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Psychophysiological investigation of false memory in amnesiac patients

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PSYCHOPHYSIOLOGICAL INVESTIGATION OF FALSE MEMORY IN AMNESIC PATIENTS

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Abstract

This thesis investigates psychophysiological characteristics of false memories in two groups of people: healthy participants and amnesic brain injured patients with Korsakoff syndrome (KS). KS patients present impairment of diencephalic structures in the brain, mainly at mammillary bodies, thalamic nuclei, fornix and mammillothalamic tract as consequence of thiamine deficit. This deficit is associated with dense anterograde amnesia with general preservation of other cognitive abilities. The main objective was to study how patients processed false memory compared to healthy age-matched controls.

To do it so, we produced several experiments. A first one was designed to validate a new false memory task that offers a language-free alternative to the classic Deese-Roediger-McDermot paradigm (DRM) along with some other improvements introduced to bias false memory production. We tested this visual false memory task (VFMT) in a sample of 20 healthy participants to study its validity as true and false memory generator under event-related potential (ERP) conditions. Results indicated that classic ERP old/new effect was present despite in showed a consistent central localization in the scalp compared to what previous ERP experiments found. Moreover, we found that true and false memory ERP signal appeared to be equivalent in localization but different in voltage.

We aimed to study true and false memory in amnesic patients and compare their performance with age-matched healthy controls. But before doing it we run an experiment to adapt VFMT to amnesic characteristics of KS sample. We decreased the amount of information to be studied engaging a shorter-delay testing time that may

overcome episodic and attentional difficulties in patients. Second version of the task, i.e. VFMT2.0 was behaviourally applied to a sample of 10 KS patients to confirm that this new version successfully produced enough amounts of true and false memories. Neuropsychological assessment was also applied to KS patients to quantify and characterize their cognitive impairment and brain damage.

Finally, ERP experiment was performed in KS patients and age-matched controls. Respect to results from first version of VFMT, ERP differences appeared in healthy participants. What behaviourally was reflected as an easier memory task, it also was associated with ERP differences in localization of ERP activity in the scalp, implicating more frontal-located electrodes for true memory processing compared to the central distribution of ERP found at VFMT1.0. Moreover, under VFMT2.0 task, healthy participants showed ERP differences when true and false memories were compared: right-frontal electrodes for true and left-frontal for false memory processing on 500 to 1000ms time window. Regarding amnesic patients, brain activity associated to true and false memory was equivalent and left-frontal sited all over the epoch. Main results indicated that true memory processing showed different ERP characteristics when patients were compared with controls despite their behavioural false memory rates were equivalent. When false memory was analysed, differences between groups were also found, mainly at early 300-500ms and later 1000 to 1500ms time windows.

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Chapter 1: General Introduction

1.1 Overview

In this chapter, we introduce the theoretical frame in which our research is based. We will discuss in more detail the concept of false memory and the theories that attempt to explain how they are caused and processed. A detailed description of one of the most important false memory tasks will be presented, with comments on its limitations considered as important points to be overcome in our research. A following section reviews the anatomical aspects related with false memory and a description of the neurological syndrome targeted for this investigation. Finally, we describe the main objectives for this thesis.

1.2 False Memory

A false memory is generally defined as an apparent recollection of an event that did not actually occur. It became a subject of interest in research in 1990, due to its important forensic and legal implications. Childhood sexual abuse declarations started to be questioned as partially induced by psychotherapy techniques in a portion of subjects (Lindsay & Read, 1995) or just falsely recovered from memory during the course of therapy (Loftus & Pickrell, 1995). Validity of eyewitness testimony in court became a vital question and scientific evidence was urgently required after debate on how reliable a retrieved memory could prove in the possible conviction of a criminal. Four reasons why recovered memories could be questioned were highlighted (Davies, 2001): a memory may not offer a sufficiently clear picture of an event; memory is a constructive process that may affect reliability; a therapeutic process may be affected by the suggestibility of the content of a memory; repetition may modify an individual memory content. It has been sufficiently demonstrated through decades of behavioural investigation that a memory may be biased, modified and also implemented in an individual (Loftus & Pickrell, 1995; Loftus, Feldman, & Dashiell, 1995; Loftus, 1996; Loftus, 2005) and assessing this phenomenon in a controlled scenario became a target.

Few attempts preceded the appearance of the first controlled laboratory task to study false memory created by Roediger and McDermott based on Deese and Underwood studies. We will describe in detail this task in the following sections of this introduction. But first, we aim to frame false memory definition in a broader context together with other "untrue" manifestations.

1.2.1 Definition and Differences with Confabulations and Delusions

A recent definition offered by Roediger and Marsh states that false memory refers to "*cases in which people remember events differently from the way they happened or, in the most dramatic case, remember events that never happened at all. False memories can be very vivid and held with high confidence, and it can be difficult to convince someone that the memory in question is wrong*" (Roediger H.L.III, 2009). This phenomenon may occur to everybody and is not necessarily linked to brain injury.

On the contrary, when an individual presents causes that drive their cognitive capacities to error or dysfunction, two main concepts should be considered: confabulations and delusions.

In brain injury, confabulation accounts for the emergence of memories of experiences which never happened (Nahum, Bouzerda-Wahlen, Guggisberg, Ptak, & Schnider, 2012). A first definition was offered by Berlyne, who described confabulation as an organic-caused falsification of memory whereby the individual had a clear conscience of what was retrieved (Berlyne, 1972). Kopelman described two main types of confabulations following Berlyne´s description: *"Spontaneous confabulation is a pathological phenomenon, which is relatively rare, and may result from the superimposition of frontal lobe pathology on an organic amnesia. On the other hand, "provoked" confabulation is common in amnesic patients when given memory tests, resembles the errors produced by healthy subjects at prolonged retention intervals, and may represent a normal response to a faulty memory"* (Kopelman, 1987). The author based his conclusions on a study with Korsakoff syndrome, Alzheimer demented patients and age matched healthy controls whereby participants were asked to remember one of Wechsler Logical Memory stories twice, once immediately after learning and as delayed recall, after 45 minutes of a non-verbal filling-the-gap task for patients and one week after for controls. Provoked confabulation was present in both groups, with a slightly different time pattern: Alzheimer patients confabulated mainly at immediate recall, Korsakoff syndrome patients at 45 minutes delayed recall and controls at one week delay.

Recently, Schnider suggested distinguishing between four types of confabulation: i) intrusions on memory tasks (i.e. Kopelman´s equivalent to provoked confabulations); ii) momentary confabulations, based on Bonhoeffer description (Bonhoeffer, 1901) and responsible for hiding a memory gap in response to questions (i.e. similarly to Kopelman´s provoked type); iii) behaviourally spontaneous confabulation caused by a confusion of reality; iv) fantastic confabulations defined as the production of implausible experiences (Schnider, 2008). Based on this categorization, a recent study by Nahum and colleagues aimed at disentangling mechanisms inducing these four distinct types of confabulation, analysing explicit memory and executive function test together with reality filtering tasks in 29 amnesic patients (Nahum et al., 2012). They found associations between momentary confabulations and some neuropsychological tests measuring task switch ability, i.e. trial making test part B minus trial making test part subtraction (Sanchez-Cubillo et al., 2009) and between executive failures such as impaired mental flexibility and momentary confabulations. They also offered information about how a proportion of momentary confabulations may account for filling memory gaps. Nahum and colleagues compelled their hypothesis on how those four types of confabulations were produced based on failure of different cognitive processes, depicted in **Figure 1**. Unsuccessful retrieval effort, dysexecutive function, monitoring problems on retrieval and definitely defective reality filtering would make up for the basis of confabulation.

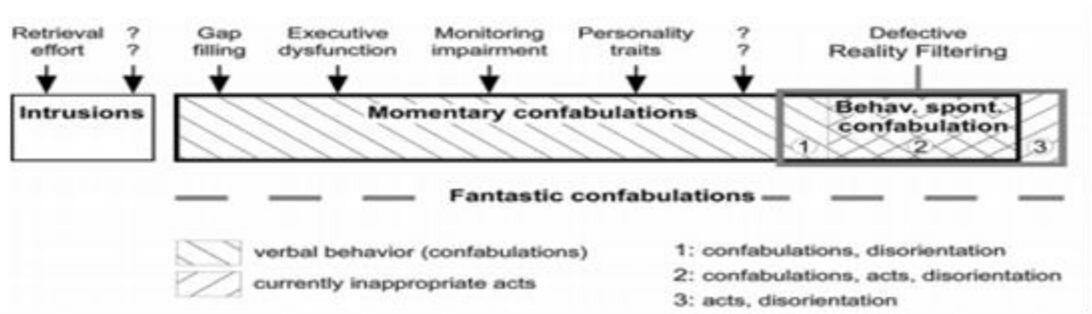

Figure 1: Model of confabulation mechanisms. Grey rectangle on the right describes the scope of disorders caused by deficient reality filtering. Causes for fantastic confabulations required multiple combinations of failures. Reproduced from Nahum et al. 2012.

Delusions may be considered similar to confabulations in some aspects. Although they may not share the same type of contents, they both share some other characteristics: both are defined as false claim production, they are resistant to counter evidence due to strong conviction, and both may show a lack of consideration regarding the consequences of the retrieved material (Turner & Coltheart, 2010). These authors studied commonalities between confabulation and delusions and proposed that both were based on the same failure, either conscious or unconscious processes causing monitoring and/or evaluation deficit. Retrieved information that needed to be checked for veracity by our executive system will not present this failure; hence, retrieval results in an unmonitored uncritical acceptance with the form of delusive or confabulated. Two factors account for both delusions and confabulation production: a conscious one involved in determining the correct content and a second unconscious one linked to the rejection of unsubstantiated thoughts. This is an interesting explicative model but it needs to be experimentally challenged.

A third concept to be considered is deception. The differential characteristic from a false memory is that deception implies a subjective feeling of the individual responding under untruthful conditions. In this case, the act of deceiving is conscious and voluntary whereas false memory is not. Despite the challenging nature of this study, there were several attempts to reveal specific features corresponding to deception. ERP experiments suggested that a positive component peaking at approximately 300ms after stimulus onset (i.e. P300) might be the electroencephalographic measure of deception (Johnson Jr, Barnhardt, & Zhu, 2003; Peter Rosenfeld et al., 1998; Rosenfeld et al., 1999; Rosenfeld et al., 2008). According to Johnson and colleagues, deception implicates a clear willing to select incompatible responses in a testing situation, hence extra-monitoring requirements took place to evaluate additional control processes defined as long-term “strategic” monitoring processes and were required to ensure response consistency and longer-term goal achievement (Johnson Jr et al., 2003). Deception would also imply important executive processes to inhibit the tendency to produce true responses and to develop additional deceptive-processing, according to these authors. Considering all the above, deception may rely on monitoring processes instead of memory processes, whereas false memories depend on both.

Functional magnetic resonance imaging techniques have been applied in a false memory task (i.e. Deese-Roediger-McDermott (DRM) paradigm, depicted in the following sections of this introduction) to elegantly compare false memory and deception as both concealing the truth (Abe et al., 2008). They analysed fMRI characteristics of deception using what they defined as a “pretending to know” process and compared it with a false memory response on the DRM paradigm. They concluded that neural correlates of deception were related with the activity of prefrontal regions of the brain, consistent with the hypothesis of executive functioning involvement on deceptive responses. Left middle-frontal gyrus activity was related with intentional cognitive processing of response manipulation and was suggested to be a reliable indicator of pretending to know responses. Left prefrontal cortex associated with “pretending to know” responses was active during both true and false memory responses, whereas the right hippocampus was only active during false memory and deceptive responses and not for true memories (Abe et al., 2008).

For this thesis, we aimed to work with healthy individuals and later with amnesic patients neurologically diagnosed with Korsakoff syndrome, as we were interested in general false memory production and particularly in how amnesic patients may produce them framed on their episodic memory impairment. We will consider confabulations and false memories equivalent in our patient sample as our experimental manipulation to produce false memories in an episodic memory task will provoke confabulation in our patients, as defined by Kopelman (Kopelman, 1995).

1.2.2 Theoretical Accounts

Historically, studies about memory were based on quantity-approaches, focusing on the amount of recalled information as the important point to be studied. On the other hand, qualitative approaches were more interested in the characteristics of what was remembered. Koriat & Goldsmith offered that distinction based on their metaphors: a "storehouse" vision of memory was related with quantitative-approaches and the alternative "correspondence" vision would be linked to how well a memory outcome referred to reality (Koriat & Goldsmith, 1994). Regarding false memory studies, both approaches had been accomplished by the main theoretical accounts that were offered to explain how false recollection processes worked. With the aim to compile all proposed theories, we will divide them here in two main accounts: the first one related with the concept of activation and how this influences encoding and testing and the second one related to the components of a retrieval process. They are not necessarily exclusive. We will describe them in more detail below.

1.2.2.1Activation Account

The general core of this account refers to the hypothesis that when something is processed in memory, collateral activation of close information with some kind of relation with the activated node takes place and may influence encoding and/or retrieval from memory. Several theoretical attempts to explain how memory processes are implicated in false production can be framed under this assumption. We will review here some of the most utilized and referenced in general false memory experiments.

James proposed that memory was based on associative processes and those were based on brain structure and functioning: *"The machinery of recall is thus the same as* *the machinery of association, and the machinery of association, as we know, is nothing but the elementary law of habit in the nerve-centres… Retention of an experience is, in short, but another name for the possibility of thinking it again, or the tendency to think it again, with its past surroundings. Whatever accidental cue may turn this tendency into actuality, the permanent ground of the tendency itself lies in the organized neural paths by which the cue calls up the experience on the proper occasion, together with its past associates, the sense that the self was there, the belief that it really happened, etc., etc. … These habit-worn paths of association are a clear rendering of what authors mean by ′predispositions′, ′vestiges′, 'traces', etc., left in the brain by past experience. Most writers leave the nature of theses vestiges vague; few think of explicitly assimilating them to channels of association".* ((James, 1890/1950) pp. 654-655). This statement by James will be present in the grounding of some of the following theories of memory retrieval.

Source monitoring account was initially suggested by Johnson and colleagues (Johnson & Raye, 2000; Johnson, Hashtroudi, & Lindsay, 1993). They stated that two elements compose memory: the content of that memory and the source where it was learnt. An individual may forget the source independently from the content of a memory as retrieval is not a strict memory process but a decision process. This theory explains that memories do not simply "come back" labelled from the store ready to be used. Rather, memory source depends upon an inferring process whereby quantity and quality of the information matters. Memories from different sources (basically perceptual and imagined sources) contain a specific type of information about those sources. However, some memory characteristics may overlap and judgement processes when attributing a memory to a source may be too lax, being the two main reasons why reality-monitoring failure may occur. This event is defined as confusion between memories for imagined and perceived events (Johnson & Raye, 2000; Johnson & Raye, 1998) and has been offered by the authors as a possible explanation for the false episodic content of false memories in the context of eye-witness recollection (Loftus, 2005) and also in the context of strong associates words inscribed on a learning list (Gallo & Roediger, 2003).

Imagination and source misattribution were suggested as the two main reasons for false episodic production (Johnson et al., 1993; Lyle & Johnson, 2006) and may underpin episodes during which individuals mistake mental pictures with real ones, as has been suggested in some childhood abuse testimonies (Lindsay & Read, 1995; Loftus & Pickrell, 1995) or whereby individuals claim to remember aspects of an event that never happened simply by mixing with features of just perceived events (Loftus, 1996; Lyle & Johnson, 2006).

Another approach, the activation-monitoring account, was developed by Roediger and colleagues (H. L. Roediger, Watson, McDermott, & Gallo, 2001) as a tool to explain their findings on false memory production using the Deese-Roediger-McDermott paradigm. This approach emphasizes similar monitoring processes as suggested by the source monitoring account. Roediger and collaborators depicted memory process as a compound of two opposing components. The first one implies the activation of critical words at study phase, whereby item-specific processing takes place to increase distinctiveness of targets to be remembered but also whereby activation of related critical lures occurs, either consciously due to elaborative processing or unconsciously because of associative network activation (McDermott & Watson, 2001). A second component of memory retrieval occurs at testing and is related to monitoring or memory editing, whereby successful distinction of activation due to real item presentation and not just internal activation is needed in order to avoid source-monitoring errors (Steffens & Mecklenbräuker, 2007). This monitoring process is implicated in the probability of false recall, which is stronger as a test item activates a critical word or, in other words, as the monitoring process becomes more difficult due to, for instance, time restrictions or lack of source information access at recognition (McDermott & Watson, 2001).

Spreading activation at encoding that may influence performance at test is a concept introduced by the aforementioned account, but was related to other theoretical attempts offered to understand how false memory production behaved. Along these lines, Foley and collaborators proposed what they defined as imaginal activation hypothesis. This hypothesis described that, when an item is presented, a broad and spontaneous activation will happen at encoding such as related thoughts, episodic related events, image-based thoughts, etc. If those elements are reactivated at recall, some participants could miss-report those items processed that way at encoding, producing false recollection (Foley & Foy, 2008; Foley, Foley, Scheye, & Bonacci, 2007; Foley, Foy, Schlemmer, & Belser-Ehrlich, 2010). All this work from Foley was based on how likely using different modalities of item presentation would engage the spontaneous process of generating visual cues associated to them, resulting in the production of false memories due to re-activation of those cues at test. For these authors, using only pictures at encoding would increase false memories for they re-activate visual cues at test and interfere with monitoring processes based on the distinctiveness of materials.

Fuzzy trace theory may also be related within this activation framework. But, here, a broader scope and more detailed assumptions about false memory productions were offered by the authors (Brainerd & Reyna, 2005; Brainerd & Reyna, 2004; Reyna & Brainerd, 1995). The main point of this theory is the suggestion of two concurrent memory traces taking place at encoding and retrieval. One is a verbatim trace related to detailed information, considering item-based information, source characteristics and every detail related with encoding and/or recollection scenarios. Verbatim contains a high amount of information, declines quickly through time and when the remaining pieces of information about that memory become associated to the wrong context, recollection errors occur (Reyna & Lloyd, 1997). The flip edge of this memory trace is the encoding and/or retrieval of general information about the memory, the gist of it, representing the meaning or theme of the stimuli. This gist is utilized when encoding or retrieval circumstances do not allow an individual to retrieve details about the memory, inferring and deciding their responses based on that gist. The gist trace is closely related with schema-based theories (Anderson, 1983) which postulates that when event details fade from memory over time (or under fuzzy-trace words, verbatim trace decreases), people unconsciously use schematic processes to complete (or embellish) those faded memories (i.e. gist is utilized to complete memory gap). The classic experiment from Brewer and Treyens is another example on how schemas may influence false recollection (Brewer & Treyens, 1981). Authors asked participants to wait for a very short period of time (only 35 seconds) in an office and then unexpectedly test their memory of what was there. Results indicated that, generally, recollection of non-present but highly semantically related items was present (i.e. items related with the schema of the office), together with recall of bizarre items present at the office (i.e. due to unusual characteristics, participants retrieved them easily based on what was defined by Brewer & Treyens as distinctiveness effect).

The criterion shift account might somehow be linked to both activation and fuzzy trace accounts. Originally suggested by Miller and Woldford (M. B. Miller & Wolford, 1999), the criterion shift was defined as any internal change in participant predisposition to respond positively to a testing item, on an item-to-item basis and depending on its relation with the theme detected (Gallo, Roediger, & McDermott, 2001). Authors suggested that, in a DRM paradigm, participants generate a meta-knowledge about the theme of the list that they use at recognition: they will prefer to respond as ‘old’ any word presented that matches with the theme they previously identified. This explained why false recognitions were produced. However, the most important conclusion of this study was their explanation of which mechanisms were involved: the error was not related with a memory process but with a decision process.

