval interactions. Although there were earlier suggestions for a similar

framework (e.g. Bower, 1967; Posner, 1969 and Cermak, 1972) the proposal of Craik and Lockhart brought earlier findings together and combined them into a single framework. The core of this approach is that 'the memory trace can be understood as a by-product of perceptual analysis and that trace persistence is a positive function of the depth to which the stimulus has been analyzed' (Craik & Lockhart, 1972, p 671). In general, this framework assumes that a hierarchy of processing stages exists, as proposed for selective attention by Treisman (1964). The first stages include sensory or perceptual analysis while later stages are concerned with the semantic or other more abstract properties of the stimuli. This conception of levels or a hierarchy of processing led to the notion of "depth of processing" where greater "depth" implies a greater degree of semantic or elaborate analysis. Specifically, Craik and Lockhart suggested that trace persistence is a function of depth of analysis, with deeper levels of analysis associated with more elaborate, longer lasting, and stronger traces. The new framework explained existing data, which seemed contradictory at the time. For example, studies of incidental and intentional learning observed that, depending on the orienting task subjects were given, they could perform better in either the incidental or in the intentional condition. According to the levels of processing framework, the instruction to learn facilitates performance only insofar as it leads the subject to process the material in a deeper manner than in the incidental condition. Thus, it is possible that with an appropriate orienting task and an inappropriate intentional strategy, learning under incidental conditions could be superior to that under intentional conditions. These conditions were met for example in a study by Segal and Mandler (1967), who showed that incidental learning during categorization of words yielded a similar recall level to that of a group who performed the same activity but who

knew that their recall would be tested. Further, Schulman (1971) had subjects scan word lists either structurally (a 'shallow' task such as words containing the letter "A") or semantically (a 'deep' task such as words denoting living things). In a subsequent unexpected recognition memory test, subjects performed significantly better in the semantic than the structural condition (see also Kolers, 1973; Seamon & Virostek, 1978). These results backed up the general ideas of Craik and Lockhart (1972), that memory performance is a positive function of the level of processing required by the orienting or encoding task. The limitation of this framework, however, is that it focuses only on encoding processes, with little regard for the nature of the subsequent retrieval processes and other researchers realized this very early.

### **Encoding specificity**

In this context the study of Tulving and Thomson (1973) is of special interest, in which Tulving and Thomson systematically varied the effectiveness of cues in a recognition memory paradigm. In three experiments they showed that the recall of a target word is dependent upon the presentation of the appropriate cue. Appropriateness refers to the finding that a cue is effective in one situation, though not in another situation. The effectiveness of a particular cue is in turn contingent upon on how the to-be-retrieved item was encoded at study as proposed by Craik and Lockhart (1972). Tulving and Thomson's findings led to the "encoding specificity principle": 'Specific encoding operations performed on what is perceived determine what is stored, and what is stored determines what retrieval cues are effective in providing access to what is stored '

(Tulving & Thomson, 1973, p353). The general principle is not new because Gestalt Psychologists like Bartlett had already claimed that the properties of an element depended on the company the element kept in the larger whole (e.g. Bartlett, 1932). Further, a long tradition of research on incidental and intentional learning came to the conclusion that what is learned depends on what happens in the learning situation (e.g. Postman, 1964).

Nonetheless, the results of Tulving and Thomson were the first systematic attempt to investigate encoding by retrieval cue interactions. Their results demonstrated that “what is stored” and “what is sought-for” varies according to the circumstances at encoding and retrieval. Together with the level of processing framework of Craik and Lockhart, these papers triggered a plethora of subsequent papers investigating these effects more systematically (see for example Craik & Tulving, 1975, and for a review see Lockhart, 2002; Craik, 2002). Nevertheless, certain theoretical assumptions, made in the levels of processing framework, were criticised. Most prominently and importantly criticised was the elusive index of ‘depth’ (e.g. Baddeley, 1978), because it is not clear how ‘depth’ is defined independently of a subsequent memory performance.

### **Transfer-appropriate processing**

In a further step, Morris, Bransford and Franks (1977) questioned the prediction of the level of processing framework that a semantic processing task should always lead to a superior memory performance relative to a phonetic processing task. They argued that this prediction may only be true for tests that use targets and foils that may be considered

appropriate for, and dependent upon, semantic modes of processing. In other words they reasoned that many results in favour of the level of processing framework are inherently biased towards the actual test used in those studies. Instead, Morris et al. propose that 'to provide a more adequate test of these aims it is necessary to consider not only the processing levels dictated by the acquisition tasks, but also the processing levels induced by the form of the memory test itself' (Morris, Bransford & Franks, 1977, p521). To test this proposal, they designed three experiments factorially crossing the factors of encoding task and type of memory test. Their results confirmed their hypotheses, in that performance in a standard recognition task was superior for a semantic encoding task relative to a rhyming encoding task, whereas in a rhyming recognition test participants performed better if they had received a rhyming encoding task than a semantic encoding task. The findings challenged Craik and Lockhart's framework by showing that 'level of processing' is important not only at encoding, but also at retrieval. More specifically, their results suggest that the critical factor is the degree of overlap of processes performed at study and the processes performed at test. Furthermore, for the first time it became clear that encoding and retrieval operations could be manipulated separately.

### **Changes in tasks and retrieval cue properties**

The realisation of separate encoding and retrieval manipulations triggered more studies trying to elucidate one and/or the other process further. The studies focused mainly on two experimental manipulations, already employed in the earlier studies: first, changes in the tasks at encoding and/or retrieval (e.g. intentional vs. incidental encoding; recall vs.

recognition) and second, changes in the properties of encoded items and retrieval cues (e.g. perceptual changes; semantic changes).

Regarding task changes, Craik and Tulving (1975) presented a wealth of data that showed that performance in memory tests varies as a function of encoding or retrieval tasks.

Furthermore, studies by Roediger and colleagues investigated especially the role of intentional vs. incidental retrieval (e.g. Weldon, Roediger & Challis, 1989; Blaxton, 1989). However, changes in the retrieval cues properties itself were left out as variables in experimental tests. Nevertheless, soon after the Craik and Lockhart paper, researchers (e.g. Tulving & Thomson, 1973) realised the importance and experimental potential of cue manipulations in memory studies because inherently the effectiveness of any memory retrieval attempt is in part contingent upon the cue given. Moreover, the work of Treisman (1964) as well as Morton (1970) emphasised how the perceptual properties of a cue can have an influence in selective attention and memory experiments. In particular, it became apparent that modality is a crucial factor in the effectiveness of cues, as demonstrated in the finding of the picture superiority effect by Paivio, Rogers and Smythe (1968) (see also Intraub & Nicklos, 1985). However, only in 1976 did Moscovitch and Craik make a systematic attempt to investigate the effect of retrieval cue manipulations in memory tests. In their experiments they manipulated the retrieval condition by i) presence or absence of cues, ii) unique or target-shared cues (i.e. sharing of the same encoding condition) and iii) cue and targets which form a meaningful unit or not (Moscovitch & Craik, 1976). They crossed these manipulations with the factor of levels of processing (shallow vs. deep encoding), and found that effect of cueing, uniqueness and congruence had beneficial effects only at deeper levels of encoding.



Further interest in the retrieval cue manipulations was expressed in priming studies. Weldon, Roediger and Challis (1989) had participants study pictures and words, followed by either an explicit free recall test or an implicit word fragment completion test. The results showed that pictures were better remembered than words in free recall (the picture superiority effect, Paivio et al., 1968). However, words produced much more priming than did pictures on the implicit word fragment completion test. In a later experiment, Weldon and Roediger again presented pictures and words during study but now participants received an implicit test of either word fragment completion or picture fragment naming. As expected, the experience of studying pictures and words transferred differentially to tests: pictures showed more priming on picture fragment completion, whereas words showed more priming on word fragment completion.

Although the findings of Roediger and colleagues and Moscovitch and Craik (1976) address different kinds of memory (i.e. implicit and explicit, respectively), both findings make a compelling case for the importance of retrieval cues and the properties of stimuli that are emphasised at encoding and retrieval.

### **Elements of episodic retrieval**

More systematic theoretical implications of the findings in the 1970s were discussed by Tulving in 1983 in the second part in his seminal publication 'Elements of episodic memory' (1983). A special emphasis was drawn towards the distinction between encoding and retrieval processes, discussed in separate chapters, which reflected the paradigm shift implemented in memory research. The chapter on encoding draws a

specific emphasis on how information or an 'engram' is stored. As known already from the levels of processing framework and the encoding specificity principle, it is possible to manipulate the formation of these engrams by means of encoding strategies or encoding orientation. More important is the fact that the retrieval stage shows similar qualities as the encoding stage, in that manipulations of task or retrieval cue properties have an effect on the retrieval of these engrams. However, Tulving states two important conditions that have to be met for retrieval to occur at all. First, the system (i.e. brain) must be in what he refers to as 'retrieval mode', and second, an appropriate retrieval cue must be present that triggers the recovery of the engram. The first condition stated by Tulving is difficult to measure by behavioural means, as it should be a tonically maintained cognitive state occurring throughout any episodic retrieval regardless of cue-related processing. Thus, whenever a stimulus becomes a retrieval cue, it is difficult to distinguish effects due to its own inherent characteristics from effects of retrieval mode. Another reason for experimental neglect of the retrieval mode may have to do with the fact that many experimental conditions including studied items tend to automatically trigger retrieval mode.

The second important factor in retrieval is the appropriateness of a retrieval cue. This is a vague term, however, because little systematic work has managed to give concrete examples of the 'appropriateness' of a cue. In his book, Tulving suggests that the appropriateness of a retrieval cue is determined by its effectiveness and specificity for the sought-for information. Hence, in daily life for example, a retrieval cue can be thought of as some salient aspects of the physical and cognitive environment that initiate and influence the process of retrieval. In terms of effectiveness, copy cues or identity cues

(Tulving & Thomson, 1973; Watkins & Tulving, 1975; Watkins, 1979) represent one extreme on the continuum of effectiveness. A copy cue is one that is physically identical with the focal element of the to-be-remembered event, as in most of the recognition memory experiments (e.g. studying the word 'cat' and being tested for memory on the word 'cat'). The idea of copy cues fits in naturally into Tulving's theoretical framework discussed above in that the effectiveness of the cue depends on its similarity or 'informational overlap' with the to-be-remembered event. Still, there are many other examples (e.g. Tulving & Pearlstone, 1966) which show that semantic associates can also be effective retrieval cues, though the testing material used seems to be crucial for the memory performance in general (for opposite results to Tulving & Pearlstone, see Underwood, Runquist & Schulz, 1959).

It follows that retrieval cues seem to be important to initiate memory search processes (e.g. retrieval attempt) and thus have a crucial role in guiding any retrieval processes. The specificity and effectiveness of cues fits well into the encoding specificity principle and the transfer-appropriate processing framework because cues, jointly with tasks, determine what information is available to the rememberer and subsequently influence performance in memory tests.

### **Classes of retrieval processes**

Tulving's proposal made clear that retrieval per se might not be a unitary process, instead it is likely to consist of multiple processes. Tulving put forward one of these processes, namely retrieval mode, which he proposed as pre-requisite for any episodic retrieval

attempt. Nevertheless, as mentioned above, it is not easy to measure different retrieval processes by behavioural means. However, functional neuroimaging methods (e.g. ERP, fMRI, PET) allow researchers to complement the behavioural data by investigating the neural correlates of different cognitive retrieval states and processes at the same time. So far four different classes of retrieval processes have been put forward by several researchers by means of ERP, PET and fMRI (Tulving, 1983; Schacter et al., 1996; Rugg & Wilding, 2000), namely, retrieval mode, retrieval orientation, retrieval effort and retrieval success. These four retrieval processes are, however, by no means exhaustive or universally agreed on. Instead, they provide concepts of the underlying processes, which still have to be supported by experimental data. Thus, I will briefly present the theoretical reasoning behind the four retrieval processes (see also Rugg and Wilding, 2000) in the next section of this chapter and I will defer a discussion of the experimental data supporting these processes to Chapter 3.

### Retrieval mode

As already mentioned above, retrieval mode is thought of as a tonically maintained cognitive state or set, which is active when people engage in episodic retrieval in general. Nevertheless, people might not be aware of this state because we attribute retrieval characteristics only to a given retrieval cue and not the retrieval state per se. Thus, neural correlates of retrieval mode should be activated at the onset of engagement in an episodic retrieval task, regardless of the retrieval cues and their study status and the processes related to mode are supposed to be maintained across the period of time episodic retrieval

is occurring. Subsequently, neural correlates of retrieval mode should only be observable in episodic retrieval tasks and not in non-episodic retrieval tasks. Hence, differential brain activation across tasks (episodic versus non-episodic) should reveal effects of retrieval mode, while the nature of the same effect should be invariant across study status (old versus new items) as well as material (e.g. modality) of the retrieval cues.

### Retrieval orientation

Rugg and Wilding (2000) further proposed that there is a fractionation of retrieval mode, into a process concerned with determining the specific processing that is applied to a retrieval cue. They called this process retrieval orientation, as it allowed subjects to directly orient themselves towards the information sought-for with a given retrieval cue. Rugg and Wilding (2000) proposed that to measure the neural correlates of retrieval orientation, researchers should contrast retrieval cues in memory tests that differ either according to the task employed at study or test (e.g. recognition memory task versus source memory task) or, if the retrieval cues differ, according to the information encoded at study (e.g. pictures versus words). Crucially, Rugg and Wilding realized that most existent data relating to retrieval orientation was confounded by retrieval success (see below). The reason was that investigators contrasted correctly recognized items (old items) as a function of the task employed, or of the encoded information. Thus, any differential activity in correctly recognized old items could be either attributed to the attempt to retrieve specific information or the content of the sought-for information itself. More importantly, the neural activity related to memory content and retrieval cue

processing could not be delineated because it was unclear what relationship these two processes might have to each other (e.g. could they be considered to be additive or not). Hence, Rugg and Wilding proposed that comparisons across tasks should be confined to retrieval cues bearing no relation to studied items (e.g. new items in a recognition memory test), in order to minimize the confound between cue processing and processes associated with successful retrieval (Rugg & Wilding, 2000). Contrasts for new items should reveal that people can directly vary the processing of retrieval cues by adopting different 'retrieval orientations' – cognitive states or 'sets' that align cue processing with the demands of a particular retrieval goal, thus increasing the likelihood of successful retrieval. Unlike retrieval mode, the retrieval orientation effect should therefore depend on the task as well as on the encoding material. The first few neuroimaging studies applying the proposed operationalization of the retrieval orientation, according to Rugg and Wilding (2000), are promising in that ERP (e.g. Robb & Rugg, 2002; Herron & Rugg, 2003; Herron & Wilding, 2004) studies do show distinct neural correlates according to what subjects are trying to remember.

### Retrieval success

Another retrieval process assumed to exist is retrieval success. This process is the most established one of all four processes because a wide range of experimental literature has examined its behavioural and neural correlates. The reason is that activity related to retrieval success is item and not cognitive state related, in contrast to the previous retrieval process. Thus, neural correlates contrasting item-related activity according to

their study status (old versus new items) as well as the subject performance (hits versus false alarms) elicit activity assumed to engender retrieval success processes (e.g. Rugg, Brovedani & Doyle, 1992). Hence, retrieval success encompasses any process associated with, or contingent upon, ecphory. It is therefore not surprising to find a plethora of data concerned with retrieval success processing, which in the last years was more oriented towards the dissociation of different types of retrieval success (e.g. recollection versus familiarity, see Yonelinas et al., 2005) or the actual retrieval content (e.g. Woodruff et al., 2005). Nevertheless, one always has to bear in mind that contrasts revealing retrieval success activity can be contaminated by numerous other processes in the retrieval (e.g. retrieval orientation, retrieval effort) as well as decision (e.g. response processes) domain.

### Retrieval effort

A more elusive retrieval process is retrieval effort (e.g. Schacter, 1996), which is understood as a mobilization of processing resources in a retrieval attempt. Thus, any retrieval attempt should mobilize some kind of retrieval effort. Further, retrieval effort might be detectable by means of behavioural performance data, as a difference in accuracy, or reaction times across tasks might be an indicator of effort across tasks. It becomes obvious that the concept of retrieval effort can be seen as a correlate of task difficulty in general. Nevertheless, there is a possibility of measuring the neural correlates of retrieval effort by contrasting the activity elicited by retrieval cues embodying qualitatively equivalent retrieval processing but that differ in difficulty (e.g. longer study lists or varying study-test intervals). Similarly to retrieval orientation, contrasts revealing



such retrieval effort-related activity should be confined to correctly rejected new items, so as to avoid interference from the neural activity of retrieval success. However, so far the detection of retrieval effort processing even under stricter criteria remains elusive or at best ambiguous.

Nevertheless, of all four proposed retrieval processes, only retrieval success, due to its item-related activity, has been investigated thoroughly so far.

Thus, the purpose of this thesis is to investigate the remaining retrieval processes further by combining retrieval cue and task manipulations with the means of neuroimaging (i.e. ERP, fMRI) methods. More specifically, my hypothesis is that cue as well as task manipulations should influence the neural correlates of retrieval orientation processes. Hence, I am in particular interested to see whether retrieval orientation effects are sensitive to manipulations of the encoding material (e.g. words vs. pictures) or the retrieval tasks (e.g. implicit vs. explicit retrieval) employed, and where in the brain the neural correlates of these processes can be located.

According to Rugg and Wilding (2000), retrieval orientation processes should be sensitive to any of those manipulations, without being confounded by any successful memory recovery and hence should reveal more pure neural correlates of retrieval cue processing. However, before presenting the specific experimental manipulations employed in the current experiments, the next chapter (chapter 2) will introduce the neuroimaging methods used in the thesis and chapter 3 will then give an overview of neuroimaging studies investigating these retrieval cue processes so far.

## **Chapter 2 – Event-related Potentials (ERP) and functional Magnetic Resonance Imaging (fMRI) Methods**

In the following chapter, I will introduce the two neuroimaging techniques, namely ERP and fMRI, employed in the experiments of the thesis before introducing the neuroimaging evidence of retrieval cue processing in general and retrieval success processes in specific in chapter 3.

The purpose of cognitive psychology is to identify the psychological processes that mediate between environment and behaviour, and to elucidate the functional characteristics of these processes (Coles & Rugg, 1995). It is thought that all psychological functioning depends on basic biophysical processes, and that a large proportion of these processes consist of neuronal transmembrane activity (e.g. Churchland, 1986). That is why it can be beneficial to complement behavioural measures with neuroimaging measurement techniques to access information about the underlying neural events corresponding to a certain cognitive process. Therefore, the recording and measurement of electrophysiological brain activity in ERP as well as the haemodynamic BOLD signal in fMRI during specific psychological tasks can inform and constrain theories of psychological function.

### **Electroencephalogram (EEG)**

The electroencephalogram (EEG) recorded from the scalp is the summation of the electrical activity of large populations of cells that is conducted through the brain and the scalp (Allison, Wood & McCarthy, 1986; Nunez, 1981). It consists of a voltage by time function. The amplitude of normal human EEG varies between approximately  $-100$  and  $100\mu\text{V}$ , and the frequency ranges from DC up to 40Hz and even beyond (Coles & Rugg, 1995). An event-related potential (ERP) is the scalp-recorded electrical activity time-locked to a specific physical or mental event (Picton, Lins & Scherg, 1995). This event is typically the experimental stimulus. The ERP is extracted from the EEG by means of averaging the signal across multiple trials of the same stimulus type. ERPs provide a trial-based measure of neural activity, in that activity is time-locked to the presentation of each experimental stimulus. This allows averaged ERPs to be formed for each experimental condition post hoc depending on performance. For example, ERPs elicited by the presentation of a studied item during a recognition memory test can be categorised according to whether the item was recognised or not. In this way, averaged ERPs can be formed both for correctly recognised studied items (so called 'hits'), for correctly rejected nonstudied items (so called 'correct rejections'), for forgotten studied items (so called 'misses') and for incorrectly recognised items (so called 'false alarms'). This event-related aspect of the electrophysiological technique differs from the blocked designs formerly employed in recognition memory studies involving haemodynamic neuroimaging methods such as PET and fMRI, which would identify activations elicited across blocks of items rather than identifying item-related activity per se (e.g. Rugg et al., 1996; Nyberg et al., 1995). For many years, ERPs could therefore provide a measure of

neural activity that reflected the subtleties of performance in a way that measures of haemodynamic neuroimaging methods could not. However, this advantage has in the last decade been weakened by the advent of event-related fMRI (Rosen et al., 1998), which can also identify neural activity contingent upon performance.

Despite this, electrophysiology stills enjoys a number of advantages as a method of studying cognitive processes. The technique's major strength is that of temporal resolution, which is in the order of milliseconds. ERPs can therefore track cognitive processes in real time, and provide information about the dynamics of neural activity such as its evolution over time, as well as interactions between the activity of multiple neural populations (Rugg, 2001). The fact that ERPs are sensitive indicators of changes in neural activity, regardless of whether these changes influence observable behaviour, means that they can be used to examine cognitive processes when direct behavioural measures are difficult to obtain. For example, ERPs have been used to examine the processes underlying implicit memory (Paller, Kutas & McIsaac, 1995; Rugg et al., 1998b), to study the neural correlates of attended versus unattended stimuli (Hillyard, Hink, Schwent, & Picton, 1973), or to investigate directed forgetting at the encoding or retrieval stage (Ullsperger, Mecklinger & Muller, 2000). The high temporal resolution of ERPs gives this technique a significant advantage over event-related fMRI when it comes to the study of recognition memory.

It is important to note that, while differences in ERPs can place an upper limit on the time by which processing differs between conditions, they cannot rule out the possibility that processing differences may have occurred at an earlier time point (Rugg & Coles, 1995). For example, ERP differences at an earlier time stage might have been too small in

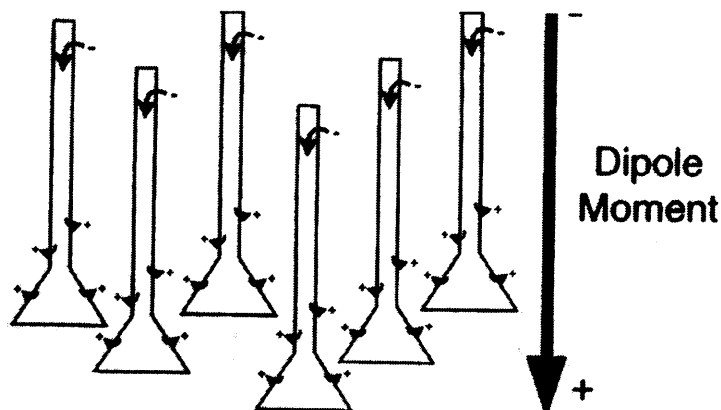
amplitude to be registered and hence recorded. Furthermore, as will be shortly discussed in the electrogenesis section, neurons with certain configurations and orientations produce electric fields that cannot be detected by ERPs. Therefore, this neural activity remains 'silent' to ERP scalp electrodes. These points illustrate a more general constraint relating to the interpretation of all kinds of functional neuroimaging data. While positive findings of differential neural activity provide support for cognitive processing differences, strong conclusions cannot be drawn on the basis of null findings.

ERPs do, however, suffer from poor spatial resolution. Because the brain acts as a volume conductor, there is no way of knowing the exact locus of the neural generators that give rise to a particular pattern of activity detected at the scalp without using other constraining sources of information. It is therefore incorrect to assume that an intracranial source can be directly inferred from the scalp location of an ERP deflection. Far greater spatial resolution can be achieved through the use of functional magnetic resonance imaging (fMRI), which records changes in neural activity and indicates loci of this activity by detecting changes in the oxygenation level of the blood flow (Ogawa, Lee, Kay, & Tank, 1990). However, this measure of neural activity is relatively indirect compared to that provided by ERPs, although a close relationship between the neural activity and the blood oxygenation levels analysed in fMRI has been established (Logothetis et al, 2001).

### Electrogenesis

An understanding of the principles of electrogenesis and of the propagation of field potentials is of crucial importance in the interpretation of ERP data. Electrogenesis

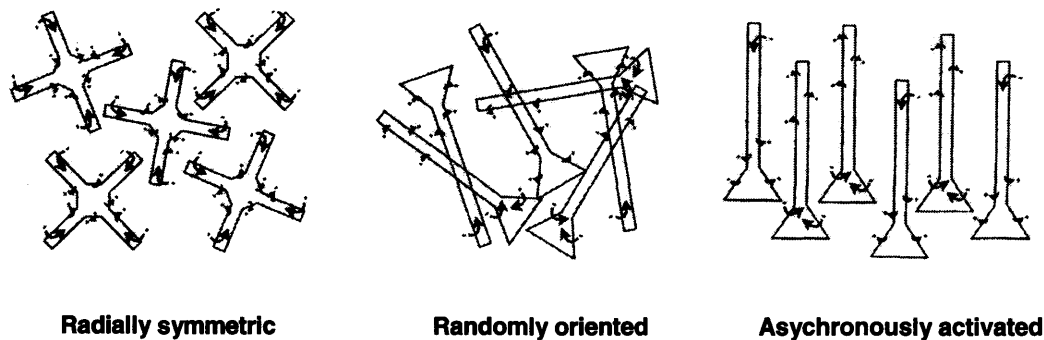
occurs at the level of individual neurons due to the bi-directional flow of positive and negative ions resulting from changes in the permeability of the cellular membrane. These individual electrical events are thought to consist largely of changes in the polarisation of inhibitory and excitatory cell bodies and dendrites of pyramidal cells rather than axonal action potentials (Allison, Wood & McCarthy, 1986). When the membranes of large groups of neurons are polarised synchronously, the resultant potentials undergo spatial summation resulting in a local field potential. The spatial arrangements of the neurons, constituting the generator, determine whether the field is 'open' or 'closed' (Coles & Rugg, 1995). An open field consists of neurons of the same orientation arranged in parallel, and is essentially a dipole as it contains both positive and negative charges between which a current can flow (Figure 2.1). A local field potential will only propagate throughout the brain, skull and scalp (which are conductive media) and contribute to the scalp EEG if it is generated by an open field, and if the arrangement of neurons generating this field is roughly perpendicular to the cortical surface. Further, the neurons have to be synchronously active to generate a field potential, which is strong enough to be detected at the scalp.



**Figure 2.1.** Open field source configuration. Adapted from Kutas and Dale (1997).

A closed field is a group of neurons, which are configured in such a way that the individual potentials cancel each other out (Wood, 1987). For example, a closed field may consist of neurons of opposite orientation, or of neurons arranged radially so that current can only flow inwards (See Figure 2.2; Kutas & Dale, 1997). The potential produced by a closed field does not propagate beyond its generators because the individual potentials cancel each other out or are in total too small and therefore cannot be detected at the scalp.

The principal brain structure that satisfies all of these constraints for detectability at the scalp is the neocortex, 70% of which consists of pyramidal cells organised by groups in columns and oriented perpendicular to the surface of the cortex (Nunez, 1981). It is therefore thought that the primary source of scalp-recorded ERPs is the synchronous excitatory or inhibitory post-synaptic potentials generated by pyramidal cells in the neocortex (Kutas & Dale, 1997).



**Figure 2.2.** Examples of self-cancelling or closed field source configurations. Adapted from Kutas and Dale (1997).



The effects of different neuronal configurations have important implications for the interpretation of ERP data as the absence of any ERP effects may simple be due to neural activity occurring in closed, rather than open, fields. Also, because of the conductive media of the brain and surrounding tissue, the laws and principles of volume conduction govern the magnitude of scalp-recorded ERPs. Given that neural tissue and the skull act as low-pass filters, a field current will diminish with increasing distance from the neuronal source and will be visible over relatively broad areas of the scalp (Davidson, Jackson & Larson, 2000).

Finally, scalp-recorded ERPs are rarely a measurement of a single local field potential, but rather a summation of potentials from multiple open fields. Open fields linearly summate as they propagate throughout the brain and reach the scalp. The principle of ‘superposition’ states that the potential at any given point represents an algebraic sum of all fields that have propagated to that point. The amplitude and polarity of the scalp-recorded ERP also varies with the distance between the electrode and the active tissue (Wood, 1987).

### **ERP recording**

Relative to the ongoing EEG, the small changes in voltage time-locked to, or elicited by, events of interest are difficult to detect. Therefore, the equipment, procedures and

parameters employed in the recording of ERP data significantly influence both the nature and the quality of the data collected. Electrode type and the quality of the interface between the skin and the electrode are both important in assuring high quality data, whereas recording parameters such as the reference site and the sampling rate employed can influence the topographical shape, the polarity, and the temporal resolution of the resulting ERPs. The recording system is also designed to minimise signal distortion and to remove artefactual noise in the signal picked up from the experimental environment and the subject.

#### Electrodes and the skin-electrode interface

Electrodes form the connection between electrical activity at the scalp and the input circuit of the amplifier. It is therefore crucial that the signal is not distorted at this interface if the recording is to be accurate. The quality of recording is significantly influenced by the type of metal from which the electrodes are made, as this determines the capacitance of the electrode, which in turn determines the degree of signal distortion. Also the integrity of the connection between the electrodes and the scalp determines the quality of signal. Usually, electrolyte solutions are sufficient to achieve an appropriate connection between the participants and the recording equipment. In terms of electrodes used, the immersion of a metal electrode into electrolyte solution can create an 'electrical double layer' of oppositely charged ions. This will cause the electrode-skin interface to act as a high-pass filter, which may distort the recorded signal. Non-polarizable Ag/AgCl electrodes are therefore most commonly used, as these are able to eliminate the electrical

double layer (Picton, Lins & Scherg, 1995) and also accurately record very slow changes in potential with minimal distortion (Picton et al., 2000). A further possible source of distortion is the quality of the connection between the electrode and the scalp as mentioned already above. The electrical impedance at this interface should be less than the input impedance of the amplifier by a factor of at least 100, or the recording is more likely to suffer from artefactual effects of electromagnetic fields (Picton et al., 2000). In a typical ERP experimental set-up, this impedance is kept below 5 k $\Omega$  by abrading the scalp beneath the electrodes. Electrodes are positioned according to standard scalp locations to allow easy comparisons between ERP experiments. The specific number and location of recording sites will depend on the particular aim and/or area of research. For example, it is necessary to employ a fairly dense array of electrodes in order to plot the scalp distributions of ERPs. In general, though, there is an even distribution of electrodes over multiple scalp locations, which typically includes mid-line and lateral sites.

### Referencing and amplification

Scalp-recorded ERPs contain both electromagnetic ‘noise’ from the environment (e.g. electrical experimental equipment such as the display monitor) in addition to the electrical brain activity of interest. As scalp-recorded activity is generally much smaller in magnitude than the electrical activity picked up from the environment, it is important to remove this environmental ‘noise’. This noise can be removed by the use of differential amplifiers which allow electrical noise in-phase at a ground electrode and the electrode of interest (known as ‘common mode signals’) to be cancelled (Picton et al.,

2000). As a potential is the difference between two points, all ERP recording must also be made with respect to a 'reference' electrode (Coles & Rugg, 1995). When using a 'referential' montage, each electrode from the array is connected to the same 'reference' electrode, which should be located at a site at which there is relatively little electrical activity of experimental interest. This common reference could be a single electrode located, say, at the nose tip, or a pair of 'linked' electrode, such as those placed over left & right mastoid processes, which provide a combination of the activity found at the two electrode sites and can be averaged off-line. Alternatively, there is also the possibility of recording from the reference of the linked mastoid electrodes and in a subsequent offline step to re-reference those electrodes to a third scalp reference, to avoid field changes. In both cases, the resulting measurement reflects the difference in voltage between that obtained at each individual electrode site and the common reference site. Therefore the location of the reference employed is of crucial importance when interpreting the scalp distribution and/or polarity of an ERP, as measurements of potentials are relative rather than absolute. The absolute values and/or the polarity of these potential differences in referenced recordings will differ according to the location of the reference employed, although the shape of the topographic profile will remain constant.

#### A/D conversion and filtering

A/D converters sample the ongoing EEG, converting these signals from analogue into digital form to facilitate data analysis (Picton, Lins & Scherg, 1995). The rate of A/D conversion is also referred to as the 'sampling rate', and this rate influences the temporal

resolution of the ERP. The resulting ERP waveform is a sequence of data points sampled at discrete intervals, each of which represents the difference in potential between the electrode of interest and the reference electrode. This sampling rate needs to be at least twice the highest frequency present in the signal (i.e., the 'Nyquist' rate). When frequencies higher than half the sampling rate (i.e., the Nyquist frequency) enter into the conversion, they may appear in the digitised data under the 'alias' of their lower harmonics (Picton, Lins & Scherg, 1995). During amplification, filtering of the analogue signals enables the recording system to detect target electrical brain activity while rejecting frequencies that are unlikely to reflect the activity of interest. Low and high cut-off frequencies specify the bandpass of the amplifier, and frequencies that fall outside of this bandpass are attenuated by the amplifiers.

### **Signal extraction**

The steps described above record an EEG that captures the electrical brain activity of interest, and which contains minimal artefactual noise. Further processing is now required in order to extract the 'signal' (i.e. the ERP) from the ongoing EEG. These steps are described below.

### **Artefact detection and elimination**

The data are examined to ensure that the ERPs only contain veridical brain activity. This is necessary because a number of artefacts can be present in the data after recording. The

waveforms are therefore usually analysed off-line in order to determine that all artefacts have been removed prior to analysis. These artefacts can take the form of baseline drifts, saturation and eye movement artefacts. A baseline drift takes the form of a linear slope, which persists throughout the epoch, and may occur if the electrode potential becomes too high, or if the skin-electrode interface is ruptured, or if the participant sweats excessively. Saturation occurs when the voltage of the signal exceeds the range of the amplifiers and thus appears as a continuous flat line throughout the epoch on the screen. Eye movement artefacts can take the form of blinks or saccadic movements. Blink-related artefacts can be eliminated in one of two ways; blinks can either be discouraged and excluded, or the contribution of the blink artefact to all other recording channels can be estimated for each individual subject and algorithmically corrected, if the electro-oculogram (EOG) was concurrently recorded. Blink-related artefacts were minimised by a blink correction algorithm in the present studies (Rugg et al., 1997b). The blink estimation and correction procedures employed in these studies also required the rejection of all trials containing saccadic eye movements.

### Signal averaging

The EEG can be considered as consisting of two parts; the 'signal' and background noise (Rugg & Coles, 1995). The signal is usually smaller than the noise in which it is embedded, and it is therefore often impossible to observe the signal in single trials (Picton, Lins, & Scherg, 1995). It is assumed that the signal is invariant across trials of the same type and time-locked to the experimental event of interest, whereas the noise is

of a random nature. Extraction of the signal from the ongoing EEG therefore requires the averaging of repeated time-locked epochs of EEG, all of which correspond to the same class of experimental event. This reduces the background noise, thus revealing the neural activity time-locked to the task (i.e. the ERP). Averaging is performed for each point by point digital value, and is performed only on artefact-free trials. As the signal is generally much smaller than the noise, the 'signal-to-noise' ratio must be increased so that the ERPs can be measured and analysed. Leading on from that, the greater the number of trials contributing to each of the experimental conditions, the higher the signal-to-noise ratio. Signal averaging gives an averaged ERP waveform for every condition at every electrode site for each subject. All statistical analyses are performed on these averaged data.

However, averaged ERPs should be interpreted with caution as signal averaging can lead to distortions of the original signal present in the single-trial data. It is possible for an averaged ERP waveform to bear little relation to the ERPs observed in individual trials, as trial-to-trial variability in either the latency or amplitude of the ERP can 'smear' the averaged ERP (Picton, Lins, & Scherg, 1995). For example, an ERP effect may differ quantitatively between two conditions, which would generally be interpreted as a graded difference in the activity of the same neural generator between the two conditions.

However, it is also possible that the two conditions differed only in the proportion of trials in which the component was evident. An additional problem is that of 'latency jitter'. This refers to the phenomenon in which timing of a component varies from trial to trial, resulting in a smeared averaged ERP with a long duration and decreased amplitude.

While it is theoretically possible to compare components in individual trials to the component observed in the average, this is not always possible if the signal-to-noise ratio is low. For a further discussion of how to quantify and compensate for the temporal jitter of signals, see Picton, Lins and Scherg (1995).

### **Interpretation of the ERP**

In general, ERP waveforms consist of a series of peaks and troughs, which are generally described in terms of their latency, polarity, scalp distribution and amplitude, measured in relation either to the pre-stimulus baseline (i.e. the mean voltage level of the waveform in the period preceding stimulus presentation), or to another feature of the waveform. To make any interpretation of these waveforms, it is necessary for the researchers to classify these troughs or peaks into so-called ERP components.

### **ERP components**

There is no unique definition of an ERP component, as the descriptive framework employed depend on whether one is adopting a 'physiological' or a 'functional' approach (Rugg & Coles, 1995). The former emphasises anatomical localisation and defines components as the activity of a single neural generator, whereas the latter emphasises the functional significance of ERP deflections and defines components in terms of the processing operations with which they are associated (these two approaches are discussed in greater detail shortly). These two approaches lie at opposite ends of a continuum, and in reality researchers take an interpretative approach that lies somewhere between these



two extremes. However, it is generally agreed that a single ERP component should represent the activity of a pool of neurons correlated with a specific processing operation. Components can either be 'exogenous' or 'endogenous'. Exogenous components are externally induced and therefore sensitive to the physical characteristics of stimuli, whereas endogenous components are internally generated and reflect the operation of higher order cognitive processes. This distinction is not categorical, and components can show sensitivity both to the physical characteristics of the stimulus and to task demands.