In the field of classic psychology, another theory tried to understand false memory production based on the level of processing account (Craik & Lockhart, 1972). Recently, it has been posited that false memories may be caused by activation-based factors depending on the depth of processing at study phase (Rhodes & Anastasi, 2000). Authors ran two experiments manipulating deep-of-processing factors (shallow and deep encoding). They predicted, according with the level of processing theories and activation-based models, that the deeper the processing of items by participants, the greater number of memory illusions will be present at recollection together with improved memory performance. They argued that this fact cannot solely be explained through the level of processing accounts and alternatively they suggest addressing the activation-based account: the deeper the processing, the higher the activation across the same conceptual node and therefore the easier it proves to generate false memories. Hence, they describe false recollection as a function of the degree of activation reached at encoding because in their experiments, shallow-processing generated less false recollection compared with deep-processing. They conclude that memory illusions are the result of semantic activation.

1.2.2.2 Dual Process Theory

This theory has classically been presented as the alternative to the aforementioned Activation Account. Dual-Process theory posits that memory retrieval is based on two main processes: familiarity and recollection (Atkinson & Juola, 1974; Jacoby, 1991; M. D. Rugg & Coles, 1995; Yonelinas, 2002). Familiarity was firstly described by James (James, 1890/1950) as a feeling of conscious penumbra related with the idea of having seen something before without being able to clearly access where or when, in contrast to recollection whereby access to detailed information about the memory is possible. Familiarity process has been defined as an automatic process, resulting as a passive consequence of stimulation, fast to be considered by the individual and easily manipulated by modulating old-new relatedness in any dimension, reflecting a "feeling of knowing" in the absence of specific knowledge about when and/or where a memory is acquired. In contrast, recollection is an intentional process, guided voluntarily by the individual, reflecting retrieval of the context in which an item was previously encountered and with a limited capacity (Curran, 2000; Jacoby, 1991).

To test these two processes in the laboratory, behavioural measures were taken from participants asking them to rate every retrieved item based on how sure they responded. This has been described as remember/know task, where participants must judge, for each positive response (i.e. HIT), their awareness about their memory performance. The remember option meant they could re-experience any information about that episode whereas the know option indicated they remembered the item but nothing else about its occurrence (Gardiner & Parkin, 1990; Tulving, 1985). It is assumed that familiarity process is related with "know" feeling-of-knowing judgements, and "remember" with recollection of proper details related with the item. It was also used by Curran and collaborators to study FM as some positive responses to critical lures were associated to high rates of "remember" judgements (Curran, Schacter, Johnson, & Spinks, 2001). The authors´ explanation for this effect suggested that: a) subjects falsely recollected illusory perceptual details about lured items and that made "remember" feeling stronger for them or b) it could reflect how semantic familiarity influence high confidence judgements (Speer & Curran, 2007). Nevertheless, some other experiments showed that true and false memories produce different rates of "remember" judgements depending on the characteristics of remembering requirements: recollection of perceptual details produced more "remember" responses in true compared with false memory (Norman & Schacter, 1997).

This dual-process account has been frequently utilized in ERP experimental settings (Friedman & Johnson, 2000). Familiarity process was firstly considered in an ERP experiment by Duzel and colleagues, who found different scalp distributions for remember and know responses during a DRM task (Duzel, Yonelinas, Mangun, Heinze, & Tulving, 1997). Later, a plurality reversal study from Curran depicted the FN400 effect as a consistent left-superior-anterior 300-500ms N400-like component, more negative for new than for old or lured items and linked to familiarity-driven recognition (Curran, 2000). On the other hand, the recollection process was associated with a left parietal-located activity showing more positive voltages for HITS compared to NEW items at around 500 to 800ms. Curran commented that this effect was functionally and topographically dissociated from other cognitive effects occurring during that very same time window, such as stimulus probability of occurrence or response confidence (Curran, 2000; Curran & Friedman, 2004), hence it could be specifically attributed to recollection.

1.2.2.3 Constructive Memory Framework

A slightly different twist from all of the aforementioned theories applies in this particular case. It has been considered as a framework that puts together notions from previously explained theories (Johnson et al., 1993; Norman & Schacter, 1997; Rumelhart & McClelland, 1986; Squire, 1992). This framework is based on the premise that experiences (i.e. memories in this case) are composed of patterns of features corresponding to different facets of that experience (Johnson & Chalfonte, 1994; Schacter, 1989), distributed widely across the brain with no specific location for a complete experience but an engram of connected features (Squire, 1992). When an experience, or in our case, a memory needs to be retrieved, a completion pattern process takes place (McClelland, 1995) allowing the reactivation of memory´s features and spreading that activation to the rest of the features associated with that memory (Schacter, Norman, & Koutstaal, 1998). Under these characteristics, the retrieval process may frequently produce errors. One could be related with a failure of the system to accurately link these features (i.e. source monitoring errors (Johnson et al., 1993)). Another error can be related with overlapping episodes ´features resulting on a recollection of only general similarities about these features and not specific information about what was learnt (Hintzman & Curran, 1994). Memory can also fail when the person access only the gist of it instead of item-specific information (Reyna &

Brainerd, 1995). Another error might occur when a failure in monitoring process, producing uncertainty on whether a memory feature belongs to a previous event or to internally generated information (Johnson et al., 1993).

But why does the human memory system requires a compound of bits/pieces to be constructed when an episodic event is required? One hypothesis explaining the importance of this type of constructive memory is related with the need of individuals to simulate or imagine future events or scenarios (Addis, Wong, & Schacter, 2007; Schacter et al., 1998; Schacter, Addis, & Buckner, 2007). The ability to retrieve information is linked with the capability to re-experience events and which is very important when an individual needs to imagine or pre-experience episodes in the future. (Schacter & Addis, 2007; Tulving, 1983; Tulving, 2002). This has to be done in a flexible manner since the future is not an exact copy of the past; hence the fact that the memory system requires flexibly extracting and recombining features of past experiences to build a plausible future. In other words, using the past to manage the future requires a constructive memory system. In fact, Tulving suggested decades ago that remembering is a mental time travel that requires consciousness about where in time events happened and a sense of subjective time (Tulving, 1983).

Authors supporting this constructive approach proposed that when false recognition is present in a memory test, rather than reflecting impaired functioning, this may indicate healthiness of this system and, in case of the opposite, result in reducing false recognition errors (Schacter & Addis, 2007). In other words, a failure of the memory system would reduce rather than increase this type of error. The authors based this assumption on previous DRM experiments completed with healthy participants and amnesic patients with medial temporal lobe damage. Patients in comparison with controls showed a decreased false recognition rate of critical lures, either semantically or perceptually related with targets (Ciaramelli, Ghetti, Frattarelli, & Ladavas, 2006; Melo, Winocur, & Moscovitch, 1999; Schacter, Verfaellie, & Anes, 1997; Schacter, Verfaellie, & Pradere, 1996). An explanation was offered by means of gist processing: healthy participants were capable of producing and retaining a well-organized semantic or perceptual representation of the gist of a learning list, allowing them to falsely recognize lured items that may match that gist but, at the same time, easily reject new items which would be far from that semantic/perceptual gist. On the other hand, amnesic patients would produce and weakly retain the gist due to their episodic memory impairment and therefore, produce less false recognition. This was experimentally induced in the Verfaellie and colleagues experiment, whereby patients were instructed to respond old to any item related with the theme of the DRM list, even if that item had not previously been presented at study. Patients showed fewer old responses compared to controls, demonstrating that their gist representation was impaired (Verfaellie, Schacter, & Cook, 2002). More details related with this approach on amnesic patients will be described below.

In summary, three main theoretical accounts exist at present trying to explain how memory is produced. The first, with a long history of experimental support, is the activation account. This theory suggests that memory is a compound of content and context, and when activation of a piece of information occurs, a spreading of that activation to related nodes of information may interfere with recollection. Several theories were formed based on this basic idea of an activation-monitoring account (H. L. 3. Roediger, Jacoby, & McDermott, 1996), a source monitoring account (Johnson et al., 1993), a fuzzy trace theory (Brainerd & Reyna, 2001) or the criterion shift explanation (M. B. Miller & Wolford, 1999). On the other hand, the dual process theory is the second major approach to memory performance, offering two processes in which retrieval is based: familiarity and recollection. A third is the constructive memory account, and attempts to combine some of the previous concepts into a new approach, whereby memory is an active process and depends upon several factors that may influence it.

We consider this constructive approach very interesting as it combines parts of previous theoretical frames but, most importantly, it offers a frame whereby episodic memory functionality is not restricted to the retrieval of events. It has been linked to another important cognitive process, executive functioning, as it was suggested that *"episodic reconstruction is just an adaptive feature of the future planning system"* (Suddendorf & Busby, 2003). We will base our theoretical explanations on this theory, in combination with the dual-process account.

1.2.3 DRM Paradigm

A significant number of false memory studies has been performed since this field of investigation reappeared in the nineties but it can be stated that most were somehow based on the Deese-Roediger-McDermott (DRM) paradigm. This paradigm rescued the concept of false recollection to offer an experimental task that allowed manipulating memory processing and therefore, brought light into how manipulation of experimental setting may influence false memory retrieval. Several studies partially modified this DRM task looking for different perspectives. Hereafter, we detail the DRM task.

1.2.3.1 The Origins: Bartlett, Underwood and Deese Experiments

Since the first results from “The War of the Ghosts” story used by Bartlett outlined in the early thirties (Bartlett, 1932), several authors have been interested in the study of memory failures. From the early studies regarding interference occurrence on memory tasks (Deese, 1959; Underwood, 1957) to the development of the classic false memory task, three decades have passed. Modeling the idea given by Deese, Roediger and McDermott designed what would lately be called the Deese-Roediger-McDermott paradigm (DRM) (H. L. 3. Roediger & McDermott, 1995).

Bartlett’s behavioural experiment was designed to study memory errors using naturalistic stimuli such as drawings and narrative stories, which participants must recall after several periods of time divided into a serial reproduction of days and weeks. He then analysed which errors appeared in the stories: i) assimilation errors regarding changes made to the story to fix participants’ cultural expectations; ii) levelling errors, when details were shortened from the story with each retelling; and iii) sharpening errors, consisting in changing the order of the story to better match their own terms or emotions (Bartlett, 1932). These results supported the hypothesis of constructive memory stating that memory retrieval may be influenced by our previous knowledge organized in schemas, which may also be influenced by cultural background.

Later, Underwood tried to offer an explanation about why false memories were produced (Underwood, 1965). His experiment consisted in a list of 200 words presented to 100 participants, which included critical stimuli, i.e. words that will elicit previously manipulated implicit responses. Participants responded to each word judging whether it was previously presented or not and results indicated that these critical words were recalled. Underwood stated that the greater the frequency of elicitation of the implicit response, the greater the likelihood of false recognition. He reasoned that, when a word is presented at encoding, participants implicitly activate associated words to that one. When a recollection task is performed, participants might recall an associate instead of a true memory and therefore produce a false memory, due to the aforementioned activation at encoding regardless of whether it was actually presented or not. This phenomenon was called implicit associative response and it became important for posterior theoretical attempts, such as the previously explained activation accounts (Ayers & Reder, 1998).

And last, but not least, the predecessor of DRM paradigm and from whom it takes its name was Deese´s extra-list intrusion study (Deese, 1959). This was an attempt to analyse why memory performance can be inaccurate. At that time, the studies focused on “intra-list” factors such as frequency and the order of emission of certain items at recall. Deese added the effect that other items had in recall and that had no direct relation with learning lists presented to subjects (i.e. “extra-list” intrusions). He used word association norms to predict the occurrence of those intrusions, building up a percentage rating of occurrence probability for the words that appeared as intrusions on a free recall memory task. His experiment had two phases: a) creation of intrusion lists, whereby subjects freely recalled a list of words presented auditory. The intrusions on that recall were counted and compared with the probability that this intrusion was matched on a paired associated task; and a second phase b) Paired association task, whereby a word was given and subjects freely produced the best paired-word that came to their minds. Relationship between frequency of occurrence of an intrusion and percentage of the same word being produced as an associate was 0.873 ($p<0.1$). He prognosticated that by using the proper association norms there was a high probability of predicting the production of a specific word as intrusion, the reason being a linear relation between probabilities of intrusion upon associative value. In his own words, he concluded that *"the probability of occurrence of an intrusion in recall is proportional to the average association strength of that item in the context of the material being recalled and is relatively independent of the distribution of association frequencies among the various items of the list"* (Deese, 1959).

It is worth to note here that, based on the same background and published in the very same journal issue than Roediger and McDermott's study, Shiffrin and colleagues also analysed false recognition effects on healthy population but their results obtained via a different theoretical approach (i.e. search of associative memory or SAM model) (Shiffrin, Huber, & Marinelli, 1995) with no remember-know task applied were lower. Influence of this work in future investigation on false recollection was not as large as DRM had, with almost 500 citations up to December 2005, according to the Social Science citation Index compared with less than 100 citations of Schiffrin and colleages work (Gallo, 2006).

1.2.3.2 Classic DRM Design

The classical false memory task described by Roediger and McDermott (DRM paradigm) has been the most used task to study false memories (H. L. 3. Roediger & McDermott, 1995). It was designed as a list-learning paradigm using a list of 15 words, all of them related semantically with a word not present on the learning list referred to as critical lure item and not presented at study.

A single-trial free-recall design for each list was applied, following the Deese procedure, but a recognition trial was also added for the DRM task. Roediger & McDermott wanted to replicate what they considered as very important results from Deese´s previous works. Authors even commented on how difficult it was to understand how such important data was actually neglected by the scientific community at the time (H. L. 3. Roediger & McDermott, 1995). To do so, two experiments were carried out. Experiment 1 utilized 6 learning lists at studyA free-recollection memory trial showed how 40% of the lists produced false memories compared to 14% of general intrusions. A recognition-trial was applied right after free-recall trials of all lists, reason why the authors suggested that false recollection of critical lures was somehow. To overcome this interference, authors designed experiment 2 with some design changes: 16 learning lists were presented to half of the participants and after them, an immediate free recall test was applied; the other half of the participants learned all the lists and performed an interference task (i.e. maths problems). Participants then performed a recognition trial, making old-new responses and remember-know judgements for items responded as old. Under these experimental circumstances, free recall produced the critical lure in 55% of the lists (an even higher percentage compared to 40% in experiment 1). A recognition task, composed by only three words from studied lists plus the critical lure, resulted in a very similar percentage of hits and critical lures indicating that participants were not able to distinguish between items previously presented and critical lures. Remember judgements for critical lures were quite high and with similar rates compared with hits. Roediger & McDermott utilized source monitoring error account (Johnson et al., 1993) to explain why remember judgements of recalled items were higher in the group of free-recall trial before recognition: participants mistook the experience of recalling the item with a real episode of studying it. Nevertheless, in this first study, they mainly submitted constructive memory theory account to explain false memory production (H. L. 3. Roediger & McDermott, 1995).

In a very complete review, Gallo (Gallo, 2006; Gallo, 2010) suggested that processes leading to false memory productions at DRM paradigm could be based on two different approaches. The first is memory-based and the participant responded to the task based on their own subjective experience of what happened at study, on a previous signal that the encoding phase left behind. When this is the case, three main theoretical explanations are given to explain false memory effects: associative activation, thematic consistency and feature overlap. With the second approach, the decision-based process explains false memory production on the participant´s own decision about a particular item being presented based on their assumptions during encoding and/or recollection. To explain this process, three main explanations are offered: response bias, criterion shift and demand characteristics.

1.2.3.3 DRM Limitations

Despite its unquestionable influence on the study of false memories, certain limitations of the DRM paradigm have been highlighted by some authors. For instance, Baoioui and colleagues suggested that using pictorial material instead of only words would increase ecological validity and facilitate broader generalization effects of memory (Baioui, Ambach, Walter, & Vaitl, 2012; Miller & Gazzaniga, 1998). Miller & Wolford stated that when the election of the critical lured items to serve as studied or lured items was predetermined instead of randomly assigned could lead to possible differences in memorability (Miller & Wolford, 1999).

One important criticism of the DRM paradigm, that we aimed to overcome in our research, was suggested by Nessler and colleagues and was related to the fact that only lured items presented a semantic association with all the other elements from learning lists, whereas old items were not necessarily semantically related with the other old items from that very same list. This certainly may affect the semantic relationship between old and lure items, which is the basis of the DRM paradigm (Nessler, Friedman, & Bersick, 2004).

1.2.4 State of the Art on False Memories

In this section we present the results of past investigations on false memories. We will focus on behavioural DRM-like studies as we consider that approach as the basis of the task we are introducing in this thesis. We will further review the most important ERP experiments on false memory in chapters 3 and 5 of this thesis, as we will utilize this same technique. For clarity we will review experiments performed with healthy participants and later comment on production on amnesic patients.

1.2.4.1 Healthy participants

Since the completion of classic nineties experiments performed on false memory, and increasing number of studies has been presented. To frame it in a general and approachable structure we have divided these studies in two main blocks: a first one whereby the focus was placed on what was required to produce or increase false recollection and a second one whereby authors focused on what processes contributed to reduce false memory. We will comment on that in the following sections.

Increasing False Recollection

Several aspects should be considered as factors that may bias false recollection and studies have been proposed to clarify some of them as described here.

Some studies disagree with the criterion shift hypothesis and the implications of priming in false recollection. One study utilized stem-completion tasks under DRM circumstances and concluded that significant priming effect was found for related lures, reflecting a long-term activation of concepts or associates at study (Tse & Neely, 2005).

Another line of investigation was established about how warning participants on the nature of false memory of DRM paradigm may influence performance. The initial premise suggested that if participants knew about the “trick” (i.e. the lured characteristic of the task), they may not be biased to produce that many false recollection responses. Surprisingly, data showed the opposite: despite that specific warning, participants did not prevent false recollection production (Gallo, Roberts, & Seamon, 1997; Multhaup & Conner, 2002), even reaching 38% of lures recollection in immediate single-item test conditions (McDermott & Roediger, 1998). Despite the fact that false recollection was not avoided when participants were warned, it was demonstrated that they were reduced in number albeit still present. Gallo designed a study aiming to investigate whether, when that warning was given, it affected false memory results (Gallo et al., 2001). Previous experiments offered warning before study phase, and Gallo designed three different warning conditions: without warning, warning-before-study (instructions were given before learning the list, therefore, it may influence encoding and retrieval of lures) and warning-before-test (instruction was given after study but right before testing, thus allowing to observe the retrieval influence process only). Data showed how lure retrieval was lower when warning was offered before study, being ineffective when offered after study, suggesting that information required to create the link to false recall was already encoded at test (Anastasi, Rhodes, & Burns, 2000; Gallo et al., 2001).

All previous data suggested that a decision-based process was in charge when false recollection happened in a DRM experiment, but as previously described, indices appeared that suggested the implication of more factors, apart from a decision making process, involved in false recollection of critical lures. This second large block of theories has been denominated as memory-based approaches, supported by works on associative activation, thematic consistency and feature overlap (see (Gallo, 2006) for review). Activation account (already commented on in section 2.2.1) offered an explanation on why an item not presented at study may be lately recollected or recognized at test based on the premise of the spreading of activation from semantically or perceptually related targets. Thematic consistency deals with the same theoretical background as fuzzy trace theory and schemas influence (introduced in section 2.2.1), focusing on the idea that memory is organized around a theme which is retrieved in testing conditions. The last approach, feature overlap, posits that an event is encoded by the system as a compound of features and the overlap of these features at retrieval conditions determines the level of familiarity and hence, the probability to mistake a memory as being real (Gallo, 2006). These three approaches of memory-based account had been experimentally analysed in studies manipulating associative relationship between study and critical lures (Deese, 1959; H. L. Roediger, Balota, & Watson, 2001) or studies using categorized lists to bias false recollection of lures which, it must be said, reached lower percentages of false recollection compared with the DRM lists

(Brainerd, Wright, Reyna, & Mojardin, 2001; Buchanan, Brown, Cabeza, & Maitson, 1999).

Reducing False Memory

The importance of the monitoring process account is to be considered when the aim is to reduce false memory production. Some experiments using exclusion tasks designs engaged a response decision pattern based on the possibility of rejecting an item if it was previously retrieved in a different context, which was called disqualifying monitoring, i.e. an explicit process involving conscious decision-making behaviour (Gallo, 2006). A different monitoring process, diagnostic monitoring, occurs when an individual, having problems in correctly retrieving an event, is capable of rejecting it purely on the basis of that retrieval difficulty. This has been referenced as a "it-had-to-be-you" effect in source monitoring literature (Johnson, Raye, Foley, & Foley, 1981) and "distinctiveness heuristic" in a Schacter experiment, studying how perceptually enhanced study environment reduced false recognition (Israel & Schacter, 1997; Schacter, Israel, & Racine, 1999).

1.2.4.2 Amnesic population

Several behavioural experiments wished to study how memory and, specifically, false memory, was processed when a brain injury impaired the previously episodic memory system.

In the early seventies Cermak and colleagues studied how interference of material previously presented affected Korsakoff syndrome patients' recollection much more than the controls because of difficulties related to material encoding (Cermak & Butters, 1972). In a subsequent experiment by the same authors specifically studying verbal encoding ability in KS patients, they concluded that even though patients were able to take advantage of cueing at recognition, they were not able to spontaneously apply this strategy (Cermak, Butters, & Gerrein, 1973). In contrast, Warrington & Weiskrantz found that similar performance on cued recall compared to free recall was present for the KS and the control group, suggesting equivalent facilitation effect (Warrington & Weiskrantz, 1971).

The debate then started as to whether episodic memory impairment may interfere or even interrupt false retrieval in a DRM-like task. The author who worked more fruitfully in this area was Schacter. It was previously presented in literature that false alarms production was different when comparing amnesic and controls, with a higher production of false alarms for patients (Cermak et al., 1973), that, together with a lower hit rate, may be reflecting a guessing tendency due to difficulties lying in distinguishing between studied and non studied items. Schacter´s first experiment using the DRM paradigm with amnesic patients wanted to disentangle why amnesic KS patients and controls false memory production was also different (Schacter et al., 1996). Under recognition testing, patients produced fewer hits, fewer false memories and more false alarms than controls. Explanation was based on two main points: a) true and false recollection were both based on the same processes, but as long as amnesic patients cannot retain semantic information and cannot retrieve episodic information as well as controls, they produced less hits and less false memories; and b) patients present an impaired ability to process semantic representations of the theme (i.e. the gist of the memory) at study and retrieve them at test, decreasing their false memory production (Schacter et al., 1996).

In a subsequent experiment (Schacter, Verfaellie, Anes, & Racine, 1998), authors aimed to study in more detail whether amnesic patients (KS, non-KS and alcoholic controls versus healthy non-amnesic participants) were able to encode the gist of the information when repeated study-test trials were applied and induction of a robust semantic gist representation was planned. In this case, the authors utilized SDT calculations, including hits minus false alarms and hits minus lures as measures of true recollection and lures minus false alarms as a measure of gist memory, as described by their tendency to rely on gist despite any influence of item-specific memory. Results indicated that due to increased gist sensitivity to gist produced by repeated trials, KS patients increased the number of false recollections whilst being strongly biased by gist and incapable of checking retrieval using episodic memory processes. Authors suggested that, given the result of this experimental manipulation they could conclude that differences on false memory performance on KS patients were due to dysexecutive problems and not to episodic memory impairment only.

Schacter experiments seemed to clarify the fact that amnesic patients, and more precisely KS patients, presented problems in encoding and retrieving the gist of memory episodes and, together with their characteristic episodic memory impairment, and as a result produced a lower number of hits and false memories and increased the number of false alarms compared with healthy controls. The question remained un-clarified: was it because they are unable to build a well-organized gist or, on the other hand, was it because KS patients are able to do so but cannot easily access it?

Verfaellie’s experiment on the false priming effect (Verfaellie, Page, Orlando, & Schacter, 2005) aimed to analyse previous findings related to false recognition in the amnesic patients (see section 2.2.3). Here authors wanted to investigate whether implicit processes may bias false recollection in amnesic patients, whereby the initial idea was that implicit processes could be considered spared for amnesic patients (Schacter & Slotnick, 2004). The authors wanted to study whether the use of an implicit stem-completion task on a DRM paradigm design may offer information about any possible impairment on gist processing in amnesic patients. Previous studies on healthy participants the existence of a false priming effect: a bias to complete stems of critical lures with previously presented lures (McDermott, 1997). When amnesic patients were engaged in this task, they showed normal priming for old words but no priming effect for critical lures, whereas control groups in this experiment showed priming effect on both (Verfaellie et al., 2005). Conclusions from this experiment suggested that memory impairment in amnesics may go beyond episodic confines and may prove to be an impoverished gist representation.

A last experiment worth including in this section was completed by Pitel and colleagues. Their work was based on the premise that cognitive deficit in KS patients belonged to a continuum with non-cognitively compromised alcoholics in one extreme and different degrees of cognitive impaired KS patients in the other (Bowden, 1990; Pitel et al., 2008). Pitel based their research on three possible explanations for episodic memory impairment for KS patients: a deficit on retrieval information, a deficit on encoding temporo-spatial features, and finally an inability to encode spatio-temporal context and/or episodic information producing a deficit in conscious recollection abilities (Pitel et al., 2008). Nevertheless, in the following study (Pitel, Beaunieux et al., 2009), Pitel and colleagues focused on how KS patients were able to learn new concepts concluding that KS semantic learning was impaired, even more impaired than alcoholic patients with no KS. This result had two main implications: one regarding the role of episodic memory in the creation of new semantic learning; and the other meant that the continuity theory could not be supported in that case.

1.3 Brain Injury and Amnesia

Four main brain anatomical blocks may be related with memory: medial temporal lobe structures (MTL), frontal lobe structures, parietal lobes and subcortical structures. A diagram of targeting brain localizations can be found in ***Figure 3***.

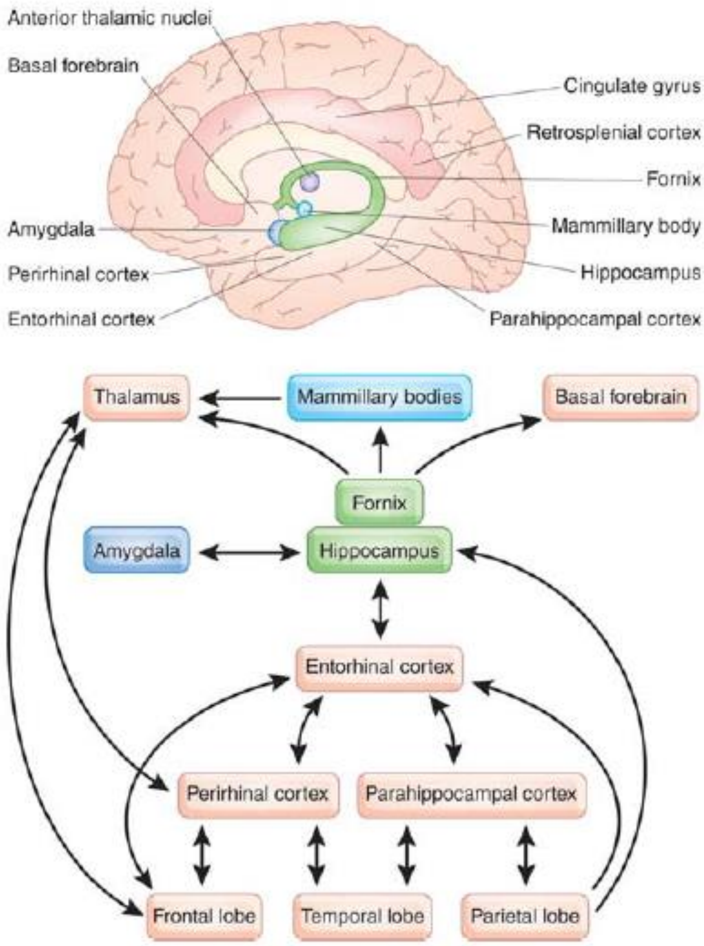

Figure 2 Brain structures involved in episodic memory. Taken from (Nadel & Hardt, 2010)

General consensus exists on the importance of medial temporal lobe structures in learning and memory processes. More specifically, four main structures have been described playing a role in episodic memory: the perirhinal cortex, the parahippocampal cortex, the enthorrinal cortex and the hippocampus. Of special interest was the explanation on the role of each of these structures offered by the binding of item and context model (i.e. BIC MODEL) (Diana, Yonelinas, & Ranganath, 2007). The authors, based on previous neuropsychological and behavioural experiments (Eichenbaum, Yonelinas, & Ranganath, 2007) described MTL functional implication in recollection. MTL structures are divided into three main structures: the hippocampus, the perirhinal cortex (PRc) and the parahipocampal cortex (PHc). The recollection process is traditionally associated with the activity from the hippocampus and posterior sits of PH whereas familiarity was associated with anterior PH. Neuroimage studies described PRc as the structure related with item characteristics (i.e. "what"), PHc with contextual information related with that item (i.e. "where") and the hippocampus as the structure responsible for binding together both pieces of information into a memory. According to the BIC model, activation of these structures will depend on the type of processing (PRc more active for items with a higher familiarity and the hippocampus and PHc more active in trials where contextual information is required to be encoded) and the cues offered at recollection (item cue will decrease activation of PRc proportionally to the degree of familiarity (familiarity-based responses produce decrease of activity at PRc) and contextual information will increase PHc and hippocampal structures (re-activation of the pattern at hippocampus and association to context on PHc modality).

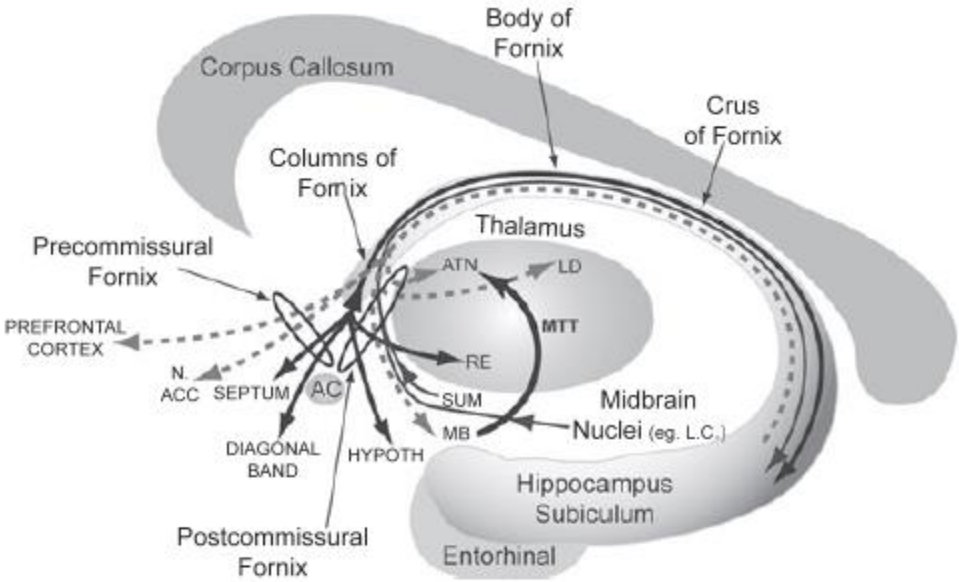

Figure 3 Diagram of subcortical structures involved in memory detailing fornix and thalamic nuclei connections. Taken from (Aggleton et al., 2010).

It is of special interest to investigate the influence of diencephalic subcortical structures in memory process. Mammillary bodies, fornix and several thalamic nuclei serve as a bridge when information is connected, managed and processed during memory encoding and retrieval (see Figure 3 for details on these structures). These structures connect cortical areas that are undoubtedly important in the memory process such as the hippocampus and MTL structures previously commented, restrospenial cortex and several structures of prefrontal cortex. Aggleton and colleagues offered an extensive review on the role of certain thalamic nuclei in the formation of three parallel temporal-diencephalic pathways (Aggleton et al., 2010): a) an anterior medial “feed-forward” system responsible for conveying hippocampal-diencephalic signals to prefrontal regions allowing cognitive flexibility and executive function; b) an anterior ventral “return-loop” system involved in optimising synaptic plasticity by means of long-term potentiation and long-term depression mechanisms (LTP and LTD respectively); and c) an anterior dorsal "head-direction" system which is thought to be involved in mental navigation and imagery manipulation (see Figure 4 for a detail on these three pathways).

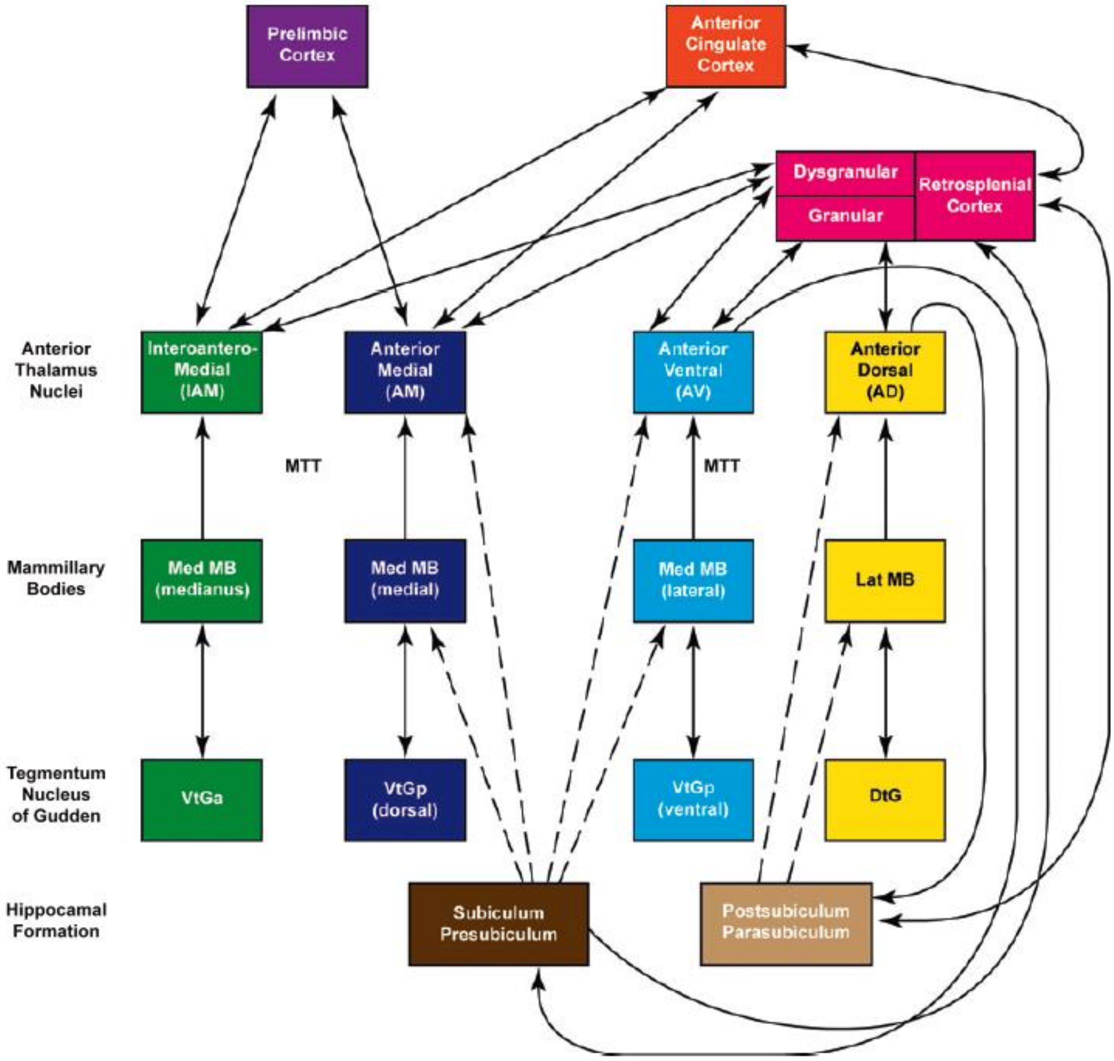

Figure 4 Detailed description of hippocampal-thalamic connections with the three main pathways described in the text. Taken from Aggleton et al 2010.

Frontal lobe involvement in memory has been related with monitoring processes of memory retrieval, especially regarding prefrontal cortex structures. These brain regions are highly connected with MTL and parietal structures and receive inputs from previously depicted diencephalic structures via cingulate cortex and corpus callosum. The importance of frontal areas is mainly related with recollection processes instead of encoding, and any disturbance of their executive intervention may result in memory errors, such as confabulations, source monitoring failures or false recollection which have been extensively considered by theoretical accounts on memory reviewed on section 2.2.

Parietal lobe is another structure classically implied in memory and attention, and has been thought to play an important role in false memory production. Drowos and collaborators (Drowos, Berryhill, André, & Olson, 2010) tested false memory production with two versions of the DRM paradigm (experiment 1 performed with lists of words and experiment 2 with lists of pictures) on two patients with posterior parietal damage. The premise was that, due to this parietal deficit, they may present episodic memory impairment and it might also be accompanied with a decrease in subjective feeling of recollection measured with remember-know task, as was previously informed (Davidson et al., 2008). Results supported the hypothesis that posterior parietal areas are involved in retrieval processes instead of encoding (Johnson & Raye, 2000) as patients despite presenting false recollection, responded with a weak feeling of recollection in the remember-know task specifically to lures but not to hits.

This offered two different hypotheses: the parietal lobe may be implicated in the recollecting of perceptual details of a memory and, being impaired, memory lacks details and patients reduce their degree of confidence (Johnson & Raye, 2000); or alternatively, the parietal cortex may be related with automatic retrieval processes that, when impaired, provoke a decrease of sense of re-experiencing events making retrieval less spontaneous in patients (Cabeza, 2008).

In a review of the role of parietal lobes in memory, Levy exposed a complete range of empirical evidence about parietal mnemonic implications, especially lateral parietal cortices (Levy, 2012). He posed important questions on the implication of these cortical regions with regards to different aspects of memory, framing all previous studies in an attempt to summarize and guide future research in this field. He concluded that no consensus has been reached so far from previous literature research in this field. He questioned important aspects: whether parietal lobes are implicated in cognitive processes or just in contents of memory; what is the temporal timing of its involvement (i.e. pre-retrieval, retrieval or post-retrieval implicated); is its correlation with the subjective impression of a memory correctly retrieved or not; what is the importance of the lateralization of parietal involvement in memory retrieval (see (Levy, 2012) for more information on these questions). The conclusion was that more research is required to clarify all these approaches.