Traditionally, each deflection was defined as a single 'component', and was labelled either in terms of its polarity and serial order in the waveform (e.g. P1, N2), or in terms of its polarity and peak latency (e.g. P200). However, it has been argued that this 'peak-picking' approach is simplistic and misleading, as a single component identified in this way may in fact represent the summation of activity from multiple sources in the brain (Kutas & Dale, 1997). It is therefore inappropriate to infer that a component identified in this way reflects the activity of a single neural generator. Although this objection is less of a problem to researchers who identify ERP components with psychological function as opposed to neural generators, the problem remains that a single ERP deflection can reflect multiple concurrent processing operations.

An additional problem with the peak picking approach is the fact that specific peaks and troughs may vary in appearance or latency according to factors such as experimental conditions or the age of subjects (Picton et al., 2000). An alternative to this method of component identification involves measuring the mean amplitude of the ERP across a specified latency region relative to the amplitude of the pre-stimulus baseline (Picton et

al., 2000), which I employed in the ERP experiments later on. The mean amplitude approach removes the focus of investigation away from 'peak-picking' and the functional significance of specific deflections, and instead examines how these mean amplitude measurements differ between various experimental conditions or response categories. These differences are known as ERP 'effects'. Mean amplitude measurements also have greater stability than those of individual deflections in that they are more resistant to residual noise. Specifying the latency region should preferably be done a priori on the basis of previous studies, but should capture the main effect of interest.

#### The 'physiological' approach

For those taking the physiological approach, the defining characteristic of an ERP component is the anatomical source of its generator(s) within the brain, and little or no attempt is made to attribute a psychological function to the component. Components are defined as the contribution to an ERP field either of the activity of a single generator, or of a neural circuit containing multiple generators. While changes in the scalp distribution of an ERP component over time imply the involvement of several generators with different time-courses, the actual localisation of these generators is difficult to determine. The fact that deflections in the ERP waveform are likely to represent a summation of the activity of multiple generators means that some way of separating and identifying these contributing sources is necessary. As stated previously, the spatial resolution of ERPs is their greatest weakness, and this obviously creates significant problems when attempting to establish the neural basis of ERP components. Although it is possible to increase the

spatial resolution of the scalp field by increasing the number of recording channels, it has been argued that over 100 channels are required before it becomes possible to distinguish the contribution of individual cortical generators to the ERP. However, even this information is unreliable due to the problem of signal distortion during volume conduction (Gevins et al., 1995). The scalp distribution of ERP effects can be represented with topographic maps which show the positions of maximum and minimum amplitudes across the scalp, in a similar way to contour maps of terrain. This mapping requires three-dimensional data to be plotted as two-dimensional representations, and data between recording sites must be interpolated from the available information. Although, purely descriptive, this technique can be used to highlight any differences in the scalp distributions of ERP effects between experimental conditions.

The difficulty in determining the neural generators of an ERP scalp field is known as 'the inverse problem'. Any attempt to solve the inverse problem is obstructed by the fact that there is no unique solution in terms of generators for any given pattern of scalp activity (Wood, 1987). Analytical procedures have been developed that allow one to infer candidate ERP sources directly from scalp fields. These ERP sources can be constrained by human intracranial recordings to scalp recordings (Halgren et al., 1980), fMRI or PET activations in analogous tasks, anatomical models drawn from animal research (Pineda & Swick, 1992) and neurological cases that allow one to relate brain lesions to distortions in scalp activity. More recent developments in the field of source localisation have applied assumptions drawn from neuroanatomical knowledge to apply specific constraints to source localisation (e.g. dipoles must be located in grey matter, dipoles must be oriented

perpendicular to the cortical sheet, dipoles must possess locally coherent activity), and take advantage of information gained from haemodynamic imaging studies employing analogous tasks to produce a single solution of 'best fit' for any scalp field (Phillips, Rugg & Friston, 2002). However, it should be noted that the coupling between electrophysiological and haemodynamic signals is not yet fully understood, although some relationship is established (Logothetis et al, 2001). Therefore, caution is advised when using haemodynamic measures to constrain the source localisation of ERP data.

#### The 'functional' approach

Cognitive psychologists commonly take the functional approach when interpreting ERP data as greater emphasis is placed on the functional characteristics of an ERP component than the location of its anatomical source. Components are largely defined as specific variations in the waveform that are correlated with the cognitive process of interest. ERPs associated with different experimental conditions are subtracted from one another in order to isolate the ERP components elicited by the experimental manipulation. These components are then considered to be correlates of whatever cognitive processes are thought to differ between the two conditions. This 'subtractive' approach rests on the assumption of 'pure insertion' which states that the experimental conditions differ only in the cognitive process of interest (Coles & Rugg, 1995, however, for a critique of pure insertion and the subtraction method, see Friston et al., 1996). The functional approach employs the spatio-temporal characteristics of ERP components to make inferences about the cognitive processes of interest. For example, the onset latency and duration of a

component are thought to reflect the temporal dynamics of the corresponding information processing operation, although these measurements are not necessarily precise as they are susceptible to residual noise in the ERP waveform. Most of the time, the fact that ERPs yield so much information in terms of information processing is of far more interest to cognitive psychologists than information regarding the anatomical localisation of such processes. Therefore, the poor spatial resolution of ERP data is less problematic for cognitive psychologist than for those taking the physiological approach.

However, the fact that ERPs directly reflect neural activity means that cognitive psychologists are required to assume some kind of relationship between the neural activity recorded and the cognitive processes inferred, and opinions differ as to the nature of this relationship. At a basic level, it is assumed that ERPs reflect some aspect of neural activity, and that cognitive processes manifest themselves in this activity. In order to make functional inferences from ERP data, it is additionally assumed that the brain is functionally segregated with different regions responsible for different cognitive functions, and that the relationship between cognitive operations and their neural substrate is invariant. This assumption is known as ‘the invariance assumption’, which has not been contradicted by empirical evidence. The invariance assumption at its most basic level argues that an invariant ‘one-to-one’ mapping exists between cognitive functions and their neural substrates. Nevertheless, it has been argued by those adopting a neural-network approach (e.g. Mesulam, 1990) that multiple brain regions may also support a single cognitive process, and that each brain region may be recruited for multiple cognitive functions. According to this view, cognitive processes are the result of

interactions between multiple networks, and as such, cannot be localised to a single neural substrate. Such an account is not necessarily problematic for functional interpretations of ERP data (which do not require the assumption that an ERP effect reflects activity of a single neural generator), as long as these other mappings are themselves invariant. It would, however, be deeply problematic for many branches of cognitive neuroscience (including ERPs) if it was demonstrated that the same cognitive process can be supported by more than one pattern of brain activity, as this would undermine the invariance assumption that in turn underpins the mapping of cognitive function to brain activity. However, no evidence has as yet been presented to suggest that this may be the case (Rugg, 1998a).

Adoption of the invariance assumption allows one to make certain inferences from differences between ERPs elicited in different experimental conditions. Inferential statistics (e.g. analysis of variance) are used to ascertain whether these differences are reliable or not. It is assumed that reliably different ERPs reflect changes in neural activity, and that these changes indicate cognitive processes that differ either in degree or in kind. The nature of these differences is inferred from whether the ERPs differ qualitatively or quantitatively. A qualitative difference is demonstrated when scalp distributions of the ERPs differ, whereas a quantitative difference takes the form of ERPs that differ in magnitude but which have statistically non-distinguishable scalp distributions. It is assumed that a qualitative difference between ERPs reflects the activation of at least partially non-overlapping neural populations, which in turn reflect functionally distinct cognitive operations. ERPs that differ quantitatively are generally assumed to reflect differential activity of the same neural population(s). It is inferred

from a quantitative difference between ERPs associated with different experimental conditions that these conditions engage functionally equivalent cognitive processes to different degrees.

Two final notes of caution are required when interpreting ERP data. Firstly, it is important to remember that one can never prove that two or more processes do not elicit qualitatively distinct patterns of electrophysiological activity through the use of ERPs, or to conclusively prove that an experimental condition is not associated with a specific ERP effect. The reason is that, as mentioned already above, a null effect may occur either because the effect is taking in place in a closed field and is therefore undetectable to the scalp electrodes, or because the level of activity associated with the condition is too weak to be detected at the scalp. One can therefore never conclude that an experimental manipulation has no effect on brain activity simply because no difference is observed in the ERPs. Secondly, as with all neuroimaging techniques including fMRI, which is presented below, ERPs are purely correlational. One cannot therefore establish a causal relationship between the cognitive function and electrophysiological activities solely through the use of scalp-recorded ERPs. ERPs must be employed simultaneously with invasive techniques (e.g. pharmacological manipulations) in order to demonstrate a causal relationship between function and neural activity.

### **functional Magnetic Resonance Imaging (fMRI)**

As mentioned at the beginning of the chapter, other non-invasive neuroimaging methods besides ERP do exist, namely MEG and fMRI. Only fMRI (functional Magnetic Resonance Imaging) is of interest for this thesis as a method, which captures images that are sensitive to blood oxygenation level-dependent (BOLD) changes in the brain (Ogawa et al., 1990) and therefore, I will describe fMRI as a measurement technique below.

### **BOLD signal**

The BOLD signal is derived from hydrogen atoms in the water molecules of any body tissue. When placed in a strong external magnetic field (often 1.5 or 3 Tesla) and excited with radio-frequency pulses, the atoms absorb this applied energy and their own energy state is altered accordingly. After the radio-frequency excitation, the hydrogen atoms emit energy at the same frequency that was applied until they return to their equilibrium state. By measuring the radio-frequency energy emitted, the MRI scanner can construct an image of the underlying tissue. Image intensities in MR images may vary because hydrogen atoms experience slightly different magnetic field strengths (inhomogeneities). For example, hydrogen atoms in fat and hydrogen atoms in free water molecules will have different relaxation times and therefore produce different signals in the MR image. BOLD fMRI procedures measure the local changes in inhomogeneity primarily due to changes in blood oxygenation. This is possible because haemoglobin can be easily applied as an endogenous contrast agent since its two physiological states,



deoxyhaemoglobin and oxyhaemoglobin, have different magnetic properties. Only deoxyhaemoglobin is paramagnetic, introducing local inhomogeneity into the magnetic field. Thus, increases in deoxyhaemoglobin result in decreased BOLD image intensity in tissue, whereas decreases in deoxyhaemoglobin lead to increases in BOLD image strength (Heeger & Ress, 2002). Simply speaking, the more activity there is in the brain due to a cognitive process the more oxygen is needed in the area(s) involved. Thus, in an activated area there is an over-proportional influx of oxyhaemoglobin in relation to deoxyhaemoglobin concentration, which can be picked up as BOLD signal by fMRI. It is now thought that BOLD contrast depends not only on blood oxygenation, but also on blood flow and blood volume (Buxton et al., 1998). Thus, BOLD fMRI can be thought of as an indirect measure of neural activity based on local haemodynamics that assume there is a tight coupling between neural activity and the haemodynamic response.

#### Relation of BOLD fMRI signal to neurophysiology

Changes in local haemodynamics are thought to occur as a result of alterations in neural activity, although exactly how neuronal activity, haemodynamic responses and BOLD signals are related is, at present, unclear (see Heeger & Ress, 2002). The underpinnings of the BOLD signal are crucial to correctly infer results of fMRI studies and place them in relation to findings from other areas of neuroscience, for example neurophysiology (Raichle, 2003). However, technical difficulties have denied researchers for a long time a direct comparison of fMRI and actual neuronal activity. Nevertheless two kinds of approaches have been made in this direction: i) the first approach involves conducting

ostensibly the same experiment in humans and non-human primates and relating the fMRI results to those from electrode recording studies in primates (Rees et al., 2000). As will be obvious from the description, this again is an indirect correlation of the BOLD fMRI signal with the neural activity; ii) the second approach is based on pioneering research where fMRI and direct measures of neuronal activity are recorded simultaneously in monkeys (Logothetis et al., 2001). Both of these methods aim to relate measurements of neuronal activity (e.g. mean firing rates, multiunit spiking activity and local field potentials; see Logothetis, 2003) to the BOLD fMRI signal.

#### Simultaneous comparison of neurophysiology and fMRI in non-humans

The superior approach is to record several measures of neuronal activity directly whilst simultaneously measuring the BOLD response in a non-human primate. Logothetis and his colleagues (2001) used an electrode implanted in V1 to record multi-unit activity (MUA) and local field potentials (LFPs) in an anaesthetized monkey. MUA is thought to represent the weighted sum of the extracellular action potentials (i.e. spiking activity) of all neurons a small distance from the electrode tip (Logothetis, 2003). Single-unit recordings tend to selectively measure the output firing rates of the large pyramidal projection neurons that constitute the output signals from a cortical area. LFPs on the other hand, are lower frequency waveforms that probably reflect the input to a given cortical area and the local processing within that region (e.g. excitatory and inhibitory interneurons; see Logothetis, 2003, for a review). Logothetis et al. (2001) found that the BOLD response directly reflects an increase in neuronal activity as measured by the

mean extracellular field potential. Moreover, at some recording sites (but not others) BOLD responses were predicted by MUA and LFPs. Overall, LFPs were slightly better at estimating BOLD responses than MUA; however, although statistically significant, LFPs accounted for only about 7-8% more variance than MUA (Logothetis et al., 2001; Heeger and Ress, 2002). This suggests that both MUA and LFP relate to BOLD signal and that there might be considerable variation across the measurement sites and therefore possibly across brain regions.

#### Nature of the BOLD fMRI effect

One interpretation of these findings is that BOLD fMRI reflects the activity of the inputs to a neural region, interneuronal activity and recurrent signals rather than the output spiking activity of the region (Logothetis et al., 2001; Logothetis, 2003). This interpretation suggests that consistent findings from electrophysiological experiments in animals and human fMRI studies will not be found when intracortical processing and output activity are decoupled within a brain region. For example, lateral or feedback signals are thought to be involved in attention and these signals should be easily observed in imaging but not necessarily observed in single-cell recording experiments. One could argue that decoupling of inputs, local processing and outputs of a brain region do not occur because interneuronal activity tends to be observed in voxels that show spiking activity, or that inhibitory synapses (e.g. certain kinds of interneurons) do not produce a measurable BOLD response (Waldvogel et al., 2000; see also Arthurs & Boniface, 2002). Moreover, Raichle (1987) has suggested that it is unlikely that large volumes of the

cortex could sustain both high inhibitory activity (producing low spiking activity) and high metabolic rate. In contrast to these views, other studies suggest that inhibition can affect the BOLD signal (Tagamets & Horwitz, 2001) and at least some brain regions appear to imply inhibition as a fundamental principle in their systems level operation, for example, the basal ganglia and the cerebellum. Clearly, more studies are needed to resolve these issues and therefore the nature of the BOLD fMRI signal remains elusive.

Alternatively, Logothetis et al.'s (2001) results could be due to the transitory nature of the MUA signals. Logothetis et al. (2001) used relatively long stimulus presentations (up to 24 seconds) commonly found in block design fMRI experiments. Both BOLD fMRI and LFPs were shown to be sustained signals, whilst MUA returned to baseline after a short period (2-4 seconds) in a number of sites. As pointed out by Heeger and Ress (2002), if shorter, more rapid representations were used, the transient activity would dominate, increasing the correlation between all measures of neuronal activity (single unit, MUA and LFP) and the BOLD response. This hypothesis should be tested because the majority of current imaging studies of human cognition use rapid, event-related designs (see below).

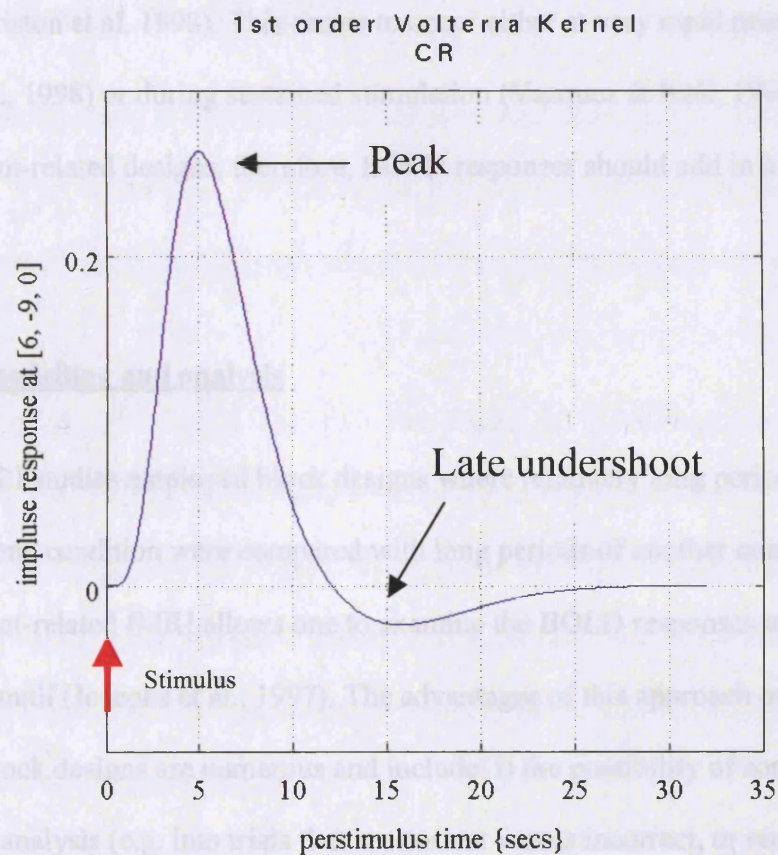
Although fMRI provides a much higher spatial resolution than ERP due to the missing volume conduction, there are some concerns about the spatial resolution achieved in fMRI (Ugurbil et al., 2003; Zarahn, 2001). For example, in earlier studies there was a concern that most of the BOLD fMRI signal came from large draining veins, distal to the location of the actual neuronal activity. This issue has been more or less resolved by

adopting suitable analysis methods. For example, retinotopic maps of visual cortex can distinguish activity that is separated by 1.5mm or less (Zarahn, 2001; Engel et al., 1994). By measuring BOLD responses as stimuli move through the visual field as Engel and his colleagues did (1994), contamination from draining veins is reduced because blood flow and oxygenation should be approximately constant in all experimental conditions in these vessels (see Heeger & Ress, 2002). It is assumed that this approach can be generalised to memory studies such as retrieval and subsequent memory because there should not be large differences in venous drainage in tightly controlled comparisons such as these.

### **fMRI in Practice: The Haemodynamic Impulse Response Function**

The haemodynamic impulse response function is the hypothesised shape of the BOLD response over time after brief stimulation. An example of this function is shown in Figure 2.3. The BOLD response reaches peak amplitude between 4-6 seconds, returns to baseline 10-12 seconds after stimulation and has a late undershoot that occurs for approximately another 10 seconds. The precise shape of this typical or “canonical” function was derived from a principal component analysis of data presented in Friston et al. (1998). Some authors have also claimed that there is an initial dip in the haemodynamic response that occurs because as neurons fire there is a slight increase in the deoxygenated blood before the vasculature can respond with a big increase in oxygenated blood to the area (for a different explanation of this phenomenon see Buxton et al., 1998). The potential benefit of imaging the initial dip is that it should have a smaller spatial spread than that of the larger positive BOLD component that peaks around

5 seconds (Zarahn, 2001). However, there is still controversy surrounding the initial dip as it has not always been found (Logothetis, 2000; Kim et al., 2000) and much more work needs to be done before it is routinely used in preference to the positive component.



**Figure 2.3.** The canonical form of the haemodynamic impulse response function.

Within a given subject, the haemodynamic response from a particular region is, in its shape and distribution, relatively consistent (Aguirre et al., 1998). However, there is considerable variability across subjects (Aguirre et al., 1998) and across brain regions

within a given subject (Schacter et al., 1997). Whether cross-subject variability is solely due to individual variation in vasculature or external factors (e.g. caffeine intake) is currently unknown. Analysis techniques (see below) have been developed to deal with some of these types of variability in haemodynamic response. Another key finding concerning the nature of the haemodynamic response is that the BOLD signal adds linearly to successive, brief presentations of stimuli (Dale & Buckner, 1997). However, the relationship between neural stimulation and the BOLD response can sometimes be nonlinear (Friston et al., 1998). This seems to occur either at very rapid presentation rates (Friston et al., 1998) or during sustained stimulation (Vazquez & Noll, 1998). For standard event-related designs, therefore, BOLD responses should add in a linear fashion.

### **Statistical modelling and analysis**

The first fMRI studies employed block designs where relatively long periods (e.g. 18-30 seconds) of one condition were compared with long periods of another condition. In contrast, event-related fMRI allows one to examine the BOLD responses to brief, rapidly presented stimuli (Josephs et al., 1997). The advantages of this approach over the more traditional block designs are numerous and include: i) the possibility of sorting trials post-hoc for analysis (e.g. into trials that are correct versus incorrect, or remembered versus not remembered, see Wagner et al., 1998) as is possible for ERP analyses; ii) trials can be presented in random or pseudo-random orders eliminating the predictability of block designs and iii) events can be defined by the subject. Finally, some events cannot be studied using a blocked design, such as an “oddball” stimulus which by definition is a

stimulus that departs from surrounding stimuli (Strange & Dolan, 2001). The nature of recognition and priming tasks dictates that the experiments conducted in this thesis will be event-related rather than blocked designs. If new and old stimuli are clustered together as in a block design experiment, it becomes very likely that subjects will realise this pattern and alter their responses accordingly.

### **Statistical Parametric Mapping (SPM)**

A very common method to analyse fMRI timeseries data is to use Statistical Parametric Mapping (SPM) (Friston et al., 1995, Ashburner & Friston, 1999; Friston et al. 1998; or see <http://www.fil.ion.ucl.ac.uk/spm>), which I also employed in the fMRI study of this thesis.

Generally speaking, the analysis comprises two stages: a pre-processing and a statistical stage. The pre-processing stage consists of processes to create a temporal and spatial reference of all scans across all subjects. Thus, at end of the pre-processing, all scans are in normalised space and hence allow statistical inferences to be made across participants. The statistical stages consist of estimating a model to fit the data, followed by F or t-test contrasts of the conditions of interest.



## **Pre-processing**

### **Slice timing**

The way SPM models different slices of the brain scans can be of a problematic nature. In the current versions of SPM (SPM99 and SPM2), data from different slices of the same scan volume are assumed to have been acquired at the same time. In reality, if an ascending sequence is used the top slice will be acquired TR seconds later than the bottom slice. This is the slice-timing problem (Henson et al., 1999a). If slices are left uncorrected, biased parameter estimates for the top-most slices may result. One solution to this problem is adopted in this thesis. During the pre-processing stage of data analysis, data from each slice will be interpolated to a reference slice as if they were acquired simultaneously (Henson et al., 1999a). It is of crucial importance as to which slice the data gets interpolated (typically the middle slice of a sequence) and more importantly, the pre-processing stage of slice-timing should be done before the data is normalised across subjects as to avoid any biased parameter estimates.

### **Realignment**

The goal of realignment is to align the functional images because of subject movements in between scans or across scan sessions. This procedure ensures that functional images are motion-corrected by estimating realignment (or motion) parameters for each session. The parameters contain three estimated translations in x, y and z directions (right/left, forward/backward, up/down) as well as three estimated rotations (pitch, roll, yaw).

Realignment works in two stages. First, the first slices from each session are realigned to the first slice of the first session. Second, within each session, the second, third, etc. images are realigned to the first slice. As a consequence, after realignment, all files are realigned to the first slice from the first session, which can be seen as a 'motion baseline'. For each file a .mat file is created containing the information of realignment, which can be used later at the statistics stages, to enter the estimated motion parameters as user-specific regressors in the design matrix.

### Normalization

The next step involves a normalization process, which is used to modify all subject's brains into a common three dimensional brain space. Normalization is therefore indispensable for any between-subjects analysis because it provides a standard brain space. There are three different ways to normalize the slice-time corrected and realigned images: i) normalization of the inplane anatomy to the MNI structural template: this method uses structural images acquired in the study to normalize them to a structural template provided by the Montreal Neurological Institute (MNI). All brain images of all subjects are thus in 'MNI space' which is a common internationally used reference space. ii) Segmentation of the inplane anatomy into gray matter, white matter and CSF: the second method uses mainly the gray matter to compute the normalization parameters. This method is not very often used, but it can be more accurate especially for basal grey matter structures such as the basal ganglia. iii) Normalization of the mean functional image to the MNI functional template: the third and last method is not so much

concerned with the normalisation of structural images but with normalising the actual functional images to a functional template provided by the MNI. The last method is becoming increasingly more common, as researchers are more concerned about the actual locus of the functional data and not necessarily the structural images overlap. It has also an advantage when the inplane anatomical image has failed to normalise well. However, this method can be inappropriate if there is large signal drop-out in parts of the functional images due to susceptibility artefacts (e.g. the orbito-frontal cortex and the temporal pole are especially prone to such artefacts due to magnetic susceptibility artefacts because of adjacent tissue (brain) and air (sinuses) regions).

### Smoothing

After normalisation all the data should have the same temporal (slice timing) and spatial (realignment & normalisation) reference. However, there might still be some between-subjects variability left which the previous steps did not account for. It is therefore necessary to smooth the data so as to compensate for any residual between-subjects variability. Further, smoothing is necessary as to allow the application of the Gaussian random field theory at the statistics inference stage. To smooth the normalised data, a Gaussian kernel defined by the FWHM (full width half maximum) is applied to the data. The size of the kernel should be at least 2.5-3 times that of the voxel size. For example, in a case of having 2 by 2 by 2 voxels, the FWHM should be at least 6 by 6 by 6, which means the Gaussian function will be a function with 6mm width, measured at the mid-point between the base of the function and its peak. The functional data are prepared for

the statistical analysis because all the voxels acquired are now in accordance with the Gaussian field theory and therefore allow statistical inferences to be made.

### **Statistical Analysis**

The statistical analysis consists of two stages. First, there is an estimation of a model, which should fit the data. This is done, by building a Design Matrix, which includes all conditions measured as well as any user-defined regressors (e.g. motion parameters etc.). Second, the actual data will be fitted to the estimation (i.e. Design Matrix) and parameter estimates for each condition and regressor are calculated. These parameter estimates are subsequently used for user-defined F-test and t-tests, which may reveal main effects and/or interactions of conditions and/or user-defined regressors. This allows one to make statistical inferences for each subjects on a first level analysis basis, which is often followed up by a second level analysis across all participants.

### **Efficiency of event-related fMRI designs**

Finally, I will mention factors that influence the efficiency of event-related designs. These include the number of events or conditions, the minimum SOA, the probability of an event occurring at a given time-point and the contrast of interest (typically, either a main effect against baseline or a differential effect). Types of design are classified depending on the probability that a specific event will occur and these can range from fully deterministic (alternating designs, e.g. ABAB) to fully stochastic (random designs,

e.g. ABBBAAB) or somewhere in between (permuted and pseudo-random designs). Furthermore, these probabilities can change over the course of an experiment (e.g. dynamic stochastic design). There are in general two types of contrast: main effects of conditions versus baseline ( $A+B$ ) and difference effects between two conditions ( $A-B$ ) (for a critique of difference effects see Friston et al., 1996). However, it is important to note that the most efficient design for one contrast is unlikely to be the most efficient design for another contrast.

Another aspect of experimental designs concerns null events. These are brief gaps between real events that are indistinguishable from the inter-trial interval (ITI). If a crosshair is presented during the ITI, then a null event appears as an ITI that is slightly protracted. The advantage of including null events is that they allow rapid multiple-event designs to be sensitive to main effects as well as differential effects (although a small amount of sensitivity to the differential effect is lost; Josephs & Henson, 1999).

For the above reasons I choose, for the fMRI experiment of the thesis, an event-related design plus null-events in my stimulus presentation to increase the design efficiency, as well as to sort conditions according to stimulus responses. I will come back to this issue in the methods section of the fMRI experiment itself, which will give a more comprehensive overview of the design and stimulus presentation employed.

### **Chapter 3 - Neuroimaging studies of retrieval cue processing**

The following chapter will give a brief overview of ERP and fMRI studies addressing retrieval cue processing. As in chapter 1, I will be selective in my choice of key studies presented and more detailed accounts can be found, for example, in the following publications (Rugg & Wilding, 2000; Rugg & Henson, 2002; Rugg, Otten, & Henson, 2002; Rugg & Yonelinas, 2003). Further, I decided to separate the studies of memory into ERP and fMRI, respectively. The reason is that the correspondence between the neural correlates of memory processing revealed by electrophysiological and haemodynamic data is less than perfect, and a one-to-one mapping is difficult to make. Thus, the first part will be mainly focused on ERP findings in the field of memory research, while the second part is concerned with event-related fMRI studies of memory processing.

#### **ERP evidence of retrieval cue processes**

All of the studies I will review employed variations on a 'study-test' recognition memory paradigm (also employed throughout the thesis), in which subjects are presented with a set of items to encode at study, and are then presented with these items together with a number of unstudied items at test. Test instructions require subjects to identify, which items have been previously studied and which items have not.

## Retrieval mode

ERP evidence so far has been relatively scarce in terms of finding evidence for other retrieval processes beside retrieval success effects (for a review of ERP retrieval success processes, see Rugg, Otten & Henson, 2002). The reason is that many retrieval processes are thought of to be tonically maintained throughout episodic retrieval and therefore state rather than item dependent, as discussed in chapter 1. However, researchers have struggled so far to delineate item and state-related retrieval effects and this has halted investigations in this direction. Thus, to my knowledge only three ERP studies so far have directly addressed retrieval mode effects. Duzel et al., (1999) recorded PET and DC ERPs on subjects performing either an episodic retrieval or a semantic decision task. The rationale behind this experiment was that according to Tulving's (1983) original formulation of the retrieval mode concept the key function of retrieval mode was to bias the cognitive system to treat external events as retrieval cues. Thus, only an episodic retrieval task instructing subjects to handle cues as retrieval cues should reveal retrieval mode effects. Further, Duzel et al. (1999) employed DC ERPs (ERPs measuring slow-wave forms), which enabled them to observe state rather than item effects for the episodic versus the semantic retrieval task. They found a sustained positive-going shift elicited by right fronto-polar waveforms during the episodic retrieval task. More importantly, the onset of this effect was in response to the task cue and sustained across the rest of the stimulus series regardless of the study status (old versus new). Thus, the effect fulfilled one of the main criteria for retrieval mode, namely the invariance across study history and the presence of the effect throughout the episodic retrieval task. The latter point further indicates that the measured effect supported the conception of retrieval

mode as a tonically maintained, item-independent state. In contrast, the semantic decision task, which also incorporated old and new items, did not elicit any such ERP effect.

Duzel et al. (2001b) reported that the scalp distribution differences between the two different kinds of blocks in Duzel et al. (1999) could be modelled by a generator in the right prefrontal cortex. However, this proposal of right frontal activation for retrieval mode is inconsistent with findings of a similar effect in ERP studies taken as an evidence that the region is sensitive to retrieval success (e.g. Wilding & Rugg, 1996; Donaldson & Rugg, 1998; and even Duzel et al., 1997).

Morcom and Rugg (2002) observed a similar ERP effect by cueing volunteers on a trial-by-trial basis to complete either an episodic retrieval task or a semantic decision task. Crucially, Morcom and Rugg (2002) recorded the ERP activity time-locked to the cue presented for each trial until the test item was presented. They found that the cue-related ERP activity was more positive-going over right fronto-central electrode sites. They reasoned that the effect reflected the adoption of retrieval mode and thus replicates the findings of Duzel et al. (1999). However, the cue-related episodic ERP effect was only apparent in conditions where a decision was preceded by the same decision and not when the decision changed between trials. Morcom and Rugg (2002) concluded that it takes at least one trial before a task-relevant set can be adopted, which they based on findings in the task-switching literature (e.g. Rogers & Monsell, 1995).

More recently, Herron and Wilding (2004) suggested that the effects measured in both earlier studies might reflect retrieval orientation effects and not a retrieval mode effect



per se. As a reminder, the difference between retrieval orientation and retrieval mode is that orientation effects should vary according to the information sought for, in contrast to retrieval mode effects. Herron and Wilding (2004) therefore incorporated a second episodic retrieval task in the original Morcom and Rugg design. This experimental manipulation allowed the measurement of retrieval mode, by contrasting the episodic retrieval tasks with the semantic decision task. Moreover, it allowed the observation of differences between the two episodic retrieval tasks, which are assumed to reflect retrieval orientation processing. ERPs time-locked to cue onset revealed a right frontal electrode site retrieval mode effect, which was invariant across episodic tasks. In contrast, an orientation effect between episodic tasks was also evident at central electrode locations (Herron & Wilding, 2004). Herron and Wilding thus provided evidence that the neural correlates of retrieval mode and orientation differ; a conclusion that could not be drawn from the two previous studies. Thus, different neural signatures for retrieval mode and orientation may exist and make it likely that the two processes are functionally distinct.

#### Retrieval orientation and retrieval effort

As a reminder, retrieval orientation is thought of as a tonically maintained retrieval strategy, which influences the cognitive operations engaged in response to each cue (Rugg & Wilding, 2000). Differences in retrieval orientation may arise because of the nature of the retrieval cue employed (e.g. verbal vs. pictorial), or because the same retrieval cues are employed to access different kind of memory representation (e.g.,

representations that arise from 'conceptually vs. data-driven' encoding operations; Roediger, Weldon, & Challis, 1989; Richardson-Klavehn, & Bjork, 1988; Jacoby, 1983). A further aspect of retrieval processing is retrieval effort – the utilisation of processing resources in attempts to retrieve a memory. Effort will vary according to the difficulty encountered when employing retrieval cues to bring back information from memory, and is a consequence of such variables as the amount of attention allocated to cue processing, and the number of retrieval attempts made. It should be noted that while orientation and effort are, in principle, independent aspects of retrieval processing, they are often likely to be confounded in practice. The combined influence on the processing of retrieval cues of these two aspects of retrieval processing will be referred to as 'retrieval set' effects.

Manipulations of retrieval set have been employed in some recent ERP studies (Ranganath & Paller, 1999; Wilding, 1999; Senkfor & Van Petten, 1998; Johnson, Kounios, & Nolde, 1997). In two of these studies (Ranganath & Paller, 1999; Wilding, 1999), ERPs elicited by correctly classified new (unstudied) items were compared directly according to the type of retrieval task in which the items were presented. In Ranganath and Paller (1999), test items consisted of unstudied pictures dissimilar to any studied item, previously studied pictures, and unstudied pictures that were perceptually similar to studied items. In one condition, subjects were required to classify both studied and similar items as 'old', responding new only to dissimilar items. In a second condition, the task was to respond old only to studied items, classifying both dissimilar and similar unstudied items as new. Ranganath and Paller (1999) reasoned that the two conditions would differ in respect of the specificity of the information that had to be

recovered from memory and, hence, would engender different levels of retrieval orientation. ERPs over left frontal scalp sites were more positive-going when elicited by new items in the test condition, which required retrieval of more specific information. Ranganath and Paller interpreted this finding as a correlate of differential engagement of memory search operations supported by the left prefrontal cortex.

Wilding (1999) compared ERPs elicited by new items in a test of source memory according to the nature of the source judgement required (speaker voice vs. type of study task). ERPs from frontal sites varied according to this manipulation, the differences demonstrating a polarity reversal across hemispheres. Wilding (1999) interpreted these findings (cf. Senkfor & Van Petten, 1998; Johnson, Kounios, & Nolde, 1997) as evidence that the requirement to retrieve different kinds of source information modulated subjects' retrieval orientation. Further, in a study by Rugg, Allan, and Birch (2000), subjects were instructed to encode words either in a shallow (alphabetic judgement) or a deep (sentence generation) way. In separate test blocks subjects performed a recognition memory experiment, which showed that the ERP neural correlates did differ as a function of the encoding task. This result was taken as evidence by the authors that participants adopt different retrieval orientations when trying to retrieve items encoded either in a semantic or in an alphabetic way.

However, these previous studies did not distinguish effects related to retrieval orientation and retrieval effort. In a more recent ERP study, Robb and Rugg (2002) instructed subjects to encode either words or pictures. In separate test phases, subjects decided for

visual words whether they had seen them before either as a word or as a picture before. More importantly, Robb and Rugg factorially crossed the factor of retrieval orientation (by way of the encoding material) with the factor of retrieval effort (by way of task difficulty). Retrieval effort was manipulated by using a combination of the variables of length of study list and study-test interval. ERPs elicited by the unstudied new words differed according to the encoding material and task difficulty in that from around 300ms post-stimulus ERPs more negative-going over central/parietal electrode sites when these items were employed to probe memory for pictures rather than words. However, difficulty ERP effects were short-lived in contrast to the prolonged nature of the study material effect. Moreover, the study material effect did not vary as a function of difficulty, and therefore the authors claimed that the retrieval orientation effect could be observed *per se*. They further concluded that retrieval orientation and retrieval effort could be regarded as independent processes.