To resume, three main neurological structures are implicated in learning and retrieval processes. The first is the temporal lobe; the second is related to diencephalic structures such as mammillary bodies, fornix and mammilothalamic tract; and a third, more recently engaged in the memory process, is the parietal lobe. In this thesis, we are targeting Korsakoff syndrome patients who present a very characteristic neurological impairment in diencephalic structures, as reviewed here, together with some other extremely significant neurological structures implicated in cognition detailed in the following section.

1.3.1 Korsakoff Syndrome

Sustained alcohol consumption can lead to a cascade of mechanisms that seriously affect health. Apart from socioeconomic reasons that evidently complicate this process, high levels of ethanol in the body together with poor nutrition may produce critical deficiency of vitamin B1 or thiamine producing acute brain damage defined as Wernicke´s encephalopathy (WE). This syndrome was described in 1881 by Wernicke (Brody & Wilkins, 1968) as a neuropsychiatric triad of symptoms such as mental confusion, ataxia and ocular abnormalities including nystagmus and ophthalmoplegia. The diagnosis of KS is straightforward when heralded by WE, especially when accompanied by characteristic acute MRI abnormalities. More frequently however, the onset of KS is insidious and its diagnosis may be elusive. An extensive autopsy series found, among individuals with the pathological hallmarks of KS, that less than one third of those with a history of alcoholism were diagnosed during their lifetime and only one twentieth of those were without a history of alcoholism. Only 8% of patients with pathologically proven KS had a history of WE (Galvin et al., 2010). Among patients diagnosed with KS during their life, only 38% presented the classic WE triad (Zuccoli et al., 2007).

Consequently, it has been suggested that KS may emerge insidiously, evolving from repeated subclinical episodes of WE (Blansjaar, Jan Vielvoye, Van Dijk, & Rijnders, 1992; Harper, Giles, & Finlay-Jones, 1986). It is perhaps not surprising that KS is under-diagnosed. Given the insensitivity of the clinical diagnosis of KS, neuroimaging signs detectable via simple visual inspection, would be of great value, but have not been previously reported (Blansjaar et al., 1992). KS is a medical emergency that requires acute parenteral thiamine replacement to reverse symptoms. If no treatment is applied, it causes metabolic failure in vulnerable brain regions, due to this thiamine deficiency, resulting in necrosis and petecchial haemorrhages in the periventricular regions of the midbrain and diencephalon, leading to death in 20% of cases (Harper et al., 1986). When treated, permanent effects lead to Korsakoff syndrome (KS) in 85% of the survivors (Day, Bentham, Callaghan, Kuruvilla, & George, 2008) associating irreversible parenchymal damage in the mammillary bodies or anterior nucleus of the thalamus (Sechi & Serra, 2007) and requiring in almost 25% of those cases, permanent institutionalization or social care (Victor, Adams, & Collins, 1989). In recent years, prevalence rates of KS in the UK are increasingly associated to socioeconomically difficult environments (Cox, Anderson, & McCabe, 2004).

KS was described by Korsakoff himself (S. Korsakoff, 1887; S. Korsakoff, 1889; S. S. Korsakoff, 1889) based on his clinical experience. The most salient clinical sign was memory disturbance as a result of different clinical symptoms in an acute state that, although Korsakoff did not link this with WS directly, included confusion and agitation associated with ophthalmoplegia, nystagmus and ataxia-like manifestations. Memory impairment occurred in a context whereby the patient seemed to be completely conscious and aware of their responses but their memory production included repeated questioning, severe episodic memory and problems to recognize people met after the onset of the disease (Kopelman, Thomson, Guerrini, & Marshall, 2009).

Semantic memory has been also tested in KS patients, with different outcomes. Preserved capability to retrieve information from semantic long-term store appeared to be intact in conceptual priming experiments (Kopelman, 1995; Talland, 1965; Verfaellie, Cermak, Blackford, & Weiss, 1990; Verfaellie, Cermak, Letourneau, & Zuffante, 1991). Two studies confirmed KS patients´ speared ability to learn new semantic information (Komatsu, Mimura, Kato, Wakamatsu, & Kashima, 2000; Van der Linden, Meulemans, & Lorrain, 1994) and one study used errorless learning procedures to ensure KS patients capability to learn (Wilson, Baddeley, Evans, & Shiel, 1994). Nevertheless, the debate exists on whether semantic learning abilities depend upon episodic memory (Squire & Zola, 1996; Verfaellie, Koseff, & Alexander, 2000) or may happen independently (Tulving, 2001) as in KS patients episodic memory impairment is core.

Two processes may be responsible for a difficult semantic processing in KS patients. The first one addresses the incapability to associate new information with previously stored data, as suggested by the context memory deficit hypothesis (Mayes, Meudell, & Pickering, 1985) as a primary deficit on encoding contextual/semantic information causing a secondary interference in recollection, and was proved in KS patients (Pitel, Rivier et al., 2009). The second process involves executive retrieval strategies suggesting that KS patients habitually process semantic information but that these do not use it efficiently. Semantic processing is an ability of special interest in the study of false memory, and the most utilized task, DRM paradigm, bases its capability to produce false recollection on semantically binding probes to non-presented items with a high semantic/categorical relation with probes (i.e. critical lures). Added to this, our VFMT strikes principally on reinforcing this semantic relatedness between what is studied and what must be recognized at test.

Amnesia is a core sign in KS but no consensus regarding the origin of this deficit has been met so far. Some authors suggested that amnesia was caused by retrieval difficulties (D'Ydewalle & Van Damme, 2006; Irle, Kaiser, & Naumann-Stoll, 1990), by impairment on encoding processes (Cermak & Butters, 1972; Kopelman, 1985) or by the incapability to effectively utilize conscious recollection abilities (D'Ydewalle & Van Damme, 2006) but none of those hypotheses have been clarified. Working memory is also another important memory component that may require further research to identify its role in KS patient memory impairment. In neuropsychological studies, the main working memory components have been described in KS patients, again with contradictory results indicating a spared phonological loop and visiospatial sketchpad (Joyce & Robbins, 1991; Noel et al., 2001) as well as altered performance in task assessing those two components of working memory (Brand, Kalbe, Fujiwara, Huber, & Markowitsch, 2003; Pitel et al., 2008). Regarding specific research on the third suggested component of working memory, i.e. the episodic buffer (Baddeley, 2000), only one work proved that it was altered, not being a KS specific feature but a reflection of chronic alcohol consumption on frontocerebellar circuitry also present in non-Korsakoff alcoholic patients (Pitel et al., 2008).

Added to memory impairment, KS patients may also present to a lesser degree and frequency other cognitive impairments such as disorientation to time (Sechi & Serra, 2007) and/or dysexecutive syndrome including behavioural signs related with apathy, blandness, mild euphoria or little reaction to events (Kopelman, 1995), arguably related with impairment of frontal lobes functionality (Brokate et al., 2003). Implicit memory, albeit infrequently informed, may reflect impairment due to interference from other cognitive functions instead of a primary impairment (Hayes, Fortier, Levine, Milberg, & McGlinchey, 2012).

Another important symptom present in a high percentage of KS patients is confabulation, defined by Victor and collaborators as “fabrication of ready answers to questions or as the fluent recitation of fictitious experiences” (Victor et al., 1989) or alternatively, as “a falsification of memory occurring in clear consciousness in association with an organically derived amnesia” (Berlyne, 1972). It has been described how this confabulation phenomenon appeared differently in the acute phase of the WE compared with the later chronic phase, being more frequently present in the chronic one (Victor et al., 1989). In the former, implication of temporal disorientation and difficulties to properly time-locate memories endowed recollection with a fictional appearance. These recollections would fit the definition of spontaneous confabulations offered by Kopelman, who described them as normal responses to a faulty memory interfered by a mixture of frontal dysfunction and organic amnesia (Kopelman, 1987), often including information related to patients’ actual occupations or environment. These confabulations might alternatively fit the labelling of provoked confabulations if they result from directly asking patients or if obtained in laboratory memory experimental environments instead of spontaneously produced by patients.

From a theoretical point of view, confabulations may also appear in the healthy population but it will be redefined as false recollection or false memory. Healthy normal people may also produce memory recollections that, even if they may be certain of their accuracy, these are not true. This phenomenon has been framed in the source monitoring account (Johnson et al., 1993). This approach is based on the idea that a false recollection is caused by a failure of the reality monitoring process, a source confusion closely related to the constructive nature of memory leading to a false recollection (Johnson & Raye, 1998). It does not necessarily implicate brain damage, as has been proven extensively in different experiments (Gallo, 2010; Loftus & Pickrell, 1995; Loftus, 2005; H. L. Roediger et al., 2001; H. L. 3. Roediger & McDermott, 1995).

Under this assumption, the focus is not on encoding strategies, but on the process that allows recollection to evaluate and monitor as accurately as possible the source and specific characteristics of that memory. This evaluation process works perfectly in situations where the required information is vague or incomplete, just by using probabilistic methods based on physical characteristics of stimuli, familiarity of them or subject's given decision criterion (Johnson & Raye, 1998). But this process can also fail or be confused, and one of the most frequent errors is based on association processes.

Source monitoring framework suggested several reasons why a false memory or confabulation may occur: a) the binding process between encoded and retrieved information is inadequate, b) consolidation or reactivation processes required for retrieval are interrupted, c) failure to effectively use evaluation processes or decision criteria for retrieval, d) the poor ability to self-generate strategies supporting successful retrieval, or e) failure to access or use general knowledge that allows a subject to evaluate the adequacy of retrieved memories (Johnson, 1991).

Neuroanatomical structures characteristically related with KS caused by permanent thiamine depletion consequences are grouped by Aggleton & Brown in two main axes: a) a central axis addressing memory production and retrieval that included the hippocampus, mammillary bodies, anterior-thalamic nuclei and the cingulate cortex as structures and the mamillothalamic tract, fornix and cingulum as white-matter connection structures; and b) the axis related with modulatory function on memory involves connections between the hippocampus and amigdala, which also connect via mediodorsal thalamic nuclei with prefrontal structures (also connected with anterior-thalamic nuclei and anterior temporal cortex structures) (Aggleton & Brown, 1999).

These structures might have an important role in the explanation of true and false memory production of KS patients.

1.4 Aims and Objectives

1.4.1 Overall objectives and motivation

Our general aim was to study neural correlates of false memory production in healthy participants and patients with amnesic syndrome due to alcohol brain injury. We aimed to utilize EEG techniques to assess brain activity during performance of a new designed false memory task. We selected KS patients as they frequently present confabulations as a clinical sign and, for the interest of this thesis, a population with a high tendency to produce false recollection was a perfect target to study false memory in laboratory conditions.

1.4.2 Specific milestones

Using the DRM paradigm as a baseline, we aim to produce a new false memory task that overcomes a series of weak points and strengthens the semantic relation between what is studied and what needs to be retrieved. Based on a dual process theory and constructive memory processes, we hypothesize that engaging participants in a task where semantic processing was induced, improved true memory performance will be produced on the basis of a deep processing account. We also expect them to activate semantic nodes at study on a broader scale, requiring them to engage monitoring memory processes, which nevertheless, would not avoid false memory production according to the activation-based account.

This scenario would be different for amnesic patients, as they present episodic amnesic impairment caused by the Korsakoff syndrome. In this case, we expect them to produce fewer true memories compared with healthy participants because of their episodic memory impairment, but we expect them to be able to produce false memories following the fuzzy-trace theory suggestion. We hypothesize that patients can codify semantic information when they learn related with the gist of it, but will have problems to store verbatim information because of their neurological condition. We also expect them to struggle with monitoring their performance, biasing false memory production. In the following chapters of this thesis, we aim to produce experimental work that allows us to study these hypotheses using ERP techniques.

We describe here the objectives we planned to achieve with the development of this research, which will be presented and explained in detail in the introductory section of each chapter in this thesis. First, chapter 2 will describe our new false memory task in detail. Once the task was designed and tested on a small sample of healthy students in a pilot experiment, we formally tested it on a bigger sample of healthy participants under EEG recording, in order to analyse distinctive ERP characteristics for true and false memory on healthy individuals. Our conclusions on this phase will be described in chapter 3. Considering that one of our main objectives with this research was to study false memory in brain injured patients, in chapter 4 we will describe the neuropsychological characteristics of the sample of KS patients selected for this purpose. We will detail the changes made to the task in order to adapt to an amnesic population and the results from a pilot study with KS patients in that same chapter. Finally, in chapter 5 we will present our study on ERP and false memories in amnesic patients compared to healthy controls, where we will discuss differences found between and within these two groups in terms of true and false memory ERP characteristics.

General discussion is offered in chapter 6.

Chapter 2: Design of a New Task: Visual False Memory Task

2.1 Overview

In this chapter we aim to describe in detail the new Visual False Memory Task (VFMT). It was designed to be utilized as a laboratory task to study confabulations and false memories. Considering previous experiments and in an attempt to optimize a paradigm of false memories, we evolved a new task. VFMT shares certain aspects with the classic DRM paradigm but has some other important and innovative qualities to create a valuable laboratory tool for studying false memories. The changes and new characteristics of this task are described in detail below.

2.2 Aims and Objectives

The classic DRM paradigm task is the most utilized in false memory studies. This task consists of learning a list of words that have a common point with another word not presented at study, called the lured item. This non-presented item lures the participant to recall it since the categorical relationship with the rest of the list at study is very high (see Introduction chapter for more details about DRM paradigm). Despite all the experimental results on how false recollection works achieved over the last thirty years thanks to this paradigm, some aspects remain partly unsolved. The aim in this chapter is to describe the aspects of our task that complement the DRM and which differ. We will discuss them in detail in the following sections.

2.2.1 Increasing Semantic Relation

One important point related with the classic DRM paradigm is that all words on a learning list will be associated with the critical lure but may not necessarily be related with one another. Some authors suggested that this aspect might be a weak point when semantic relationship between items is targeted (Beato, Boldini, & Cadavid, 2012; Nessler, Friedman, & Bersick, 2004).

The first idea for the design of our task was inspired by a behavioural experiment carried out by Brewer and Treyenes on schemata-related inferences from memory (Brewer & Treyens, 1981). They left participants waiting in a room full of objects for 35 seconds with no other instruction but to wait for the examiner to return. Right after, participants were taken to a different room to perform a free recall memory test on what they could say about the "testing" room. A recognition test was also completed immediately after. Brewer and Treyenes divided the items into schemata-related and saliency-related based on a previous rating from volunteers. The latter described how noticeable they were rated and the former how likely they were in the context of that room. Using this classification, they showed a correlation of 0.75 ($p<0.05$) between recognition and schemata-relation, 0.69 ($p>0.05$) for saliency. This showed how strong the memory interference can be when related semantically with the target and was the basis for our semantic-related visual lured items, which we will describe in detail later.

We aimed to create strength of semantic relationship between old and lured items that might later influence the false recognition rate (Nessler, Mecklinger, & Penney, 2001). This relationship was presented in Deese's original work, where he described how *"the probability of occurrence of an intrusion in recall is proportional to the average association strength of that item in the context of the material being recalled …"* (Deese, 1959).

The Associative Activation Account was behind this aim. Gallo described it as *"the activation of concepts stored in semantic memory due to the processing of other concepts found at the same conceptual level"* (Gallo, 2006). This linked with the theory of spreading activation that explained how the use of a concept or a word activates a node in the lexicon and that secondarily spreads activation to surrounding nodes which are semantically related (Collins & Loftus, 1975), setting the basis for all posterior semantic priming experiments. Nevertheless, priming effect is quite a short-term process, and false memories can last not only minutes but days or months.

False memory tasks summarize the activation effect from several words at study and therefore the trace can be stronger. Hence, the participant may consciously think of the related lure and encode it as an episodic memory trace per se, allowing its recollection in a memory task due to a source monitoring error described by Johnson and Raye (Johnson & Raye, 1981).

It has been suggested that the influence of what was intended during learning could influence the probability of false memories on a recognition task. A first explanation was given by Underwood and his implicit associative response account (Underwood, 1965), indicating that when a word was presented at encoding, participants implicitly activated words associated to that one. When the recollection task was performed, participants recalled an associate and hence produced a false memory, because it was already activated at encoding regardless of whether it was actually present or not. This explanation was at the core of posterior source of activation confusion account for memory retrieval (Ayers & Reder, 1998) which also offered another explanation on why semantic activation may be at the centre of false memory production. Ayers & Reader, with classical level-of-processing theories on their background (Craik & Lockhart, 1972), suggested that memory performance depended on both the number of times an item was activated and the degree of its activation, and that those same conditions might produce an increase of false recollection.

A later experiment by Rhodes and Anastasi manipulated two degrees of processing (shallow versus deep-processing tasks) on a learning task. They concluded that the deeper the processing during learning, the higher the probability of producing produce false recollections at recognition task. They predicted that the deeper participants were engaged in the item processing, the greater amount of memory illusions they might present at recollection together with an improved memory performance. The reason they argued was that, beyond levels of processing accounts, activation-base theories might complement the explanation: the deeper the processing, the higher the activation across the same conceptual node and therefore the easier it would be to generate false memory. Hence, they described false recollection as a function of the degree of activation reached at encoding. In their experiments, shallow-processing generated less false recollection compared with deep-processing task and they concluded that memory illusions were the result of semantic activation (Rhodes & Anastasi, 2000).

Taking all the aforementioned and considering that our aim was to increase the probability of false memory production by the participant in a memory task, we focused on two main strategies. First, we designed a different encoding scenario compared to DRM item lists, including only one single picture that recreated a complete and detailed contextual and semantic theme to be processed at encoding phase of the experiment. Every single item presented on that scene belonged to a single thematic category; hence, all the information presented at encoding had a strong semantic relation. For example, on one of our scenes we presented a picture of a beach and all the items presented on it were related solely to a proper beach scenario, with no items from a different semantic context unrelated to that category (for a complete list of scenes and items utilized in our task, see Appendix Chapter 1).

The second strategy focused on the list of items to be used at recognition task. We will describe the task in more detail in the following sections but, as a matter of example, let us say that for the beach scene, we selected fifteen items for the recognition memory task. Those items included five already presented on that scene, five completely new and non-related with the theme and another five that, although not present on the scene, were semantically related. Those first and last five items correspond to our old and critical lures items. Both retained a high semantic relation between them and with the scene at encoding (See **Figure 6** for another example of scene and testing items).