Dzulkifli, Sharpe and Wilding (2004) also tried to tease apart effects of retrieval effort and retrieval orientation in an ERP study. However, Dzulkifli and colleagues manipulated task difficulty not by means of encoding task, as Robb and Rugg did, but by collecting data from a larger group of subjects to allow a between-subject analysis between high and low memory performing subjects. In addition, subjects encoded study words either in a semantic or phonological way to induce different retrieval orientations in the test phases for the two conditions. Strikingly, their results showed that an ERP retrieval orientation effect was only evident for the low performing group, i.e. those subjects who had to make more effort to recognise and to reject test items correctly, and not for the high performing

subject group. These results indicate that the neural correlates of retrieval effort and retrieval orientation are not as easy to delineate as first thought because the effects were both apparent only in the low performing group. Hence, researchers should take caution in interpreting an ERP effect as related to retrieval orientation unless they: i) either employ an experimental design showing no behavioural performance differences between conditions, thus making it unlikely that retrieval effort was part of the ERP difference effect or ii) investigate task cue time-locked ERP effects which should be not as prone to require effort as the item-related effects mentioned. The reason is that the cue effects should reflect more preparatory retrieval processes (like retrieval orientation) and not the actual effort of an retrieval attempt. Nevertheless, both experimental constraints are by no means established and need to be further scrutinised.

In a further study Herron and Rugg (2003) investigated whether the blocking of the study phases influenced the building retrieval orientation effects in the test phase. More specifically, subjects encoded mixed lists of words and pictures, and then performed a recognition memory task with words as test items. In one block, the requirement was to respond positively to test items corresponding to words, and to reject both new items and items corresponding to studied pictures. In the other block, positive responses were made to test items corresponding to pictures, and items corresponding to words were rejected along with new items. Similar to Robb and Rugg (2002), new item ERPs differed according to the sought-for information. More importantly, Herron and Rugg (2003) argued that the findings demonstrate that ERP retrieval orientation effects can be found when both relevant and irrelevant items are encoded in a common study context. They

further show that the effects are obtained even when the test list contains retrieval cues corresponding to both classes of study item. Hence, the adoption of a retrieval orientation may not only serve to maximise the probability of retrieving targeted memories, as argued before, but may also reduce the likelihood of retrieving irrelevant memories.

### **fMRI evidence of retrieval cue processes**

The final part of this chapter will describe fMRI studies investigating retrieval cue processes and I will refrain from reporting retrieval success studies. Similarities of neural correlates in fMRI and ERP studies will only be highlighted when relevant, and I will mainly refer to recent event-related fMRI memory studies.

### **Retrieval mode**

To my knowledge only a few fMRI studies so far have systematically investigated effects of retrieval mode. However, a number of PET studies (Cabeza et al., 1997; Duzel et al., 1999; Grady et al. 2001; Nyberg et al., 1995; Rugg et al., 1998a) have attempted to localise effects of retrieval mode in the human brain. Most of the studies suggest that Brodmann area 10, in the right prefrontal cortex represents the neural signature of retrieval mode because it shows activity invariant across episodic retrieval tasks and invariant to the nature of the retrieval cue and study status (old versus new). For example, Cabeza and colleagues (1997) found right prefrontal activity in a PET experiment for a cued recall and a recognition test in comparison to a non-episodic baseline. Duzel et al.

(1999) and Nyberg et al. (1995) investigated whether high or low-density proportions of old words in a recognition memory test would show retrieval mode activity in comparison to a control task. Further, Grady et al. (2001) investigated whether different encoding material would lead to different neural signatures to a control task but not to each other. All of the above studies reported right prefrontal activations across retrieval tasks and were insensitive to the nature of the cue. Although these studies were run in a blocked fashion, and thus the results might reflect item- rather than state-related right prefrontal activity, the pattern of results suggests that this region is activated across episodic retrieval tasks and different retrieval cues employed, which fulfils the criteria of a retrieval mode effect as put forward in chapter 1 (see also Lepage, 2001 for a meta-analysis of retrieval mode PET studies). Hence, all the studies concluded that the right prefrontal activity should be attributed to retrieval mode processing.

This notion was challenged by Rugg and colleagues (1998c) who showed in a PET, as well as in a subsequent fMRI study (Rugg et al., 1999), that the right prefrontal activation is task-sensitive and thus not likely to represent retrieval mode processing. In their study, Rugg et al. (1998c) contrasted word stem cued recall with recognition memory tasks. Crucially, they factorially crossed the two retrieval tasks with two density lists, which they compiled as follows: a low density list with 0% old items and a high density list with 80% old items. Right prefrontal activity was observed in the cued recall list, regardless of which density list was employed. However, activation in BA10 could only be observed in high density lists in the recognition memory test. This pattern of right-prefrontal activity (BA10) is difficult to reconcile with the idea that this region should be the neural

signature of an adoption of a task-invariant retrieval mode. Rugg and colleagues suggested on the basis of these and earlier findings (Rugg et al., 1996) that the activity in the right prefrontal region might be more due to memory monitoring operations, as the activity in this region increases with target density, although this notion was challenged (see below, retrieval effort, Wagner et al., 1998).

Further, Donaldson and colleagues (Donaldson et al., 2001b) contrasted item- and state-related fMRI activity to reveal transient (i.e. retrieval success) and sustained (i.e. retrieval mode) retrieval processing in a recognition memory task. Their results showed the common network of transient retrieval success effects (see above) and more interestingly, frontal brain regions sensitive to sustained retrieval processing (i.e. retrieval mode correlates). However, in contrast to the PET studies, retrieval mode activity was mainly observed in the frontal areas of the left hemisphere (e.g. left inferior frontal gyrus), which supports Rugg et al. (1998c) findings that the right prefrontal cortex might not be the brain region responsible for retrieval mode processing. More strikingly, Donaldson et al. showed also that retrieval success and mode processing can be associated with the same brain region, which leaves again open the question as to whether retrieval success and more general retrieval cue processes are truly orthogonal to each other.

### Retrieval effort

As mentioned in chapter 1, the concept of retrieval effort is ill-defined and elusive, as any mobilization of retrieval processes can be regarded as such a process. Still, Schacter et al. (1996) reported in a PET study that, at a subsequent test, word stems encoded shallowly



showed greater anterior prefrontal activity than word stems encoded deeply. However, an fMRI study by Buckner and colleagues (1998) found the opposite result, in that prefrontal regions were more activated for items encoded deeply than shallowly. Further doubt was cast on the proposal of neural correlates of retrieval effort in prefrontal cortex by the earlier mentioned study of Wagner and colleagues (1998). Wagner et al. (1998) varied the factors of encoding task (shallow versus deep) which affected the accuracy and reaction times greatly in favour of deeply encoded test items, while having no effect on activation in the prefrontal cortex regions. Together, these findings indicate that retrieval effort has so far no neural correlate or signature which can be easily identified.

### Retrieval orientation

As discussed earlier, the recording of neural correlates of retrieval orientation has so far been mainly attempted in ERP recognition memory studies. To my knowledge no published fMRI study has directly targeted retrieval orientation processes. However several studies, briefly outlined below, have investigated encoding and retrieval task manipulations, which are related to retrieval orientation investigations.

McDermott et al. (1999) collapsed activity elicited by old and new items in a recognition task and contrasted this with the activity of items at encoding. McDermott and colleagues reported various regions for which activity was higher in the retrieval than the encoding condition, including lateral and medial parietal cortex, and right dorsolateral prefrontal cortex. However, due to collapsing activity across old and new items it is difficult to

attribute these activities to either retrieval orientation or retrieval success. Similar problems can be found in a study by Nolde et al. (1998), in which retrieval-related activity was contrasted for old items with regard to whether a yes-no recognition task or a source memory task was performed by subjects. Nolde and colleagues reported in particular regions in the left prefrontal cortex which were more active in the source than the yes-no task, which they attributed to additional 'reflective' retrieval operations. However, as in the McDermott study, the response related-activity cannot be attributed to either retrieval success or retrieval processing per se.

A study by Ranganath and colleagues (2000) made a more promising approach towards this problem. In their study, subjects encoded pictures perceptually which differed in size. In two subsequent test phases, participants had to decide in the 'general' retrieval task whether they had seen the picture before, or in the 'specific' retrieval task whether the items were larger or smaller at study. Ranganath et al.'s (2000) results indicated that left anterior prefrontal cortex (BA 10) showed a relative increase in signal for the specific task, regardless of whether items were correctly identified as old or new. Ranganath and colleagues reasoned that this activity is due to some kind of monitoring or evaluative function carried out on the products of retrieval attempts. On the other hand, according to Rugg and Wildings (2000) proposal, these results could also be an effect of task-related retrieval cue processing (i.e. retrieval orientation). A subsequent study by Dobbins et al. (2003) reported similar results for retrieval orientation by contrasting recency with source task performance in a memory test. Source memory in comparison to recency decision exhibited increased activity especially in frontal, as well as in parietal cortices, while the

opposite contrast (i.e. recency > source memory) revealed activity mainly in frontal brain regions. Prefrontal regions therefore seem to be the most likely candidate for the so-called retrieval orientation effects (Rugg & Wilding, 2000) because of the differential activation of this region according to the task sought-for. However, the reported differences could also be due to the relative difficulty levels of the two tasks (i.e. retrieval effort; Schacter et. al, 1996) because specific tasks (i.e. source memory) should demand more processing and therefore retrieval effort than general tasks (i.e. recency). This possible confound needs to be further investigated in future fMRI studies.

From the above summary of neuroimaging studies of retrieval cue processes it is clear that more thorough and systematic investigations are needed to elucidate these processes further. Thus, in the following experiments, I combined some of the encoding, retrieval and retrieval cue manipulations mentioned in chapter 1 with the ERP & fMRI neuroimaging techniques to see how these manipulation change the neural correlates of retrieval orientation in particular. The specific experimental manipulations and their associated hypotheses will be introduced at the relevant point of each experimental chapter.

## **Chapter 4 – General ERP Methods**

Methods common to all ERP experiments presented in this thesis are described in the following chapter. Methods for the fMRI experiment and procedures more specific to the individual experiments can be found in the method sections of the relevant chapters. All experiments were approved by the joint ethics committees of the University College London and the University College London Hospitals.

### **Experimental paradigm**

For most of the experiments reported here, an explicit yes-no recognition memory paradigm was employed. Only experiment 5 included an incidental retrieval task as found in implicit memory paradigms (e.g. Richardson-Klavehn & Bjork, 1988; Richardson-Klavehn et al., 1994).

Each experimental session comprised several numbers of experimental blocks, which differed across experiments: four blocks (Experiments 1 & 4), two blocks (Experiment 2 & 3) or one experimental block for each of two groups (Follow-up study of experiment 2). Each experimental block represented a single experimental condition and consisted of two phases: study and test. The only exception was experiment 5 where each experimental block consisted only of one phase.

## **Participants**

Participants were drawn from a population of undergraduate and graduate student volunteers from UCL recruited via a group-based subject database. All participants were right-handed and spoke English as their first language. They were aged between 18 and 35 years, and had normal or corrected-to-normal vision. Participants gave informed consent before taking part in all experiments and were reimbursed at the rate of £7.50 per hour (plus travel expenses).

## **Stimuli**

The experimental item pool consisted of 320 colour pictures of nameable objects (collated from picture databases and the internet) and 320 words corresponding to the names of these objects (name agreement was tested initially in a pilot study, where at least 4 out of 6 subjects gave the identical name to an object). 288 pictures and words were chosen as critical items in experiment 1. The remaining items were used in practice sessions or were employed as filler items. For experiments 2-4, the experimental materials consisted of 164 colour pictures of nameable objects (a subset of those employed in experiment 1), along with their corresponding names. In addition, 164 auditory presentations of these names were created. 144 stimulus triplets (i.e. picture plus corresponding visual and auditory names) were selected as critical items. The remaining stimuli were employed as practice or filler items.

The physical characteristics of the pictures and visual words were the same as in experiment 1. Auditory words were spoken by a male native English speaker and

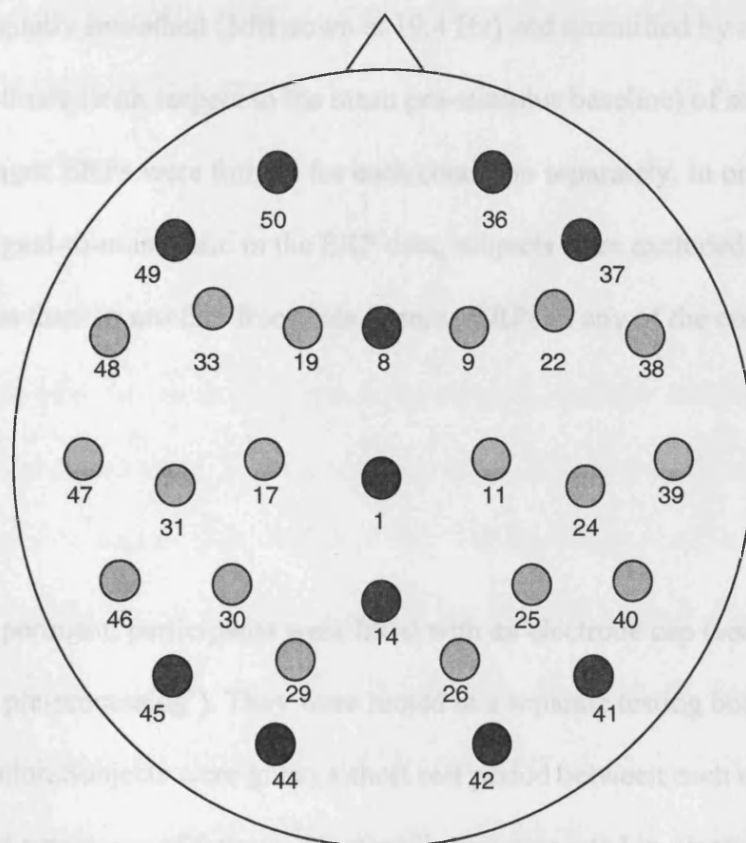
recorded in stereo with a sampling rate of 44.1 kHz and 16 bit resolution. The waveforms were filtered to remove ambient noise and edited so as to onset at the beginning of an auditory 'frame' that lasted for a total of 1500 ms.

In each experiment, the pictures, visual words or auditory words were randomly allocated to the separate study and test lists, and for each list the order of critical items was randomly changed. Study lists were buffered with two filler items at the beginning. Test lists contained four filler items, two at the beginning to avoid recency effects and two in the position immediately after a mid-list pause. Study lists of all experiments comprised 36 critical stimuli and test lists of all experiments comprised the studied 36 stimuli plus 36 new stimuli. For experiment 1 & 4 a total of four study-test lists were created, while experiments 2 & 3 consisted of two study-test lists. The ordering of the study-test lists (i.e. experimental conditions) was counterbalanced across subjects and short practice blocks preceded the experiments proper.

### **ERP recording and pre-processing**

EEG was recorded from 31 silver/silver chloride electrodes. Twenty-nine of these were embedded in an elasticated cap (these 29 sites were a subset of the 'montage 10' provided by the supplier of the electrode cap; see Figure 4.1). The equidistant placement of the electrode sites was done according to the international 10-20 system (Jaspers, 1951). The remaining 2 electrodes were placed on each mastoid process. Vertical and horizontal electroculogram (EOG) were recorded from electrode pairs situated above and under the right eye and on the outer canthus of the left and right eye. Recordings were made with

reference to the mid-frontal electrode ('Fz' of the international 10-20 system) and were re-referenced offline to the average of the two mastoids.



**Figure 4.1.** Twenty-nine electrode sites of the 'montage 10' equidistant recording system used in all ERP experiments.

EEG and EOG were amplified with a bandwidth of 0.03-35 Hz (3dB points) and digitized (12 bit resolution) at a sampling rate of 8ms per point (125 Hz). For each test trial, the recording epoch lasted for a duration of 2068ms, which included a 128ms pre-stimulus baseline period to give a post-stimulus recording epoch of 1940ms. A correction procedure was applied to minimize trials rejected due to blink artefact, using linear regression to estimate and correct the contribution of blink artefact to the EEG (similar to Rugg, Mark, Gilchrist & Robert, 1997). Trials containing excessive horizontal and

vertical eye movements other than blinks were rejected via visual inspection, as were trials with A/D saturation or drifts in the baseline exceeding  $\pm 55\mu\text{V}$ .

ERPs were digitally smoothed (3dB down at 19.4 Hz) and quantified by measurement of the mean amplitude (with respect to the mean pre-stimulus baseline) of selected latency regions. Averaged ERPs were formed for each condition separately. In order to achieve an adequate signal-to-noise ratio in the ERP data, subjects were excluded if they contributed less than 16 artefact-free trials forming ERPs to any of the critical conditions.

### **Procedure**

Prior to the experiment, participants were fitted with an electrode cap (see 'ERP recording and pre-processing'). They were seated in a separate testing booth facing a computer monitor. Subjects were given a short rest period between each of the study-test blocks to avoid symptoms of fatigue. All stimuli were presented in central vision within a light grey background frame that subtended a vertical and horizontal visual angle of 3.8 degrees. Colour pictures were shown within the frame subtending a vertical and horizontal visual angle of 3.7 degrees. Words were displayed in black upper case letters on a light grey background subtending a vertical visual angle of 0.4 degrees and a maximum horizontal angle of 3.7 degrees.

Each subject received a short practise study-test block prior to the first study phase for each condition to become familiar with the experimental procedure and the presentation of the items. They were informed as to which experimental block they were about to study before the appearance of the first item in the test list of each block.



Subjects made their decisions by pressing one of the two response keys in front of them with their index finger. The subjects were told before the first study phase how the keys were configured. The configuration was alternated across subjects but remained constant across blocks for each participant.

### **Data analyses**

Behavioural and ERP data were analysed using repeated measures ANOVA for all experiments. Where necessary, F-ratios are reported with degrees of freedom corrected for non-sphericity (Greenhouse & Geisser, 1959). For the behavioural analyses, ANOVAs were performed on accuracy and reaction time (RT) data and any contrasts of interest were followed up with t-tests. For the ERP data, all statistical tests used an alpha level of .05. In all cases, effects that did not involve factors of study material or retrieval task are not described (effects involving the factor of Old/New can be found in the appendix of the thesis). Magnitude and topographic analyses of the ERP data were conducted as detailed below.

### **Magnitude analyses**

The waveforms for each condition were quantified by measuring the mean amplitude (relative to the pre-stimulus baseline) over four latency regions: 100-300 msec, 300-600 msec, 600-900 msec, and 900-1200 msec. These regions were selected to correspond with those typically employed in previous comparable studies (e.g. Herron & Rugg,

2004) while also taking into account visual inspection of the waveforms in the present experiments. Analyses within each latency region took the form of initial global ANOVAs conducted on data from a distributed grid of 18 electrode sites (indicated in light grey in Figure 4.1) in order to identify which scalp locations were sensitive to the experimental manipulations. This grid was factored according to hemisphere, anterior-posterior chain (frontal, temporal, parietal) and site (inferior, mid-lateral, superior) and included lateral frontal sites (48, 33, 19, 38, 22, 9; see Figure 4.1), lateral temporal sites (47, 31, 17, 39, 24, 11) and lateral parietal sites (46, 30, 29, 40, 25, 26). First, data from each condition were analysed separately in order to establish reliable differences in the ERPs between the study material and/or task conditions. When the overall ANOVA gave rise to significant effects of study material and/or task, subsidiary ANOVAs were conducted to separately contrast ERPs according to the material and/or the task. Further for experiments 1 & 2, the three midline electrodes (8, 1, 14) were also analysed along the lines of the above analysis.

### **Topographic analyses**

Differences in the scalp topography of reliable study material and encoding task effects were investigated, both within and across condition, as well as across different latency regions (as described above). The use of topographic analyses provides a means of assessing whether ERP effects differ qualitatively (i.e. due to the activation of different neural generators) across different experimental conditions and/or latency regions. These analyses were conducted on difference scores derived from all 29 electrodes and reveal

reliable differences when significant condition x site interactions are obtained. As a standard procedure the topographical analysis was conducted on all electrode sites because the effects reported were widely distributed over the scalp and hence, it was seen as not necessary to conduct any further focused topographical analyses on selected electrode sites only. There are potential problems, however, when using an ANOVA model, as changes in the activity of neural generators have multiplicative, rather than additive, effects on the amplitude measures detected at the scalp. Therefore, when an experimental manipulation elicits a simple change in dipole strength, differential changes in amplitude will be detected at different electrode sites, resulting in a misleading condition x site interaction. In order to satisfy the additivity assumption of the ANOVA, the ERP data was rescaled prior to analysis by using the min/max method (McCarthy and Wood, 1985). This method calculates the amplitude of the ERP effect of interest at each electrode site relative to all other sites and maintains a pattern of relative differences in the size of the effect across the scalp while removing differences in amplitude. More specifically, this method finds the minimum and maximum mean values in each condition, subtracting the minimum from each data point, and dividing by the difference between minimum and maximum (McCarthy and Wood, 1985). Finally, the scalp distribution of ERP effects were displayed using spline maps showing the relative size of the effect (in microvolts) across the surface of the scalp. This technique was used to highlight any significant differences in the scalp distribution of ERP effects between experimental conditions.

## **Chapter 5 – Experiment 1: The employment of different classes of retrieval cues and their influence on the retrieval orientation effect**

### **Introduction**

I presented in an earlier part of the thesis the theoretical and experimental background of item- and state-related retrieval cue processing. As a reminder, the ERP findings of Robb and Rugg (2002), Herron and Rugg (2003) and Dzulkifli, Sharpe and Wilding (2004) support the proposal that subjects process retrieval cues differently depending on the nature of the targeted memory representations, even in yes/no recognition tests, which do not require from the subject to retrieve specific study information. The functional significance of the ERP effect (greater negativity in new word ERPs when attempting to retrieve pictures rather than words) identified in the studies of Robb and Rugg (2002) and Herron and Rugg (2003) is unclear however. The findings of Robb and Rugg (2002) suggest that the effect is not due to the greater difficulty of using words as cues to search for picture- rather than word-based memories (but see Dzulkifli, Sharpe & Wilding, 2004). Nevertheless, the design of the Robb and Rugg (2002) and Herron and Rugg (2003) studies confounded the manipulation of study material with the degree of similarity between study and test items. This confound makes it difficult to determine whether the ERP effect is a consequence of attempting to retrieve words vs. pictures (a material effect), or using cues that differ in their similarity to the sought-for information (a cue similarity effect). If the former would be true, it would mean that the ERP effect is encoding material dependent and new word ERPs should always be more negative when

attempting to retrieve pictures. In contrast, according to the latter explanation it is expected to see more negative ERP waveforms if the test and study material differ in their overall perceptual similarity.

The aim of the following first thesis experiment was to address this issue by crossing the variables of study material and retrieval cue, allowing an assessment of whether previous findings reflect material or similarity effects. This was achieved by extending the study of Robb and Rugg (2002) to include two additional conditions in which pictures rather than words served as the retrieval cues. Thus, the design crossed the factors of stimulus material and study-test similarity to generate four conditions: study words – test words; study words – test pictures; study pictures – test pictures, and study pictures – test words.

## **Methods**

### **Participants**

Thirty subjects participated. Data are reported from twenty subjects (9 female), aged between 18 and 33 years (mean 24). Data from the remaining ten subjects were rejected due to the failure to form ERPs from fewer than 16 artefact-free trials in one or more of the critical experimental conditions.

## Experimental Materials

From the pool of 320 experimental items (described in chapter 4), 288 pictures and words were chosen as critical items. The remaining items were employed as practice or filler items.

For each subject, four study lists were created by random sampling from the item pool. Each list contained 36 critical stimuli along with 2 filler items, which padded the beginning of the list. Two of the lists contained pictures, and two words. Test lists, one corresponding to each study list, contained a random ordering of the 36 critical items belonging to the study list, along with 36 unstudied items. A further four filler items were used to pad the beginning of the list (2 items) and to act as the first 2 stimuli after the mid-way break. The unstudied items employed in the four test lists were selected randomly, without replacement, from the item pool.

Each subject received a different ordering of the four study-test cycles (word-word, picture-word, word-picture, picture-picture). Each of the study-test cycles comprised one experimental condition so that all four conditions had separate or blocked study-test cycles. The hand employed for the test judgements was held constant within subjects, but counterbalanced over them.

## Procedure

Study trials consisted of the presentation of a fixation character ('+') for 500ms. The screen was blanked for 120ms, and followed by the presentation of the stimulus for a

duration of 1500ms. The screen was then blanked until the subject responded, after which the next trial was initiated. The study task varied depending on whether pictures or words were presented. For pictures, subjects decided whether each displayed object would, at its real-life size, fit into a shoebox. For words, the judgement was whether the denoted object was more likely to be found indoors or outdoors. The rationale for this procedure was to maximize the distinctiveness of the memory representations resulting from the encoding the two classes of study material, and hence to maximize the likelihood that subjects would adopt different retrieval orientations when searching for each class of material.

Test trials began with the presentation of a fixation character ('+') for 1200ms, after which the screen was blanked for 120ms. This interval was followed by the presentation of the test item for 500ms. A second fixation character ('\*') then appeared for 2400ms. The screen was then blanked and the next trial initiated 200ms later. The task was to judge whether each item (or the corresponding item in the case of the word-picture and picture-word conditions) had been presented in the immediately preceding study phase.

### ERP recording and analysis

(see chapter 4 for a detailed description)

## **Results**

### Behavioural Performance

Mean percent correct and reaction time (RT) are shown for each condition in Table 5.1.

Recognition accuracy was assessed using the discrimination index  $Pr$  ( $pHit - pFalse$  Alarm; Snodgrass & Corwin, 1988). These values were .86, .82, .92 and .72 for the word-word, picture-word, picture-picture and word-picture conditions respectively.

ANOVA of these data [factors of cue type (word vs. picture) and study-test match (same vs. different)] gave rise to significant effects for match condition ( $F_{1,19} = 48.00$ ,  $p < .001$ ), and for the interaction between match condition and cue type ( $F_{1,19} = 15.81$ ,  $p = .001$ ). Follow-up ANOVAS revealed that, in the matching conditions, performance was better for picture than for word cues ( $F_{1,19} = 6.66$ ,  $p < .025$ ). Conversely, when study material and cue mismatched, performance was better for the word cues ( $F_{1,19} = 17.14$ ,  $p < .001$ ). Additional contrasts revealed no reliable difference in performance for the word cues according to whether words or pictures were being retrieved, but a significant enhancement in the picture-picture compared to word-picture condition ( $F_{1,19} = 51.00$ ,  $p < .000$ ).

**Table 5.1.** Percent accuracy, RT (ms) and PR by condition and item type.

Condition	Accuracy (SD)		RT (SD)		PR
	Old	New	Old	New	Hit-FA
Word-Word	0.92 (0.08)	0.95 (0.06)	869 (267)	963 (269)	0.86
Word-Picture	0.82 (0.1)	0.9 (0.07)	1042 (307)	1262 (315)	0.72
Picture-Picture	0.95 (0.04)	0.97 (0.03)	803 (192)	849 (278)	0.92
Picture-Word	0.9 (0.08)	0.92 (0.06)	969 (259)	1139 (180)	0.82

ANOVA of correct rejection RTs (i.e. the condition from which the ERP data reported below were derived) also gave rise to a main effect of match condition ( $F_{1,19} = 107.80$ ,  $p < .000$ ).



.001) and an interaction with cue type ( $F_{1,19} = 16.28, p < .001$ ). Follow-up tests revealed that for both words and pictures RTs were shorter when cue and study material matched ( $F_{1,19} = 56.98, p < .000, F_{1,19} = 60.75, p < .000$ , respectively). For the match condition, RTs were shorter for picture than word cues, whereas the converse was the case when cue and study material did not match ( $F_{1,19} = 12.94, p < .01$  &  $F_{1,19} = 5.32, p < .05$ , respectively).

### ERP Data

Grand-average ERP waveforms elicited by correctly classified new items are shown for selected electrode sites in Figures 5.1 & 5.2. The mean numbers of trials (range in brackets) forming individual subjects' ERPs were 28 (16-36), 27 (17-35), 30 (24-35) and 28 (16-33) for the word-word, word-picture, picture-picture and picture-word conditions respectively. As is evident from the figure, when the retrieval cues are words, ERPs are more negative-going when pictures are the sought-for material from around 300ms post-stimulus onwards. In contrast, when memory is cued by pictures the effect reverses, such that waveforms are more negative-going when words are targeted for retrieval from around 300ms post-stimulus onwards.

The ERP data were quantified and analysed according to the procedure described in Chapter 4 with ANOVAs employing the factors of cue type (word vs. picture) and study-test similarity (match/non-match) in the magnitude analysis. Only effects that do involve the factor of study-test similarity are of interest in the current context, and are therefore reported (see Table 5.2). A summary of effects involving the factor of Old/New for experiment 1 can be consulted in appendix 1 of the thesis.

In addition to the analyses of ERP amplitude described above, the scalp topographies of the study-test similarity effects were contrasted according to the procedure described in Chapter 4. The initial ANOVA employed the factors of retrieval cue (word vs. picture), latency region, and electrode site.

**Table 5.2.** Exp. 1 – Summary of ANOVA results in each ERP latency region including the factors of match and cue.

Main effects & interactions	100-300 msec	300-600 msec	600-900 msec	900-1200 msec
18 main electrode sites				
MT	$F_{1,19} = 11.39, p < .01$	$F_{1,19} = 9.81, p < .01$	$F_{1,19} = 26.36, p < .000$	–
MT x HM	–	–	$F_{1,19} = 9.71, p < .01$	–
MT x ST	–	$F_{1,2,23.4} = 12.40, p = .001$	$F_{1,1,21.2} = 7.07, p < .025$	$F_{1,2,22.3} = 4.99, p < .05$
WP x MT x AP	–	$F_{1,2,22.7} = 5.80, p < .025$	$F_{1,2,21.9} = 10.45, p < .01$	$F_{1,2,23.4} = 9.64, p < .01$
MT x HM x AP	–	$F_{1,3,25.0} = 3.88, p = .05$	–	–
MT x AP x ST	–	–	$F_{1,9,36.6} = 3.69, p < .05$	–
3 mid-central electrode sites				
MT	$F_{1,19} = 6.02, p < .025$	$F_{1,19} = 15.35, p = .001$	$F_{1,19} = 19.81, p < .00$	–

MT = match type; WP = cue type; HM = hemisphere; AP = location; ST = site

### *Magnitude analyses for 18 electrode sites*

#### **100-300ms**

ANOVA of the 100-300ms latency region only revealed a main effect of match condition ( $F_{1,19} = 11.39, p < 0.01$ ).

#### **300-600ms**

ANOVA of the 300-600ms data gave rise to a main effect of match condition ( $F_{1,19} = 9.81, p < .01$ ) and to its interactions with site ( $F_{1.2, 23.4} = 12.40, p < .001$ ), and with cue type and anterior-posterior chain ( $F_{1.2, 22.7} = 5.80, p < .025$ ). A subsidiary ANOVA on the data for the word cues only gave rise to a match effect ( $F_{1,19} = 8.72, p < .01$ ). ANOVA of the picture data revealed interactions between matching condition and chain, and matching condition and site (respectively:  $F_{1.3, 24.5} = 6.36, p < .025$ ;  $F_{1.2, 22.6} = 7.95, p < .01$ ). This pattern of effects suggests that match effects were reliable for both cue types, but that their scalp distributions differed (see topographic analyses below).

#### **600-900ms**

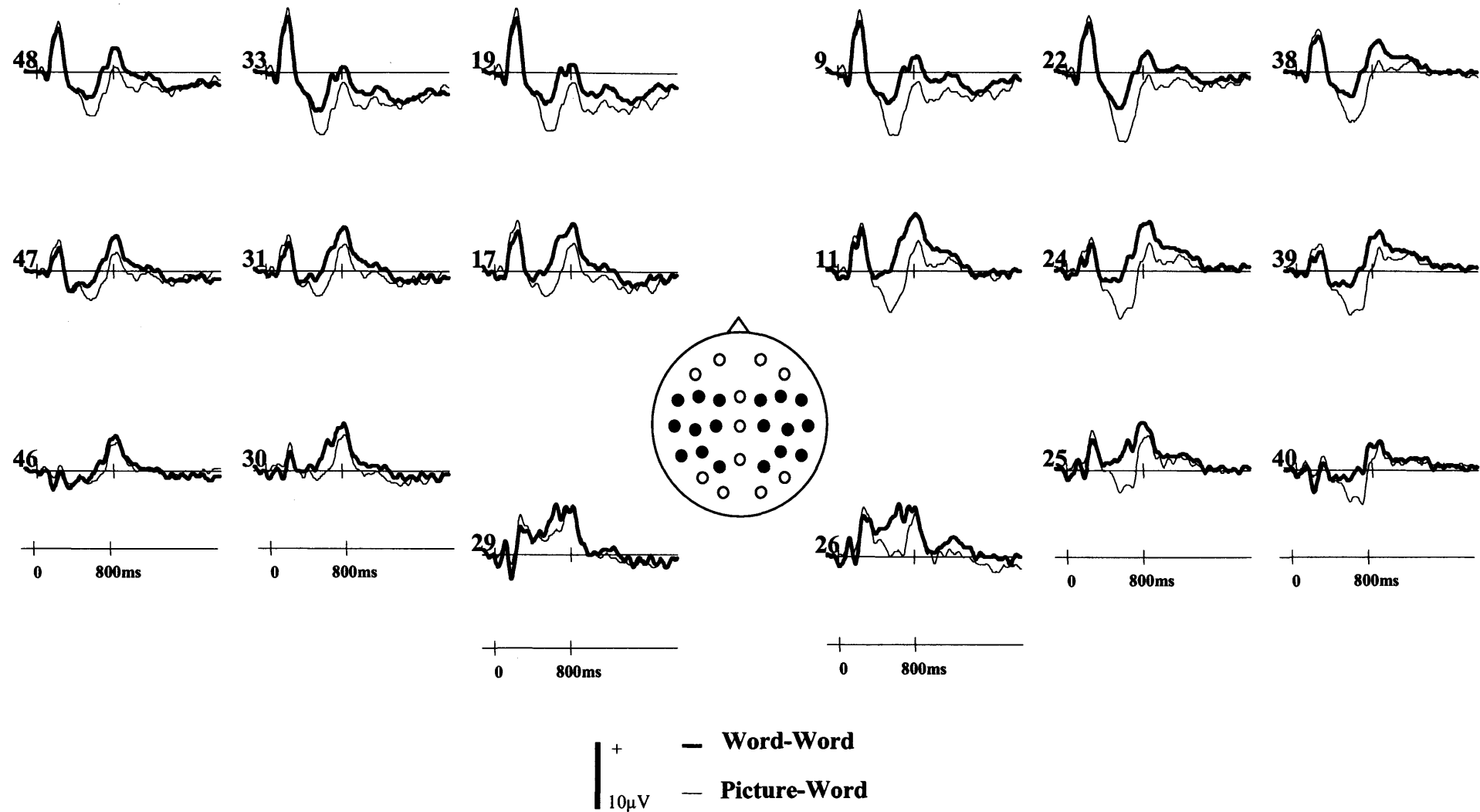
ANOVA of the 600-900ms data again gave rise to a main effect of matching condition ( $F_{1,19} = 26.36, p < .000$ ), as well as its interaction with hemisphere and site ( $F_{1,19} = 9.71, p < .01$ ;  $F_{1.1, 21.2} = 7.07, p < .025$ ), and with cue type and anterior-posterior chain ( $F_{1.2, 21.9} = 10.45, p < .01$ ). A follow-up ANOVA on the data for the word cues gave rise to a match effect ( $F_{1,19} = 16.76, p < .001$ ), and to its interaction both with hemisphere ( $F_{1,19} = 5.13, p < .05$ ), and chain ( $F_{1.6, 30.8} = 9.19, p < .001$ ). In the case of the picture cue data, a main effect of matching condition was again found ( $F_{1,19} = 19.57, p < .001$ ), along with match

x hemisphere and match x site interactions (respectively:  $F_{1,19} = 4.80, p < .05$ ;  $F_{1.1, 20.5} = 7.61, p < .025$ ). These results once again demonstrate robust match effects for each class cue type, with a tendency in both case for the effects to be larger over the right hemisphere. Again echoing the findings for the previous latency region, there is also a suggestion that the scalp distribution of these match/non-match effects might vary with cue type.