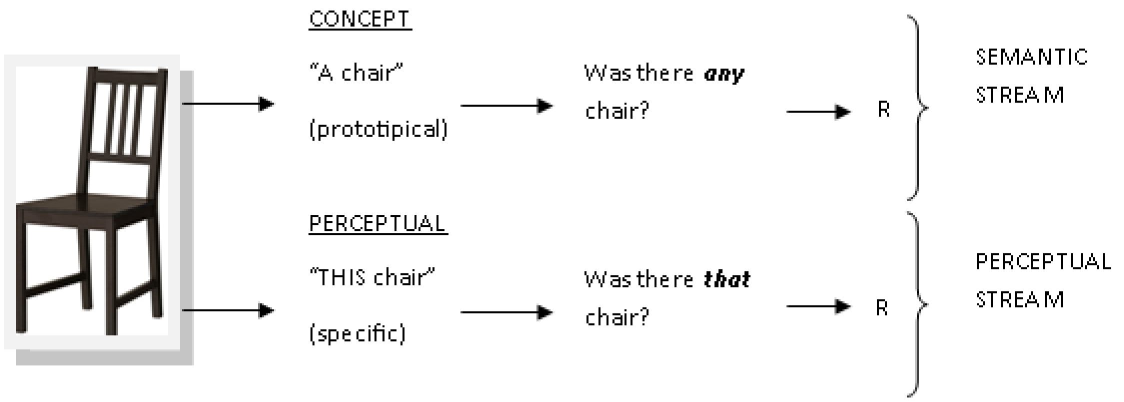

Figure 5 Differences between semantic and perceptual responding requirements during a memory task. In our experiment, participants were engaged to use the semantic stream and were trained and prevented to do it so, avoiding an item-specific approach

We used different exemplars at recognition test as compared with the items present at studied scenes because we wanted to minimize any possible perceptual processing effect at recollection phase

Using general standard images at recognition was also a way of biasing abstract processing, for no visual but categorical information was therefore processed and no pictorial or visual memory was engaged on the task. Visual stimuli lead to a categorical memory access to perform memory recognition instead of a pure visuo-perceptual memory task (see Figure 5).

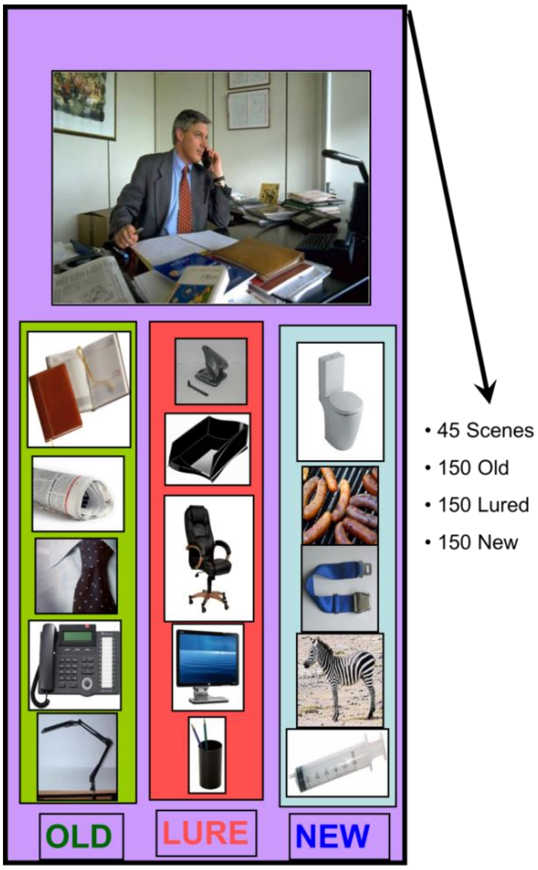

Figure 6 Example of a contextual scene utilized at encoding. Below, a detail of all fifteen items presented at recognition memory task for this specific scene.

Despite our efforts to increase the semantic relationship described, we were aware that we did not strictly measure the degree in which that effect was produced. We acknowledge that some scenes and/or items might produce a stronger semantic effect compared to other, and that was not measured. We did not control quantitatively for relatedness among our stimuli and that could be a weakness in our task. The election of the scenes and the related items was done to the experimenter´s criterion of semantic relation, but no formal measure of that was planned. To select items to be used as old and lured items, the experimenter with the help of her team selected from a pool of possible pictures the ones that they considered that might produce easier and stronger semantic connection with the scene. It can be argued that some of the selected items might not be the best to do the job, but no further measure was considered, being this one of our weak points regarding the design of the VFMT. For future adaptations and versions of this task, we need to include measures of how likely each scene and each item generated the semantic context and relation sought, as previously described in the literature during other DRM experiments using words (Beato et al., 2012; Deese, 1959).

2.2.2 Influence of Retention Interval

What happens between the end of the study phase and the beginning of recollection trials on a false memory task (either a general or a specific DRM-like task) could be important in terms of recollection success. In the literature there are different tendencies. Some experiments left that time out with no task at all (Curran et al., 2001; Swick, Senkfor, & Van Petten, 2006) but others suggested filling that gap with several types of tasks, with the precaution of not interfering with the material to be recollected from memory: mathematical calculations (Herron & Rugg, 2003), judgment tasks (Garoff-Eaton, Kensinger, & Schacter, 2007), verbal tasks (Henkel, Johnson, & De Leonardis, 1998), working memory exercises (Nessler et al., 2001; Nessler &

Mecklinger, 2003), listening to music (Geng et al., 2007) or just using that time to place the electrode cap at the EEG laboratory (Duzel et al., 1997).

The length of that interval was also important, ranging from immediate recollection trial after learning (Van Damme & D'Ydewalle, 2009a; Watson, McDermott, & Balota, 2004) to several milliseconds between learning and recollection (Nessler & Mecklinger, 2003; Swick et al., 2006), several minutes (Curran et al., 2001; Henkel et al., 1998; Kim & Cabeza, 2007; Kuo & Van Petten, 2006; Kuo & Van Petten, 2008; Nessler et al., 2004; Vilberg & Rugg, 2007), delays of more than half an hour (Duzel et al., 1997), twenty four hours (Payne, Elie, Blackwell, & Neuschatz, 1996) or even after one month of the memory manipulation (Zhu, Chen, F Loftus, Lin, & Dong, 2010).

Our false memory task had an immediate recollection task, with no interval between study and test phase longer than 3 seconds of fixation of the screen.

2.2.3 Instructions for the Task

There was some controversy related with whether or not participants being aware of the nature of the false memory task might allow themselves to generate any type of metacognition related with it which might optimize their memory performance. Miller and Wolford explained how participants on a DRM paradigm task generated a meta-knowledge about the theme of the list and later on, at recollection or recognition task, they were more prone to respond positively to any word that met that theme. They generated a rather liberal response strategy that produced a high percentage of false recollection responses (i.e. lured items met the general theme) (M. B. Miller & Wolford, 1999). But arguably, the most important conclusion of this study was the authors´

explanation of this effect: it was not related with a memory process per se but was a decision process failure.

Another debate point was related with how false memory production might be interfered with or biased depending on whether experimenters explained the real meaning of those lured items to participants or not. In Gallo et al. experiment, they forewarned participants on the nature of lured items (i.e. items never studied before) and engaged them not to respond to them positively (Gallo et al., 1997). They saw that the false recollection ratio decreased but was still significantly higher than false alarms. They concluded that the strategy for reducing false memories must be more complex than only shifting their response criteria or knowing the lured nature of the task. They were uncertain as to whether false recollection depended on the encoding or decision making processes, because previous studies always warned participants before the study phase. A way to deal with this was to control when the warning was given to participants. Gallo and collaborators suggested that if warning was given after study but before testing, false recollection might depend on shifting criteria and not on other explanations such as associative activation (H. L. Roediger et al., 2001; Underwood, 1965) or strong gist trace (Reyna & Brainerd, 1995). Warning after study would not affect false recognition because by then, information leading to false recognition had already been codified. In the other hand, if warning was offered before study, experiments would not distinguish between shift control and association accounts. Their results concluded that false recollection effect was very strong even in the group warned after study, indicating that false recollection is beyond participants' conscious control.

Another work by McDermott and Roediger also warned participants before the study phase about the illusory nature of the critical lures but they did not avoid false remembering although their rate dropped but not as much as Gallo and colleagues experiment (Gallo et al., 1997). They concluded that the illusion was very strong even in fore- warned conditions (McDermott & Roediger, 1998).

These two studies indicated that warning participants had no significant effect on false recollection; therefore, instructions of our VFMT were not explicit on the lured characteristics of the items. We will describe in more detail instructions given to participants below.

Experimenters gave specific explanations to participants in order to avoid visuo-perceptual encoding and to engage conceptual-semantic processing of the items presented at the study scene. We warned participants that, at recognition task, the items to respond to would not be the same as at the studied scene. Instead, there would be prototypical items belonging to that general category. Participants must not respond based on whether testing items were exactly the same ones as the scene, but whether they belonged to the same prototypical category (i.e. we might present a bottle of wine that, even though it will not be exactly the same one as in the scene, it will still be a prototypical bottle of wine and not a bottle of milk or water, which would be completely different and would correspond to a negative response on the recognition task). Following this approach, we were pushing participants to process the information in a categorical manner, engaging them to create a semantic context where all the features presented at study matched and from where they could subsequently identify old items at recognition task. In other words, we were implicitly warning participants before encoding phase to produce a thematic context (i.e. a gist of the scene) that they could use at recognition (Brainerd & Reyna, 2001; Brainerd & Reyna, 2004; Reyna &

Brainerd, 1995). For a detailed description of the instructions given to participants, see below.

2.2.4 To Design a Powerful Task to be Used at the EEG Laboratory

One of the problems of the classic DRM paradigm is the quantity of useful trials where production of false memories was present. Having only one lured item per list made it complicated to pursue the number of trials needed for a psychophysiological experimentation context (Beato et al., 2012). Experiments in the literature with an ERP design to study generally false memories need a great amount of usable trials to reach significant signals when they are added into segments and grand averaged in voltage. Even though some authors using the DRM paradigm tried to increase the number of critical lures utilizing not only the more semantically related critical lure described but also the two (A. R. Miller, Baratta, Wynveen, & Rosenfeld, 2001) or the three (Wiese & Daum, 2006) most highly semantically associated with the list, this partial solution could also meet some methodological complications related with the probability of those extra-words being falsely recalled when they were not clearly equivalently lured (Beato et al., 2012).

Some of the most recent experiments utilizing the DRM paradigm are shown in Table 1, with a detailed description of the number of lured items they included at recognition-testing phase and the ratings of true memory and false memory achieved. All of them used lists of words, presented either visually or auditory at encoding, and the majority of them kept the modality of presentation constant at encoding and test (except for (J. C. Chen, Li, Westerberg, & Tzeng, 2008; Curran, 2000).

Only one experiment, to our knowledge, used the DRM paradigm with pictures instead of words, but their results did not include ERP data (Baioui, Ambach, Walter, & Vaitl, 2012). Their hypothesis was that a true memory will differ from a false memory on psychophysiological measures such as skin conductance, respiration rate, heart rate and finger pulse, intentionally based on the Concealed Information Test (CIT) (see (Verschuere, Ben-Shakhar, & Meijer, 2011).

Table 1

Description of latest studies using DRM paradigm on ERP experimental design.

	TOTAL[a]	LURES[b]	%HIT	%FM	%FA	Notes
(Fabiani, Stadler, & Wessels, 2000)	144	24	72.6	71.19	20.07	DRM-like task
(Curran et al., 2001)	288	96	63	53	23	Results from general performance
(Nessler et al., 2004)	180	80	84.6	19.6	9.5	
(Urbach, Windmann, Payne, & Kutas, 2005)	200/400	20/40	80/91	56/47	10/2	Data from exp1 and exp2 respectively
(Wiese & Daum, 2006)	144	48	80.6	47.9	4.5	
(Geng et al., 2007)	384	48	74	63	12	
(J. C. Chen et al., 2008)	120	24	87	49	4	Lure2 presentation produced a 64% of false memories
(Beato et al., 2012)	120	30	78.3	44.8	8.2	
(H. Chen, Voss, & Guo, 2012)	384	96	87	55	3	

Note: [a] Total number of items at test; [b] total number of lured items included at test.

In our experiment, VFMT creates a new experimental design where the rate of critical lures was increased with only one presentation at encoding, producing a valid number of trials for subsequent ERP analysis. As depicted lower in this chapter, our

VFMT will include a total of 150 critical lures over only 30 scenes presented at encoding, pursuing a reliable false memory.

2.2.5 Using Linguistic-Free Material

Another point addressed was related with the development of a free linguistic memory task. DRM paradigm task and the majority of the experiments performed to study false memory production were based upon linguistic material, mainly lists of words. They were visually or auditory presented in some experiments (Boldini, Beato, & Cadavid, 2013; Duzel et al., 1997; Geng et al., 2007; Nessler et al., 2001; Nessler & Mecklinger, 2003; Wiese & Daum, 2006); other studies changed the plurality of the words to create lured probes (Curran, 2000). On the other hand, other experiments utilized non-verbal material, such as faces (MacKenzie & Donaldson, 2007; Paller, Gonsalves, Grabowecky, Bozic, & Yamada, 2000), line drawings of objects or shapes (Kuo & Van Petten, 2006; Slotnick & Schacter, 2004), fractals (Speer & Curran, 2007) or coloured pictures of objects on grey backgrounds (Vilberg, Moosavi, & Rugg, 2006). Nevertheless, something rather infrequently included in those studies was the use of non-verbal material to create false memories at both learning and test.

Several studies focused on how stimuli presentation modality may affect false recognition. A series of experiments by Foley and collaborators followed this idea. In one experiment (Foley et al., 2010) the authors found that false memories rates were lower when lures were visually presented as pictures at different ages, dropping from 68 to 30% of false recollection. Following several experiments on this subject, Foley and collaborators offered what they named *imaginal activation hypothesis* (in the line of the *source-monitoring framework* (Johnson et al., 1993)). This hypothesis described that when an item was presented, a broad and spontaneous activation occurred at encoding, such as related thoughts, episodic related events, image-based thoughts, etc. If these were reactivated at recall, some participants could miss-report the items processed that way at encoding, producing false recollection (Foley & Foy, 2008; Foley et al., 2007; Foley et al., 2010). All this work was based on how likely it was that using different modalities of item presentation would implicate e the spontaneous process of generating visual cues associated with them that can be re-activated at test and bias a higher proportion false memory production. For these authors, using only pictures at encoding would increase false memories for they re-activate visual cues at test, interfering with monitoring processes based on the distinctiveness of materials.

Another experiment evaluated age differences in false memory production regarding false recollection induced by photographs with older and younger adults (Koutstaal, Schacter, Johnson, Angell, & Gross, 1998) and later on with elderly adults (Schacter, Koutstaal, Johnson, Gross, & Angell, 1997). In both of them, authors utilized photographs of events that participants previously saw on a videotape. Participants saw a videotape and were then asked to rate several aspects of the acting set up (i.e. judgment task). After an interference task lasting 20 minutes, they showed drawn photos of actions to participants and asked them to rate how similar those drawn events were to the ones presented previously on the videotape. Verbal recognition task was performed two days later: they were given a brief verbal description of objects and were to respond old when that object was on the videotape, being careful not to give that answer if the object was present on the photograph but not on the videotape. For the old-rated objects, they performed a R/K judgment. Under these conditions, results indicated that presenting photographs increased the probability of falsely remembering events and this was significantly higher for older adults compared with younger. The age related differences may reflect impaired source-monitoring abilities in the elderly group.

In a second experiment, these same authors modified the experimental conditions, not biasing cognitive processing of the photos that may help to distinguish between false and true photos (i.e. they were asked to rate how similar they were compared with the previous videotape, and how helpful to link photos and videotapes) but a different setting where learning and testing conditions developed a higher false recollection rate. To do so, they changed four aspects: a) during videotape viewing, participants were asked to simply count how many times actors went in and out of the scenario; b) photos were shown two weeks later, when participants returned to the laboratory; c) photo rating was related with pleasantness array and no reference to the previous videotape was required and d) after 20 minutes of interference task, verbal recognition task was performed, with R/K judgment. Under these conditions, authors expected to increase false recognition among younger adults, but rather than that, they did not. However, in older adults, false recognition of objects was constant during their two experimental designs, indicating that older adults usually confuse the origin of events that did happen and produce incorrect recollections (Schacter et al., 1997).

Doctoring photographs has been used to prove that photographs help subjects to imagine details about the event that they later confuse with reality (Garry & Gerrie, 2005). Based on the “lost in the mall” paradigm (Loftus & Pickrell, 1995) where a complete false narrative episode of being lost in a mall at childhood was implanted in participants´ memory, Wade and collaborators tried to lead similar false experiences based on four doctored photographs where participants´ own pictures were included in the picture of an event (e.g. hot-air-balloon ride). After 2 weeks of reviewing these photographs at least three times per week, half of the participants remembered something related with that ride (Wade, Garry, Read, & Lindsay, 2002).

To our knowledge, only one experiment used a single presentation of pictures with a clear thematic background as probes (M. B. Miller & Gazzaniga, 1998) in a close parallelism with our design. In that case, 12 scenes were presented one after the other at learning phase, and experimenters asked participants to remember as much as possible. After a 30 minute interval filled with fluency and perceptual tasks, an auditory recognition test with 72 words read out loud by the examiner was administered to participants together with a remember/know judgment task. Recognition task included 24 words being old, 24 critical lures previously removed from the scene but with a semantic relation with it, and 24 new. They also applied the DRM paradigm task to the same participants to analyse any possible differences between the modalities in false memory production. Results indicated that an equivalent number of lured responses appeared in both experimental displays (50% for pictures and 51% for words) with similar false alarms (9% and 12% respectively) and no differences between participants regarding the visual or verbal modalities. Authors concluded that this picture paradigm was as effective as the classic DRM paradigm to create false memories. They pointed out three main advantages in the abovementioned word task: a) it required only one single presentation; b) items at recognition can be counterbalanced to ensure their effects on memory could not be attributed to any characteristics of the items; and c) this picture paradigm avoided the source confusion effect, because in this case, the lured item was part of the scene and subjects were not generating a picture based on a series of events (as in the DRM paradigm). On the contrary, the mechanism involved in false memory in this picture paradigm may be related with how participants utilized the schema of the picture (Anderson, 1983): “they rely on the schema of the event and integrate expectancies from those schemas with stored perceptual details that actually occurred” (M. B. Miller & Gazzaniga, 1998). The classic experiment from Brewer and Treyens commented here was another example of how schemas may influence false recollection (Brewer & Treyens, 1981).

Compared with the picture paradigm (M. B. Miller & Gazzaniga, 1998), our VFMT presented the following differences: a) we maintained visual modality at recognition task instead of their auditory recollection test; b) we increased the number or critical lures to 5 per scene, a total of 150 critical lures instead of only two per scene and a total of 24; c) no 30-minutes interference task between encoding and retrieval was applied to participants (we applied the recognition task right after encoding); d) a small number of scenes (three on VFMT1.0 and only one on VFMT2.0) were presented at study; e) VFMT had 30 scenes instead of only 12; f) We presented scenes for 12 seconds with a 1 second interval between scenes, whereas the Miller presentation of scenes lasted 10 seconds ith a countdown of 5 seconds between each; and g) they modified original scenes to remove critical lures from the pictures whereas our critical lures came from the semantic and thematic context emerging from the scenes utilized during the test.

Recently, Baioui and collaborators investigated false memories with a rather similar design. Authors based their design on the DRM paradigm but created a visual procedure for both study scenes and recognition test items (Baioui et al., 2012). Encoding phase included 13 drawn scenes with a thematic context (e.g. cleaning) and recognition phase included six drawn items extracted from each scene: three studied items, two completely new and one critical lure. Their hypothesis was that a true memory will differ from a false memory on psychophysiological measures such as skin conductance, respiration rate, heart rate and finger pulse. Authors used the Concealed Information Test (CIT) (Verschuere et al., 2011). This procedure compares physiological measures involving crime-relevant responses, comparing characteristics from known objects to unknown objects, where a typical pattern of activity had already been described (Ben-Shakhar & Elaad, 2003). Results from Baioui and collaborators indicated how behavioural false memory percentage was lower compared with previous experiments with a similar design (39.5% compared with a 50% from the pictorial paradigm by Miller and Gazzaniga (M. B. Miller & Gazzaniga, 1998) but with a consistent very low false alarm rate of 3.1%. Regarding phychophysiological measures they concluded that true recognition showed higher electrodermal activity compared with false recognition.