### **900-1200ms**

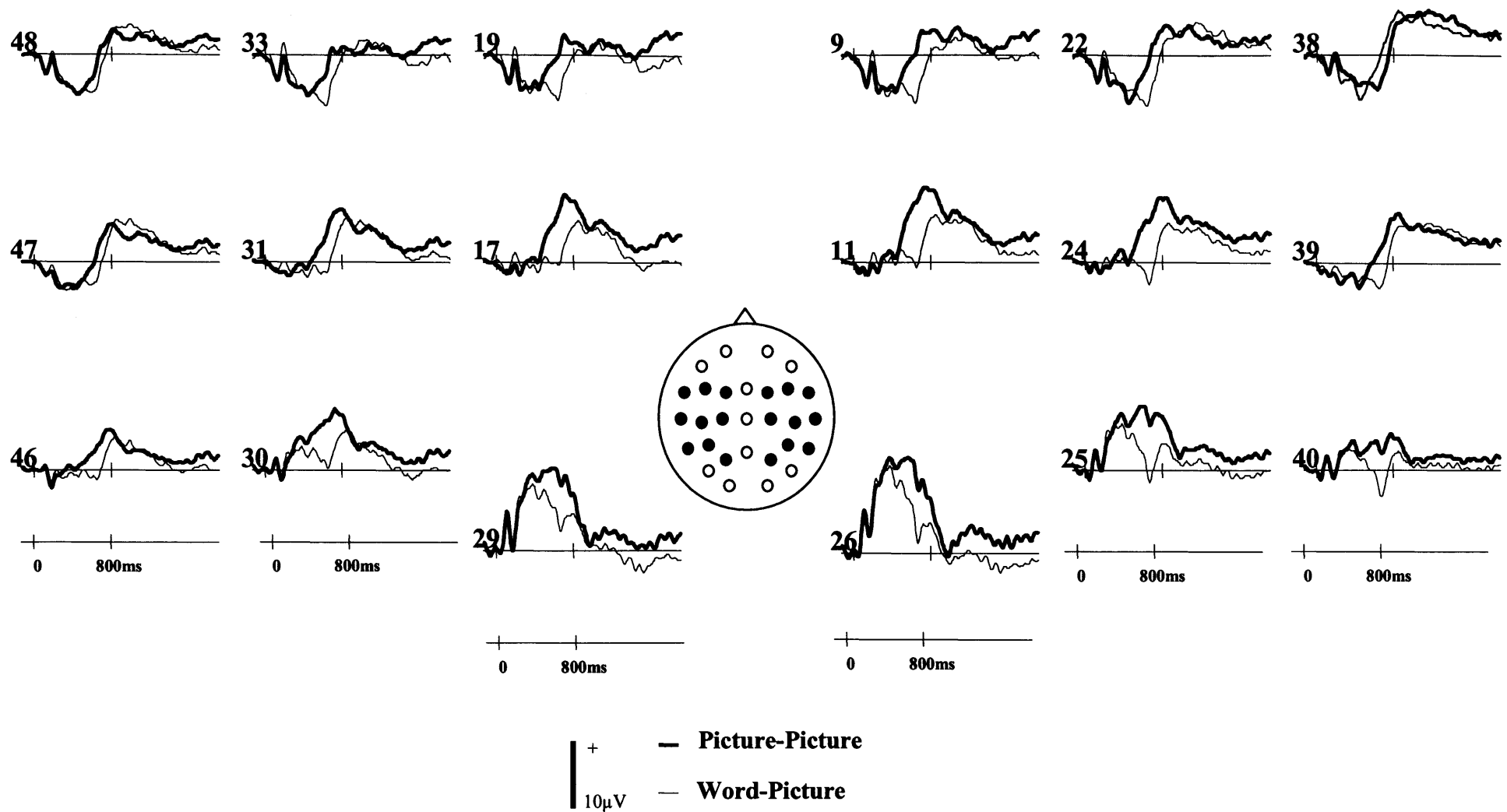
For the 900-1200ms region, ANOVA revealed interactions between match condition and site ( $F_{1.2,22.3} = 4.99, p < .05$ ), and between match condition, cue type, and anterior-posterior chain ( $F_{1.2,23.4} = 9.64, p < .01$ ). However, separate ANOVAs gave rise to no effects involving the match/non-match factor for either the word or picture cue data.

## Word retrieval cue condition



**Figure 5.1** Exp. 1 – Word retrieval cue conditions: Grand average ERP waveforms elicited by correctly rejected new items at lateral frontal (48, 33, 19, 38, 22, 9), lateral temporal (47, 31, 17, 29, 24, 11) and lateral parietal sites (46, 30, 29, 40, 25, 26).

## Picture retrieval cue condition



**Figure 5.2** Exp. 1 – Picture retrieval cue conditions: Grand average ERP waveforms elicited by correctly rejected new items at electrode sites described in Figure 5.1.

### *Magnitude analyses for 3 selected electrode sites*

As evident from Figures 5.1 & 5.2, the scalp distribution for the matching effects for word and pictures cues are widely distributed, including mid-central electrode sites.

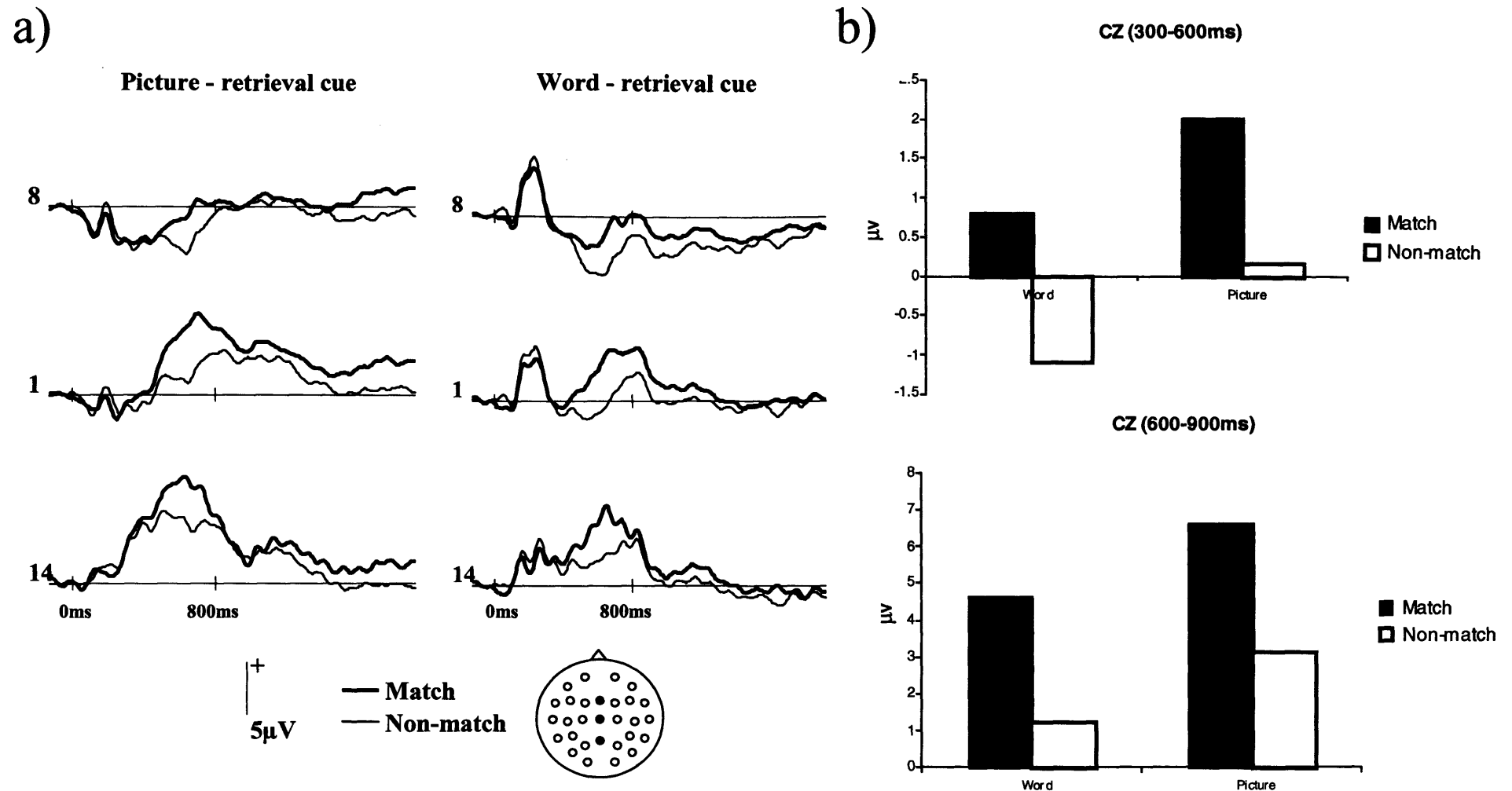
However, these three electrode sites are not included in the main analysis. Therefore, I conducted a further analysis encompassing only the three mid-line electrode sites (see Figure 5.3).

The latency regions of 100-300ms, 300-600ms, and 600-900ms gave rise in an ANOVA to a main effect of match condition ( $F_{1,19} = 6.02, p < .025$ ;  $F_{1,19} = 15.34, p = .001$ ;  $F_{1,19} = 19.81, p < .000$ ), but no interactions with cue type. Further ANOVA of the 900-1200ms latency region indicated only a trend of match condition ( $F_{1,19} = 3.55, p > .07$ ) and no interaction with cue type.

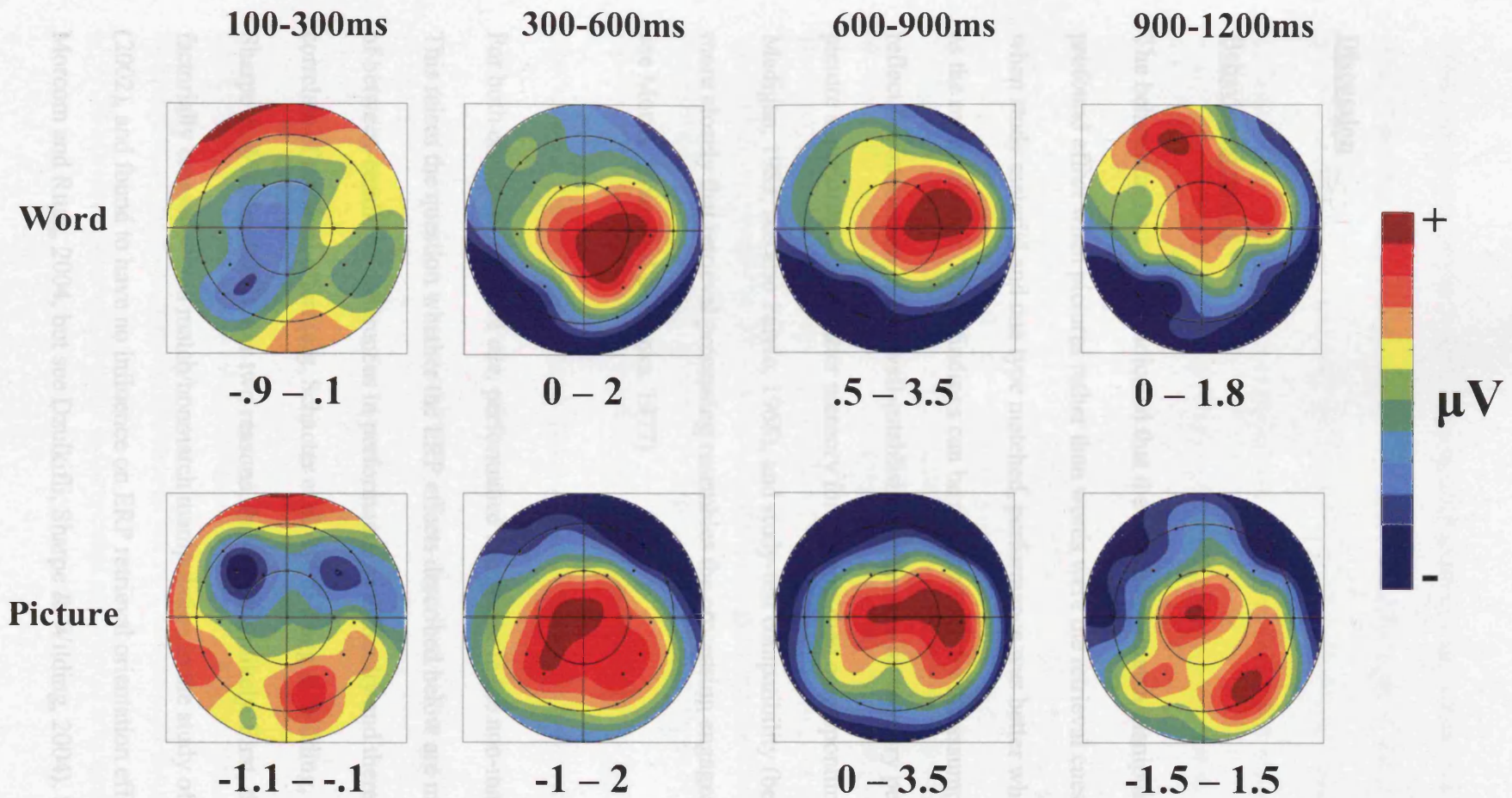
### *Topographic Analysis*

The scalp topographies of the match effects associated with the word and picture cues are illustrated in Figure 5.4 for each latency range. ANOVA demonstrated a cue type x site interaction ( $F_{4,3, 82.6} = 2.88, p < .025$ ), unmodified by the factor of latency region ( $p > .1$ ), indicating a significant difference in the topography of the two effects. As can be seen in Figure 5.4, this difference appears to have a more anterior distribution for the effects associated with the word cues.





**Figure 5.3** Exp. 1 – **a)** Mid-line electrode sites for Picture and Word retrieval cue conditions: Grand average ERP waveforms elicited by correctly rejected new items. **b)** Bar graphs showing ERP magnitudes in microvolt ( $\mu V$ ) at electrode site CZ for two selected latency regions (300-600ms; 600-900ms).



**Figure 5.4** Exp. 1 – **Top Panel:** Scalp topographies for the word retrieval cues (match – non-match) for all latency regions. **Lower panel:** Scalp topographies for the picture retrieval cues (match – non-match) for all latency regions. Values below each spline map denote minimum and maximum microvolt ( $\mu\text{V}$ ) values of each map.

## **Discussion**

### **Behavioural results**

The behavioural measures indicated that the match/non-match manipulation had a more profound effect when pictures rather than words were the retrieval cues. In addition, when study material and cue type matched, performance was better when pictures served as the retrieval cues. These findings can be accommodated by the assumption that they reflect the interaction of two well-established influences on memory performance: the picture superiority effect (better memory for pictures than corresponding words; Madigan, 1983, see also Paivio, 1968), and study-test compatibility (better memory the more closely that retrieval processing resembles the processing engaged during encoding; see Morris, Bransford & Franks, 1977).

For both classes of retrieval cue, performance was worse in the non-match condition. This raises the question whether the ERP effects described below are merely a correlate of between-condition differences in performance or difficulty and therefore merely a correlate of retrieval effort (e.g. Schacter et al. 1996; Rugg & Wilding, 2000; Dzulkipli, Sharpe & Wilding, 2004). For two reasons, this seems unlikely. First, difficulty was factorially crossed with a match/nonmatch manipulation in the study of Robb and Rugg (2002), and found to have no influence on ERP retrieval orientation effects (see also Morcom and Rugg, 2004, but see Dzulkipli, Sharpe & Wilding, 2004). Second, whereas

differences in performance were considerably more marked when pictures were retrieval cues rather than words, there was no corresponding difference in the magnitude of ERP retrieval orientation effects (see Figure 5.3, bar graphs). However, the issue of retrieval difficulty/effort effects remains unresolved unless the same effect could be observed when retrieval performance is equivalent for the different classes of study material.

### ERP results

The principal aim of the present experiment was to contrast two alternative explanations for the ERP retrieval orientation effects reported by Robb and Rugg (2002) and Herron and Rugg (2003), namely, that the effects reflect the consequences of searching for words vs. pictures as opposed to the employment of matching vs. nonmatching retrieval cues. The presented findings support the latter explanation: for both types of retrieval cue, ERPs were more negative-going when the cues were used to probe memory for nonmatching items. It thus appears that a crucial condition for the manifestation of the ERP effects is a variable level of similarity between material in memory and the retrieval cue used to probe for the material. When similarity is high, ERPs elicited by retrieval cues are more positive-going than when similarity is low.

I defer further comment on what the notion of ‘similarity’ might mean in this context and the question of the functional significance of the ERP effects until the general discussion of the thesis. An issue more specific to the present experiment concerns the possible

significance of the topographic differences observed between the ERP retrieval orientation effects elicited by word and picture cues.

The present orientation effects for the word cues closely resemble those reported in two previous studies (Robb & Rugg, 2002; Herron & Rugg, 2003). As in these earlier studies, the effects onset around 300 ms post-stimulus (although there was a main effect of study material in the 100-300ms latency region), and demonstrated a rather diffuse scalp distribution which remained statistically invariant across latency regions. The ERP effects observed for the picture cues were similar to those elicited by the words in respect of their time-course and overall magnitude. However, the scalp topographies of the effects elicited by the two classes of cue differed. Those elicited by words demonstrated the more anterior and symmetrical distribution (see Figure 5.4). This finding indicates that the two effects reflect activity in neural populations that are either partially distinct, or in which the distribution of activity varies in a material-dependent fashion. This should not be surprising because just as the neural activity supporting word and picture identification differs, so, one might expect, will the activity engaged by the two classes of item when they act as retrieval cues. More impressive, in my opinion, are the similarities between the ERP effects associated with the two classes of item. In the light of these similarities I think it possible that the functional significance of ERP retrieval orientation effects does not vary according to whether they are elicited by words or pictures. Nevertheless, it is difficult to claim one or the other for certain at the present stage.

## **Chapter 6 – Experiment 2: Is the occurrence of the retrieval orientation effect contingent upon the presentation of copy cues?**

### **Introduction**

Leading on from experiment 1, the findings of Robb and Rugg (2002) were replicated and extended in that there was a sustained negative ERP waveform onsetting at around 300ms and ending at around 900ms post-stimulus for test items not encoded as ,copy cues‘ and that the ERP retrieval orientation effect is not specific for visual words as retrieval cues, instead a similar effect is apparent in the picture retrieval cue conditions. As mentioned earlier, retrieval orientation is a process which enables subjects to align themselves with the cue processing to a certain retrieval task. Hence it follows, that any cue information from the encoding stage is crucial to help in aligning retrieval processing, and therefore processing resources specific to the encoding modality should be re-instated at retrieval as to increase the likelihood of a successful retrieval.

It follows that ,matching‘ a retrieval cue with its encoded information appears to be an important variable in eliciting the ERP retrieval orientation effect (see Nairne, 2002). This process would also explain nicely Robb and Rugg’s (2002) findings, as well as the results of Herron and Rugg (2003) who showed that intermixed study items of different modalities can reveal the ERP retrieval orientation effect at test. The question remains, how much overlap between retrieval cue and encoded information is necessary to reveal retrieval orientation effects in scalp ERPs? The experimental material used in experiment 1 provided two levels of overlap for both retrieval cue materials i) a complete overlap of

retrieval cue and encoded information (visual word-visual word; picture-picture) or ,copy cues‘ and ii) an incomplete overlap of retrieval cue and encoded information (visual word-picture; picture-visual word). The former level provides the rememberer with information on all levels (perceptual and semantic) for encoded items while the latter level provides only semantic overlap of encoded information and retrieval cues. So, is the ERP retrieval orientation effect contingent upon the presentation of ,copy cues‘ at retrieval or can two retrieval conditions, which do not employ copy cues, give rise to the above ERP effect?

To summarise the following issues remain unsolved: i) is the presentation of ,copy cues‘ in at least one of the test conditions necessary to elicit the ERP retrieval orientation effect? ii) is the ERP effect still observable in retrieval conditions which are matched in terms of task difficulty? iii) is the simultaneous change of study material and encoding task in experiment 1 responsible for the observed ERP effect (see below)? And finally iv) where in the brain might the retrieval orientation process be located, as the ERP distributions are widespread and thus a localisation is difficult to make?

To address the first three issues I conducted a further ERP experiment (experiment 2) plus a follow-up ERP study, while the last issue was addressed in an fMRI study (experiment 3, see chapter 7). The first of the two ERP experiments investigated whether ERP retrieval orientation effects can be obtained when retrieval cues do not resemble either class of study material, thus avoiding any possible ,copy cue‘ processing. This was accomplished by modifying the procedure of Robb and Rugg (2002) such that the two classes of study item comprised pictures and auditory, rather than visual words. The

second issue was addressed in a subsidiary follow-up experiment. In all previous studies, including experiment 2, manipulation of study material was associated with a parallel manipulation of encoding task – in the present studies, this took the form of a size judgment task for pictures and an indoor/outdoor judgment task for words. However, this raises the possibility that ERP retrieval orientation effects depend on the employment of different encoding tasks and therefore I removed in the follow-up experiment the confound of a parallel study material and encoding task manipulation.

## **Experiment 2**

### **Methods**

#### **Participants**

Twenty subjects participated. Data are reported from 16 subjects (9 female), aged between 18 and 22 years (mean 19). Data from the other 4 subjects were rejected due to there being fewer than 16 artefact-free trials in one or more critical condition.

#### **Experimental Materials**

The experimental materials consisted of 164 stimulus triplets pictures, visual words and auditory words (a subset of those employed in experiment 1, see also chapter 4). 144 triplets were selected as critical items and the remaining stimuli were employed as practice or filler items.



As in the previous experiment, study and test lists were created anew for each experimental subject. In each case, two study lists were created, each comprising 36 critical stimuli, either pictures or auditory words, preceded by 2 fillers. Test lists were constructed as for the previous experiment but consisted exclusively of visually presented words. Thus, each subject underwent 2 study test cycles in which studied items were either pictures or auditory words, and test items were always visual words.

### Procedure

The experimental procedure was very similar to that adopted in experiment 1. That for the picture study phase was identical to the previous experiment. For the auditory word condition, the sequence of events was the same as for the word study condition of experiment 1 except that stimulus presentation took the form of the presentation over headphones of a 1500ms auditory frame containing the study item. Subjects were instructed to listen carefully to each word and classify it according to whether it referred to an indoors or outdoors object.

The test phases were identical to those employed in the word conditions in experiment 1. As in the previous experiment, the study-test ordering was counterbalanced across subjects. Each of the study-test cycles comprised one experimental condition so that the two conditions in this experiment had separate or blocked study-test cycles (picture-word, auditory-word).

### ERP recording and analysis

(See chapter 4 for a detailed description.)

## **Results**

### Behavioural Performance

Mean percent correct and RTs are shown for each class of study material in Table 6.1, where it can be seen that performance was very similar for the two conditions. The contrasts for Pr and correct rejection RT were both far from significant ( $F_{1,15} = 0.55$ ,  $p > .4$ ,  $F_{1,15} = 0.40$ ,  $p > .5$ , respectively). Further, both conditions (pictures-visual words and auditory words-visual words) showed no reliable reaction time differences for hits ( $F_{1,15} = 1.44$ ,  $p > .2$ ).

**Table 6.1.** Percent accuracy, RT (ms) and PR by condition and item type

Condition	Accuracy (SD)		RT (SD)		Pr
	Old	New	Old	New	
Picture - Visual Word	0.87 (0.11)	0.93 (0.06)	915 (223)	1012 (230)	0.79
Auditory Word - Visual Word	0.86 (0.11)	0.93 (0.08)	896 (187)	995 (242)	0.76

### ERP Data

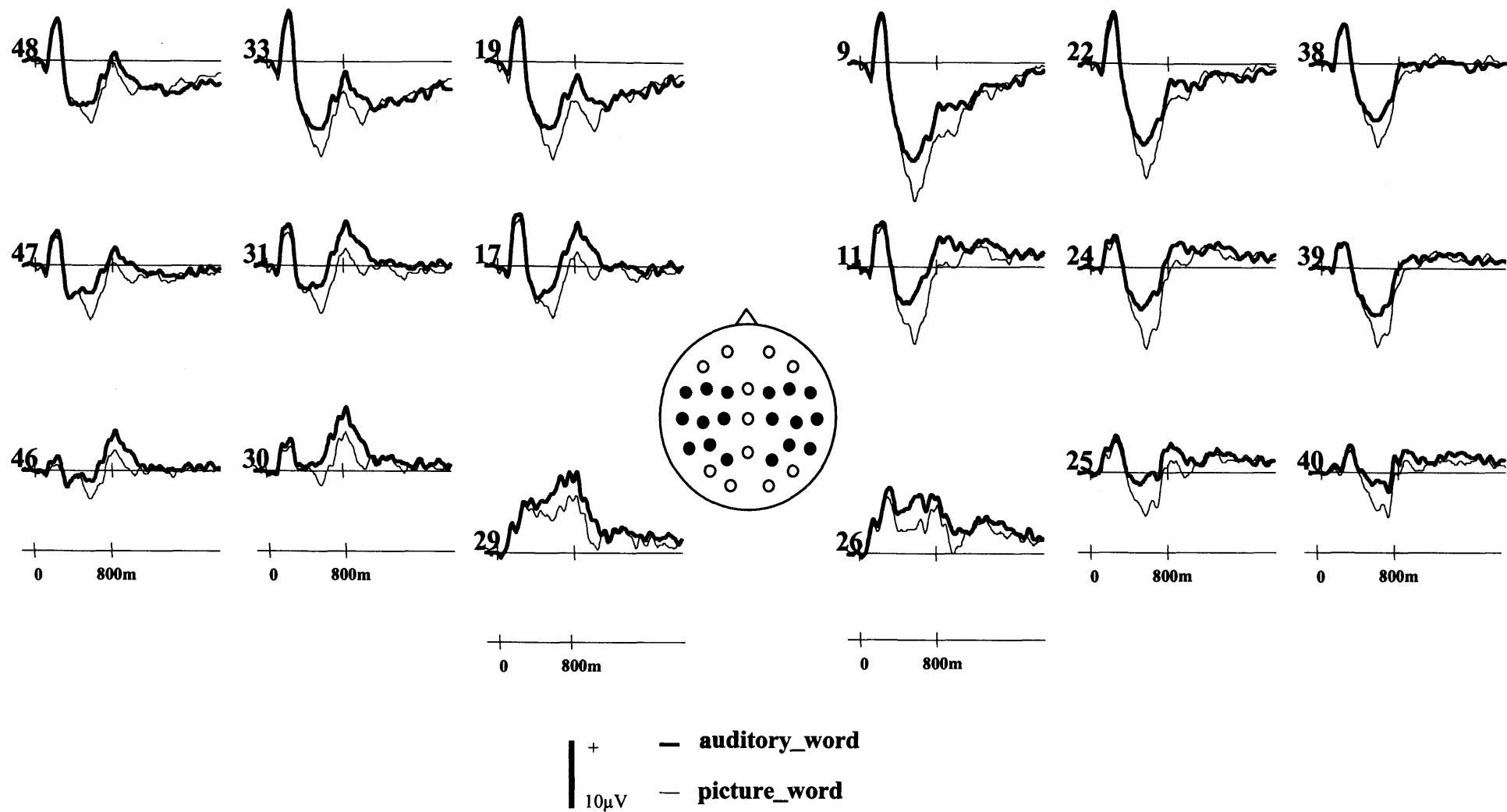
Grandaverage waveforms are shown in Figure 6.1. The mean numbers of trials (and range) forming the ERPs were 29 (25-36) and 29 (21-35) for the picture and auditory word conditions respectively. It is evident from the figure that the ERPs are more negative-going when pictures were the sought-for material rather than auditory words.

ERPs were quantified and analyzed as in chapter 1 (see also chapter 4) and the Old/New effects of experiment 2 can be found in appendix 2. For a summary of the analysis results see Table 6.2.

**Table 6.2.** Exp. 2 – Summary of ANOVA results in each ERP latency region including the factor of study material.

Main effects & interactions	100-300 ms	300-600 ms	600-900 ms	900-1200 ms
18 main electrode sites				
PA	–	$F_{1,15} = 5.76, p < .05$	$F_{1,15} = 20.82, p < .00$	$F_{1,15} = 4.01, p = .06$
PA x ST	–	$F_{1.3,19.2} = 5.27, p < .05$	$F_{1.1,16.2} = 5.45, p < .05$	–
3 mid-central electrode sites				
PA	–	–	$F_{1,15} = 13.00, p < .01$	$F_{1,15} = 3.52, p = .08$

PA = study material; HM = hemisphere; AP = location; ST = site.



**Figure 6.1** Exp. 2 – Grand average ERP waveforms elicited by correctly rejected new items at lateral frontal (48, 33, 19, 38, 22, 9), lateral temporal (47, 31, 17, 29, 24, 11) and lateral parietal sites (46, 30, 29, 40, 25, 26).

### *Magnitude analyses for 18 electrode sites*

#### **100-300ms**

ANOVA of the 100-300ms latency region did not give rise to any main effect or interaction including the study material as a factor (see Table 6.2).

#### **300-600ms**

ANOVA of the 300-600 ms data revealed a main effect for study material ( $F_{1,15} = 5.76$ ,  $p < .05$ ), and for its interaction with site ( $F_{1.3,19.2} = 5.27$ ,  $p < .05$ ).

#### **600-900ms**

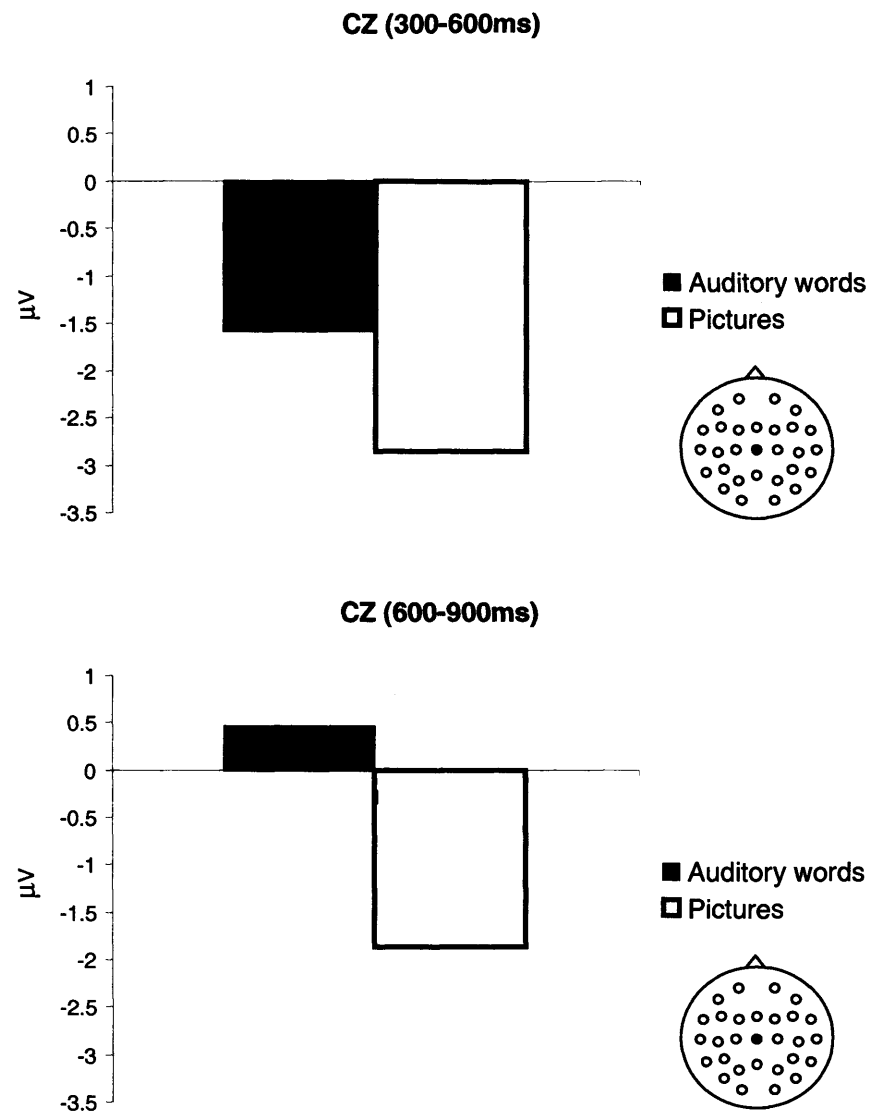
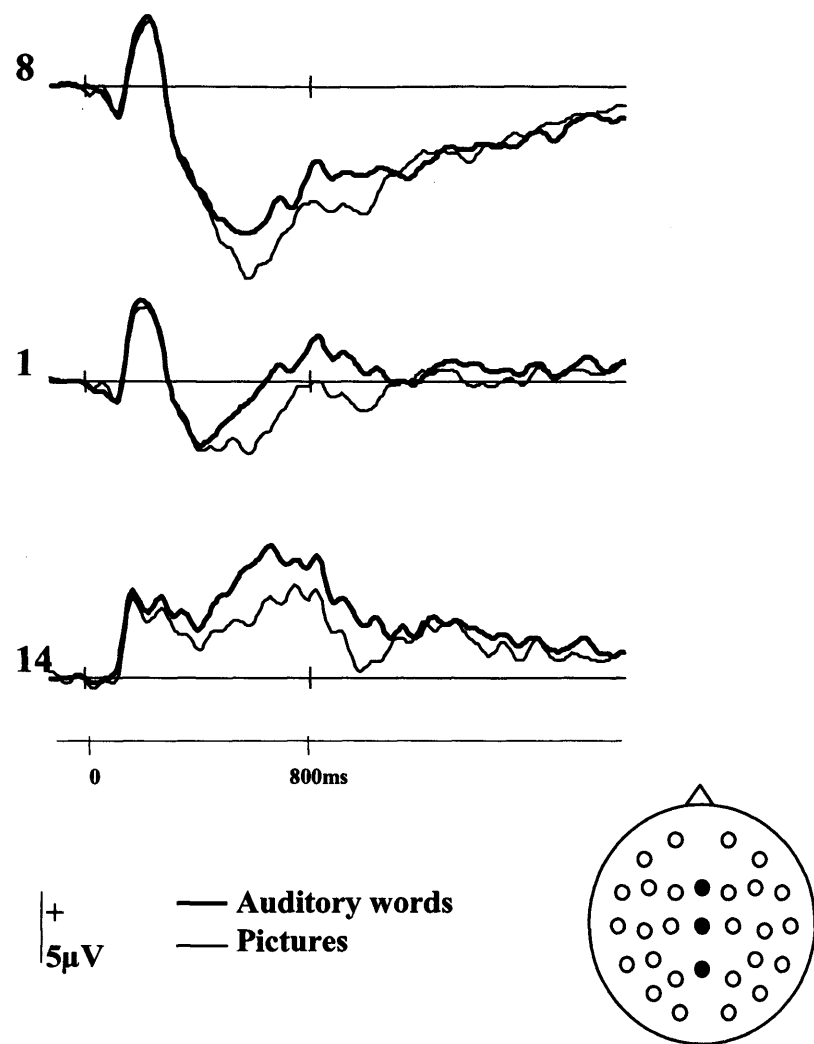
The same two effects were also found for ANOVA of the 600-900 ms data (respectively:  $F_{1,15} = 20.82$ ,  $p < .000$  and  $F_{1.1,16.2} = 5.45$ ,  $p < .05$ ).

#### **900-1200ms**

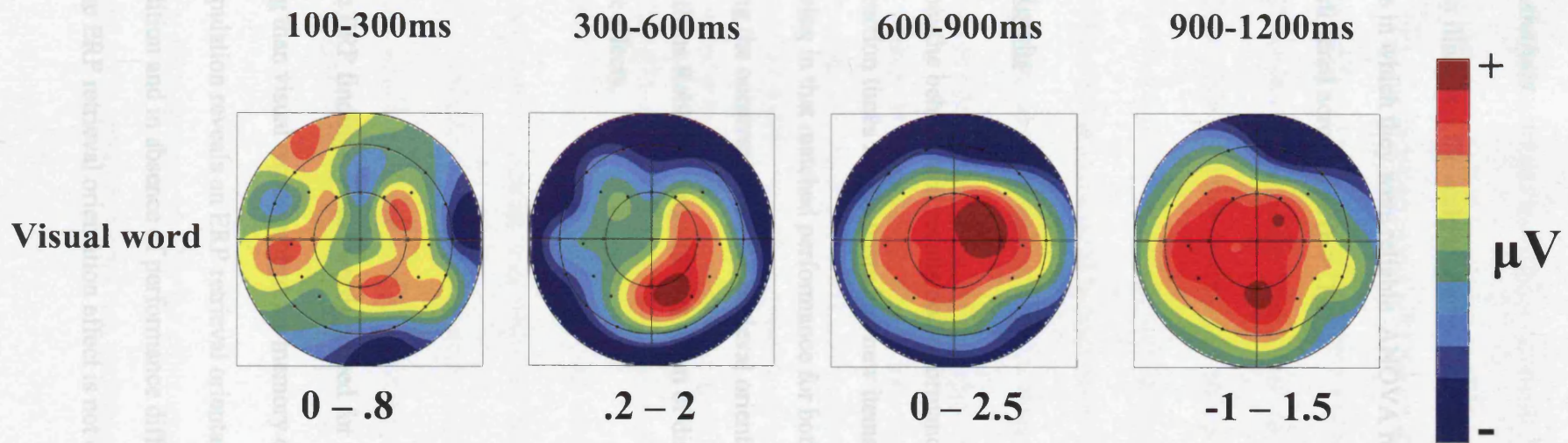
No effects involving the factor of study material were reliable for the 900-1200 ms latency region.

### *Magnitude analyses for 3 selected electrode sites*

Similar to experiment 1, I conducted a planned post-hoc analysis on three central midline electrodes, which however revealed no effect of study material, except for the 600-900ms latency region ( $F_{1,15} = 13.00$ ,  $p < .01$ ) (see Figure 6.3).



**Figure 6.3** Exp. 2 – **Left:** Mid-line electrode sites for visual word retrieval cue condition: Grand average ERP waveforms elicited by correctly rejected new items. **Right:** Bar graphs showing ERP magnitudes in microvolt ( $\mu\text{V}$ ) at electrode site Cz for two selected latency regions (300-600ms; 600-900ms).



**Figure 6.4** Exp. 2 –Scalp topographies for the visual word retrieval cues (auditory words – pictures) for all latency regions. Values below each spline map denote minimum and maximum microvolt ( $\mu V$ ) values of each map.



### *Topographic Analysis*

Figure 6.4 also illustrates the scalp topographies of the study material effects in the two latency ranges in which they were reliable. ANOVA revealed no evidence that these topographies differed across time ( $p > .1$ ).

## **Discussion**

### **Behavioural Results**

As evident from the behavioural results no performance differences were found for accuracy or reaction times for the unstudied new items. In view of the ERP findings, this is very reassuring in that matched performance for both experimental conditions seems to be not affecting the occurrence of ERP retrieval orientation effects, which in turn indirectly confirms Robb and Rugg (2002) claim of dissociable retrieval orientation and retrieval effort effects.

### **ERP Results**

In terms of the ERP findings, visual words probed for memory of pictures were more negative-going than visual words probed for memory of auditory words. Thus, the study material manipulation reveals an ERP retrieval orientation effect even in the absence of a copy cue condition and in absence of performance differences between conditions. It follows that the ERP retrieval orientation effect is not contingent upon the presentation of

a literal copy cue in the test phase, rather a difference in overlap between retrieval cue and encoded information on certain levels is sufficient to elicit the effects. Hence, it seems that the less overlap between encoded information and retrieval cue, the more negative-going the ERP waveform is. This translates to the experiment in that in the auditory words-visual words condition, the visual words test cues share a semantic overlap with the encoded auditory words and also a pre-semantic overlap of information (e.g. lexical or phonological). In contrast, the pictures–visual words condition can rely on the same semantic overlap as the condition above, however, there is no pre-semantic overlap between pictures and visual words. It is therefore not surprising to observe a retrieval orientation effect because the higher degree of information overlap in the auditory words-visual words condition should help facilitate any orientation towards the encoded information, even though there is no behavioural difference for the new items across conditions. Moreover, the reduced amplitude and shorter latency of the ERP retrieval orientation effect in this experiment (e.g. missing statistical study material effects in the 300-600ms and 900-1200ms latency regions) can also be explained in terms of overlap between study items and retrieval cues because the study material changed its form in both conditions in contrast to experiment 1 which employed two copy cue conditions. Still, the similarity of effects in terms of scalp distributions allows us to conclude that the same kind of cue processing activity (i.e. retrieval orientation) reported in experiment 1 was also active in experiment 2.

However, the question remains whether the effect reported above is due to the study material encoded or the actual encoding task performed. The reason is that, as mentioned

earlier, in all previous studies, including experiment 2, manipulation of study material was associated with a parallel manipulation of encoding task as mentioned in the introduction. As a reminder, the rationale for this procedure was to maximize the distinctiveness of the memory representations to maximize the likelihood that subjects would adopt different retrieval orientations when searching for each class of material. However, the employment of this procedure raises the possibility that ERP retrieval orientation effects depend on the employment of different encoding tasks. Therefore, in a control experiment with only ten subjects (due to the strong ERP effects observed), I repeated experiment 2 but without the confound of manipulating the encoding task in parallel to the study material.

## **Follow-up study of Experiment 2**

### **Methods**

#### **Subjects**

Twelve subjects participated in this experiment. Data are reported from ten subjects (3 female), aged between 20 and 26 years (mean 23). Two subjects were rejected due to there being fewer than 16 artefact-free trials in one or more experimental conditions.

### Experimental materials, procedure and EEG recording

These aspects of the experiment were identical to those in experiment 2 with the exception of the encoding tasks employed with the study materials. Rather than having subjects make a size discrimination on the pictures, and an indoor/outdoor judgment on the words, all items were subjected to the same judgement. Half of the subjects made size judgments in the two study phases, and the remainder performed the indoor/outdoor task.

### Results

#### Behavioural Performance

Performance indices are summarized in Table 6.3. Pr was higher for the auditory word than the picture condition ( $F_{1,8} = 8.19$ ,  $p < .025$ ), but correct rejection RTs did not differ significantly ( $p > .1$ ).

**Table 6.3.** Percent accuracy, RT (ms) and PR by condition and encoding task.

Condition	Accuracy (SD)		RT (SD)		Pr
	Old	New	Old	New	
Picture - Visual Word	0.89(0.04)	0.91(0.07)	932 (189)	1045 (269)	0.81
Auditory Word - Visual Word	0.93(0.05)	0.96(0.06)	931 (227)	989 (217)	0.88

### ERP data

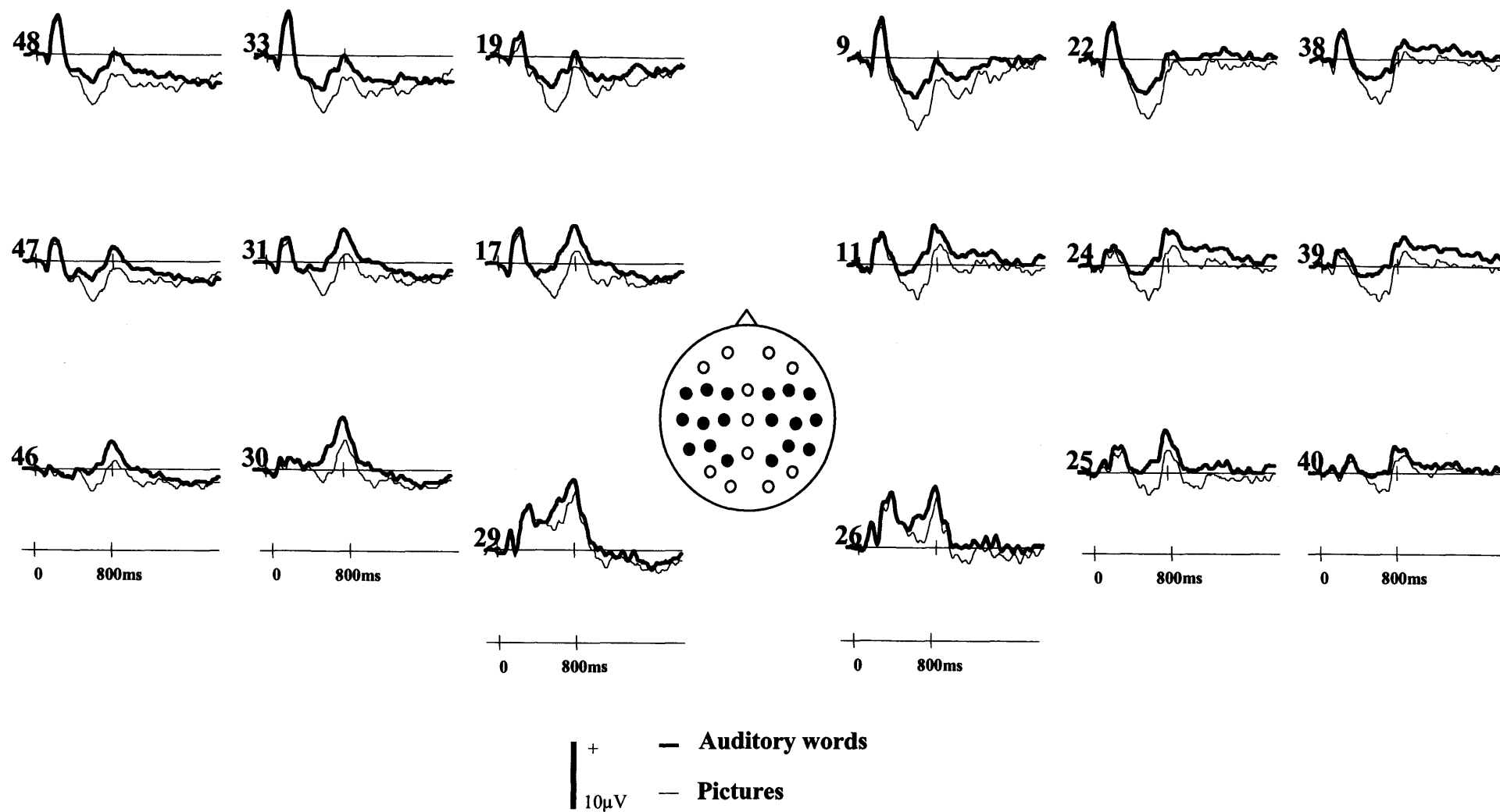
Grand-average ERPs are shown in Figure 6.5. Waveforms were based on a mean (range) of 33 (26-36) trials in the word condition, and 30 (25-36) trials when pictures were the study material. It appears from the figure that the differences between the ERPs resemble those found in experiment 2. This impression was confirmed by statistical analysis of the same four latency regions and eighteen electrode sites as were employed previously (see experiment 2 or chapter 4).

#### *Magnitude analyses for 18 electrode sites*

ANOVA of the 100-300ms latency region did not reveal any significant effects of study material. However, the effect of study material was a trend in the 300-600 ms data ( $F_{1,8} = 4.23$ ,  $p = .074$ ), and reliable in the two succeeding latency regions (600-900:  $F_{1,8} = 18.08$ ,  $p < .01$ ; 900-1200:  $F_{1,8} = 6.31$ ,  $p < .05$ ).

#### *Topographic Analysis*

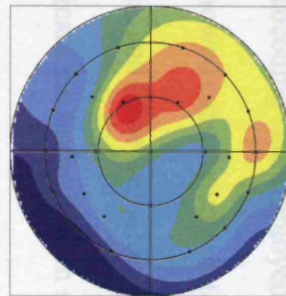
The analysis of the scalp topographies revealed that the effect measured does not change over time in the latency region of 300-1200ms ( $F_{3,2,12.7} = 1.27$ ,  $p > .3$ ).



**Figure 6.5** Follow-up study – Grand average ERP waveforms elicited by correctly rejected new items at same electrode sites as above (Figure 6.1) collapsed across both judgement groups.

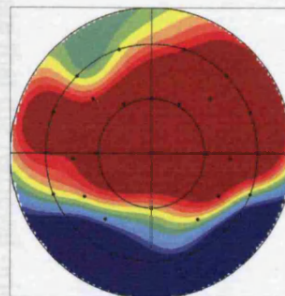
Visual  
words

100-300ms



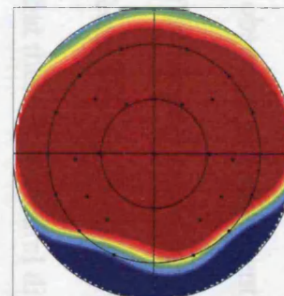
0 – .9

300-600ms



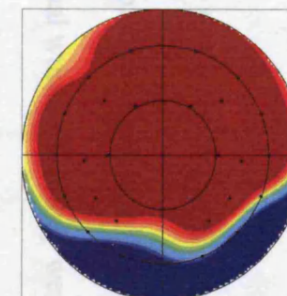
-1 – 2

600-900ms



0 – 3.5

900-1200ms



-1.5 – 1.5



**Figure 6.8** Follow-up study –Scalp topographies for the visual word retrieval cues (auditory words – pictures) for all latency regions. Values below each spline map denote minimum and maximum microvolt ( $\mu\text{V}$ ) values of each map.

## **Discussion**

### **Behavioural Results**

The behavioural data show that there is a performance difference between the auditory word-visual word and the picture-visual word condition, in that subjects are more accurate in identifying visual words when they were encoded auditorily than as pictures. This findings might indicate that there are actual test difficulty differences between conditions which were not observed in experiment 2. Thus, it is difficult to decide whether these performance differences might have influenced the ERP data and hence, the retrieval orientation effects. Nevertheless, the data of experiments 1 & 2 and Robb and Rugg (2002) indicate that these behavioural differences should not affect the occurrence of the retrieval orientation ERP effect.

### **ERP Results**

The ERP data clearly indicate that the retrieval orientation effect can be elicited regardless of the semantic encoding task employed in this follow-up experiment. Both encoding task conditions showed robust study material effects in the 600-900ms and the 900-1200ms latency regions, and there was a trend in the 300-600ms latency region. I think that these results replicate the findings from experiment 2 in that people can vary how to probe their memory.



However, the above conclusion seems problematic in that both encoding tasks were of a ,deep‘ or semantic nature and hence, it is not clear whether the same effects could be observed by contrasting a ,shallow‘ with a ,deep‘ encoding task. Moreover, according to the transfer-appropriate processing and the encoding specificity principle the overlap between encoding and retrieval should depend on the processing tasks and the study material used. Thus, not only the study material should be responsible for any retrieval orientation effects, but also the task performed either at encoding or retrieval (as stated in Rugg & Wilding, 2000). Indeed, Rugg, Allan and Birch (2000) reported an ERP difference for new test items according to whether subjects performed a deep or shallow encoding task, with waveforms encoded semantically showing sustained negative ERP waveforms from 300ms post-stimulus onwards. Thus, there might be a retrieval orientation difference for different semantic encoding tasks, which, however, was too subtle to be picked-up by the ERP grand-averages. On the other hand, no significant changes over time were observed on the topographic analysis, replicating the topography findings of experiment 1 & 2 and hence, arguing against a proposal of a split into study material and encoding task orientation effects, at least in this follow-up study.

## **Chapter 7 – Experiment 3: fMRI correlates of retrieval orientation**

### **Introduction**

The previous three thesis experiments have shown that the retrieval orientation effect is a robust ERP effect whose neural correlates are still present even by a change of retrieval cue modality (experiment 1) or by the absence of a 'copy cue' condition (experiment 2), or by a change of the semantic encoding task (follow-up study). However, the ERP retrieval orientation effects have so far always been manifested as a mid-central electrodes effect sustained across several latency regions. This centrally located, widespread activity makes it very difficult to estimate a neural origin of the underlying process, because of the volume conductivity of the scalp (as described in the inverse problem in chapter 2). Results of similar ERP neuroimaging studies are comparable to my experiments, in that some studies (e.g. Robb & Rugg, 2002; Herron & Rugg, 2003) do show a similar mid-central distribution for new item ERP contrasts. However, other studies also investigating new items effects according to study or retrieval conditions show a more mid-frontal distribution (e.g. Dzulfikfli, Sharpe & Wilding, 2004), a lateralized frontal distribution (e.g. Johnson, Kounios & Nolde, 1997), or a combination of both (e.g. Rugg, Allan & Birch, 2000). Further, a study which investigated cue-related activity preceding the presentation of the actual stimulus when volunteers were preparing to retrieve information from memory reported a left prefrontal distribution for the ERP retrieval orientation effect for new items requiring different episodic source judgements

(Herron & Wilding, 2004). These differences in scalp-distributions may have arisen due to several factors including ERP references employed or task differences.

On the whole, however, the ERP retrieval orientation effects reported in the above studies are generally widespread over the scalp, with an amplitude maximum at mid-central electrodes when using a mastoid reference (though see Johnson et al., 1997; Rugg et al., 2000; Dzulkipli et al., 2004; Herron & Wilding, 2004, for more lateralized, frontal scalp distributions). This widespread activity makes it difficult to estimate the neural generator(s) of the ERP effect, particularly given that the brain and skull act as spatial low-pass filters for electrical fields (Davidson, Jackson & Larson, 2000).

One potential solution to this problem is to use haemodynamic methods like fMRI. To my knowledge, no fMRI study has contrasted conditions that would meet the criteria set out by Rugg and Wilding (2000) for isolating retrieval orientation.

As a reminder, Ranganath and colleagues (2000) (based on a previous ERP experiment, Ranganath & Paller, 1999), contrasted successfully recognized and rejected items according to different levels of specificity of retrieval. In the study phase, participants made size judgements about visually presented objects. In a subsequent test phase, they judged whether objects had been presented in the same size at study (i.e. "specific" condition) or whether object had been seen at all, regardless of its size (i.e. "general" condition). Ranganath et al. found that regardless of the study status (old versus new) of the test items, left anterior prefrontal cortex (BA 10/46) showed greater activity in the specific than general conditions. Thus, the left prefrontal cortex is a likely candidate for a neural origin of retrieval orientation, being more active when participants need to focus

their memory search for specific information, regardless of whether that search is successful. A subsequent study (Rugg et al., 2003), however, failed to activate left prefrontal cortex when comparing a condition that required retrieval of specific source information (the left/right position and colour of studied words) with a condition that did not. In fact, they found greater activity in the left prefrontal region identified by Ranganath et al. for correct recognition of old items than for correct rejection of new items, suggesting that this region is more concerned with successful retrieval from memory. The reason for the difference between these two studies is unclear, but could relate to the different material used (pictures vs words), the different type of source information tested (size versus position/colour) or differences in the precise task instructions (e.g, the use of three responses in the specific condition of Ranganath et al., but only two in their general condition; see Rugg et al., 2003 for further discussion).

Another event-related fMRI study by Dobbins and colleagues (2003) contrasted neural activity in a source task with neural activity in a recency task for both successful and unsuccessful retrieval of information. At test, participants were presented with two words, and cued to indicate either 1) which one was encoded in the context of a specific study question (the source task), or 2) which one was more recent, regardless of study question (the recency task). They proposed that retrieval orientation differed for the two types of test condition. Like Ranganath et al. (2000), Dobbins et al. found that lateral prefrontal (and lateral parietal) regions were more active in the source than recency task, regardless of whether or not their two-alternative choice was correct. However, the use of two old items at test (rather than a single item that was either old or new, as in Ranganath

et al., 2000, and Rugg et al., 2003, studies) complicates the comparison of the "retrieval success" effects across the studies (as does the use of another different type of source information).

One potential problem with all three studies cited above is that the contrasts used to isolate retrieval orientation may be confounded by generic difficulty effects (or "retrieval effort", Buckner et al., 1998), given that accuracy tended to be lower, and/or reaction times longer, for the source memory tasks. While Rugg et al. (2003) factorially varied retention interval, and Dobbins et al. (2003) varied inter-item lag, in attempts to address difficulty effects, neither manipulation was completely successful. More fundamentally, all three studies tested retrieval orientation by changing the retrieval task. According to Rugg and Wilding's (2000) proposal, a manipulation of the type of study material being sought, while holding the retrieval task constant, should also induce differences in retrieval orientation. The recent ERP data using this approach, discussed earlier, have shown that the retrieval orientation effect associated with different types of study material is not affected by factors that affect difficulty (but see Dzulkifli, Sharpe & Wilding, 2004). For example, Experiment 2 found a retrieval orientation effect even though accuracy and reaction time did not differ reliably across the conditions. Based on these findings, I used a very similar design to Experiment 2: participants studied either pictures or auditory words (in different blocks), and were tested using visual words as cues within the same basic yes/no recognition task. By contrasting new test items as a function of whether participants were trying to remember pictures or auditory words and hence, should identify regions sensitive to retrieval orientation. Based on previous fMRI

experiments (e.g. Ranganath et al., 2000), I expected to find the neural correlates of retrieval orientation in prefrontal cortex regions.

## **Methods**

### **Participants**

Eighteen volunteers participated. Data are reported from seventeen participants (10 female), aged between 18 and 35 years. Data from the remaining participant was rejected due to behavioural performance that was two standard deviations below the mean of all participants.

### **Experimental Materials**

The same experimental material and design, as in Experiment 2 was used in this study.

The only difference from Experiment 2, was the addition of 36 "null events"

(presentation of a fixation cross) that were randomly interspersed within each test list.

These null events achieve a stochastic distribution of stimulus onset asynchrony (SOA) between the events of interest (the test words), which is necessary in fMRI to separate BOLD responses to new test words (versus baseline) from BOLD responses to old test words (Josephs & Henson, 1999).

## Procedure

Each participant underwent four blocked study-test cycles, two for each type of study material (picture-word, auditory-word). As in the previous experiment, the study-test ordering was counterbalanced across subjects. For study phases, auditory words and pictures were presented for 1500ms with an SOA of 5000ms. Each stimulus was preceded for 3500ms by a cue (a '+' symbol). Participants decided whether each item would, at its real-life size, fit into a shoebox. In contrast to Experiment 2, the study task was the same regardless of whether study items were pictures or auditory words.

For test phases, words were presented for 500ms with an SOA of 3240ms (1.5 TRs; see fMRI acquisition). Participants were instructed to judge whether each item had been presented in the immediately preceding study phase (either seen as a picture, or heard as a word, depending on the condition).

Participants performed all study and test phases while lying in the scanner, though fMRI data was only acquired in the test phase. fMRI data were not acquired in the study phase in order to avoid compromising audibility in the auditory condition.

## fMRI Acquisition

A 1.5T Sonata system (Siemens, Erlangen, Germany) was used to acquire 24 T2\*-weighted transverse echoplanar (EPI) images (64x64 3x3mm<sup>2</sup> pixels, TE=50ms) per volume, with blood oxygenation level dependent (BOLD) contrast. EPIs comprised 3mm-thick axial slices taken every 4.5mm, acquired sequentially in a descending direction. Four test sessions with 175 scans for each test phase were acquired. Volumes were collected continuously with a repetition time (TR) of 2.16s. The first 5 volumes per

session were discarded to allow for equilibration effects. The ratio of SOA to TR ensured that the impulse response was sampled every 1.08s (over trials).

### Behavioural Analysis

Test trials with RTs less than 200ms or greater than the SOA (3240ms) were marked as invalid. For each experimental condition, trials were sorted into six types: 1) studied items called old ("hits"), 2) unstudied items called new ("correct rejections"), 3) studied items called new ("misses"), 4) unstudied items called old ("false alarms"), 5) filler items, and 6) invalid trials. Only the first two trial-types had appreciable numbers and were of interest for the fMRI analysis, leading to a 2x2 factorial design with factors study material ("picture" vs. "auditory") and study status ("hit" vs. "correct rejection").

### efMRI Analysis

Analysis of the fMRI data was performed with SPM2 (<http://www.fil.ion.ucl.ac.uk/spm>). All volumes were coregistered to the first volume, and unwarped to allow for interactions between EPI distortions and participant movement (Andersson et al., 2001). Scans in which the mean or variance of the difference between one or more slices and those in the previous scan exceeded 5 times the standard deviation of such differences over all scans per session (N=170) were marked as outliers (to be modeled separately; see below). The data in each slice were interpolated in time to match the acquisition time of the middle slice. Spatial normalization parameters were estimated by warping each participant's



mean EPI to a standard EPI template based in Talairach space (Ashburner & Friston, 1999). Normalized EPI images were resliced to 3x3x3mm voxels and smoothed with an isotropic 8mm FWHM Gaussian kernel (final estimated smoothness was 10x10x10mm<sup>3</sup> FWHM). The timeseries in each voxel was highpass-filtered to 1/128 Hz and scaled to a grand mean of 100, averaged over all voxels and scans within a session.

Statistical analysis was performed in two stages. In the first stage, neural activity was modeled by a delta function at stimulus onset. The BOLD response was modeled by convolving these delta functions with a canonical haemodynamic response function (HRF, Friston et al., 1998). The resulting time courses were downsampled at the midpoint of each scan (corresponding to the middle slice) to form covariates in a General Linear Model. Covariates were modeled for each condition (see Behavioral Analysis above), plus separate covariates for each outlier scan (consisting of a single delta function) and a single covariate representing the mean (constant) over scans. Temporal autocorrelation of the errors was accommodated by an AR(1) model, the parameters of which represent hyper-parameters governing the nonsphericity of the error covariance, and which were estimated together with the parameters for each covariate using Restricted Maximum Likelihood (Friston et al., 2002).

Contrasts of parameter estimates comprised the data for the second-stage analyses, which treated participants as a random effect. SPMs were thresholded at  $p < .001$  uncorrected. The maxima were localized on a normalized mean EPI across participants. Stereotactic coordinates correspond to the standard Montreal Neurological Institute brain. These

coordinates bear a close, but not exact, match to the atlas of Talairach and Tournoux (1988), which was used to estimate Brodmann Areas (Brodmann, 1909).

## **Results**

### **Behavioural Performance**

Mean percent correct and reaction time (RT) are shown for each condition in Table 7.1. Recognition accuracy was assessed using the discrimination index  $Pr$  ( $pHit - pFalse$  Alarm, Snodgrass & Corwin, 1998). These values were .87 and .85 for the auditory and picture conditions respectively. ANOVA on  $Pr$  revealed no main effect of study material ( $F_{1,16} < 1.97$ ,  $p > .1$ ). ANOVAs for RTs including the factors of study material (auditory vs. pictures) and test status (hits vs. correct rejections) showed a main effect of test status, ( $F_{1,16} = 34.34$ ,  $p < .001$ ), with longer RTs for correct rejections than hits, but no main effect of study material, nor an interaction of these factors, ( $F_{1,16} < 2.06$ ,  $p > .1$ ). Separate planned comparisons for correct rejections failed to find any effect of study material on accuracy, ( $F_{1,16} = 0.07$ ,  $p > .7$ ), or RTs, ( $F_{1,16} = 1.83$ ,  $p > .1$ ).

**Table 7.1.** Percent accuracy and RT (ms) by study material condition.

Condition	Accuracy (SD)		RT (SD)	
	Old	New	Old	New
Picture - Visual Word	0.88(0.07)	0.95(0.04)	1128 (186)	1259 (208)
Auditory Word - Visual Word	0.92(0.06)	0.95(0.04)	1114 (202)	1231 (234)

### efMRI Data

I will report first the basic “old-new” or “retrieval success” effect (Hits versus Correct Rejections); the main effect of study status, averaging across study material. The rationale of reporting first the Old/New effects was to compare the results with previous fMRI studies because no fMRI study so far has targeted directly retrieval orientation effects. It would be reassuring for any retrieval orientation effects measured, if the well-established networks of frontal and parietal Old/New effects would be also apparent in the data. Therefore, I exclusively masked this Old/New main effect with the interaction between test status and study material, in order to remove voxels in which the old-new effect varied with study material. This interaction mask was thresholded very liberally at  $p < .05$  uncorrected, making the result a more stringent test of those old-new effects that were of comparable size for both picture and auditory conditions. I then report the results of the planned comparisons of the Picture and Auditory conditions on correct rejections alone - i.e, the test of retrieval orientation. Finally, the interaction between test status and study material, which is one way to investigate differences in “retrieval content” - i.e. old-new effects that differ according to whether the old items were previously studied as pictures or auditory words can be found in appendix 3 & 4.

#### *Old-New (“retrieval success”) effects*

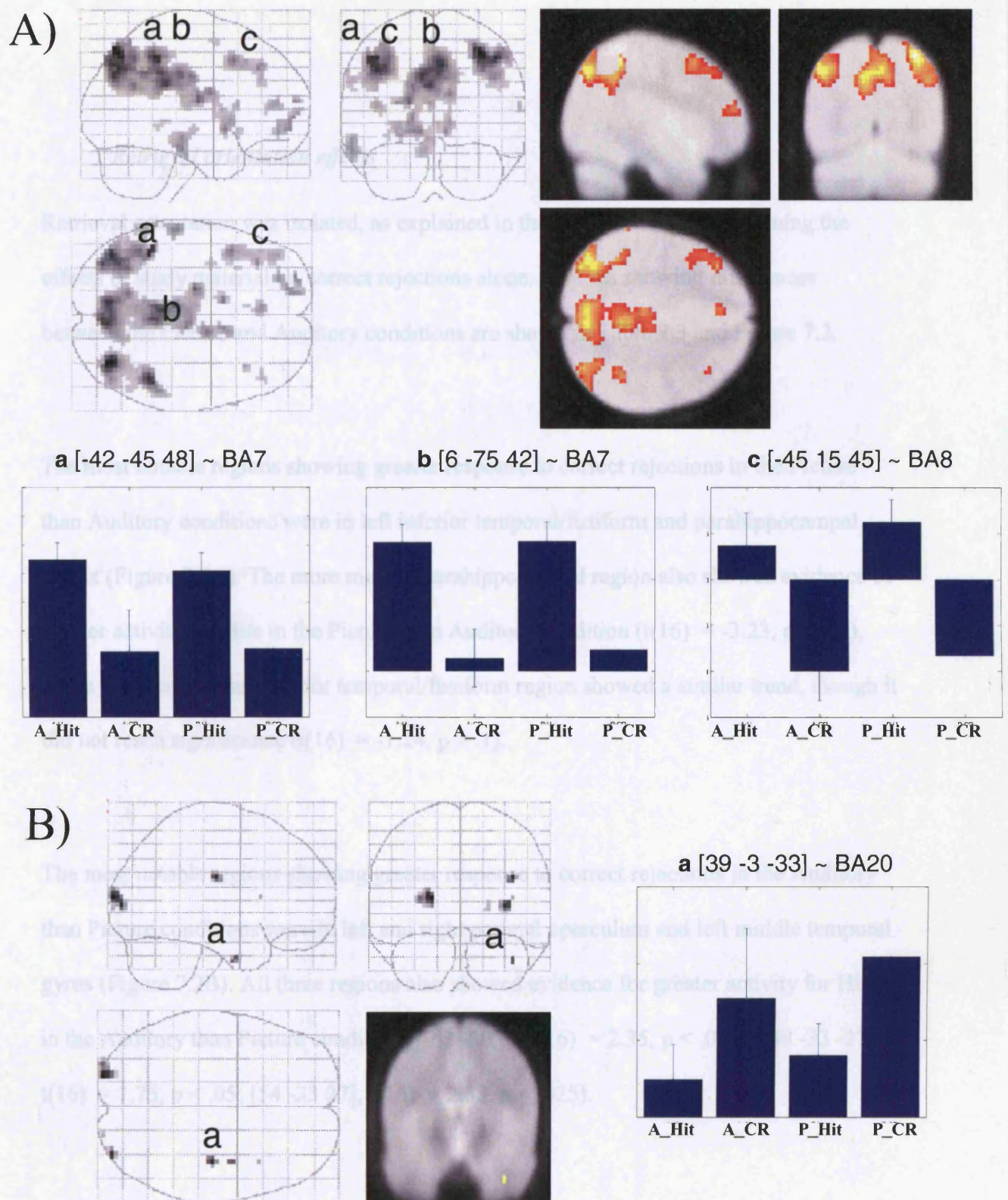
The regions showing greater responses to Hits than Correct Rejections were highly consistent with previous studies (e.g. Rugg & Henson, 2002), most notably parts of

bilateral inferior and superior parietal cortices, bilateral precuneus, posterior cingulate and left dorsolateral and frontopolar cortex (Table 7.2 and Figure 7.1A). As can be seen from the plots in Figure 7.1A, these regions show activations related to successful retrieval regardless of the study material.

Only a few regions showed a greater response to Correct Rejections than Hits, most notably in right anterior MTL and bilateral occipital cortex (Table 7.2 and Figure 7.1B). The former is consistent with previous findings of activity reductions for old relative to new items in a meta-analysis across four studies (Henson et al., 2003). It may correspond to perirhinal cortex, though is slightly more lateral than previous findings (it is difficult to be precise with such group, normalised, smoothed data).

**Table 7.2** Exp. 3 – Regions showing elevated activations for study status as a factor

Contrast	Region	Side	Size	BA	MNI coordinates			Z-value
		(L/R)	(cm <sup>3</sup> )		x	y	z	
Hits > CR								
	Frontopolar gyrus	L	.35	10	-27	60	15	4.29
	Frontopolar gyrus	L	1.32	10	-15	57	-6	4.33
	Middle frontal gyrus	L	.97	10	-42	48	15	3.96
	Superior frontal gyrus	L	.68	8	-6	36	42	4.22
	Middle frontal gyrus	R	.27	9	45	36	33	3.46
	Middle frontal gyrus	R	.27	8	36	24	45	3.97
	Inferior frontal gyrus	R	.14	45	63	18	12	3.67
	Lateral orbital gyrus	L	.16	47	-33	18	-9	3.37
	Middle frontal gyrus	L	3.13	8	-45	15	45	4.58
	Olfactory area	L	.76		-12	9	-6	4.47
	Medial caudate nucleus	R	2.51		12	-3	21	4.49
	Middle temporal gyrus	L	1.43	40	-60	-24	-21	4.40
	Pons	L	1.16		-6	-24	-18	3.96
	Corpus callosum	R	.27		3	-42	-3	3.45
	Angular gyrus	L	12.47	7	-42	-45	48	5.61
	Superior temporal gyrus	R	.16	40	51	-54	27	3.21
	Occipital gyrus	R	11.34	7	33	-72	51	5.92
	Precuneus	B	34.13	7	6	-75	42	5.30
CR > Hits								
	Frontal operculum	R	.03	45	39	15	12	3.37
	Inferior temporal gyrus	R	.11	20	39	-3	-33	3.83
	Frontal operculum	R	.32	41	39	-18	27	4.22
	Occipital gyrus	R	.41	18	33	-90	6	4.18
	Occipital gyrus	R	.11	18	21	-96	3	3.32
	Occipital gyrus	L	1.24	18	-21	-96	12	4.36



**Figure 7.1** Exp. 3 – **A)** Sagittal, coronal and transverse views of the Hit (H) > Correct Rejection (CR) activations consisting of at least 5 contiguous voxels surviving  $p < .001$  uncorrected, shown on a maximal intensity projection (left) and normalised EPI (right). Below are plots of the amplitude of the best-fitting canonical haemodynamic impulse response across the four conditions for three maxima within: (a) left inferior parietal cortex, (b) posterior cingulate and (c) left dorsal prefrontal cortex. Error bars show standard errors of respective differences: Auditory\_Hit – Auditory\_CRs, Auditory\_CR – Picture\_CR and Picture\_Hit – Picture\_CR. **B)** Views of the Correct Rejection > Hit activations consisting of at least 2 contiguous voxels,  $p < .001$  uncorrected and plot of activity across the four conditions for the (a) right anterior temporal region.

### *Retrieval orientation effects*

Retrieval orientation was isolated, as explained in the Introduction, by examining the effects of study material on correct rejections alone. Regions showing differences between the Picture and Auditory conditions are shown in Table 7.3 and Figure 7.2.

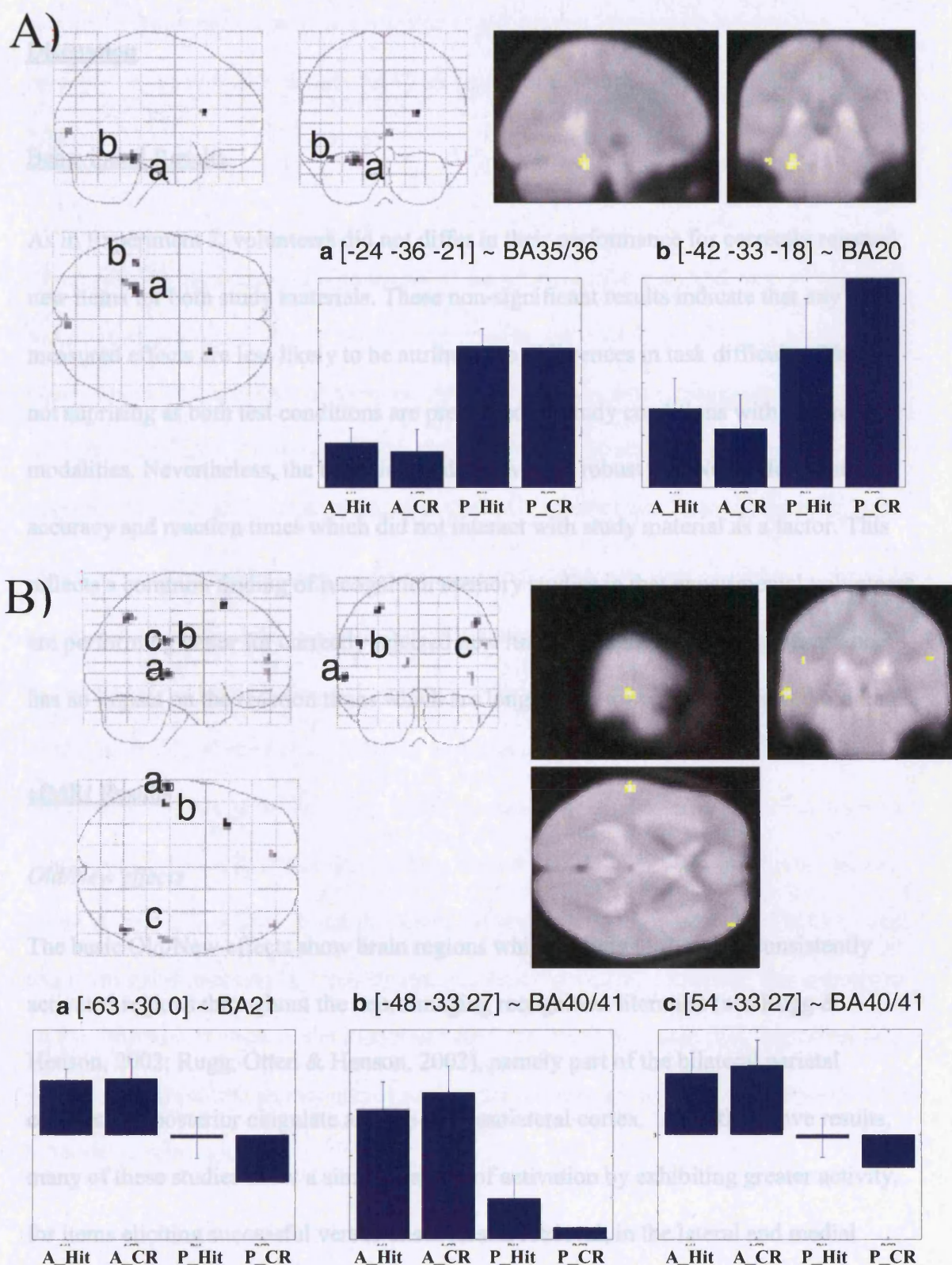
The most notable regions showing greater response to correct rejections in the Picture than Auditory conditions were in left inferior temporal/fusiform and parahippocampal cortex (Figure 7.2A). The more medial, parahippocampal region also showed evidence of greater activity for Hits in the Picture than Auditory condition ( $t(16) = -3.23, p < .01$ ), while the more lateral, inferior temporal/fusiform region showed a similar trend, though it did not reach significance ( $t(16) = -1.24, p > .1$ ).