Nevertheless, we were not able to strictly control a language-free environment for our task, because even though scenes and items did not contain any language, we could not control participants´ own learning and retrieval strategies used for this task. We collected informal reports from participants about their “tricks” remember better and collected qualitative information about the tendency of some participants to “translate” into words what was presented on the screen. We suggested that, even though the contents of the task were language-free, verbal encoding was possibly present in some participants and we did not control this aspect in our experiments.

2.3 Description of VFMT

2.3.1 Material and Stimuli

The task had a stimulus pool with a total number of 45 visual colour pictures, each recreating a proper semantic context (we will refer to as "scenes") and 450 visual colour images representing a single item or object (henceforth "items"). Scenes and items were selected from public internet resources ensuring that some basic conditions were met, such as being free for public use, having a proper size to be displayed on a computer screen, avoiding language coded information (unless necessary to clearly compose semantic meaning) and being complex enough to ensure a number of components that allow a memory task. Minor changes were made using Photoshop software in a small number or scenes and items to guarantee that basic characteristics were met. A maximum of 950 pixels of height or width were used for all scenes, depending on orientation (i.e. horizontal or vertical layout), to keep format as constant as possible. A similar procedure was applied for items, with 400 pixels most.

The scenes were presented with a visual angle of 14.16 by 10.39cm for landscape display and 8.66 by 10.39cm when they were portrait-like oriented. Regarding items, visual angle for landscape display corresponded to 6.94 by 4.77cm and for portrait-like orientation was of 6.94 by 4.34 cm.

Scenes were selected in order to provide a clear semantic context, a situation with a thematic meaning. There was a specific context for each scene, for example, scene number 1 represented a wedding thematic context and no items in that scene or in the associated items at recognition task were displayed that could belong to any other scene of the experiment to avoid either mistaken semantic relation or contextual information.

Hence, each scene created a semantic context from which we drew the specific semantic items for recognition memory.

The study phase of the experiment randomly selected 30 from the 45 scenes for each participant. Randomization of scene usage for each participant aimed to avoid any biasing of response as a way to reliably create an homogeneous performance among participants for all scenes. All scenes and items were presented once only during the whole experiment. Each scene was associated with 15 items, 5 of which represented old components of that scene (i.e. old items); another 5 items represented objects that were semantically related with the scene or its context but were not present (i.e. lure items), and the last 5 were not related semantically with the scene nor presented previously at study and randomly selected from a pool of old and lured items corresponding to the 15 scenes not included in the task (i.e. new items) (see Figure 6 for a detailed description).

2.3.2 Pilot Study

In order to prove that this new procedure was successful in developing a sufficient memory task, a pilot study using a pool of 45 scenes and 450 items with a small number of volunteers was carried out. Participants in this pilot will not participate again in the following experiments using this task.

The objective was to select the best scenes, remove those that were insufficient to generate either true or false percentages of responses and check task design features, such as stimulus presentation timing, presentation and response displays. Bangor University students were recruited using the same methods as described in chapter 3 of this thesis. Information about the experiment was given, on this occasion only for the behavioural aspect, as no EEG recording was required. Participants signed a consent form for participation (see Appendix Chapter 2 for information sheet and consent form) and the task was performed following the same instructions detailed in chapter 3 of this thesis for experiments with healthy students (i.e. experiment 1 with VFMT1.0).

Participants

Eight healthy participants were recruited amongst the students at Bangor University by SONA advertisement and by word of mouth. All participants gave their informed consent and were paid for their collaboration according to Bangor University rates. The mean age was 28 years old, (range 22-35) and half were male.

Material and Stimuli

A total of 45 scenes with five old and five lure items associated to each were utilized for this pilot. 30 scenes were selected for each participant from the pool of 45 together with the corresponding 5 old and 5 lured items and adding 5 new items for each scene. These new items belonged to the pool of items corresponding to the other 15 scenes not included in the study and had no semantic relationship with those studied

Procedure

In a quiet laboratory at the School of Psychology, Bangor University, the eight participants received information about the experiment and they were asked to sign a consent form for their collaboration. Instructions about experimental requirements were the same as described in chapter 3 of this thesis. At the end of the experiment, they were debriefed.

Results

Behavioural percentages of responses are described in Table 2. A total of correct hits of 76.33%, together with a low false alarm rate of 0.92% supported the validity of this task as a memory task, showing significant differences between hits and false alarms ($t(7) = 24.02$; $p<.001$). Its validity as a false memory task was certified, with significant differences between the percentage of 43.25% positive responses to lures against false alarms ($t(7)=8.853$, $p<.001$). The quickest response time corresponded to hits, followed by correct rejections of new items and false memories (see Table 2 for details on times). Significant differences on response time were found between hits and false memories (the former being quickest) $t(7)=-5.846$, $p=.001$) but no difference appeared between hits and correct rejections of new items, nor for false memories compared with correct rejections of lures.

Table 2
Behavioural results of Pilot Experiment.

	OLD	LURE	NEW
Percentage of R			
Yes	76.33	43.25	8.67
No	23.17	56.25	90.42
Response Time (in milliseconds)			
Yes	1008.85	1102.56	1232.27
No	1080.89	1166.05	1027.08

2.4 Summary

The rationale for a new design of false memory task was approached in this chapter. Overcoming some previous weaknesses of the DRM paradigm, opting for a new language-independent task and increasing the number of trials for successful ERP experiments were the objectives for this new task.

A randomized presentation of scenes for each participant compensated the lack of specific analysis regarding how likely each scene generated semantic context to each participant and with each of the items. Experimenters acknowledge that, without quantitative information on this aspect, the way to prevent any possible response biasing was to randomly present encoding material. This would also compensate any possible influence of some specific scenes, which evaluators acknowledge they might content specific cultural-related contexts (e.g. bullring scene). The alternative to random presentation of scenes was not considered by experimenters, because fixing the presentation order for each scene might have influenced response-rate of some of them due to the classically described primacy and/or recency effect (Murdock Jr, 1962).

The pilot study was performed to try out this new task, and was proved to be sufficient in generating a valid number of hits and an acceptable rate of false memories to be utilized as a false memory task. Participants discriminated successfully between hits and false alarms and their positive response rate to lure items was significantly different from false alarms.

Chapter 3: ERP Study Using a False Memory Task (VFMT1.0) on Healthy Participants

3.1 Overview

In this chapter, we will investigate neural correlates of false memory production on a sample of healthy students under an ERP design experiment. For the first time, the VFMT1.0 was used on ERP experimental design. This false memory task is based on visual-pictorial material only, within a thematic context, which we suspect engages a stronger semantic processing. Together with the high amount of critical lures trials available at recognition in this new task, we expected to obtain information on whether there are ERP differences between false and true memories. We will comment results in correlation with those of previous classic DRM experiments and some other ERP studies on episodic memory with a healthy population.

3.2 Introduction

The event-related brain potential technique (ERP) has become a key tool in cognitive science for it provides the precise time measurement of neural electrical activity related with an event. Additionally, thanks to new investigation techniques, which include larger electrodes arrays and special filtering methodologies, ERP provides information about the localization of cortically generated activity (Friedman & Johnson, 2000). It has been proven that introducing scalp-recorded ERP on episodic memory investigation helps to disentangle the processes taking part in this cognitive ability.

The first ERP experiment to be reviewed here which was based on true and false memory was Duzel and colleagues´ awareness experiment (Duzel, Yonelinas, Mangun, Heinze, & Tulving, 1997). They wanted to study subjective awareness of memory retrieval. They defined two ways of accessing information stored in memory: autonoietic awareness (corresponding to remembering, re-living, and traveling back in time) and noetic awareness (corresponding to knowing, to the present moment). They related these two processes with the remember/know paradigm used in false memory experiments, and tested them with a DRM paradigm. Their hypothesis was that ERP signals for Autonoietic awareness associated with "remember" judgements would be the same for true and false memories. Furthermore, they suggested that ERP components that appeared to be different from "remember" and "know" judgements, but are indistinguishable from true and false memories, corresponded to conscious awareness and that these were independent of non-conscious processes. Their experiment concluded that there were no ERP differences in response categories (i.e. true or false memory) but they found ERP differences regarding the awareness-based response (i.e. judging "remembering" or "knowing" for the given answer). Authors suggested that neural changes associated to consciousness might account for these differences.

Curran´s study on familiarity and recollection memory effects was the following work carried out on false memory, stating the ground basis for the ERP Dual Process Theory (Curran, 2000). This theory, as previously reviewed in the Introduction chapter of this thesis, stated that memory retrieval depends on two processes: familiarity and recollection. Classic ERP studies on true memory (Allan, L Wilding, & Rugg, 1998; Johnson, 1995; Rugg & Coles, 1995) described an ERP component related with the recollection process: the parietal old/new effect. This component can be found from 400-800ms at parietal sites and described a higher positivity for HITS compared to CR. It also state that this particular component was associated with the recollection of specific information such as study modality (Wilding & Rugg, 1997b) or the speaker´s voice (Wilding & Rugg, 1997a). The other process related with the Dual-Process theory is familiarity. ERP studies showed how this component was related to the N400 ERP component in a frontal area of the scalp showing more positive voltages for HIT compared to CR. Curran named this component as FN400 (Curran, 1999). It was previously studied by Rugg and colleagues as not being influenced by deep of processing (Rugg et al., 1998).

For this experiment (Curran, 2000), the author designed a plurality recognition procedure based on Hintzman and Curran´s previous experiment (Hintzman & Curran, 1994). Participants studied a list of words and executed a recognition test with three different types of items: same words, opposite plurality words and new words. Participants had to respond “yes” to the words that were the same and “no” to opposite plurality and new words. Curran’s aim was to replicate the FN400 and parietal old/new effect as familiarity and recollection ERP signatures, proving also that both familiarity and recollection were different processes for they appear at different times and in varied scalp locations. To prove so, he analysed familiarity comparing ERP voltages of similar words responded as yes to the voltage corresponding to new words responded by participants as no (equivalent to our HITS/CR), and recollection comparing voltage from studied words responded as yes to voltage corresponding to positive responses to similar words (equivalent to HIT/LURE). He found a consistent familiarity effect reflected in a left-superior-anterior NF400-like component peaking from 300 to 500ms with more negative values corresponding to CR when compared to HITS and FM. Results also showed a more positive left-parietal 400-800ms effect with higher voltages corresponding to HITS.

Curran´s final conclusion in this experiment was that familiarity and recollection ERP signatures (i.e. FN400 and parietal old/new effect) were generated in different areas of the scalp and can therefore be considered as two different processes according to the Dual-Process theory. Added to that, he found a time overlap between these two processes, suggesting that FN400 old/new ERP effects were associated to both recollection and familiarity processes. The parietal old/new ERP effect was associated to recollection processes.

Another important question to be solved was whether brain potentials could reflect behavioural differences in true and false recognition. In the literature of that time, controversial results complicated a clear resolution for this point. ERP studies to that date showed more similarities than differences between true and false memories (Duzel et al., 1997; Johnson et al., 1997). fMRI studies also suggested a similar activation of memory-related brain structures such as the parahippocampal cortex and the hippocampus during true and false recollection (Schacter, Buckner, Koutstaal, Dale, & Rosen, 1997). A positron emission tomography study using a DRM paradigm task also concluded a bilateral prefrontal activity associated to both true and false memory responses (Schacter et al., 1996).

Even though they did not use the DRM paradigm, Gonsalves and Paller study offered data suggesting that true and false recognition can be distinguished using ERP measures (Gonsalves & Paller, 2000). They framed their study on the idea of reality-monitoring errors that can be manipulated when increasing the perceptual vividness of an imagined event. To prove so, they designed a list of strong semantic associates that produced a semantic activation of the lured item from the study phase of experiment. Their experimental task required participants to create a visual image of the written word presented on the screen. For half of those words, a real picture of it was also shown. At recognition task, they had to decide whether the word was presented with a real picture or not. They recorded ERP during both study and recognition phases in order to compare them for those items correctly recognized.

Their hypothesis was that true memories would associate more perceptual details than false memories and that will be reflected on ERP, being related with memory-related imagery processes. Items correctly recognized would show a more positive occipital ERP signal at study compared with items forgotten during the recognition phase.

Gonsalves and Paller concluded that ERP signals of true and false recognition differed because of the lack of perceptual details available for reality-monitoring processes used for false memory items. Visual imagery played a role in the formation of false memory: the more the item was visually imagined, the higher the possibility that reality-monitoring processes failed and produced a FM.

Curran and colleagues designed an ERP experiment to give some light on the issue about differences between true and false memory (Curran, Schacter, Johnson, & Spinks, 2001). Their experimental design was based on DRM paradigm but it took into account participants´ response rate to create two different groups. In the one side, poor performers were those with a lower discrimination accuracy rate measured based on the proportion of HITS versus false alarm rates. On the other side, good performers' accuracy rate was higher. Authors described three response categories (i.e. old(yes), lure(yes) and new(no)) and eight scalp regions to analyse three main ERP effects described before (i.e. FN400, parietal old/new effect and left-frontal old/new effect).

This was the first experiment to consider the analysis of HIT versus FM responses as a false memory measure.

Results from this experiment proved very significant to establish the basis of ERP false memory research. Authors demonstrated that the late right-frontal ERP effect was related with a post-retrieval evaluation process that was engaged more frequently by good performers compared to poor performers, and that it was used as a measure to distinguish between these two groups. On top of this, they also described a parietal old/lure 400-800ms ERP effect, consisting in a higher voltage for HITS compared to FM responses on the parietal-left side recorded from poor performers group, finding no differences between response categories for good performers. A final result from this experiment was related with FN400 early 300-500ms ERP effect: no differences were found between poor versus good performers, neither between voltages corresponding to HIT and FM response categories.

After Curran´s investigations, Nessler soon produced a couple of studies that would also be very important in this field. The first one, in collaboration with Mecklinger and Penney, was focused on how encoding strategies may influence false memories production (Nessler, Mecklinger, & Penney, 2001). There were two possible explanations: first, false memories may arise by means of familiarity processes and secondly, by means of spreading activation of mental lexicon nodes, making difficult to correctly identify the source previously activated (Roediger and McDermott supported this last approach (Roediger & McDermott, 1995)). Nessler and colleagues indicated that a lured item was activated at encoding thanks to the associative activation with the rest of the items of the list, and therefore, at testing phase, lures and olds would be equally activated and ERP of true and false memories were found equal. This was also linked with the fact that DRM paradigm lists were built based on the semantic relation of one single word (i.e. the lured word) with the rest of the list, but with no guarantee of the same semantic strength between them, a fact that authors pointed out as a weakness of the DRM paradigm. To ensure a semantic connection between all items, authors created experimental lists based on a categorical noun generation experiment with students. The ten most typical words were selected for each category list for the study phase and all were equivalent with regards to typicality. They also ensured a high categorical relation for lured items. They selected lures from the seven most typical words for each category. The recognition test included five old items, five lured and ten completely new items.

ERP data was pooled into six regions of interest: left-frontal (F9, AFz, Fz, F5, FT9, FT7, Fc5), medial-frontal (AFz, AF3, AF4, Fz, F3, F4, FCz), right-frontal (F10, AF8, F8, F6, FT10, FT8, FC6), left-parietal (TP9. TP7, CP5, P9,P7, P5, PO7), medial parietal (CPz, Pz, P3, P4, PO3, POz, PO4) and right-parietal (TP10, TP8, CP6, P10, P8, P6, PO8). Time analysis was restricted to three intervals: 300 to 500, 500 to 700 and 1200 to 1600 ms.

Nessler and collaborators hypothesized that, considering experimental engagement on categorical processing of items at study, if false recognition was based on both familiarity and active recollection processes, then early fronto-medial old/new effect and parietal old/new effect would be equivalent for both true and false recognition. If false recognition was, on the contrary, based only on familiarity, no parietal old/new effect would be present.

To test this hypothesis, authors ran two different experiments. The first enabled to observe that false recognition was present for both familiarity and recollection ERP signatures. Smaller parietal ERP old/new effect was found for false recognition compared to true recognition; hence, authors suggested that false recognition was based to a lesser extent on recollection rather than true recognition.

Nevertheless, authors questioned whether differences between true and false recognition may be due not only to the semantic activation but to the encoding strategy of participants. They suggested that the recall strategy might also be important: the group of participants with a higher false recognition rate showed similar fronto-medial and parietal ERP effects for both true and false memory unlike the low false recognition rate group (no old/new false recollection ERP at all). Authors designed a second experiment to disentangle how the encoding strategy may influence false memory production.

A second experiment manipulated a type of encoding forcing participants to focus on conceptual similarities (category group) or perceptual features (item category) at study. Their hypothesis was that the category group will present same old/new ERP for both TM and FM as both will be related with familiarity and recollection processes. On the other hand, the item group will not show old/new early fronto-medial nor parietal ERP.

Results from experiment 2 showed that ERP differences were found despite similarity of category and item groups false recognition rates. True and false recognition showed similar old/new ERP in the category group (TM and FM are both based on an early fronto-medial familiarity effect and a parietal recognition effect) but different old/new effects for the item group (FM did not evoked early fronto-medial ERP as no familiarity was involved contrary to TM).

Nessler and colleagues suggested analysing new and old responses to lured items (i.e. FM versus CRL) as an alternative measure for familiarity, as they suggested that a lure word responded as yes should be more familiar than a lured word rejected with a no response. They found no early fronto-medial ERP signal but a small parietal positivity for false recognition in the item group. This may indicate that automatic spreading activation may happen in the absence of familiarity and may lead to false recognition. Results from the second experiment indicated that ERP voltages at early time window (300-500ms) for FM were more positive compared to CRL only when participants were engaged in the category processing of the items, finding no difference when item-based processing was engaged.

As a final conclusion based on these two experiments, authors suggested that differences in ERP patterns of true and false recognition depend on the encoding strategy: when based on categorical relationships, both TM and FM recalls depended on both familiarity and recollection processes; when based on item specific features, FM depended on recollection but not familiarity (Nessler et al., 2001).

To obtain further results that may resolve whether ERP may distinguish between true and false memory or not, another experiment was designed to find a distinctive ERP signature (Wiese & Daum, 2006). This experiment was also based on the Dual Process Theory and authors designed a DRM paradigm task maintaining the same presentation-of-items modality at study and test, to ensure item-specific strategies at retrieval. Experiment also asked participants to produce R/K judgement response, to study monitoring versus retrieval processes associated with true and false recognition.

The Wiese and Daum hypothesis was that familiarity effects could not solely explain false memory, because participants usually rated false memories as "Remembered" in a DRM task. Authors expected to find similar parietal old/new effect for FM and TM. They also expected to find an ERP anterior-frontal difference between TM and FM at late time window, which would be based on post-retrieval processes.

To test these hypotheses, authors analysed the old/new effect based on three factors: the response category (HIT, false alarm to lure (FM), the correct rejection of lure (CRL), the correct rejection to distractor (FA)), the anterior/posterior electrode distribution (Frontal, central, parietal) and the left/right electrode position (left, central, right) was performed for old/new ratings. They only selected 400-700ms for analysis and F5, F6, Fz, C5, C6, Cz, P5, P6 and Pz as electrodes.

They found an ERP old/new memory effect (400-700ms) for TM in the case of the left and middle electrode positions, but only at P5 for FM. Authors did not find any parietal ERP old/new effect differences between HITS and FM, in the line of previous studies (Curran et al., 2001; Nessler et al., 2001). In the case of frontal sites, a higher positive deviation for HITS compared to FM was found. FM differed on scalp distribution from hits and CR-L over left-posterior areas. This, again, gave evidence that frontal areas may distinguish between true and false recollection, whereas posterior areas might not.

Another important aspect to be considered was whether time intervals might influence true and false memory production. Nessler and his group reviewed previous experiments related with different retention delays in memory tasks and designed an experiment with two time delays between study and recognition testing (40 and 80s) (Nessler & Mecklinger, 2003). Authors assured that these two delays would implicate long-term memory structures. They also included in this experiment the analysis of an error-related negativity (ERN) ERP component, peaking at about 50-100ms when a participant committed an error in a reaction time task. This has previously been reported as electrophysiological evidence for the brain mechanism dedicated to monitoring performance (Falkenstein, Hohnsbein, Hoormann, & Blanke, 1990) and compensating errors (Gehring, Goss, Coles, Meyer, & Donchin, 1993).

The same six ERP regions of interest from previous studies of the group (Nessler et al., 2001) but only two time windows were selected in this case: early 300-600 and late 1000-1600ms. Results indicated that false recognition rates were higher at long delays compared to short delays. ERP signatures were also different regarding delay, finding an early mid-frontal familiarity ERP for false recognition at 40s but not present at 80s delay time. This fact revealed how the weakening of memory trace along time does not allow for familiarity-based recognition, being the reason why no midfrontal ERP was present at long delay.

Based on this time-dependent effect consideration, Chen and colleagues designed a very short-delay experiment to distinguish between a false memory production based on episodic memory processes versus a priming effect (Chen, Voss, & Guo, 2012). Authors collected ERP in their short-term-DRM task and included a repetition priming manipulation. Chen and colleagues suggested that, in this kind of short-term design, N400 ERP effect for lures (a component associated with semantic/conceptual processing) would play a very important role for false retrieval, but priming effects might be controlled in order not to interfere in the recollection process of this type of short-term design.

They also pointed out what previously was described by Nessler (Nessler et al., 2004) regarding the inconvenience of using NEW responses as a baseline to FM to define illusory retrieval. These authors also suggested using a FM versus CRL comparison to better isolate neural processing associated specifically to false recognition processes.

Data analysis was executed each 100ms time window with two main factors: condition (X3 HITS, FM, CRL) and location (X5 frontal: F3, Fz, F4; fronto-central: Fc3, Fcz, Fc4; central: C3, Cz, C4; centro-parietal: CP3, CPz, CP4; parietal: P3, Pz, P4). The first conclusion from this experiment was that a short-term DRM task produced a typical false memory effect. Clear N400 old/new effect was found from 300-500ms for HITS and FM (both relative to CRL as baseline) and it was localized on posterior electrodes for both TM and FM, but only TM produced a reliable frontal N400 ERP. This may account for semantic/conceptual activation to recognition judgements. Authors concluded that the N400 analysis gave preliminary evidence of a different neurocognitive processing for long-term and short-term memory displays: a short-term display relied more on a semantic/conceptual processing and fluency compared to long-term. Chen’s suggestion was that long-term designs depended upon monitoring-failure processes to produce FM and for short-term, the highest implication was for semantic/conceptual priming processes. ERP late positive component (i.e. LPC) peaking from 500-700ms and related with retrieval of specific details was present for TM but not for FM, in the line of a previous sensory-reactivation hypothesis formulated by Schacter and Slotnick (Schacter & Slotnick, 2004). For the later 700-onwards time window, classically related to monitoring processes rather than activation processes, a negative ERP effect appeared for FM but not for TM.

Chen concluded that the cause of short-term FM production may be a combination of three scenarios: a higher semantic/conceptual priming (as N400 showed) together with a failure to retrieve specific details (as proved by an LPC-like ERP) and a less effortful retrieval and/or monitoring of performance (reflected by post 700ms ERP).

A last significant contribution to the study on true and false memory using ERP techniques was offered by Nessler and his group. On this occasion, they focused on how classic true memory experiments might differ from new false memory approaches (Nessler, Friedman, & Bersick, 2004). Authors explained how classic old/new recognition studies would measure ERP voltages four old and new responses and would find what was previously reported: a difference in positivity (old being more positive than new) at early 300-500ms mid-frontal sites (i.e. medial-frontal episodic memory effect) and the same difference in positivity at posterior 500-800ms parietal sites (parietal episodic memory effect) (Friedman & Johnson, 2000; Rugg & Allan, 2000).

On the contrary, false memory designs (i.e. based on DRM task) presented an important difference from the classic approach. The problem was that lured items were the only ones associated with all other members of the study list, whereas old items were not necessarily related with other old items on that list. To overcome this problem, authors suggested creating lists of words and extracting both lures and old items from the same category, leaving new words to be used from a very different and not studied category. This design raised an issue regarding ERP signals: new items on false memory design stood out very easily from the rest of the items (both lures and old) due to their absence of semantic relation to the concept. Therefore, authors suggest that ERP analysis from false memory designs must not focus on new responses as classically performed (Curran, Schacter, Johnson, & Spinks, 2001; Nessler et al., 2001) but on correct rejections to lure items (i.e. CRL) instead. This was the authors´ statement of the old/not lured effect of false memory experiments, suggesting to be the equivalent to old/new effect in classic memory designs.

The main difference between these two designs appeared at test phase according to Nessler and colleagues. Classic designs used both old and new items from the same semantic category extracted from the study phase whereas false memory designs used old and lure items from the same semantic category but new items were not. The classic method did not allow selecting responses using semantic strategies and the false memory design capable of rejecting new but not lures based on a semantic strategy.

Nessler and collaborators´ aim of this experiment was to replicate old/new early and posterior ERP effects on classic design using a false memory design. They based analysis on similar procedures, with two time windows of interest (i.e. early 400-500ms, late500-700ms) and five regions of interest (Anterior-frontal: AF7, AF3, AFz, AF4, AF8; Frontal: F7. F3, Fz, F4, F8; Central: C5, C3, Cz, C4, C6; Parietal: P7, P3, Pz, P4, P8; Parieto-occipital: PO7, Po3, POz, PO4, PO8) and laterality (X5 Far left: AF7, F7, C5, P7 PO7; Left-medial: AF3, F3, C3, P3, PO3; Medial: AFz, Fz, Cz, Pz, POz; Right-medial: AF4, F4, C4, P4, PO4; Far-right: AF8, F8, C8 P8 PO8) to analyse two groups of participants separately (i.e. implementing a classic versus false memory design).

Data suggested that new responses behaved on ERP differently in classic versus FM design experiments: the classic approach showed new items were rejected based on item-specific strategies whereas in FM design a semantic strategy was utilized to reject new items. Added to this, both early and late ERP memory effects were present in FM design when comparing HITS versus correct rejections of lured responses. Hence, conclusion from this experiment stated that false memory designs must consider effects of semantic novelty to explain true and false memory production.

A last experiment that needs to be commented here was Beato and colleagues´ optimized design of a DRM paradigm classic task, suitable to be used in an ERP experiment. Experiments reviewed so far in this introduction were adaptations or different versions of the classic DRM paradigm task, providing more trials of false memory responses in order to successfully record ERP. An alternative was to utilize category lists (Goldmann et al., 2003; Nessler, Mecklinger, & Penney, 2001) but the degree of semantic association with the lure is not quantified as it is for the DRM paradigm. Beato and collaborators used 10 DRM lists with 3 lures and tested them with students at university so as to study how the level of processing at study may influence false memory production (Beato, Boldini, & Cadavid, 2012).

Regarding ERP effects, they were expecting to find that, from 500-800ms where old/new effect had been stabilised at parietal sites, ERP for HITS would be equal to ERP for FM. At this same time window and effect, they expected deep processing to produce a larger parietal effect than shallow processing. At the late time window, from 1000-1500ms where a right-frontal old/new effect had been described, authors expected to find the same ERP signal for HIT and FM corresponding to monitoring processes. On the other hand, regarding levels of processing, they expect more positive voltages for deep processing compared to shallow.

Results from Beato´s experiment suggested that ERP correlates of false memory retrieval were equivalent to true recognition, in all time windows (300-500, 500-800 and 1000-1500ms) and all electrodes of analysis (Fz, P3, F6) when a DRM classic paradigm is used. This might be indicating that both true and false memory depend on the same underlying processes. On top of that, authors suggested that false memory is not the result of an early familiarity response to items at recognition test, but a failure of retrieval and/or monitoring process intervening later on. Regarding the level of processing during the study phase, results indicated there were no differential effects on true and false memory.

In our experiment, we will base our analysis on previously reviewed studies and we will include specific time windows and regions of interest. We will also follow the suggestion to include CRL analysis as a valid measure of false memory when compared to FM responses (i.e. FM versus CRL to measure false memory as opposite to HIT versus CR to measure true memory), as we consider it an important piece of information to explain and discuss memory performance within a dual-process framework without the influence of a salient effect of new responses in this task. We also increased the number of lures per list and the categorical relationship between all items in the testing list to engage deeper semantic processing, and utilized a short space of time between encoding and recognition tasks. In addition, we will finally focus on the previously described three main ERP effects: early frontal 300-500ms familiarity effect, a parietal-left 500-800ms recollection effect and the late right-frontal 1000-1200ms monitoring effect.

In this experiment, we aim to replicate results from our pilot study (see chapter 2 for details) suggesting that this VFMT 1.0 is a suitable task to produce true and false memory responses at a similar rate to those used in previous studies (Beato et al., 2012; Curran et al., 2001; Wiese & Daum, 2006).

We expect to replicate ERP old/new effects at three main time windows of analysis using VFMT1.0. We aim to find a positive voltage related with HITS when compared to CR at frontal localizations in an early time window (300-500ms) that may account for familiarity influence on retrieval, as has been found previously in the literature (H. Chen et al., 2012; Curran, 2000; Nessler et al., 2001; Nessler et al., 2004; Wiese & Daum, 2006). We hypothesize that true and false memory at this very early time and with our short-term retrieval memory design, they will both depend upon familiarity and semantic-activation related processes, therefore we expect no differences between ERP signals corresponding to true and false memory retrieval (i.e. HIT versus FM)(Nessler et al., 2001). Regarding the alternative measure of false memory (i.e. FM versus CRL), which has been suggested a better tool to use in this false-memory designed type of experiments (H. Chen et al., 2012; Nessler et al., 2004; Wiese & Daum, 2006), we expect to replicate ERP voltage differences found at this early time window following previous studies (H. Chen et al., 2012).

For the next time window of the analysis, we aim to replicate classic old/new positive voltages for HIT responses when compared to CR from 500-800ms peaking at parietal sites. Regarding false memory measures, we also expect to find differences in voltages, being HITS more positive than FM, and FM more positive when compared to CR. In addition, we predict that comparison between FM versus CRL will produce no differences in voltage at this time window, because none of these measures are based on recollection processes.

We finally predict to find at the last time window of analysis, from 1000 to 1200ms, the previously documented old/new effect, with HITS voltages being higher when compared to CR at right-frontal areas of the scalp. As this time window has been related with monitoring processes, we are expecting to find differences between HIT and FM voltages here, resulting from a distinct evaluation-of-response process.

3.3 Material and Methods

3.3.1 Participants

Twenty healthy adults (45% men and 55% women) mainly right-handed (85% right-handed and 5% ambidextrous) participated in this experiment. They presented a mean age of 29 years old (SD = 7.18) with normal or corrected to normal vision. All participants were able to read the Information Sheet and after asking any required questions, they signed the consent form. They were paid for their participation in the study based on Bangor University´s standard rates. Ethical approval was given by School of Psychology at Bangor University for this experiment.

3.3.2 Stimuli

For this experiment, we utilized the same stimuli depicted at Chapter 2. See Figure 7 for a description of the experimental setting.

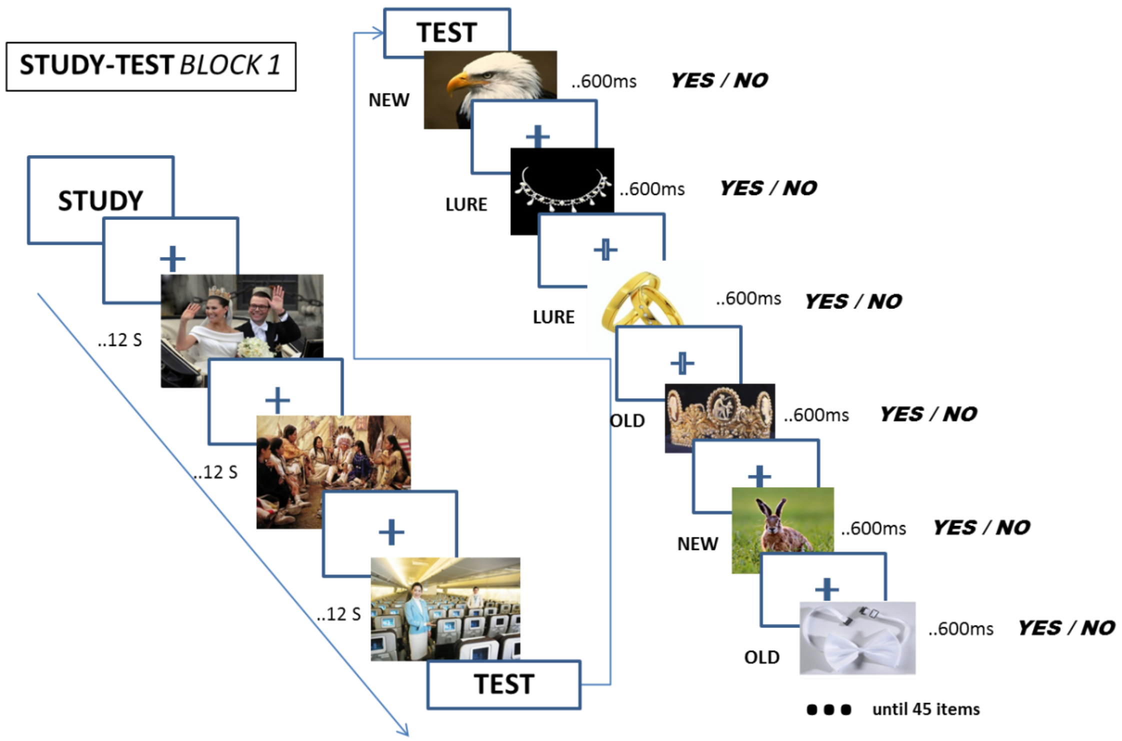

Figure 7 Description of a single study-test block with detailed timing and characteristics of testing conditions.

<u>*3.3.3 Procedure*</u>

The experiment was designed as study-test consecutive phases, naming a complete study-test phase as “block”. In the study phase, the participant saw the word STUDY on the screen for 2 seconds, after which, a series of 3 scenes were presented for 12 seconds each, with a fixation cross of 300ms between them. After that, the test phase started with the word TEST appearing on the screen for 2 seconds while participants got ready to use the response buttons on a keyboard laying on their lap: the F key for “yes” responses with the right hand and the J key for “no” responses with the left hand (counterbalanced order across participants) after each item presentation. The items to be tested were presented on screen during 600ms after 300ms of fixation cross and participants had 1400ms of blank screen to complete response until the next fixation cross was shown, indicating the end of responding time and the next item presentation. Following the presentation of all the items (45 items including 15 old, 15 lures and 15 new for each scene), another STUDY screen display indicated that a new block started. The whole experiment lasted about 35 minutes and was composed by 3 blocks, separated with a blank screen of 5 seconds: the first block with four study-test sets, the second with three sets and the last one with another three, all of them with relax periods self-managed by participants in between (see Figure 8).

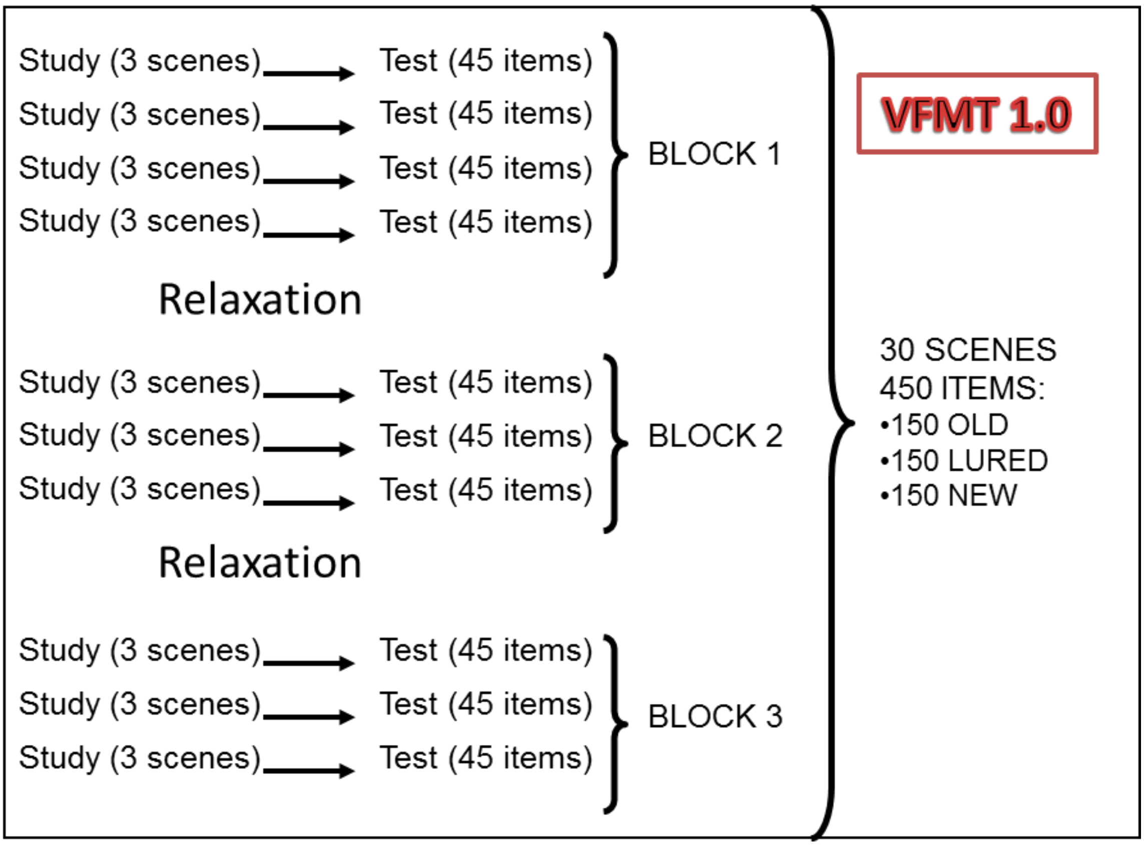

Figure 8: Study-test block and detail of the number of scenes and items tested.

Each item was defined by four different response categories as hit, correct rejection, false memory and correct rejection of a lured item depending on the participant´s responses. We considered hit-category an old item responded by the participant as “yes” (HIT); a false memory-category as a lured item responded as “yes”

(FM); a new-category as new item responded as “no” (CR); and a correct rejection of a lured-category as lured items responded as “no” (CR-L) (see Table 3).