The most notable regions showing greater response to correct rejections in the Auditory than Picture conditions were in left and right parietal operculum and left middle temporal gyrus (Figure 7.2B). All three regions also showed evidence for greater activity for Hits in the Auditory than Picture condition ( $[-63 -30 0], t(16) = 2.35, p < .025$ ;  $[-48 -33 -27], t(16) = 1.75, p < .05$ ;  $[54 -33 27], t(16) = 2.33, p < .025$ ).

**Table 7.3** Exp. 3 – Regions showing elevated activations for factor study material.

Contrast	Region	Side	Size	BA	MNI coordinates			Z-value
		(L/R)	(cm <sup>3</sup> )		x	y	z	
<b>P &gt; A</b>								
	Subcortical - intramedullary	R	.14		27	24	18	3.83
	Inferior temporal/fusiform gyrus	L	.14	20	-42	-33	-18	3.51
	Parahippocampal gyrus	L	.89	35/36	-24	-36	-21	3.66
	Striate area	R	.24	17	6	-90	0	3.38
<b>A &gt; P</b>								
	Frontomarginal gyrus	R	.19	10	45	54	0	3.39
	Frontopolar gyrus	L	.14	9	-9	54	12	3.51
	Middle frontal gyrus	L	.27	6	-33	15	57	4.10
	Middle temporal gyrus	L	.38	21	-63	-30	0	3.97
	Parietal operculum	L	.19	40/41	-48	-33	27	3.89
	Parietal operculum	R	.19	40/41	54	-33	27	3.34
	Angular gyrus	R	.35	7	48	-63	45	3.75





**Figure 7.2 Exp. 3 – A)** Views of the Picture > Auditory activations for correct rejections only,  $p < .001$  uncorrected and plots for (a) left fusiform and (b) left inferior temporal regions. **B)** Views of the Auditory > Picture activations for correct rejections only and plots for (a) left middle temporal and (b) left and (c) right parietal operculum. See Figure 7.1 legend for more details.

## **Discussion**

### **Behavioural Results**

As in Experiment 2, volunteers did not differ in their performance for correctly rejected new items for both study materials. These non-significant results indicate that any measured effects are less likely to be attributed to differences in task difficulty. This is not surprising as both test conditions are preceded by study conditions with different modalities. Nevertheless, the behavioural data revealed robust Old/New effects for accuracy and reaction times which did not interact with study material as a factor. This reflects a common finding of recognition memory studies in that experimental volunteers are performing better for correctly rejected new items, though this higher performance has an impact on the reaction times which are longer than for correctly rejected old items.

### **efMRI Results**

#### *Old/New effects*

The basic Old/New effects show brain regions which belong to the most consistently activated regions throughout the neuroimaging recognition literature (see Rugg & Henson, 2002; Rugg, Otten & Henson, 2002), namely part of the bilateral parietal cortices, the posterior cingulate and the left dorsolateral cortex. As in the above results, many of these studies show a similar pattern of activation by exhibiting greater activity, for items eliciting successful versus unsuccessful retrieval, in the lateral and medial parietal cortices (Rugg & Henson, 2002). In addition, many studies suggest that the

activity in these regions may be a function of the amount of episodic information retrieved in response to a specific test item (e.g. Henson et al., 1999b; Eldridge et al., 2000).

The parietal fMRI activity is reminiscent of the ERP 'left parietal' Old/New effect. Such a cross methodological comparison is reassuring in that a similar neural signature can be observed for the same class of items by means of different neuroimaging techniques. As evident from Figure 7.1, the data show the same pattern of activity in that correctly rejected old items are more activated than correctly rejected new items in these regions.

Similar findings of old items engaging more activity than new items can also be found in the dorsolateral prefrontal cortex region of the data. A functional interpretation of this region has so far been elusive and has been attributed to either retrieval success (Henson et al, 1999b; McDermott et al., 2000) or to monitoring processes that operate on the products of retrieval (Fletcher et al., 1998; Henson, Shallice & Dolan, 1999 but see also Ranganath, Johnson & D'Esposito, 2000). The present findings indicate that the former might be true in that items being successful retrieved show greater levels of activity than test items being successfully correctly rejected (see Figure 7.1). However, this appears to be a problematic in view of the Ranganath findings which indicated that, regardless of the study status, there was an increase of activity for the amount of encoded perceptual detail retrieved in this region.

### *Retrieval orientation and retrieval content effects*

The patterns of activity presented in Figure 7.2 and Table 7.3 show that effects of study material are common to both studied and unstudied items and hence, no differential activity for correctly rejected new items can be observed. Therefore, I will discuss orientation and content effects together because the results do not seem to allow delineating both effects.

### **A-P contrast**

The contrast of words encoded auditorily versus words encoded as pictures reveals main responses in auditory cortex regions (BA 21, BA 40/41). As mentioned above the elevated activity is apparent for two of the auditory encoded test word conditions (Hits and Correct Rejections) and thus does not seem to be influenced by the status of test items. For the studied items this seems to be not surprising in that it is assumed that episodic retrieval involves reinstatement of cortical activity engaged during processing of an episode when it was initially experienced. Thus, different retrieval content should be associated with distinct cortical regions (e.g. Vaidya et al., 2002; Wheeler & Buckner, 2003; Woodruff et al., 2005). In this study it means that to retrieve words encoded auditorily it is beneficial to re-activate auditory cortex regions. Nevertheless, the same response for the correctly rejected unstudied items is not explained via this phenomenon. Still, the re-activation of the encoding-relevant cortex regions might not be constrained to old items, instead the same activity could help volunteers to reject unstudied items as to

avoid unwanted retrieval information. This would run along the lines of the Herron and Rugg (2003) conclusion that retrieval orientation might help to avoid retrieving false positive information and thus, helping to probe memory retrieval. In terms of a functional interpretation the activation in the auditory cortex regions would mean that all test items are covertly ‘sounded out’ by the subjects which subsequently can be used to probe memory for a given retrieval cue.

### **P-A contrast**

In a similar way, the activity in fusiform cortex observed for the P-A contrast can be interpreted. Namely, words encoded as pictures show greater responses than words encoded auditory in fusiform cortex (BA 20, BA 35/36) regardless of their study status. More strikingly, elevated activation in the fusiform cortex has been reported for encoded pictures by several researchers (e.g. Vaidya et al., 2002; Wheeler & Buckner, 2003). However, in all of the above studies an increase of activity was observed for the correctly recognized studied items only, and not for the correctly rejected unstudied items, as reported here. Similar to the explanation I suggested above, one can assume that this extrastriatal activity could be interpreted as retrieval cue effect per se, which can be beneficial to the subjects to correctly recognize or reject each item. More specifically, in the condition where subjects receive words as retrieval cues which were encoded as picture, imagining each word as a picture might help the volunteers to orient their memory probing towards a given retrieval cue.

To summarize, surprisingly the findings of experiment 3 did not replicate the results of Ranganath, Johnson and D'Esposito (2000). That is, no left prefrontal cortex activation was observed for the contrast of correct rejections when they differ according to study material retrieved. However, more interestingly other retrieval cue effects surfaced along with robust Old/New effects, which might in the end be more relevant to cue processing per se. More specifically, there was evidence that at the retrieval stage the same regions are activated for old as well as new items depending on the study material. For words encoded auditorily this means that regardless of study status the auditory cortex regions are activated for each test item. Similarly, the extrastriatal cortex regions showed greater response for words encoded as pictures than words encoded auditorily. In this case, activity in the infero-temporal cortex enables participants to imagine each visual test word as an object, which again should be beneficial in making a correct recognition judgement. Thus, both effects measured should be actual retrieval cue effects, as they are not influenced by retrieval success as a factor. According to Rugg and Wilding's (2000) retrieval orientation definition, the measured effects could be interpreted in terms of retrieval orientation as the effects should help people to align themselves with the information given for a specific retrieval cue and thus support successful retrieval. Nevertheless, with regard to the above findings this would mean that the retrieval orientation process per se might be not detectable, as I can only report the activity related to the encoded information (auditory words and pictures). I will discuss and interpret these findings in a broader context in the General Discussion of the thesis.

## **Chapter 8 – Experiments 4 & 5: Effects of indirect versus direct retrieval task on the neural correlates of retrieval processing, and is retrieval orientation a pure imagination process?**

### **Introduction**

The previous experiments provided several new facts about retrieval orientation. Nevertheless, many issues remain and one crucial aspect is whether the appearance of ERP retrieval orientation effects are contingent upon episodic retrieval per se. Leading on from Tulving's hypothesis that subjects must be in a tonically maintained cognitive state called "retrieval mode" to evoke interactions between retrieval cues and stored memory representations (Tulving, 1983), several researchers contrasted tasks of episodic versus semantic retrieval to observe retrieval mode effects (Duzel et al., 1999; Morcom & Rugg, 2002; see also chapter 3). According to Rugg and Wilding's (2000) definition, retrieval mode should thus be: i) time-locked to the onset of an episodic retrieval task and maintained throughout the duration of the task, ii) task invariant across different episodic retrieval tasks and most importantly in this context iii) sensitive to contrasts between episodic and non-episodic tasks as shown in the above studies. Rugg and Wilding further concluded that the adoption of retrieval orientations can be thought of as subprocesses to retrieval mode and thus retrieval orientation processes should only be apparent if subjects are in retrieval mode. However, in contrast to retrieval mode, retrieval orientation should be sensitive to different episodic retrieval tasks as well as to the study material, which was demonstrated in the previous chapter and by other researchers (Robb & Rugg, 2002;

Herron & Rugg, 2003; Herron & Wilding, 2004). Hence, factorially crossing the factors of study material and retrieval task (episodic versus non-episodic), should reveal: i) retrieval mode effects apparent in the episodic retrieval tasks but invariant to the study material; ii) retrieval orientation effects again only observable in the episodic retrieval task, however sensitive to the encoded information. These contrasts should reveal whether there is a qualitatively dissociation between retrieval mode and orientation effects. To my knowledge, most studies so far have only been interested in one (retrieval mode; Duzel et al., 1999; Morcom & Rugg, 2002; Wilding & Sharpe, 2003) or the other (retrieval orientation; Robb & Rugg, 2002; Herron & Rugg, 2003) form of process, and only one study has attempted a direct dissociation of retrieval mode and retrieval orientation by means of ERP (Herron & Wilding, 2004).

Herron and Wilding (2004) asked volunteers to complete either a semantic retrieval task or one of two episodic retrieval tasks depending on the cue which preceded each test item. The data of the experiment were compiled by measuring the cue-related ERP activity for each cue class, similar to the recordings of Morcom and Rugg (2002) and Duzel et al. (1999). Their results showed that there are dissociable neural correlates of retrieval mode and orientation. The former showing a right frontal scalp distribution, similar to Morcom and Rugg's (2002) and Duzel et al.'s (1999) findings, while the latter showing a fronto-central scalp distribution, similar to the previously presented and Robb and Rugg's (2002) findings. In contrast to Herron and Wilding (2004), the thesis results so far conveyed item and not cue-related ERP activity. Thus, in experiment 4, I investigated whether one could observe dissociations of retrieval mode and orientation



for item-related ERP activity by factorially crossing the factors of study material (auditory words vs. pictures), as employed in experiment 2, with a new factor of retrieval task (Direct vs. Indirect). The factor of retrieval cue (visual words) was held constant across the experiment. All items denoted concrete objects. Subjects performed the same task in all study phases (an indoors/outdoors decision about each object), and then either performed a yes/no recognition memory test (Direct task) or a different semantic decision (decision about the object size; Indirect task). I expected to: i) replicate the ERP retrieval orientation effect of experiment 2 for new items in the Direct task; ii) to see no evidence of the same ERP effect for new items in the Indirect task; iii) to find a neural correlate of retrieval mode by comparing Direct and Indirect retrieval task whose signature should be not affected by study material as a factor.

## **Experiment 4**

### **Methods**

#### **Participants**

Nineteen subjects participated. Data are reported from sixteen subjects (11 female), aged between 18 and 35 years. Data from the remaining three subjects were rejected due to the failure to form ERPs from fewer than 16 artefact-free trials in one or more of the critical experimental conditions.

### Experimental Materials

The same experimental material and design as in experiment 2 was employed. In addition, two study-test cycles were added for the indirect retrieval task conditions with the same number of stimuli at study and test (see chapter 4).

### Procedure

Study trials consisted of the presentation of a fixation character ('+') for 500ms. The screen was blanked for 120ms, and followed by the presentation of the stimulus for 1500ms. For the auditory word condition the stimulus presentation took the form of the presentation over headphones of a 1500ms auditory frame containing the study item. The screen was then blanked until the subject responded, after which the next trial was initiated. The study task remained consistent across all four study phases. In each study phase each subject was asked to decide whether the denoted object was more likely to be found indoors or outdoors.

Test trials began with the presentation of a fixation character ('+') for 1200ms, after which the screen was blanked for 120ms. This interval was followed by the presentation of the test item for 500ms. A second fixation character ('\*') then appeared for 2400ms. The screen was then blanked and the next trial initiated 200ms later. The task at test differed according to whether the subject was required to make a yes/no recognition judgement (i.e. direct retrieval task) or a semantic size judgement (i.e. indirect retrieval

task). In the two direct test conditions, subjects judged whether each test item corresponded to a study item (either a picture or an auditory word) in the immediately preceding study phase. In the two indirect test conditions, the judgement was whether or not each presented item would, in real life, fit into a shoebox. Subjects were told that some items in the test phase of the indirect conditions were studied previously, but this was irrelevant to their task, so they should concentrate on the semantic judgement.

The order of the direct/indirect task, and of the two types of study material, was counterbalanced across subjects, as were the hands employed for 'yes' and 'no' responses. As in the previous experiment, the study-test cycles were ran in a blocked fashion in that each experimental condition (e.g. auditory-word, picture word) comprised one study-test cycle.

#### ERP recording and analysis

(See chapter 4 for a detailed description.)

### **Results**

#### Behavioural Performance

Accuracy and RTs are shown in Table 8.1. For the two Direct memory conditions, recognition accuracy was assessed using the discrimination index  $Pr(pHit - pFalse Alarm)$ ; Snodgrass & Corwin, 1988). These values were .79 (.10) and .78 (.12) for the

Auditory and Picture conditions respectively, which did not differ reliably ( $F_s < 1$ ,  $p > .7$ ). In all subsequent analyses, New items in the Direct task are restricted to those that received correct responses (i.e. correct rejections) as in previous experiments. For the two Indirect memory conditions, accuracy of the semantic judgments was close to 100%, and in any case, the size decision is debatable for some items. For these reasons, all New items were analysed for the Indirect task.

RTs were subjected to a two-way ANOVA with factors retrieval task (Direct/Indirect), study material (Auditory/Pictures), and study status (Old/New). There was a reliable interaction between study material and study status ( $F_{1,15} = 4.95$ ,  $p < .05$ ), which appeared to be driven by slower responses to New items in the Picture conditions. No other interactions reached significance. Follow-up, planned comparisons on New items showed a reliable difference between Picture and Word conditions in the Direct task ( $F_{1,15} = 7.88$ ,  $p < .025$ ), but not in the Indirect task ( $F_s < 1$ ,  $p > .6$ ).

**Table 8.1.** Percent accuracy, RT (ms) and PR by condition and retrieval task

Condition	Accuracy (SD)		RT (SD)		
	Old	New	Old	New	Pr
<b>Direct retrieval task</b>					
Auditory Word - Visual Word	0.85 (0.09)	0.94 (0.05)	1035 (188)	1081 (237)	0.79
Picture - Visual Word	0.84 (0.11)	0.95 (0.03)	1035 (157)	1146 (243)	0.79
Condition	Accuracy (SD)		RT (SD)		
	Old	New	Old	New	Pr
<b>Indirect retrieval task</b>					
Auditory Word - Visual Word	-	-	1038 (244)	1046 (233)	-
Picture - Visual Word	-	-	1027 (256)	1063 (231)	-

## ERP Data

Given the hypotheses concerning retrieval orientation, I began by examining ERPs to New items only. These are shown for Picture and Auditory conditions at selected electrode sites, and separately for Direct and Indirect tasks, in Figures 8.1 & 8.2. The mean numbers of trials (range in brackets) forming individual subjects' ERPs were 29 (18-35), 29 (21-34), 33 (28-35) and 31 (24-35) for the Direct-Auditory, Direct-Picture, Indirect-Auditory and Indirect-Picture conditions respectively.

In the Direct task, ERPs from about 400ms onwards were more negative-going when pictures rather than auditory words comprised the sought-for material, replicating previous findings. This difference was widespread and apparent over all electrode sites as seen in Figure 8.1. In the Indirect task (Figure 8.2), ERPs were also more negative-going in the Picture than Auditory conditions. However this difference occurred in an earlier time window, from around 250ms to 600ms, and appeared to be stronger over more posterior sites.

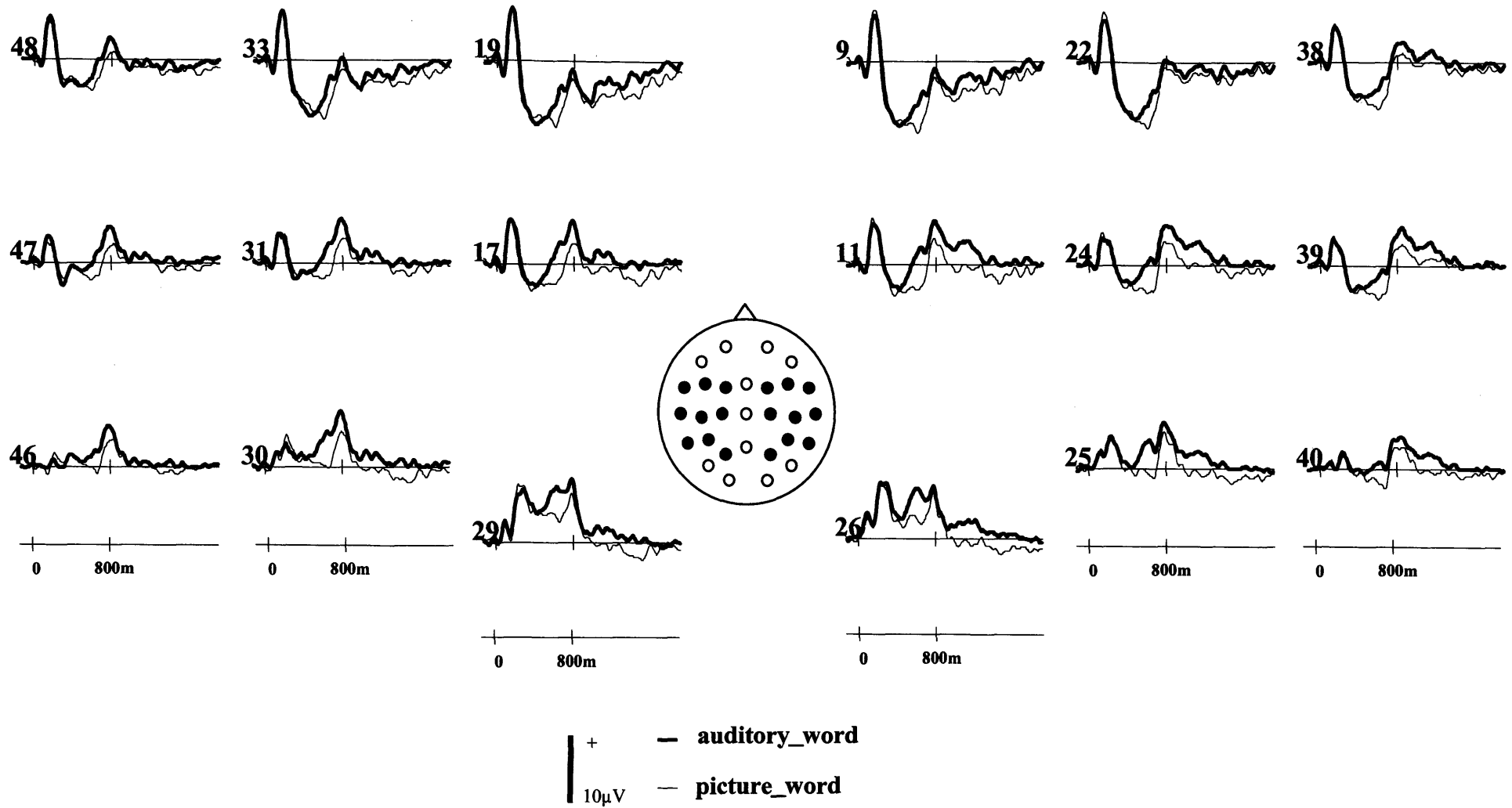
To test these effects, data were quantified and analysed over the same latency regions and electrode sites as in the previous experiments (chapter 5 & 6; see also chapter 4). Effects that do not involve the factor of study material are not reported (see Table 8.2 for a summary of the study material effects), however a summary of the Old/New effects can be found in appendix 5.

**Table 8.2.** Exp. 4 – Summary of ANOVA results in each ERP latency region including the factor of study material and retrieval task.

Main effects & interactions	100-300 msec	300-600 msec	600-900 msec	900-1200 msec
18 main electrode sites				
El	–	$F_{1,15} = 18.52, p < .001$	$F_{1,15} = 9.05, p < .01$	$F_{1,15} = 5.20, p < .05$
PA	–	$F_{1,15} = 3.95, p = .6$	$F_{1,15} = 5.04, p < .05$	–
El x PA	–	–	$F_{1,15} = 5.54, p < .05$	–
El x PA x ST	$F_{1,1,16.5} = 6.13, p < .025$	–	–	–
El x PA x AP x ST	$F_{2,2,32.3} = 3.33, p < .05$	–	–	–
El x PA x HM x AP	–	–	–	$F_{1,8,27.3} = 3.50, p < .05$

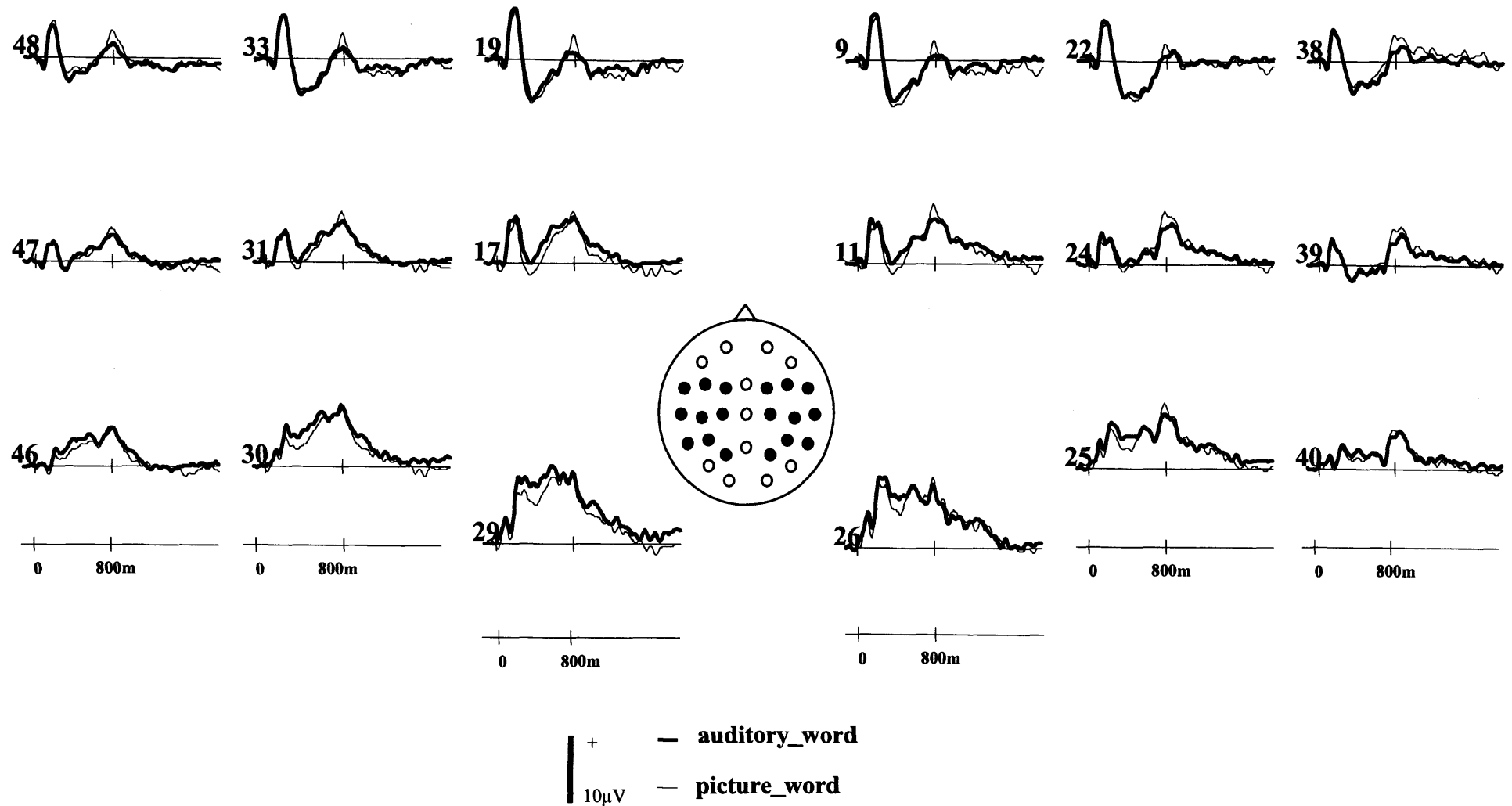
El = retrieval task; PA = study material; HM = hemisphere; AP = location; ST = site.

## Direct retrieval task



**Figure 8.1** Exp. 4 – Grand average ERP waveforms elicited by correctly rejected new items at lateral frontal (48, 33, 19, 38, 22, 9), lateral temporal (47, 31, 17, 29, 24, 11) and lateral parietal sites (46, 30, 29, 40, 25, 26) for the direct retrieval task.

## Indirect retrieval task



**Figure 8.2** Exp. 4 – Grand average ERP waveforms elicited by new items at same electrode sites as above (Figure 8.1) for the indirect retrieval task.



*Magnitude analyses for 18 electrode sites*

**100-300ms**

ANOVA of the 100-300ms region revealed an interaction of retrieval task, study material, anterior-posterior chain and inferior-superior chain ( $F_{2.2,32.3} = 3.33, p < .05$ ). Follow-up ANOVAs on Direct and Indirect tasks separately revealed an interaction of study material with the inferior-superior chain ( $F_{1.1,16.3} = 4.94, p < .05$ ) only for the Indirect task.

**300-600ms**

ANOVA of the 300-600ms region revealed a marginal main effect of study material ( $F_{1,15} = 3.95, p = .6$ ) and a reliable main effect of retrieval task ( $F_{1,15} = 18.52, p < .001$ ).

**600-900ms**

ANOVA of the 600-900ms region revealed a main effect of retrieval task ( $F_{1,15} = 9.05, p < .01$ ) and an interaction of study material and retrieval task ( $F_{1,15} = 5.54, p < .05$ ). Subsidiary ANOVAs on Direct and Indirect tasks separately showed a main effect of study material only in the Direct task ( $F_{1,15} = 14.94, p < .01$ ).

**900-1200ms**

For the 900-1200ms region, ANOVA revealed a main effect of retrieval task ( $F_{1,15} = 5.20, p < .05$ ) and an interaction between study material, retrieval task, hemisphere and anterior-posterior chain ( $F_{1.8,27.3} = 3.50, p < .05$ ). Separate ANOVAs on Direct and Indirect tasks gave rise to a main effect of study material only in the Direct task ( $F_{1,15} = 8.14, p < .01$ ).

### *Magnitude analyses across latency region*

The above analyses suggest an effect of study material specific to the Indirect task early on (100-300ms), and specific to the Direct task later (600-1200ms). However, the two effects were clearly overlapping in time (e.g. from 300-600ms). To test for a latency difference more formally, I selected via visual inspection a latency region in which the effect was maximal in the Indirect task (250-600ms) and a latency region in which the effect was maximal in the Direct task (450-850ms). ANOVA including latency region and all electrode sites as further factors revealed a reliable interaction between latency region, retrieval task, study material and site ( $F_{3,2,47.8} = 4.24$ ,  $p < .01$ ).

### *Task order effects*

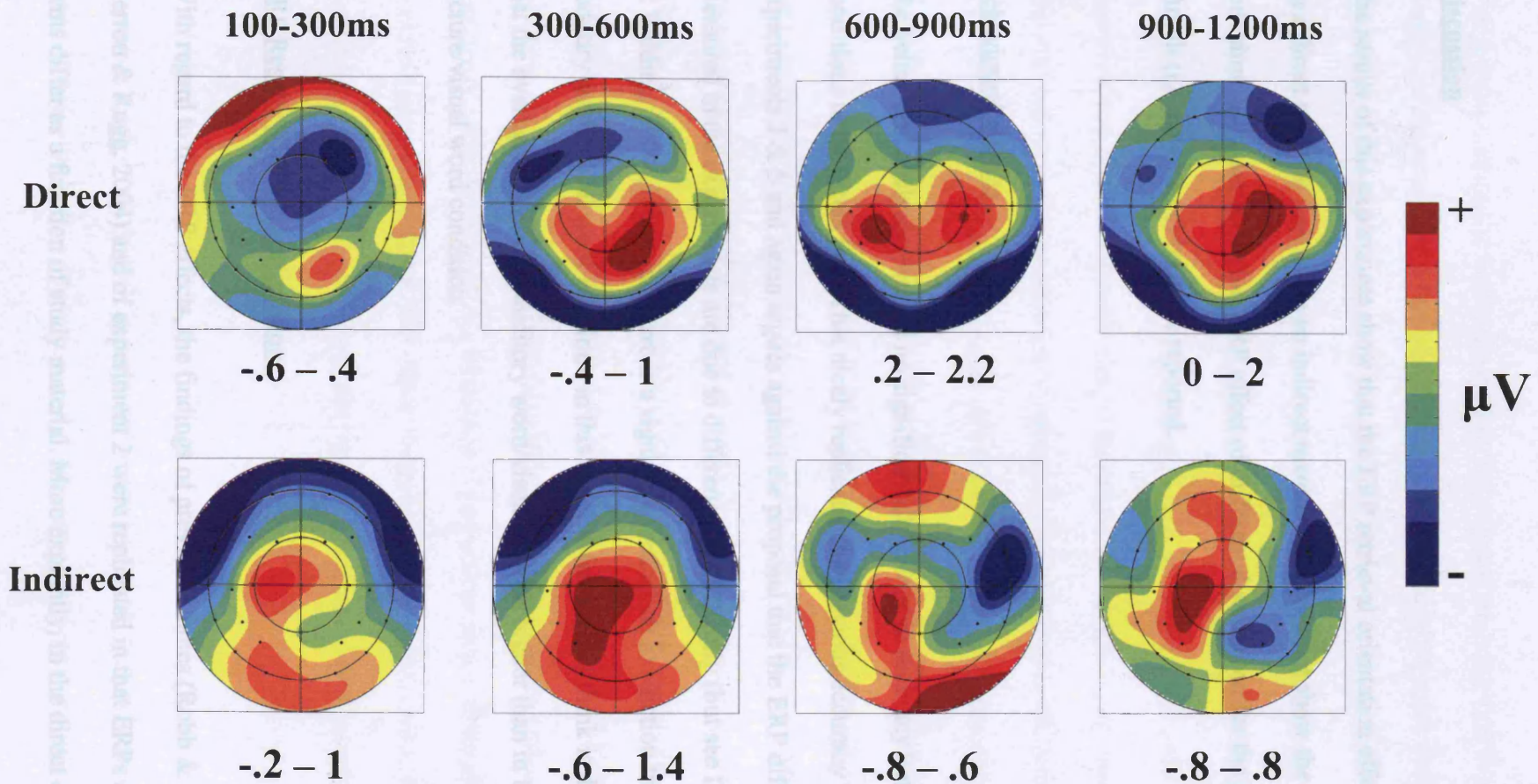
Although the order that subjects performed the Direct and Indirect tasks was counterbalanced across subjects, I was concerned that the effect of study material on New items in the Indirect task might only arise for subjects who performed the Indirect conditions after the Direct conditions. In other words, I was worried that the experience of having previously performed a task that required searching episodic memory might bias the manner in which subjects processed items in the subsequent Indirect task, such that they thought about whether each test item had previously been studied, even though this was not relevant to their task (and despite being told not to). To test this possibility, I split the 16 subjects into 2 groups (one of them comprising 7 subjects: explicit task followed by implicit task, and the other one comprising 9 subjects: indirect task followed by direct task) by the order that they performed the Direct and Indirect tasks. ANOVAs

showed no interactions involving study material and this additional “group” factor (or involving retrieval task and group), for any latency region.

### *Topographic analysis*

In addition to the above analyses of ERP amplitude, the scalp topographies of the ERP effects of study material were contrasted as a function of retrieval task. These topographies are shown for each retrieval task and latency region in Figure 8.3. ANOVAs on these scaled differences were performed for each latency region with the factors of retrieval task (Direct/Indirect) and electrode site (1-29). However, no interactions between task and site reached significance for any latency region: 100-300ms ( $F_s < 1.1$ ,  $p > .05$ ); 300-600ms ( $F_s < 1$ ,  $p > .05$ ); 600-900ms ( $F_s < 1$ ,  $p > .05$ ); 900-1200ms ( $F_s < 1$ ,  $p > .05$ ); 1200-1400ms ( $F_s < 1$ ,  $p > .05$ ).

I also conducted a topographical analysis contrasting the early Indirect (250-600ms) vs. the late Direct (450-850ms) conditions, but this did not reach significance either ( $F_s < 1$ ,  $p > .05$ ). Thus, while the interactions with electrode factors in the above amplitude analyses imply a different pattern of study material effects across time over the scalp, there is no evidence that these scalp differences are robust enough to be brought out by the present analyses.



**Figure 8.3** Exp. 4 –Scalp topographies for the visual word new items of the direct and indirect retrieval task (auditory words – pictures) for all latency regions. Values below each spline map denote minimum and maximum microvolt ( $\mu\text{V}$ ) values of each map.

## **Discussion**

The results of this experiment show that the ERP retrieval orientation effect is dependent on a direct retrieval task while an indirect memory test does not show the same pattern of activation, although an earlier ERP effect of different distribution for the same class of stimuli (i.e. new items) could be reported.

## **Behavioural Results**

The behavioral analysis revealed no significant difference in accuracy between both test conditions in the direct task. This nicely replicates the previous accuracy results of experiments 2 & 3 and again argues against the proposal that the ERP differences measured in the experiments are due to differences in difficulty (but see Dzufliki, Sharpe & Wilding, 2004). However, there is a significant reduction in reaction times in the auditory word/visual word condition in this experiment which I think is due to the fact that the overlap between the auditory word/visual word is higher than in the picture/visual word condition.

## **ERP Results – retrieval orientation**

With regard to the ERP effects, the findings of previous studies (Robb & Rugg, 2002, Herron & Rugg, 2004) and of experiment 2 were replicated in that ERPs elicited by new items differ as a function of study material. More explicitly, in the direct conditions ERPs

of new items encoded as auditory words are more positive-going than those encoded as pictures. More importantly, the indirect conditions in this experiment did not show the same effect, however, new items in the indirect task show an earlier effect of new items in the same direction. As stated in the above analysis both effects show an overlap in the 300-600ms latency region, with the indirect effect starting and finishing earlier (~250-600ms) and the direct effect starting later but being more prolonged (~450-1200ms). Therefore, the direct effect resembles, in its extent, the results of previous experiments, while the indirect effect is less clear to interpret. The topographic analysis of the new items in both direct and indirect tasks also failed to clarify a difference between the effects in both tasks, because for both topographic analyses (original and modified latency regions), no interaction of tasks (direct vs. indirect) by sites can be found and therefore any functional interpretation of the difference between the two effects should be done cautiously. However, I am confident that the two effects are functionally different because, as evident from amplitude analysis, the effect of the indirect task can be found more at posterior sites, in contrast to the direct task being reported at mid-central electrode sites. I propose therefore, that the non-significant results in the topographic analyses are due more to the lack of statistical power than an actual functional similarity of both effects, although the ERP effect observed in the indirect condition has still to be explained, which I will do in the adjoint paragraph together with the retrieval orientation findings.

As stated in earlier chapters it is proposed that subjects can vary in how they process retrieval cues. Implicit in this notion is the assumption that participants can explicitly

vary this cue approach. It follows that only a task designed to set subjects in a retrieval state (or mode), should allow participants to apply the cue constraining observed in the ERP retrieval orientation effects. More explicitly, any task designed in terms of indirect retrieval (e.g. implicit retrieval; Graf & Mandler, 1984; Richardson-Klavehn et al., 1994) should fail to elicit the ERP retrieval orientation effect, in that subjects are not in a 'retrieval mode' (Tulving, 1983). Thus, subjects should not process upcoming items directly (or explicitly) as retrieval cues and any occurring retrieval should be, in this case, incidental and not intentional. In terms of the ERP retrieval orientation effect, this means that no retrieval orientation should occur because of the explicit nature of this effect. This is exactly what was found in that new item ERPs in the indirect condition do not show an effect in the same latency region as the direct conditions. In terms of a functional interpretation of the earlier ERP effect in the indirect conditions, the early difference might be a cross-modality attention effect (e.g. Talsma & Kok, 2001; Eimer & Schroger, 1998). The posterior-occipital distribution (see Figures 8.2 & 8.3) and the early time window would comply with this proposal, although I am aware that the comparison of results across different research fields is difficult to make. Other functional interpretations can only be made cautiously because of the indirect (or implicit) nature of the task. However, I am also aware that the results for the indirect conditions might not be process pure (i.e. implicit). One reason for this is that subjects might have disregarded the test instructions and were doing an explicit retrieval of information in any case. A second and related reason is that only the task and not a change of test cue (e.g. use of word stems for implicit retrieval) was determining whether participants were applying an implicit or explicit approach towards the test cues. As reported in the Methods section, to

avoid any confounds of task order a strict counterbalancing was applied to reduce any risk of such effects. Further, the experimental instructions were made very clear to the subjects and the importance of succeeding in the test by following exactly the study and test instructions was stressed to each of them. In addition, each subject was quickly debriefed after the experiment finished and asked about how they approached each task and whether they changed this approach. None of the above ‘checks’ revealed any consistency of subject behavior across the different retrieval tasks. To rule out any further doubt, a post-hoc analysis was conducted for which subjects data was split into two groups according to the order of task they received (direct task followed by indirect task vs. indirect task followed by direct task). The between subject ANOVA did not give rise to an interaction of group by task by study material by sites in any of the latency regions, revealing that direct retrieval (e.g. explicit) processing of cues in the indirect conditions is less likely. However, as already mentioned, at this stage it cannot be established whether any attentional processing is really responsible for the reported ERP effect in the indirect conditions.

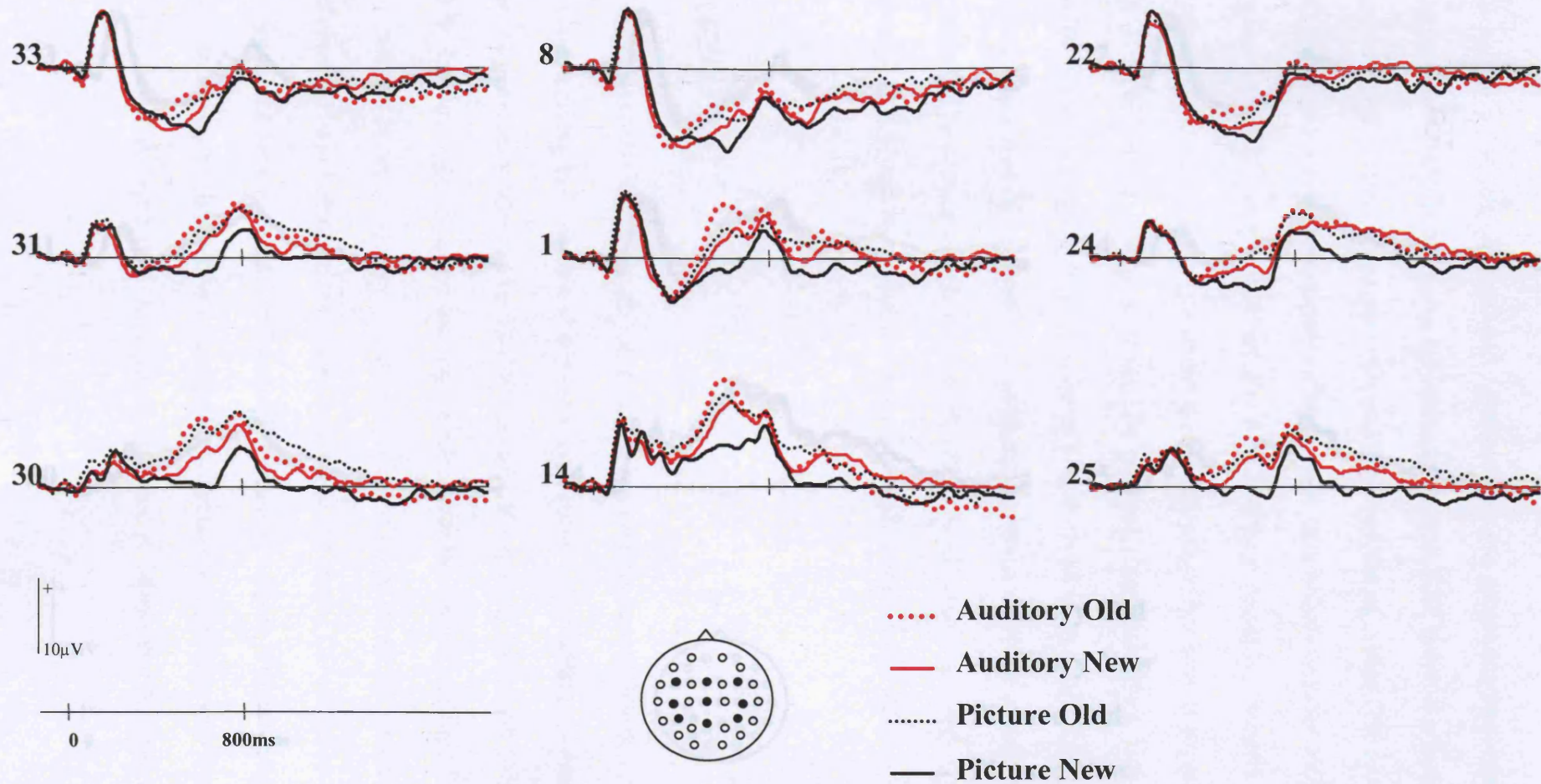
### ERP Results – retrieval mode

As evident from Figures 8.4 & 8.5, the ERP waveforms show a difference between retrieval tasks regardless of the study material. This difference onsets at around 300ms post-stimulus and is sustained until the end of the recording epoch, and shows more negative-going ERP waveforms for the direct task especially at frontal and central electrode sites. This observation is confirmed by significant retrieval task main effects for



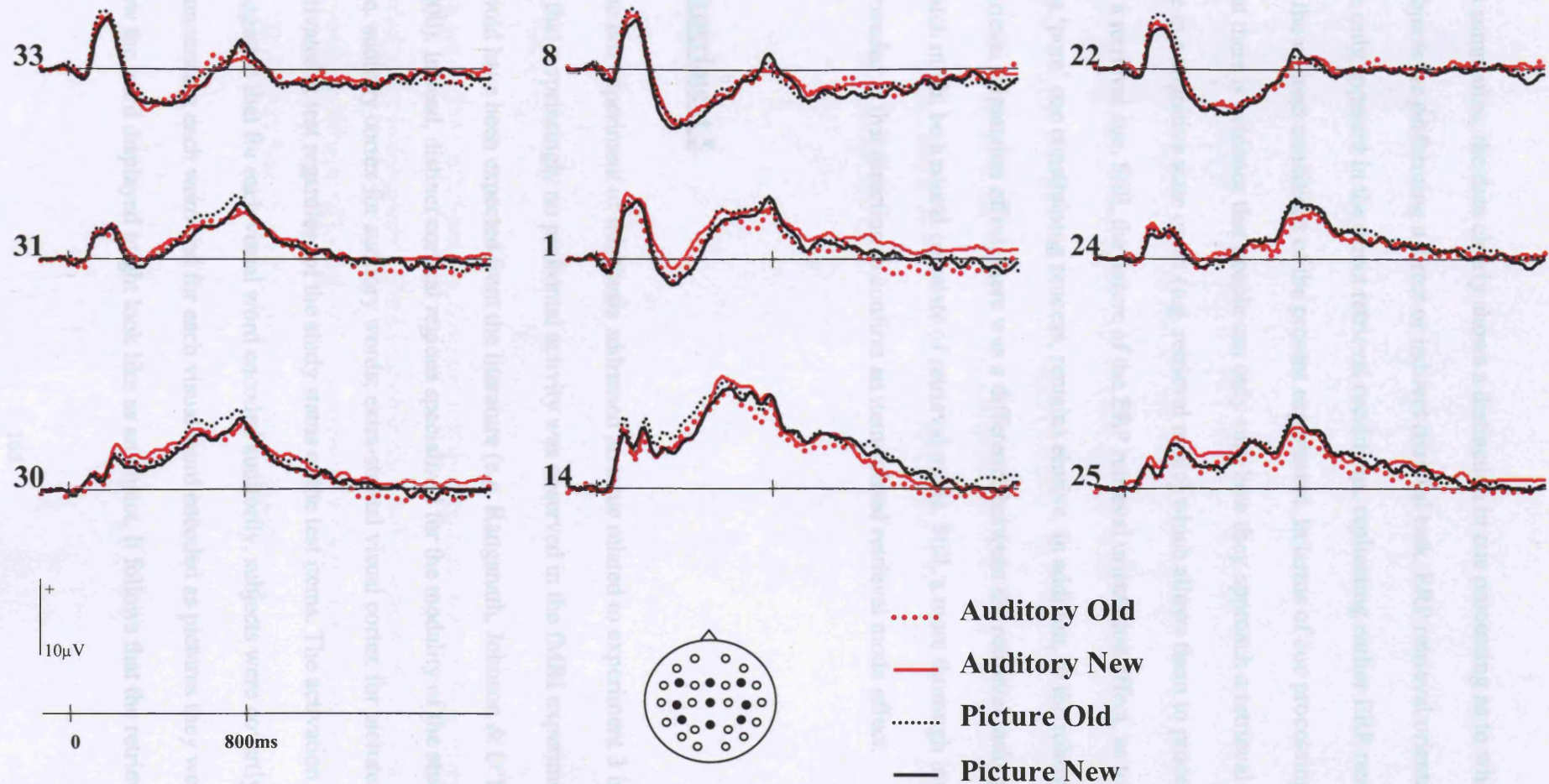
the 300-600ms and 600-900ms latency regions, (see Table 8.2). According to Tulving (1983) and Rugg and Wilding (2000) the differential activity for an episodic versus a non-episodic retrieval task which is invariant across study materials and status could be interpreted as a neural correlate of retrieval mode. However, this conclusion seems to be problematic on two grounds. First, retrieval mode should be a tonically maintained process which should be apparent throughout memory retrieval. In contrast, the data indicates that an effect of retrieval task is missing for the earliest and latest latency regions and hence appears only from 300ms to 900ms. It is of course possible to argue that episodic retrieval processing onsets only in this time region when subjects are not cued towards a specific retrieval, as in the studies of Herron and Wilding (2004). Still, the data leaves open the question of whether this is true. Second, the direction of the retrieval mode effect observed is opposite to the one measured in the studies of Duzel et al. (1999) and Morcom and Rugg (2002), namely these studies observed more negative going ERP waveforms for the non-episodic than for the episodic condition. Still, these differences can be accommodated with the present findings in that i) different ERP activities (i.e. cue versus item-related activity) were measured and ii) different non-episodic tasks were employed across the present and previous studies.

## Direct task



**Figure 8.4** Exp. 4 – Grand average ERP waveforms elicited by new and old items at lateral frontal (33, 22), lateral temporal (31, 24) and lateral parietal (30, 25) and mid-central sites (8, 1, 14) for the direct retrieval task.

## Indirect task



**Figure 8.5** Exp. 4 – Grand average ERP waveforms elicited by new and old items at lateral frontal (33, 22), lateral temporal (31, 24) and lateral parietal (30, 25) and mid-central sites (8, 1, 14) for the indirect retrieval task.

To summarize, the data clearly shows a distinction in cue processing as to whether subjects are performing a direct or indirect retrieval task. ERP retrieval orientation effects are only apparent in the direct retrieval conditions, replicating earlier ERP results, and not in the indirect conditions of the present experiment. In terms of cue processing, I believe that there is evidence that people can only vary how they approach a retrieval cue if they are in a cognitive state or set (e.g. retrieval mode) which allows them to process each cue as a retrieval cue. Still, the nature of the ERP retrieval orientation effect, as to whether it is a 'pure' cue constraining process, remains elusive. In addition, to the robust ERP retrieval orientation effect, there was a difference between the retrieval tasks per se, which might be a neural correlate of retrieval mode. Still, a more thorough investigation is needed in that direction to confirm an item-related retrieval mode effect.

## **Experiment 5**

The last experiment of this thesis addressed an issue related to experiment 3 in chapter 7, in that surprisingly no prefrontal activity was observed in the fMRI experiment, as would have been expected from the literature (e.g. Ranganath, Johnson & D'Esposito, 2000). Instead, distinct cortical regions specialized for the modality of the study material (i.e. auditory cortex for auditory words; extra-striatal visual cortex for pictures) were activated at test regardless of the study status of the test items. The activation patterns suggested that for each visual word encoded auditorily, subjects were covertly pronouncing each word and for each visual word encoded as pictures they were imaging how the word displayed might look like as an object. It follows that the retrieval



orientation effect might ,trigger‘ the engagement of specific cortical regions related to the encoded information as to increase the likelihood of successful retrieval. Nevertheless, another possibility might be worth pursuing, in that the actual retrieval orientation is an imagination process and not a retrieval cue process per se.

To test this possibility, I conducted a further ERP experiment, in which I presented subjects with visual words and instructed them in one condition to imagine how each word sounds like if spoken out loud and in a second condition to imagine how a corresponding picture to the object might look like. The hypothesis was that no retrieval orientation effect would be apparent because subjects are not in a retrieval mode in these conditions and hence, according to Rugg and Wilding’s (2000) definitions no retrieval orientation should occur.

## **Methods**

### **Participants**

The same nineteen subjects as in experiment 4 participated because experiment 5 was run directly after experiment 4. Five of the nineteen subjects were excluded from the experiment, because of excessive eye movements throughout the experiment, which resulted in less than 16 artefact free trials per condition.

### Experimental Materials

The experimental material was compiled out of a pool of 90 visual words. For each subject, random sampling from the item pool created two experimental lists. Each list contained 36 words along with 3 filler words, which padded the beginning of the list. The order of the critical items was randomized for each subject and the order of task as well as allocation of words into the picture or auditory imagination was rotated across subjects.

### Procedure

All trials began with the presentation of a fixation character ('+') for 1200ms, after which the screen was blanked for 120ms. This interval was followed by the presentation of the test item for 500ms. A second fixation character ('\*') then appeared for 2400ms. The screen was then blanked and the next trial initiated 200ms later.

For the auditory imagining condition, participants were instructed to look at the screen and to imagine how each visual word would sound if it were spoken out loud. It was stressed to each volunteer to covertly pronounce each word and not to speak the actual word out loud. In the picture imaging condition, participants were instructed to look at the screen and to imagine how each visual word would look like as an object.

Prior to the presentation of the first list proper, 2 short practice lists cycles were administered, one for each condition, to familiarise subjects with the experimental tasks and procedures. The order of the conditions was counterbalanced across subjects.

### ERP recording and analysis

(See chapter 4 for a detailed description.)

## **Results**

### Behavioural Performance

There were no behavioural data collected for this experiment, as subjects were not required to make any judgements via the response keys.

### ERP Data

ERPs for both conditions at selected electrode sites are shown in Figure 8.6. The mean numbers of trials (range in brackets) forming individual subjects' ERPs were 31 (22-34), and 29 (19-35) for the Auditory and Picture imagination conditions respectively.

ERPs for visual words covertly pronounced showed from about 400ms to 900ms post-stimulus more positive-going ERP waveforms over frontal electrode sites than visual words imagined as pictures. In contrast, from around 500-600ms onwards the visual words imagined as pictures displayed more positive-going ERP waveforms at posterior scalp locations until the end of the recording epoch.

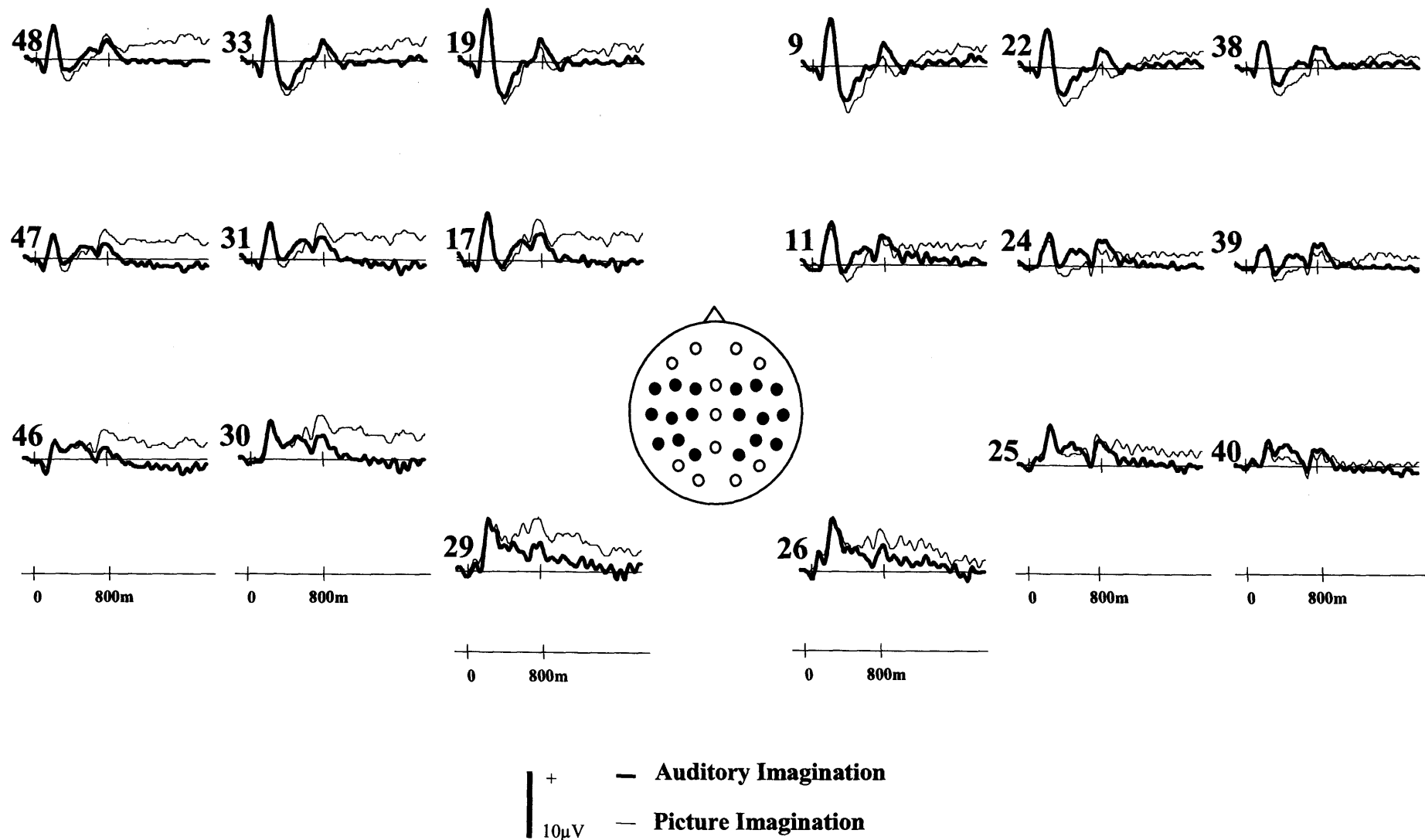
To test these effects, the same latency regions and electrode sites as in previous experiments were employed. Effects that do not involve the factor of imagination are of no interest in the current context, and are not reported.



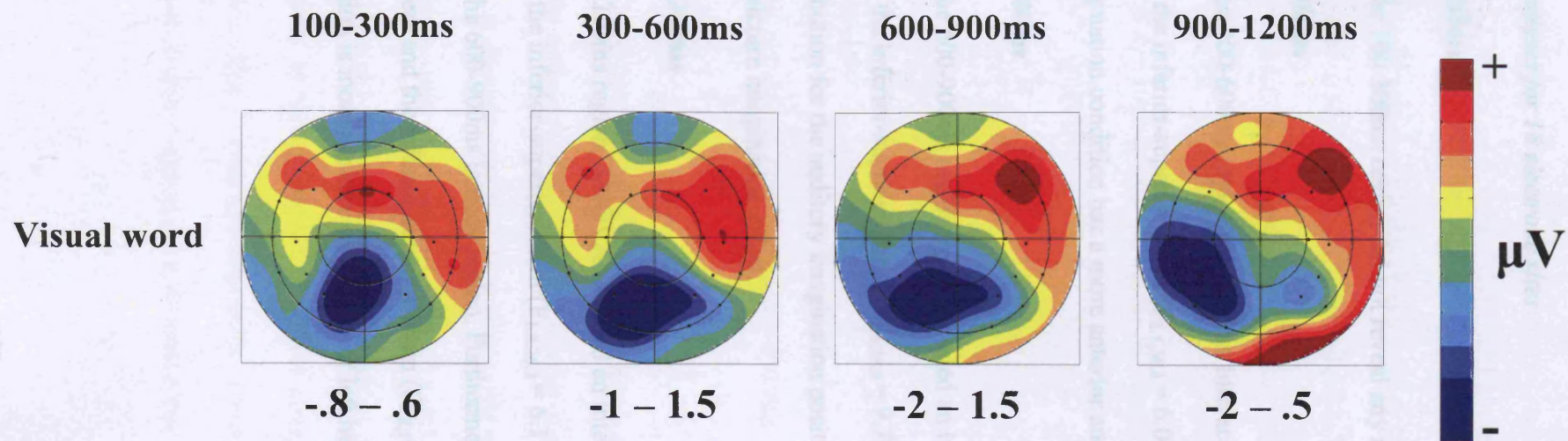
**Table 8.3** Exp. 5 – Summary of ANOVA results in each ERP latency region including the factor of type of imagination.

Main effects & interactions	100-300 msec	300-600 msec	600-900 msec	900-1200 msec
18 main electrode sites				
PA	–	$F_{1,15} = 3.74, p = .07$	–	–
PA x AP	–	$F_{1,1,17.1} = 8.83, p < .01$	$F_{1,2,18.4} = 19.14, p < .000$	$F_{1,2,18.4} = 11.98, p < .01$
PA x HM x ST	–	–	–	$F_{1,2,17.9} = 4.67, p < .05$
PA x AP x ST	–	$F_{2,5,36.8} = 6.06, p < .01$	$F_{2,6,38.9} = 9.78, p < .000$	$F_{1,8,26.3} = 6.11, p < .01$

PA = type of imagination; HM = hemisphere; AP = location; ST = site.



**Figure 8.6** Exp. 5 – Grand average ERP waveforms elicited by visual words imagined auditorily or as pictures at lateral frontal (48, 33, 19, 38, 22, 9), lateral temporal (47, 31, 17, 29, 24, 11) and lateral parietal sites (46, 30, 29, 40, 25, 26).



**Figure 8.7** Exp. 5 –Scalp topographies for the visual word items of the imagination task (auditory words – pictures) for all latency regions. Values below each spline map denote minimum and maximum microvolt ( $\mu\text{V}$ ) values of each map.

### *Magnitude analyses for 18 electrode sites*

#### **100-300ms**

ANOVA of the 100-300ms region did not reveal any main effects or interactions.

#### **300-600ms**

ANOVA of the 300-600ms region revealed an interaction of condition with the anterior-posterior and the inferior-superior chain ( $F_{2.5,36.8} = 6.06, p < .01$ ), indicating that the auditory imagination condition has a more anterior and inferior distribution.

#### **600-900ms**

ANOVA of the 600-900ms region again revealed an interaction of task with the anterior-posterior and the inferior-superior chain ( $F_{2.6,38.9} = 9.78, p < .000$ ), reflecting the anterior-inferior distribution for the auditory imagination positivity and the posterior superior-positivity of picture imagination effect.

#### **900-1200ms**

For the 900-1200ms region, ANOVA revealed an interaction of task with the anterior-posterior and the inferior-superior chain ( $F_{1.8,26.3} = 6.11, p < .01$ ), reflecting the same pattern as in the 600-900ms latency region. Furthermore there was an interaction of task with hemisphere and the inferior-superior chain ( $F_{1.2,17.9} = 4.67, p < .05$ ) revealing that the picture condition is more positive over superior left hemispheric electrode sites.

### *Contrast of experiment 4 vs. experiment 5*

From the observations of Figures 8.6 & 8.7 and the amplitude analysis above, it is clear that the imagination effects appear very different to the retrieval orientation effects reported in the previous experiment. Nevertheless, to make sure that there is no relationship between both ERP effects, I contrasted the unstudied new items of experiment 4 with the imagined conditions in experiment 5. To test these effects, data were quantified and analysed the same way as experiments 4 & 5 with an additional factor experiment (Experiment 4 vs. 5).

### *Magnitude analyses for 18 electrode sites*

#### **100-300ms**

ANOVA of the 100-300ms region did not reveal any main effects or interactions.

#### **300-600ms**

ANOVA of the 300-600ms latency region reveals an interaction of experiment with material and the anterior-posterior and the inferior-superior chain ( $F_{2,9,43.0} = 6.17$ ,  $p < .01$ ). Subsequent analysis, revealed an interaction of material with the anterior-posterior and the inferior-superior chain for experiment 4 and 5 ( $F_{2,9,43.6} = 2.93$ ,  $p < .05$ ;  $F_{2,5,36.8} = 6.06$ ,  $p < .01$ ; respectively) indicating the fact that in both experiments the ERP waveforms related to pictures are more negative-going over anterior electrode sites than those related to auditory words as imagination or study material. However, the ERPs for pictures are more negative-going in experiment 5 than in experiment 4.

Further, ANOVA revealed an interaction of experiment with the factors hemisphere and inferior-superior electrode chain ( $F_{1.3,19.1} = 4.18$ ,  $p < .05$ ). Planned post-hoc analyses showed an interaction of hemisphere and inferior-superior chain only in experiment 4 and not in experiment 5 ( $F_{1.4,21.3} = 3.88$ ,  $p = .05$ ;  $F_{1.6,23.6} = 0.61$ ,  $p > .5$ ; respectively).

### **600-900ms**

ANOVA of the 600-900ms latency region reveals an interaction of experiment with material and the anterior-posterior and the inferior-superior chain ( $F_{2.5,36.8} = 6.69$ ,  $p < .01$ ). Subsequent analysis revealed an interaction of material with the anterior-posterior and the inferior-superior chain for experiment 5 and not experiment 4 ( $F_{2.6,38.9} = 9.78$ ,  $p < .00$ ;  $F_{2.3,35.1} = 1.75$ ,  $p > .1$ ; respectively) indicating that in experiment 5 ERP waveforms related to pictures are more positive going over posterior electrode sites than those related to auditory words.

### **900-1200ms**

ANOVA of the 900-1200ms latency region reveals an interaction of experiment with material and the anterior-posterior and the inferior-superior chain ( $F_{2.3,34.3} = 4.33$ ,  $p < .025$ ). Subsequent analysis, revealed an interaction of material with the anterior-posterior and the inferior-superior chain for experiment 5 and not experiment 4 ( $F_{1.8,26.3} = 6.11$ ,  $p < .01$ ;  $F_{2.7,40.7} = 1.40$ ,  $p > .2$ ; respectively) indicating the same effect as in the 600-900ms latency region.

Furthermore, ANOVA gave rise to an interaction of material with hemisphere and the inferior-superior chain ( $F_{1.3,16.6} = 4.53$ ,  $p < .05$ ).

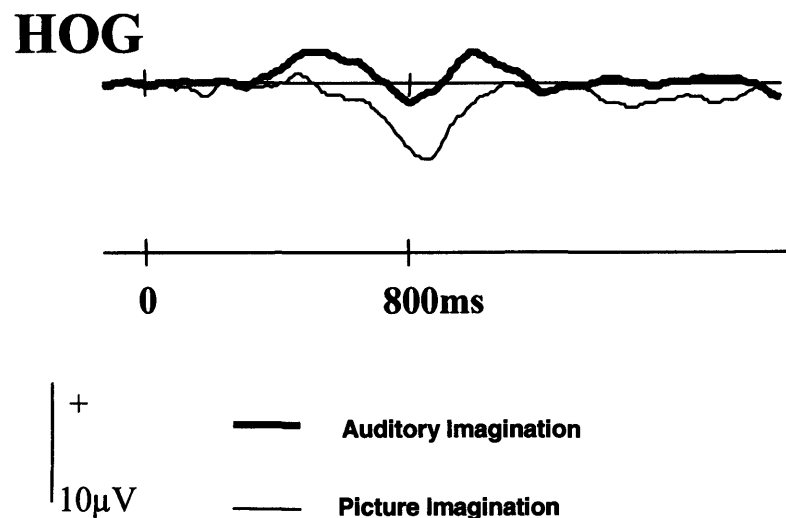
## **Discussion**

### **ERP Results**

The data of experiment 5 do not support the idea that the retrieval orientation effect is based on pure imagination by the subjects. More explicitly, the neural signature of the imagination processes were different in comparison to the ERP retrieval orientation effect. This was also reflected by a direct contrast of the correctly rejected new items of the direct condition in experiment 4 and the two imagination conditions of experiment 5. The contrast revealed interactions involving the factor experiment for the 300-600ms, 600-900ms, and 900-1200ms latency regions. Further analysis showed that in the 300-600ms latency region, both retrieval orientation and imagination do show a similar effect especially at frontal electrode sites. However, the experimental interactions in the following two latency regions clearly indicate that the ERP waveforms differ in that in the imagination experiment show more positive-going waveforms at all electrode sites. This positivity for imagined pictures of visual words is in stark contrast to the more negative going ERP waveforms for correctly rejected words encoded as pictures in the retrieval orientation effect. Thus, it seems unlikely that the same process is underlying the imagination of pictures and auditory words and the orienting towards pictures and auditory words.

Further, although the results of experiment 3 suggest that reinstatement of cortical regions related to the modality of the studied material is part of the retrieval orientation

process, a mere imagining of visual words as spoken out loud or as objects does not suffice to evoke the same effect (at least in ERP). Still, it is difficult to compare data across different methodologies as a one-to-one matching between ERP and fMRI data is very difficult to make (see chapter 2 & 3). Also, the ERP data displayed an HOG (horizontal oculogram) artefact in the ERP grand-average (see Figure 8.8) which was due to the fact that people were moving their eyes when thinking of either an object corresponding to the presented word or imagining the visual word spoken out.



**Figure 8.8** Exp. 5 – Grand average ERP waveforms elicited by visual words imagined auditory or as pictures at the horizontal eye movement electrode (HOG).

Although this is an interesting findings itself, it was not possible to remove the HOG artefact completely to remain sufficient trials for the statistical analysis and therefore especially the frontal effect in the imagination conditions has to be interpreted cautiously. Furthermore, even though there are other techniques to remove eye movement (e.g.



principal component analysis), these techniques are for the current data in my opinion not a feasible approach. The reason is that, commonly, an HOG artefact is reflected on both frontal hemisphere electrode sites, in that one hemisphere shows a positive deflection, while in the same time window the other hemisphere displays a negative deflection. (This is due to the fact that the eye constitutes itself a dipole with the cornea being in general more negative and the retina being more positive. Hence, if the eyes turn, one frontal head region should become more negative while the opposite side should become more positive.)

However, although there is a more negative deflection on the right frontal electrode sites for the picture condition, there is no 'polarity reversal' (i.e. more positive ERP amplitudes) at the left frontal electrode sites for the same condition. It follows, that the right frontal ERP difference is ambiguous in that it could constitute on the one hand a genuine ERP effect or on the other hand an HOG artefact. At the present stage, I believe the former is true in that the ERP reversal effect at left frontal sites is missing. Still, future research, employing more stringent constraints on eye movements, might elucidate the above findings further and might also clarify any further similarities and differences between ERP retrieval orientation and imagination effects.

## **Chapter 9 – General Discussion**

In the presented thesis I contrasted new unstudied items in recognition memory tasks to see whether these show differences according to manipulations of the encoded information, the retrieval cue or the retrieval task. The rationale of constraining analyses to unstudied new items allowed, according to Rugg and Wilding (2000), to separate processes related to retrieval attempts per se, namely retrieval mode, orientation and effort, from processes related to retrieval success. Although these new operationalizations offer a more controlled approach of retrieval process dissociations, it is still difficult to delineate processes belonging to different retrieval classes. Moreover, it remains undefinable whether those retrieval processes are actual orthogonal to each other, as outlined in chapter 3 of this thesis. Nevertheless, the data provide strong support for separate neural correlates to the different classes of retrieval processes. To highlight these dissociations of retrieval processes, and specifically the functional characteristics of the retrieval orientation effect, I will in the following chapter first summarize the outcomes of each experiment, followed by the theoretical implications for retrieval orientation as well as other measured retrieval processes and finally, I will outline possible future research in this field.

### **Experiment 1 – Summary**

Experiment 1 can be thought of as an extension and replication of the experimental design of the Robb and Rugg (2002) study which investigated whether ERPs of unstudied new items differ according to the encoded material while holding retrieval cues constant. Similar to Robb and Rugg (2002) I found that from around 300ms post-stimulus onwards ERPs of visual words encoded as pictures were more negative-going than visual words being encoded as words. Furthermore, I also reported a similar effect in the picture retrieval cue conditions, in that ERPs for pictures encoded as words show more negative ERP waveforms than pictures encoded as pictures. Thus, the results of experiment 1 are a clear indication of the ERP retrieval orientation effect being a more general or even amodal process, which is not constrained to words as retrieval cues per se. Still, the topographical difference between the word and picture retrieval cue conditions argues against such as proposal, because it shows that the picture and the word effect do have very likely different neural origins and thus are unlikely to be supported by the underlying process. On the other hand it should be not surprising that different retrieval cue modalities necessitate different ERP scalp distributions because the processing of different modality test stimuli should be specific to different cortical areas. Yet accepting this explanation would mean to abandon the idea of the retrieval orientation process as a more abstract or a modal process not being affected by the retrieval cue modality. This is of further particular interest of the later findings in experiment 3, which showed cortical activity not related to the retrieval cue itself, but instead to the study material encoded.

Another important finding in experiment 1 was that the behavioural data for the new item conditions differed according to the encoding as well as the retrieval material. It follows that different degrees of difficulty were apparent across experimental conditions, changing according to the factors of match and material of the encoding and retrieval cues. Hence, it can be suggested that different levels of retrieval effort had to be employed especially for the more difficult non-matching conditions, which could explain the observed ERP differences in terms of retrieval effort. I believe that this is not likely, because Robb and Rugg (2002) manipulated in their study the factor of task difficulty in parallel to the factor of study material, revealing no effect of the former factor, and because the first study is based on the experimental design of Robb and Rugg (2002) I believe that this also holds true for experiment 1.

### **Experiment 2 - Summary**

The main findings of experiment 2 were ERP waveform differences for new unstudied items even when neither of the encoded information had a structural overlap with the retrieval cues. Hence, the missing copy cue condition does not affect the occurrence of the ERP retrieval orientation effect, even though the neural signature in terms of the scalp distribution and the sustained activity of the effect appears to have changed in comparison to experiment 1. More specifically, the effect onsets as in experiment 1 at around 300ms post-stimulus but ends earlier (900ms post-stimulus) and shows a mid-central distribution. Nevertheless, I believe that into the same retrieval orientation process as in experiment 1 was tapped, because a change of modality in both encoding

conditions might diminish the actual ERP differences. In addition, there were no behavioural differences across conditions observed for the correct rejections, thus allowing us to conclude that the ERP retrieval orientation effect is also apparent between conditions which are matched for difficulty, again supporting the findings and the conclusions of experiment 1.

The follow-up study of experiment 2 was designed to remove an experimental confound employed in the previous two experiments (and as well in Robb & Rugg, 2002). The confound took the form of simultaneous change of encoding task and encoding material. Thus, in experiment 1 words and pictures employed different encoding tasks and the same was true for the encoding tasks for auditory words and pictures in experiment 2. The manipulation of encoding task was employed to increase the differences at encoding for each class of study material. Rugg and Wilding (2000), generally stated that manipulations of encoding material as well as encoding task should lead to different retrieval orientations (see also chapter 3), however a simultaneous change of both variables should not allow to delineate whether the ERP retrieval orientation was due to one of them. Nevertheless, the follow-up study found that a change of the semantic encoding task does not affect the general occurrence of the retrieval orientation effects.

### **Experiment 3 – Summary**

Leading on from the previous experiments, the design of experiment 2 allowed to show retrieval orientation effects without obvious behavioural condition differences. Thus, I

employed the same design in an efMRI experiment to see where the neural origins of retrieval orientation can be localized in the human brain. As there are no published fMRI experiments investigating retrieval orientation experiment under the conditions set out by Rugg and Wilding (2000), I decided for this experiment to analyse retrieval success effects as well, by contrasting activity associated to successful recognized and successful rejected test items (i.e. so called Old/New effects). Retrieval success processes have shown common patterns of brain activation across several studies (see chapter 3 and Rugg & Henson, 2002), therefore replicating Old/New activation patterns in the data would reassure the reliability of any other retrieval processing effects (e.g. retrieval orientation). Fortunately, the findings showed robust Old/New effects by showing elevated activations for Old in comparison to New items in lateral and medial parietal cortices, as well as in the left prefrontal cortex, which belong to the common pattern of retrieval success brain activation. This was reassuring in relation to the validity of any other retrieval process effects. In terms of retrieval orientation processing, there were two regions which were activated regardless of the study status of test items, namely auditory cortex and fusiform cortex regions. Contrasts of visual words being encoded auditorily showed auditory cortex activation for new as well as old visual word test items, while contrasts of visual words encoded as pictures revealed activity in the fusiform cortex regardless of study status. These findings propose that in any retrieval attempt, cortical regions specific to the sensory information given at encoding are reinstated at retrieval to support the likelihood of successful retrieval and successful rejection.

#### **Experiment 4 & 5 – Summary**

In experiment 4, the factors of retrieval task (direct vs. indirect) and encoding material (auditory words vs. pictures) were crossed to see whether Rugg and Wilding's (2000) definition of retrieval mode holds true in that a contrast of new item ERPs should reveal a difference between the direct and the indirect retrieval task conditions. As mentioned before, according to Rugg and Wilding (2000), retrieval orientation can be thought of as a subprocess of retrieval mode and thus should only occur in an episodic retrieval task. Translated to the experimental design, only the direct retrieval conditions should elicit neural correlates of retrieval orientation. This is exactly what was found in that in the direct retrieval conditions, correct rejections ERP waveforms differed according to the encoded material and hence, replicated the findings of experiment 2. In addition, the onset and scalp distribution of the direct conditions in experiment 4 reflected the descriptions of earlier retrieval orientation effects. In contrast, the indirect conditions did not elicit any similar effect, although there was an earlier ERP effect which I interpreted as a cross-modality attention effect (e.g. Talsma & Kok, 2001; Eimer & Schroger, 1998) because of its latency region and occipital distribution. More strikingly, I also observed a difference of retrieval task not affected by the factor study material and hence, being a likely candidate for retrieval mode processing. This would mean that in the direct retrieval task conditions there are two dissociable processes namely, retrieval orientation and retrieval mode, which would be the first time these processes have been shown in item-related ERP experiment.

Further, the results of experiment 5 showed that there is an ERP difference between visual words being imagined either auditorily or as pictures. However, this difference did interact with the new item contrast of the direct conditions in experiment 4, thus, showing different neural correlates than the ERP retrieval orientation effect. Nevertheless, I am aware that a more strict experimental setting for an imagination experiment, as well as the removal of the HOG artefacts common in this experiment, might provide more reliable results.

### **Theoretical implications**

The experiments presented in this thesis try to provide a more consistent picture of item-related retrieval processes and, to scrutinise, in particular retrieval orientation processes. The manipulations employed in the experimental designs support the notion that retrieval orientation is a common and robust process. The findings from the five experiments described here demonstrate that i) the ERP orientation effects reported by Robb and Rugg (2002) arise from differences in the similarity between retrieval cues and sought-for study items, and not merely in the form of the study material; ii) the effects do not reflect differential processing of copy cues relative to other cue types, nor do they depend on the employment of different semantic encoding tasks; iii) retrieval orientation is not contingent upon or reflects performance differences across conditions; iv) the fMRI neural origins of retrieval orientation show reinstatement of distinct cortical region activity specific to the encoded material; v) the ERP orientation effects are dependent on



direct (i.e. explicit) episodic retrieval tasks and they are dissociable from retrieval mode item-related activity; vi) the effects do not simply reflect imaginative processing.

What might be the functional significance of these findings? In keeping with Robb and Rugg (2002) and Herron and Rugg (2003), I have assumed that the neural correlates of retrieval orientation predominantly reflect the differential 'pre-retrieval' processing (Rugg & Wilding, 2000) of retrieval cues aimed at optimizing the likelihood of successful retrieval. As noted by Robb and Rugg (2002), however, while the onset of the ERP effects is short enough to reflect processing occurring prior to successful retrieval on at least some proportion of trials, their duration (here, around 800 ms) is long enough to encompass processes that might occur subsequent to a retrieval attempt. This means that the effects may reflect multiple retrieval processes, some of which might more properly be regarded as 'post-retrieval' (Rugg & Wilding, 2000). While this possibility cannot be ruled out at present it is worth noting that, as in two earlier studies (Robb & Rugg, 2002; Herron & Rugg, 2003), there was no evidence that the scalp distribution of the effects varied with time, and thus no evidence to suggest that different neural generator populations (and thus different cognitive operations) were engaged at different points in time. One possibility is that the extended time course of the effects indexes the period during which cue representations were maintained and employed to probe memory in the face of retrieval failure.

If one assumes that the ERP retrieval orientation effects reflect differential pre-retrieval processing, it still leaves open the question of the aspects of cue processing that are

modulated. One possibility, discussed also by Herron and Rugg (2003), is that the effects reflect differential reliance on recognition based on familiarity versus recollection. This proposal derives from 'dual process' theories of recognition memory (for review see Yonelinas, 2002b), and the notion that recognition judgments can be based either on a relatively automatic, acontextual sense of familiarity, or a more effortful and deliberate process of recollection. According to this argument, ERP retrieval orientation effects emerge when retrieval cues are more likely to engender high levels of familiarity in one condition than another. If, for example, copy cues are more likely to engender familiarity than are cues in a different modality or format, the effects observed in Robb and Rugg (2002), Herron and Rugg (2003), and the present experiment 1 could all be explained as reflections of the differential processing applied to retrieval cues depending on the likelihood of familiarity-driven recognition. For example, one might argue that more effort would be made towards a cue to prompt recollection when the likelihood of familiarity-driven recognition is low.

Herron and Rugg (2003) argued against this account on the grounds that behavioural evidence supporting the proposal that familiarity-driven recognition would be less probable in their picture-word than in their word-word conditions is not conclusive. The present findings provide further evidence against the account. In experiments 2 and 4 robust ERP retrieval orientation effects were observed even though study and test items changed format in both retrieval conditions. The evidence suggesting that familiarity is weakened by format change is as strong when the change is between auditory and visual words as when it is between pictures and visual words (see Yonelinas, 2002b). Thus,

there should have been the same amount of recollection in both retrieval conditions and, consequently, an absence of ERP retrieval orientation effects.

An alternative possibility is that ERP retrieval orientation effects directly reflect familiarity differences between matching and non-matching test cues. This proposal derives from 'global matching' models of recognition memory (for review, see Clark & Gronlund, 1996), in which it is assumed that the familiarity of a retrieval cue is the sum of its match with all the stored items presented in a specific study context. By this argument, matching cues (for example, words in the 'study words' condition of experiment 1 or pictures in the 'study pictures' condition of that experiment) will be more familiar than will non-matching cues in that they have greater overall similarity to the sought-for study items. This proposal seems problematic for at least three reasons. First, studies designed to characterize the ERP correlates of familiarity, as manifest in recognition memory experiments, suggest that these correlates take the form of a relatively transient (ca. 300-500 ms) positive-going modulation with a maximum over the mid-frontal scalp (what Curran has termed the 'FN400'; e.g. Curran, 2000; Curran & Cleary, 2003; Mecklinger, 2000; Rugg et al., 1998). The present effects, by contrast, are considerably more sustained in time and demonstrate invariant scalp distributions over time with broadly distributed across the scalp. Second, retrieval orientation effects have been reported with mixed study lists that comprised both words and pictures (Herron & Rugg, 2003). Since the two classes of study item were encoded in the same list context, the global match, and thus the familiarity, of the new test words in that experiment would

have remained constant regardless of whether words or pictures were the sought-for material.

Third, according to the above proposal retrieval orientation effects should be found for old as well as new items. This follows because the overall familiarity of matching cues should still be greater than the familiarity of non-matching cues because of their higher average similarity with the study set. Nevertheless, the comparison of old items seems problematic because any effects of retrieval orientation on old item ERPs are confounded with effects due to successful retrieval. Further, the two classes of effect cannot be assumed to be additive; to name only two of the variables potentially confounded with study material manipulations, success effects will vary: i) as a consequence of differential variability in the latency of recognition judgments; ii) as differences in the proportion of judgments accompanied by recollection (see also Herron & Rugg, 2003). However, the influence of such confounds will be at a minimum when recognition performance is similar across the two study conditions, as was the case in experiment 2. The old item ERPs of experiment 2 are illustrated in appendix 6, where it can be seen that the effects evident for new items (Figure 6.1) appear attenuated. Consistent with this impression, ANOVA failed to reveal significant effects of study condition in either the 300-600 or 600-900 ms latency ranges. This result does not appear to be compatible with the idea that the ERP retrieval orientation effects described here and elsewhere reflect differences in the global similarity of the test cues to the study set. I assume that the failure to find such effects in the old item ERPs of experiment 2 reflects the fact that successful retrieval often occurred rapidly after only minimal cue processing. Thus, the effects of such processing were apparent only when retrieval was unsuccessful, as in the case of new

items. Nevertheless, the findings of experiment 3, lead me to the conclusion that retrieval orientation processes were common to both classes of test items (i.e. old and new items).

Although the present findings argue against the idea that ERP retrieval orientation effects reflect differential familiarity, a related proposal might be worth pursuing. According to this idea, the effects reflect different dependence on semantic/conceptual information taken from from retrieval cues. The reason is that the potential for overlap between cue representations and memory representations at non-conceptual levels is greater in some conditions than others. For example, let's consider the different conditions in experiment 1. In both the word-word and picture-picture conditions, recapitulation of the cognitive operations engaged at study will result in cue-target overlap at all representational levels. In contrast, when the study items and retrieval cues are dissimilar, mere recapitulation will not be enough; whereas this will result in representational overlap at the semantic/conceptual level, there will be little or no overlap at nonconceptual levels (there would be zero overlap, for example, between the presemantic 'structural descriptions' encoding a picture and the 'orthographic descriptions' representing its name (Tulving & Schacter, 1990). To maximize cue-target overlap, it would therefore be beneficial to focus attention and processing resources on only those attributes of a retrieval cue that could potentially be shared with the targeted memory representations (cf. Nairne, 2002). In the present example, these attributes would primarily be conceptual/semantic. This account can be easily extended to the findings of experiment 2. As already noted, while the processing of auditory and visual words does not overlap at initial input stages, these items are likely to share pre-semantic representations at lexical and phonological levels

(Price, 2000). Thus, the potential for overlap between auditory and visual word representations at non-conceptual levels is greater than that which is possible between pictures and visual words. Therefore, there would have been less need to constrain cue representation to the semantic level in the word-word conditions of experiments 2, 3 and 4.

According to this proposal, the present ERP retrieval orientation effects reflect differences in the need to constrain cue processing. Specifically, it can be proposed that the more that a cue representation must be constrained to the semantic/conceptual level, the more negative-going will be the ERPs. This proposal receives support from the findings of Rugg, Allan and Birch (2000). In that experiment, study task was manipulated rather than study material. Subjects encoded words in a 'deep' (sentence generation) or 'shallow' (alphabetic judgment) study task, and subsequently made yes/no recognition decisions on a mixture of studied and new items. ERPs elicited by new items were more negative-going when the recognition lists contained deeply rather than shallowly studied old words, the effect demonstrating a time-course and scalp distribution similar to those described here. Rugg et al. (2000) suggested that the effect reflected differences in the extent that retrieval cues were subjected to semantic processing in the two test conditions. Specifically, they argued that in keeping with the transfer appropriate processing principle (see chapter 1), subjects were more likely to derive semantic representations of test items when the study task involved semantic rather than orthographic processing.

Furthermore, there is the question of the loci of the neural activity reflected by these ERP effects. This question cannot be answered from the findings of experiment 1 & 2: the diffuse scalp distributions of the effects offer little guide to their likely intracerebral origins.

As stated above, in the previous ERP experiments using a slightly different design (Experiment 1), I identified retrieval orientation effects when comparing conditions in which participants used test cues to retrieve either matching, or non-matching type of study material. Because this “match-nonmatch” effect did not appear to differ according to the type of material (visual words vs. visual pictures), I inferred that the ERP effect reflected the degree of constraint applied to the processing of the test cues (with greater constraint in the non-matching conditions). Therefore, when there was a similar ERP effect using exactly the same paradigm as here, I suggested that visual words are subjected to more constraints when employed as retrieval cues for studied pictures than for studied auditory words. More specifically, I suggested that when word cues are used to retrieve pictures it is necessary to focus on semantic/conceptual attributes of the cue to maximize the probability of overlap between the cue and targeted memory representations. When visual words are employed in an attempt to retrieve auditory words, by contrast, cue-target overlap will exist at multiple levels of representation (e.g. lexical and phonological as well as semantic), reducing the requirement to constrain the representation of the retrieval cue to its semantic features.

This hypothesis would not seem to be supported by the present fMRI data: I did not find that brain regions associated with semantic processing (anterior temporal cortex, e.g., Thompson-Schill et al (1999); Graham & Hodges (1997), or left inferior frontal cortex,

e.g, Wagner et al (2001)) were more active in the Picture than Auditory condition. Instead, the fMRI data are highly suggestive of an alternative basis of retrieval orientation in the present paradigm. This is the hypothesis that when participants were trying to retrieve pictures or auditory words from the visual test cues, they either imagined a visual depiction of objects named by each test word, or imagined the auditory/phonological correspondence of each test word, respectively. This would be consistent with both the greater left inferior temporal and left fusiform (BA 20, 35/37) activity in the Picture than Auditory conditions, given that such regions are known to be involved in visual object processing (e.g. Chao, Haxby, & Martin, 1999; Ishai et al., 1999) and in particular visual imagery (e.g. Ishai, Ungerleider, & Haxby, 2000). It would be also consistent with the greater left middle temporal gyrus / bilateral parietal opercula (BA 21, 40/41) activity in the Auditory than Picture conditions, given that such regions are known to be involved in auditory/phonological processing (e.g. Demonet et al., 1992), and in particular auditory imagery (e.g. Shergill et al., 2001). This alternative hypothesis would appear to be generally consistent with the transfer appropriate processing principle (Morris, Bransford & Franks, 1977). Further it can be also regarded as an extension of the “cortical re-instatement theory” (Wheeler & Buckner, 2003), in that engaging the same material-specific cortical regions during retrieval that were engaged at encoding increases the likelihood of successful recognition, or rejection, of retrieval cues in a memory test.

Unlike previous fMRI studies that involved comparisons related to retrieval orientation (Dobbins et al., 2003; Ranganath et al., 2000), I did not find effects in left anterior prefrontal cortex. This most likely reflects the different approaches to isolating retrieval orientation: Ranganath et al. and Dobbins et al. compared different retrieval tasks, and



found greater left prefrontal activity when the task placed greater emphasis on retrieving source information from the study phase, regardless of whether that attempt was successful or not (though see Rugg et al., 2003). Here I kept the retrieval task constant (yes/no recognition), and contrasted attempts to retrieve different types of study material. Furthermore, there was no behavioral evidence for a difference in accuracy or reaction times between the Picture and Auditory conditions of the present study, unlike the Ranganath et al. and Dobbins et al. studies, in which the "source tasks" showed evidence of being more difficult (i.e, lower accuracy and/or longer reaction times). Instead, the regions in left anterior prefrontal cortex showed greater activity for Hits than Correct Rejections, regardless of study material (see below). This effect of "retrieval success", rather than of "retrieval orientation", is consistent with a recent study using a recognition memory paradigm (Rugg et al., 2003). Interestingly, a right anterior prefrontal region also showed an effect of retrieval success, but only for words studied as pictures.

So, the data of experiment 3 suggest either that my previous interpretation of ERP retrieval orientation effects is incorrect (including the possibility that different orientation effects arise in different contexts, e.g. across Experiments 1 and 2), or that the neural generator(s) of the ERP retrieval orientation effect are not the same as the regions showing haemodynamic retrieval orientation effects.

Several other regions also showed an effect of retrieval success (i.e, greater activity for Hits relative to Correct Rejections) that did not vary significantly as a function of the study material. These findings, particularly regarding the lateral parietal cortices, posterior cingulate and dorsolateral prefrontal cortex, are highly consistent with previous studies (e.g. Rugg, Otten, & Henson, 2002, Rugg & Henson, 2002). The superior parietal

and dorsolateral prefrontal activations may have more to do with target effects, rather than memory effects per se (Henson et al., 2000; Herron, Henson, & Rugg, 2004). In contrast, the posterior cingulate and more inferior lateral parietal regions may reflect true memory effects, possibly recollection of study context (Henson et al., 1999b; Henson, Hornberger, & Rugg, 2005; Yonelinas et al., 2005). In the latter case, the failure to find any evidence that the activity of inferior/medial parietal regions is modulated by study material, suggests that the recollected information does not relate solely to the study material (i.e, whether seen as a picture or heard as a word), consistent with the data of Woodruff et al. (2005). It thus remains an interesting question as to what aspects of the study episode, if not study material, activate these regions during recollection.

There was also decreased activity for Hits than Correct Rejections in a right anterior medial temporal region, again seemingly regardless of study material. Signal reductions associated with recognition in extra-hippocampal anterior medial temporal cortex have been found in several previous studies (Brozinsky et al., 2005; Henson et al., 2005; Henson et al., 2003; Rombouts et al., 2001; Weis et al., 2004). The reductions are often in the vicinity of perirhinal cortex, though the present effect appears too lateral to be located in this structure. It has been suggested that these effects are neural correlates of familiarity (Henson et al., 2003), and if so, the present lack of a study material effect would be consistent with a conceptually- rather than perceptually-based perirhinal familiarity signal (O'Kane, Insler, & Wagner, 2005).

Further, it seems also important to consider the neural correlates of retrieval content in this context (see appendices 3 & 4 for results). Previous studies have shown that some brain regions exhibit "retrieval content" effects, i.e. greater activation when retrieving a

particular type of study material or studied associate (Nyberg et al., 2000; Vaidya et al., 2002; Wheeler & Buckner, 2003, 2004; Wheeler, Petersen, & Buckner, 2000; Woodruff et al., 2005). These are typically brain regions believed to be specialized for perceptual processing of the specific class of study material. For example, Wheeler and colleagues (2003; 2000) had subjects study visual words together either with a sound or with a picture. At test, subjects decided whether visual words had been paired with a sound or picture. Greater activity in extrastriate cortex [-45 -69 -6] and auditory cortex [-57 -39 14] was found for correctly retrieved words that had been paired either with pictures or with sounds respectively. A subsequent study (Wheeler & Buckner, 2004) found greater activity in left anterior fusiform ([-25 -37 -26], coordinates from Woodruff et al., 2005) for words paired with pictures when those words were given a "Remember" response than when they were given a "Know" response. This would be expected if effects of retrieval content only arise when study modality is explicitly recollected (e.g. "reinstated", according to the cortical reinstatement theory). This result was replicated by Woodruff et al. (2005), with coordinates [-24 -42 -20] and [-32 -34 -20].

These coordinates are very close to those showing greater activity for Correct Rejections in the Picture than the Auditory conditions in Experiment 3 ([-24 -36 -21] and [-42 -33 -18]). Like the previous studies, these regions also showed greater activity for Hits in the Picture than Auditory conditions. However, there was no evidence for the interaction between Hits/Correct Rejections and study material that would be expected if the activity also reflected retrieval content (i.e. a greater old-new effect in these regions in the Picture than Auditory condition). Likewise, the coordinates of left temporo-parietal regions that

showed greater activity for Correct Rejections in the Auditory than Picture conditions showed the same pattern for Hits, but no evidence of an interaction with study material.

One reason for the lack of interactions with retrieval content in the present study might be a low level of recollection of the study material (i.e. if old items were recognized mainly on the basis of conceptually-based familiarity; see Woodruff et al., 2005). However there is also an important procedural difference between Experiment 3 and the previous studies of “retrieval content effects”. In experiment 3, test items were deliberately blocked according to study material, in that participants could adopt a clear retrieval orientation. In the previous studies, the different types of old items were intermixed at test (as is necessary, if one wants to examine differences in retrieved content, regardless of participants’ expectancies about that content). This means that the differential activations in material-specific regions in previous studies were probably not influenced by effects of retrieval orientation. In experiment 3 however, the effects of retrieval orientation in these regions may have combined or interacted with effects of the retrieval content. For example, increased activation owing to retrieval of the relevant content for Hits may have been counter-acted by decreased activation owing to a truncation of processing related to retrieval orientation (as alluded to above). This would prevent an interaction between Hits/Correct Rejections and study material – i.e. a greater effect of study material for Hits than for Correct Rejections - that might be expected from a version of the cortical reinstatement theory that considered only the effects of retrieval content (and not of retrieval orientation). One way to test this possibility might be to intermix old items studied as different materials within a recognition memory test in which participants were strongly oriented towards trying to retrieve one particular type of study material. Old

items studied as the non-target material might then show effects of retrieval content – i.e., activation in material-specific brain regions - without activation of those regions by retrieval orientation. More generally, whether the regions showing retrieval orientation and retrieval content effects are the same, or anatomically distinct, is not possible to conclude from experiment 3.

Further, the contrast of direct versus indirect retrieval tasks in experiment 4 showed a striking pattern in that ERP retrieval orientation effects were only apparent in the direct and not the indirect retrieval task. These results give a first idea of retrieval orientation as a process which is engaged only in declarative memory. Arguably, the indirect test used in experiment 4 might not allow the best possible incidental retrieval, in that only the task instructions were hindering the subjects from direct retrieval. Nevertheless, from the subjects' debriefing and the task order contrasts, I think one can be confident that it was unlikely that direct retrieval was taking place in the indirect conditions. Still, future research employing, for example, word fragment tests might be more stringent in their measure of incidental/indirect retrieval. In terms of the absence of a ERP retrieval orientation effect in the indirect conditions (though presence of an earlier ERP effect) I would also make the suggestion that the ERP orientation effect in the direct task reflect an explicit and therefore active process. The reason is that participants were only able to direct themselves explicitly towards the retrieval cues and the previously encoded information in the direct retrieval task. Hence, the assumption of retrieval orientation as an automatic/passive process seems not to support in my eyes in that there was no comparable ERP effect in the indirect conditions. Still, the proposal of an active process

needs to be further scrutinized by more stringent experimental designs. On a related note, future research might also investigate the relationship between retrieval orientation and retrieval mode processes. In experiment 4, retrieval mode processes, being invariant to the encoding material, occurred only in the episodic (i.e, direct) task, thus being in compliance with Rugg and Wilding (2000) retrieval process definitions. In contrast, retrieval orientation, which is thought of as a subprocess of retrieval mode appeared in its known scalp distribution only in the direct conditions and as a function of the encoding material. Nevertheless, at the present stage it is not possible to determine the exact relationship between these two processes, in that they could for example be inherently linked or exclusive to each other.

Finally, the findings of experiment 5 showed that the ERP retrieval orientation effect is not a pure imagination effect, that is, it is not the case that participants imagine either hearing or seeing the corresponding encoded items. The results of experiment 5 stand therefore in stark contrast to the results of experiment 3 which, as mentioned above, indicate a link between retrieval content and orientation effects. At the present stage it is difficult to make any interpretation on the imagination ERP experiment, in that it is not established what the underlying processes of the recorded ERP effects are. Still, it is reassuring for the cue constraining hypothesis that it does not suffice for participants to merely imagine the encoding material to elicit an ERP retrieval orientation effect. Still, the nature of the ERP retrieval orientation effect itself, as to whether it is a 'pure' cue constraining process, remains elusive.

### **Future directions**

The foregoing account leaves open numerous issues, only three of which are highlighted here. First, it is unclear whether the cue constraining proposal applies specifically to cue processing at the semantic/conceptual level, or whether it generalizes to any pair of test conditions where cue processing is differentially constrained. For example, might one see similar ERP differences in a comparison between the present word-word conditions and a condition in which it was beneficial to confine cue processing to the phonological level? It is also unclear to what extent the ERP effects reflect the initial derivation of cue representations, as opposed to their subsequent maintenance and deployment. Given the extended time-course of the effects (see above), it would perhaps be surprising if these latter processes were not implicated to some degree. Further, how much structural or semantic overlap is necessary between the encoded information and the retrieval cues as to see the ERP neural signature of the retrieval orientation effect. And finally, the findings of the fMRI study should be addressed to see whether retrieval orientation and retrieval content effects are anatomically separable and independent from each other. Future studies addressing these issues might help to elucidate further retrieval cue processing in general and retrieval orientation processes in particular. Nevertheless, I think that the data presented in the thesis make a strong case for reliable ERP retrieval orientation effects and how these effects can be modulated by experimental manipulations. It shows furthermore that new and more thorough lines of research into retrieval cue processing are necessary and that this topic has been overshadowed by research into retrieval success for far too long.

## **Appendix:**

**Appendix 1.** Exp. 1 – Summary of ANOVA results in each ERP latency region including the factors of old/new, match and cue type.

Main effects & interactions	100-300 ms	300-600 ms	600-900 ms	900-1200 ms
18 main electrode sites				
ON	–	$F_{1,19} = 79.8, p < .00$	$F_{1,19} = 81.38, p < .00$	$F_{1,19} = 44.71, p < .00$
MT x ON	$F_{1,19} = 17.11, p = .001$	$F_{1,19} = 17.96, p < .00$	$F_{1,19} = 9.96, p < .01$	$F_{1,19} = 14.15, p = .001$
ON x HM	$F_{1,19} = 7.29, p < .025$	–	–	–
ON x ST	–	$F_{1,1,21.7} = 47.09, p < .00$	$F_{1,3,24.7} = 125.46, p < .00$	$F_{1,3,24.2} = 12.77, p = .001$
WP x SD x ON	–	$F_{1,19} = 6.30, p < .025$	–	–
MT x ON x AP	$F_{1,2,23.0} = 5.19, p < .05$	–	–	–
MT x ON x ST	–	–	$F_{1,1,20.8} = 6.59, p < .025$	$F_{1,2,22.7} = 25.52, p < .00$
ON x HM x ST	–	–	$F_{1,4,26.7} = 4.20, p < .05$	$F_{1,2,21.9} = 5.64, p < .025$
ON x AP x ST	–	$F_{1,5,29.4} = 8.28, p < .01$	$F_{1,6,31.1} = 9.45, p = .001$	$F_{2,0,38.7} = 4.16, p < .025$
WP x MT x ON x HM	–	–	$F_{1,19} = 6.83, p < .025$	–
WP x ON x HM x ST	$F_{1,7,31.7} = 7.69, p < .01$	–	–	–
MT x ON x AP x ST	$F_{2,5,47.2} = 5.24, p < .01$	$F_{2,2,41.7} = 4.62, p < .025$	–	–

ON = Old/New; MT = match type; WP = cue type; HM = hemisphere; AP = location; ST = site.



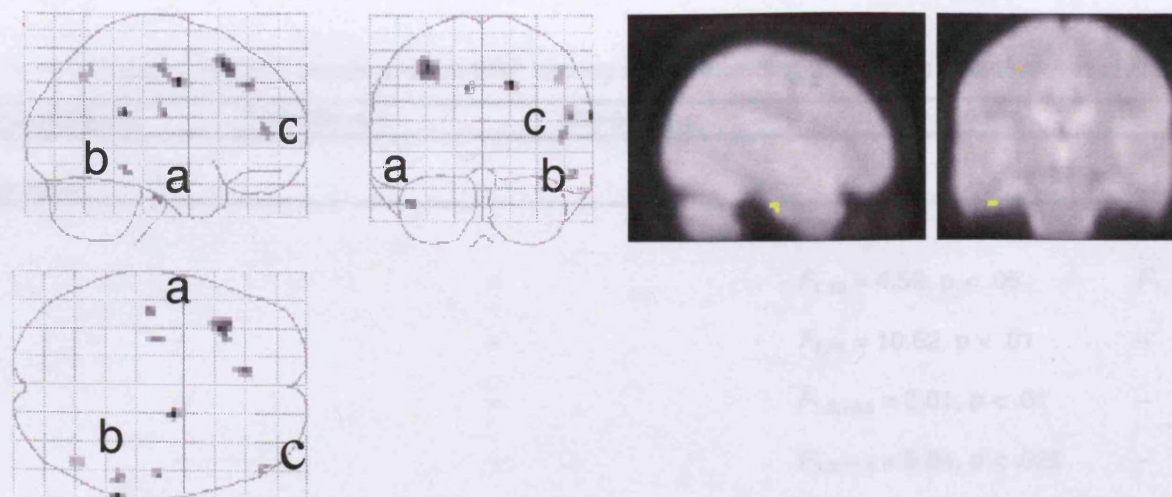
**Appendix 2. Exp. 2 – Summary of ANOVA results in each ERP latency region including the factors of old/new and study material.**

Main effects & interactions		100-300 ms	300-600 ms	600-900 ms	900-1200 ms
18 main electrode sites					
ON	–		$F_{1,15} = 3.91, p < .025$	$F_{1,15} = 20.76, p < .00$	$F_{1,15} = 13.341, p < .01$
ON x ST	–		$F_{1.2,18.0} = 10.62, p < .01$	$F_{1.1,16.0} = 20.26, p < .00$	$F_{1.2,17.6} = 10.47, p < .01$
ON x AP x ST	–		$F_{1.8,26.4} = 3.55, p < .05$	–	$F_{2.0,30.1} = 7.64, p < .01$

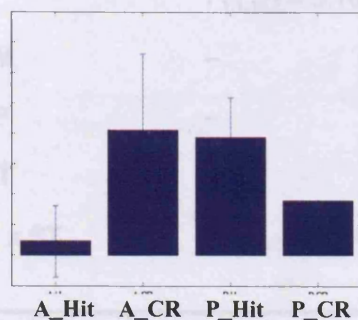
ON = Old/New; PA = study material; HM = hemisphere; AP = location; ST = site.

**Appendix 3.** Exp.3 - Regions showing elevated activations for study status as a function of study material.

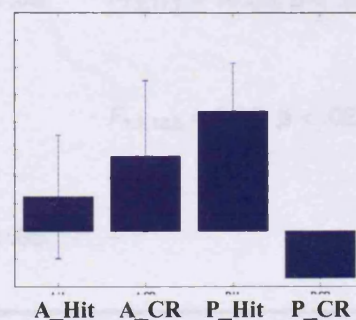
Contrast	Region	Side	Size	BA	MNI - coordinates			Z-value
		(L/R)	(cm <sup>3</sup> )		x	y	z	
<b>P &gt; A (Hits – CR)</b>	Middle frontal gyrus	R	.24	10	48	48	9	3.44
	Superior frontal gyrus	L	.32	8	-9	36	39	3.70
	Middle frontal gyrus	L	1.107	6/8	-33	21	51	4.01
	Superior frontal gyrus	R	.3	6/4	18	-6	42	4.27
	Parietal operculum	R	.19	40/41	54	-15	21	3.59
	Precentral gyrus	L	.24	4	-27	-18	51	3.56
	Fusiform gyrus	L	.16	36/20	-45	-21	-30	3.61
	Superior temporal gyrus	R	.14	40/22	66	-39	21	4.08
	Inferior temporal gyrus	R	.22	20	57	-39	-12	3.52
	Angular gyrus	R	.3	7/1	45	-66	45	3.26
<b>A &gt; P (Hits – CR)</b>	Lingual gyrus	L	.22	18	-12	-75	-12	3.42
	Striatum	R	.24	17	12	-84	9	3.63
	Striatum	L	1.13	17	-15	-84	9	5.88



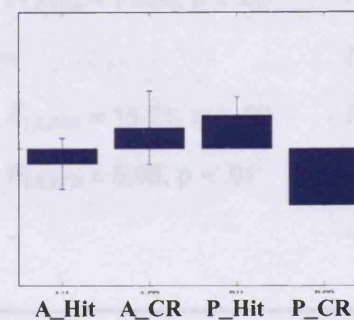
**a** [-45 -21 -30] ~ BA20



**b** [57 -39 -12] ~ BA36/20



**c** [48 48 9] ~ BA10

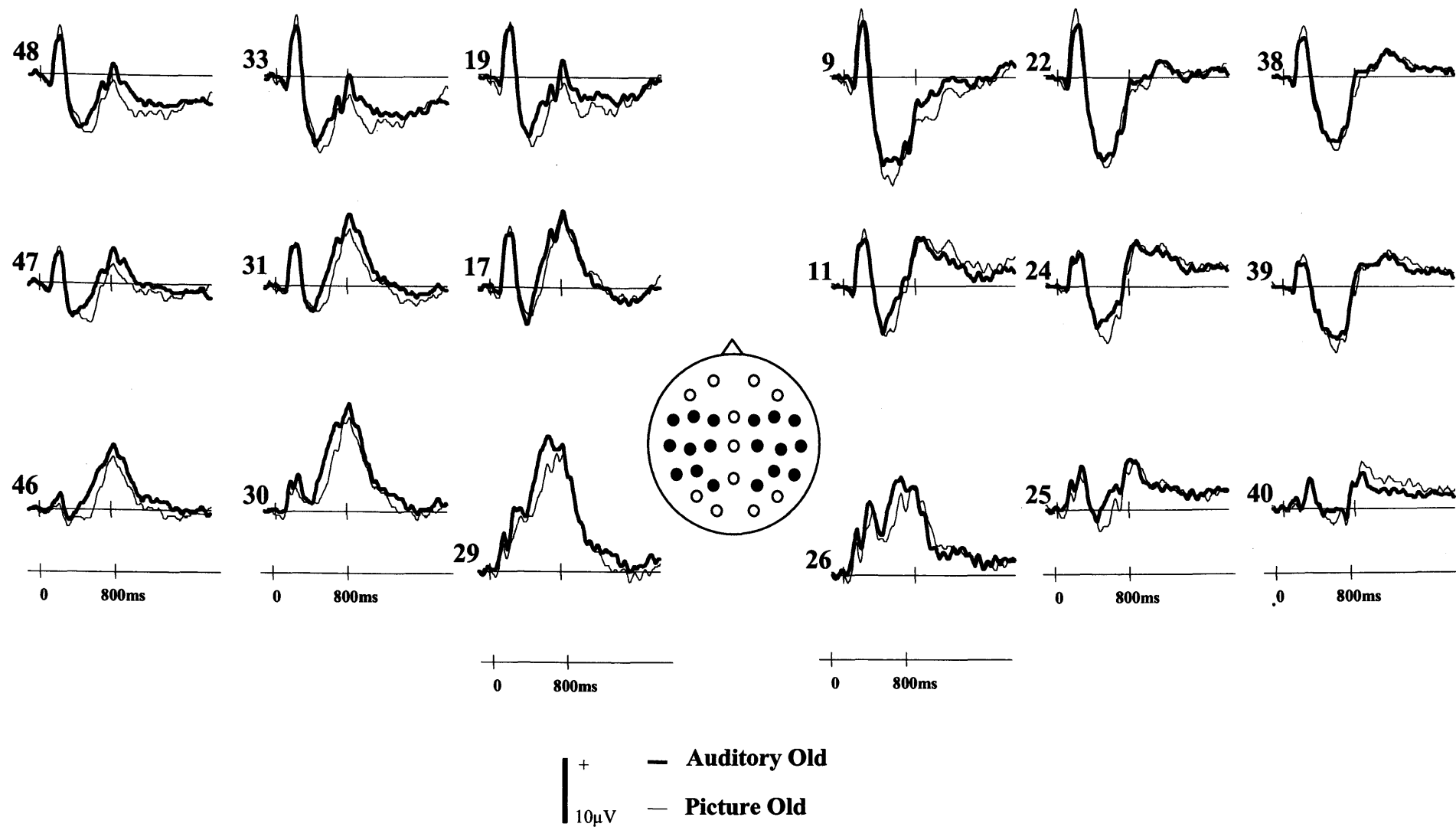


**Appendix 4.** Exp.3 – Views of greater old-new effects (H-CR) for the Picture than Auditory conditions (interaction) and plots for (a) left inferior temporal, (b) right middle temporal, and (c) right frontopolar regions.

**Appendix 5. Exp. 4 – Summary of ANOVA results in each ERP latency region including the factors of old/new, study material and retrieval task .**

<b>Main effects &amp; Interactions</b>	<b>100-300 ms</b>	<b>300-600 ms</b>	<b>600-900 ms</b>	<b>900-1200 ms</b>
<b>18 main electrode sites</b>				
<b>ON</b>	–	–	$F_{1,15} = 4.59, p < .05$	$F_{1,15} = 5.21, p < .05$
<b>ON x HM</b>	–	–	$F_{1,15} = 10.62, p < .01$	–
<b>ON x AP</b>	–	–	$F_{1,3,19.5} = 8.01, p < .01$	–
<b>ON x ST</b>	–	–	$F_{1,2,17.4} = 5.84, p < .025$	–
<b>EI x ON x AP</b>	$F_{1,1,16.5} = 13.37, p < .01$	$F_{1,1,16.4} = 7.20, p < .025$	$F_{1,2,17.5} = 6.78, p < .025$	–
<b>EI x ON x ST</b>	$F_{1,1,16.2} = 5.16, p < .05$	$F_{1,2,17.7} = 10.06, p < .01$	$F_{1,2,17.9} = 11.26, p < .01$	$F_{1,3,20.0} = 7.29, p < .01$
<b>SD x ON x HM</b>	–	–	–	$F_{1,15} = 4.60, p < .05$
<b>SD x ON x AP</b>	–	$F_{1,2,18.5} = 6.00, p < .025$	$F_{1,5,22.1} = 15.21, p < .00$	$F_{1,5,22.8} = 11.21, p = .001$
<b>ON x HM x ST</b>	–	–	$F_{1,8,27.2} = 6.96, p < .01$	–
<b>EI x ON x AP x ST</b>	$F_{2,2,33.3} = 3.84, p < .05$	–	–	–

EI = retrieval task; ON = Old/New; PA = study material; HM = hemisphere; AP = location; ST = site.



**Appendix 6.** Exp. 2 – Grand average ERP waveforms elicited by correctly recognised old items at lateral frontal (48, 33, 19, 38, 22, 9), lateral temporal (47, 31, 17, 29, 24, 11) and lateral parietal sites (46, 30, 29, 40, 25, 26).

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