Table 3
Description of the Different types of responses codified

	ITEMS		
RESPONSES	Old	New	Critical Lure
Yes	*HIT*	*FALSE ALARM (FA)*	*FALSE MEMORY (FM)*
No	*MISS*	*CORRECT REJECTION (CR)*	*CORRECT REJECTION OF LURE (CRL)*

Testing sessions were executed individually. Evaluators gave participants information about the experiment and a consent form that they must read and sign to carry on with the task (see Appendix Chapter 3 for Consent Form and Information Sheet). Experimenters asked participants to wash their hair with baby shampoo in order to ensure connectivity of the electrodes from the EEG cap that was used by the experimenters to record participant´s brain activity during the memory task. They were conducted to a Faraday electrically-isolated room in the EEG laboratory. Small amounts of alcohol to clean the skin surface and some electrolytic gel were used on each electrode, to ensure optimal electrical connection. The more suitable size of cap was used for each participant (i.e. 56 or 58 diameter size cap. Memory task was displayed using Presentation 14.0 software on a 38cm computer screen placed at approximately 80-100cm from the participant, producing the same visual angle that was depicted at Chapter 2. Response keyboard was placed on participants´ lap to facilitate response pressing without general body movement that could interfere with the EEG signal. Prior to the memory task,20 trials of eye movement testing for each four directions (i.e. up, down, left and right) and for blinking trial was performed to posteriorly remove eye movement artefacts from our signal. Right after the eye movement task, experimenter introduced VFMT to participants.

Verbal instructions were given to participants, asking them to study a series of scenes in order to perform a later memory task on them. Examiner informed participants that they will see the word STUDY on screen and right after that, they will see three different scenes for a short period of time each. During study phase there was no response required from them, they were simply asked to look carefully at those scenes and remember as much as they could from them. After these three scenes, participants will see the word TEST on screen, and a series of single items will appear on the screen for a very short period of time, one after the other. They were asked to indicate, via button presses, whether they remembered each item being shown in any of the previous presented scenes. The response assignments were counterbalanced across subjects. The instructions were specific with the fact that items were not the ones exactly from the scene but general representations of that particular object (i.e. the item “bottle of wine” shown during the test phase would not be exactly the same one shown in the scene, but still is a prototypical bottle of wine and not a bottle of whiskey, so the response should be “yes”) to facilitate conceptual/semantic processing. Participants were asked to respond as fast and accurately as possible, even though some of the responses might be difficult to decide on. Time to respond for an item ended when the next item to be tested appeared on screen and participants were instructed not to respond retrospectively as that response would not be considered. No explicit instructions related with lured items were given to participants, hence they could respond naively regarding this matter. After testing all items related to the studied scenes, participants would see the word STUDY again on screen and learning and later tasting were done under the same conditions.

3.3.4 ERP procedures

Sixty-four scalp positions were continuously recorded on EEG (FP1, FP2, APz, F9, F7, F5, F3, F1, Fz, F2, F4, F6, F8, F10, FT7, FC5, FC3, FC1, FCz, FC2, FC4, FC6, FT8,T7, C5, C3, C1, Cz, C2, C4, C6, T8, TP9, TP7, CP5, CP3, CP1, CPz, CP2, CP4, CP6, TP8, TP10, P9, P7, P5, P3, P1, Pz, P2, P4, P6, P8, P10, PO9, PO7, POz, PO8, PO10, O1, Oz, O2, Iz). Following the extended10-20 system, electrical recording activity using Brainamp DC, Brain Vision Recorder V2 was collected. All electrodes were embedded in an elastic cap (Easy Cap) and fixed both to the chest and below participant´s chin. Two extra electrodes were placed below both eyes (IO1 and IO2) to measure ocular eye movements. During recording, reference electrode was AFz and FPz was ground. Later on, experimenters re-referenced offline to the average reference by adding the estimated original reference. During EEG recording, channels close to saturation were manually reset, and impedance was kept below 5khz. Recordings were made with amplified and digitalized channels each with bandwidth DC-250hz, 1khz sampling rate and 10 mega-amperes input impedance. Experiment took place within a Faraday room to minimize the effect of electrical noise.

Control of visual artefacts required a previous measure of 20 trials each of 5 prototypical eye movements (left, right, up, down, blink) in a calibration phase prior to the proper experiment. Experimenters used this data to train an ICA to detect eye movement components, selecting the appropriate components by visual inspection before offline removing them from the experimental data.

Offline, raw EEG data was band-pass filtered to include voltages from 0.1 to 35Hz below. EEG processing was divided into epochs starting 200ms before stimulus onset and finishing 1500m after independent component analysis was used to reduce eye movement and blink artefacts and epochs with clear drift or noise were excluded. ERP were time-locked to stimulus presentation and segmented according to responses: for positive responses to old items (HITS), positive responses to lured items (FM), negative responses to new items (CR) and negative responses to lured items (CR-L).

3.3.5 Statistical Analysis

Behavioural analysis was based on two-tailed paired t-test calculations for both RT and response percentage. Levene´s corrections were applied when homogeneity of data was violated. We took into consideration ERP mean amplitude measures for each relevant response (i.e. HITS, FM, CR and CR-L) and difference waves for memory related effects (i.e. HIT versus CR, HIT versus FM and FM versus CR) where considered for statistical analysis.

Statistical analysis for ERP data was based on previous studies in the literature, reviewed here at introduction section. We selected and analysed separately the following specific time intervals of interest to study main ERP effects: 300 to 500ms for the early midfrontal effect, 500 to 800ms for parietal old/new effect and 1200 to 1500ms for the late right-frontal effect.

In order to avoid an inflation of type I error due to the large number of tests involved, (Oken & Chiappa, 1986), we selected electrodes based on previous studies (reviewed at introduction section of this chapter), focusing statistical analysis on areas previously found of interest for ERP memory design. In our case, from the 64 available channels we selected only the following: F7, F5, F3, F1, Fz, F2, F4, F6, F8, T7, C5, C3, C1, Cz, C2, C4, C6, T8, P7, P5, P3, P1, Pz, P2, P4, P6, P8. They were grouped into three factors: localization (frontal, central, parietal), lateralization (left, central, right) and electrode (x3).

We calculated four-way repeated measures ANOVA with response category as a factor with two values, either HITS or FM versus CR responses, and the corresponding three factors of region of interest. We focused on the main effects related to response category and any interaction effect that might relate response category to any of the localization and lateralization included in this analysis.

Bonferroni correction for multiple comparisons was calculated and post-hoc analysis was executed for significant interactions between factors. Significance level of 0.05 was considered.

3.4 Results

3.4.1 Behavioral Results

T-test analysis between HITS and false alarms proved the classical memory effect in the case of this memory task that showed a significant difference between them ($t(19)=30.1$; $p=.000$). False memory effect was also proved to exist in this task, with a difference between FM and false alarms production ($t(19)=13.58$; $p=.000$) (see Figure

9**Error! Reference source not found.** and Table 4 for percentages).

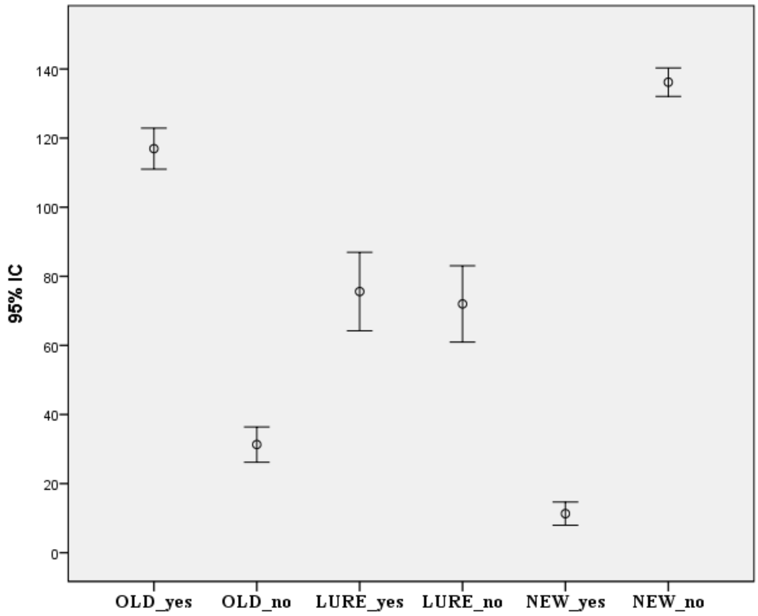

Figure 9 Estimated means for each item type and response with 95% of interval of confidence. Responses at horizontal axis are described depending on the original type of item (old, lured or new) and the actual participant´s response (yes or not).

On average, participants correctly responded to old items 116 times over a total of 150, reaching a percentage of HIT responses of 77.9%. Percentage of false alarms to new items was very low (7.2%) and interestingly enough, a very similar amount of positive and negative responses to critical lures were counted in this sample (see Table 4 for detailed behavioural results).

The analysis of response times showed that, in general, responding correctly to any category was faster than responding incorrectly (in this case a "yes" response to a lured item was considered a correct response). The fastest response corresponded to HITS, followed by correct rejections to new items, this last category having a similar time compared to FM. Significant differences were found when comparing response time for HITS with FM $t(19)= -4.9$, $p< .001$, with CR $t(19)=-2.811$, $p=.011$, and with

FA t(19)=-4.87, p<.001. Responses to FM were faster compared to CRL´s responses t(19)=-5.288, p<.001 and FA t(19)=-3.124, p=.006. CR responses were significantly faster than FA t(19)=3.814, p=.001. Detailed information about response performance and response time can be found in Table 4.

Table 4
Mean response time values in milliseconds for each response category.

	CATEGORY ITEM					
	OLD		LURED		NEW	
	Yes	No	Yes	No	Yes	No
% R	**77.97**	**20.87**	**50.4**	**48**	**7.5**	**90.8**
Total R	116.95	31.3	75.6	72	11.3	136.2
	(12.7)	(10.9)	(24.3)	(23.6)	(7.2)	(8.9)
RT	942.03	1071.5	1010.7	1129.7	1135.6	1006.2
	(219.5)	(248.2)	(232.5)	(259.2)	(235.4)	(239)

Note: R responses; RT response time in milliseconds. Standard deviation values between brackets.

3.4.2 ERP Results

Visual inspection of the waves indicate how higher differences between HITS and CR can be found at middle line electrodes, from frontal to parietal electrodes but proving maximal at central sites (i.e. Cz and CPz) and from 400 to 700ms approximately. This difference is also present at right-sided fronto-central electrodes. A step-like distribution of voltages appears at mid-central electrodes, with a higher voltage for HIT, followed by FM, CRL and finally CR. It is worth noting that the fronto-central electrode seems not to distinguish voltages from FM and CRL, but shows a clear old/new effect. Another interesting fact is that FM voltage is closer to HIT´s voltage and, on the other hand, CRL voltage is similar or closer to CR´s voltage at CP4 and Pz electrodes. A last comment on these waves is that similar voltages for all response categories appeared in left-sided electrodes (see Figure 10).

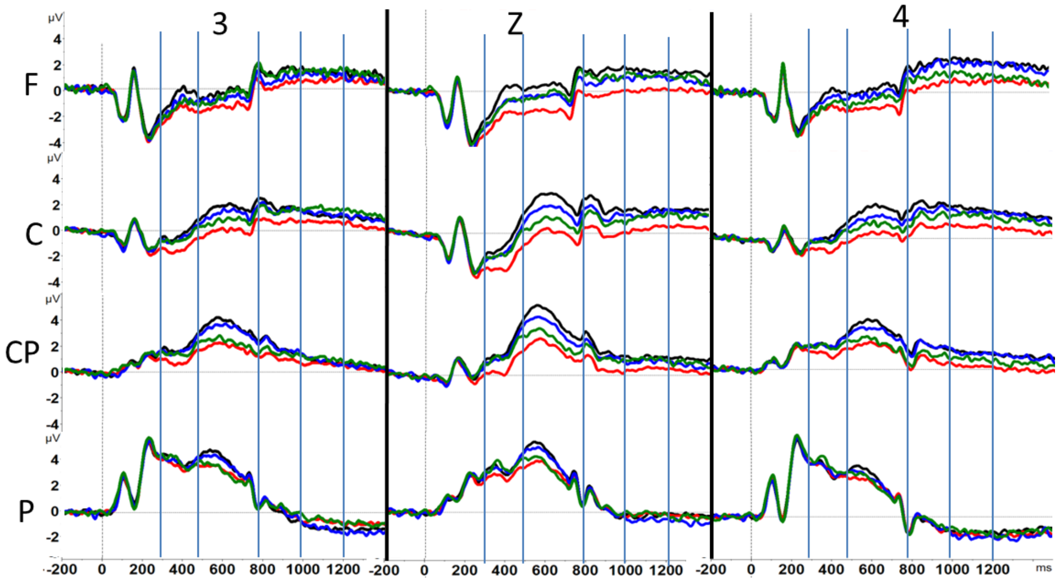

Figure 10: Mean voltages for all four response categories (HIT in black, CR in red, FM in blue and CRL in green) displayed for three lateralization (3 for left, Z for middle and 4 for right) and four localization sites (F, C, CP and P). Milliseconds are displayed in X axis and microvolts in Y axis.

Topographies of the relevant difference waves (hits minus CR, hits minus FM, FM minus CR and FM minus CRL) showed a distribution in each time window of interest that matches some of previous results reviewed in the introduction of this chapter (i.e. mid-frontal early effect) but also different localizations for some other effects (500-800ms parietal effect) (see Figure 11). We will describe in more detail each memory effect on the three time windows of interest.

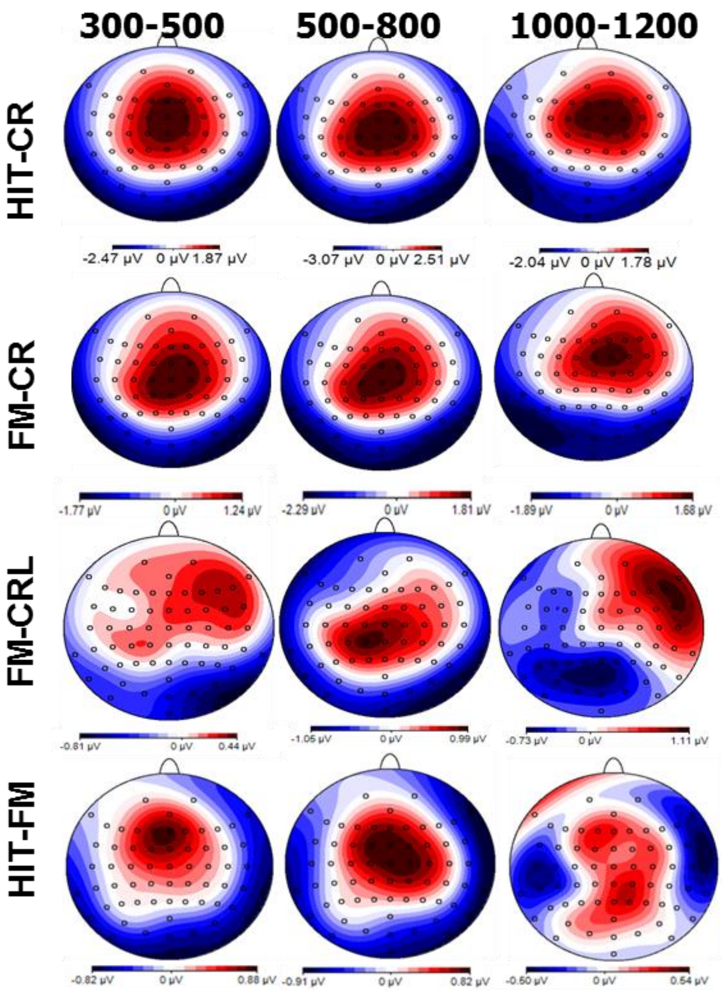

Figure 11: topographical maps of voltage distribution from difference waves corresponding to HIT-CR, FM-CR, FM-CRL and HIT-FM

TRUE MEMORY: HIT versus CR

On the early 300-500ms time window data indicated main effect of response category, confirming significant differences between HIT and CR, $F(1, 19) = 77.1$, $p < .001$, being HIT more positive compared to CR ($M = 0.51$; $SE = 0.113$ and $M = 0.06$; $SE = 0.113$ respectively). Interaction was found between lateralization and response category, ($F(2, 38) = 29.22$, $p < .001$) and follow-up paired comparisons indicated that

HIT voltage was significantly more positive compared to CR only in the case of middle electrodes, $F(1, 19) = 60.60$, $p < .001$, with HIT M = 1.024, SE=0.347, and CR M = -0.244, SE = 0.318; no differences reported for left $F(1,19) = 0.629$, $p = .44$ and right $F(1,19) = 0.001$, $p = .98$ hemispheres. Interaction between localization and response category was also significant $F(1.18, 22.5) = 15.15$, $p < .001$. Post-hoc contrasts showed significantly more positive voltages for HIT responses at frontal (M = -0.79, SE = 0.47, $p<.001$) and central (M = -0.46, SE = 0.28, $p<.001$) electrodes when compared to CR (M = -1.59, SE = 0.47 and M = -1.2, SE = 0.241 at frontal and central respectively), but not at parietal electrodes, where HIT showed an equivalent mean voltage compared to CR (M = 2.77, SE = .49 and M = 2.96, SE = .44 respectively, $p = .2$).

This indicates how HIT responses at this time window were systematically more positive in voltage than CR responses; therefore indicating the presence of the classic old/new effect. Localization for this effect was mid-frontal and mid-central with no differences at parietal localizations.

When analysing the following time window corresponding to 500-800ms, a main effect was found for response category $F(1, 19) = 98.04$, $p < .001$ with higher voltages corresponding to HIT responses compared to CR voltages (HIT M = 0.82, SE = 0.1 and CR M = 0.23, SE = 0.11). An interaction effect was found between localization and response category $F(2, 38) = 8.14$, $p = .007$ and follow-up paired comparisons indicated that HIT was more positive than CR at frontal (M = -0.3; SE = 0.5 and M = -1.12, SE = 0.43 respectively, $p = .002$) and central localizations (M = 1.15, SE = 0.22 and M = 0.001, SE = 0.21 respectively, $p<.001$), but not at parietal localization (HIT M = 1.6, SE = .58 and CR M = 1.81 , SE = .45, $p = .45$). Interaction effect of lateralization with response category showed significantly higher voltages for HIT $F(1.85, 34.7) = 31.23$, $p < .001$ only at middle areas (HIT $M = 2.1$; $SE = 0.32$ and CR $M = 0.43$; $SE = 0.32$) but no differences were found between HIT and CR at left (HIT $M = .28$, $SE = .16$ and CR $M = .3$, $SE = .16$, $p = .89$) or the right hemisphere (HIT $M = .09$, $SE = .16$ and CR $M = -.04$, $SE = .17$, $p = .35$).

These results indicated that at this time window, the old/new effect was also present, being HIT responses systematically more positive than CR. No differences in voltage were present between hemispheres. This old/new effect presented mainly a fronto-central localization.

In the 1000 to 1200ms time window, the amplitude for HITS of $M = 0.51$, $SE = 0.13$ was more positive than for CR, $M = 0.06$, $SE = 0.113$, as indicated by a significant main effect of response category, $F(1, 19) = 77.1$, $p < .001$. The interaction between response category and localization was significant, $F(2, 38) = 15.15$, $p < .001$. Post-hoc comparisons showed that the amplitude of HITS compared to CR was more positive in the case of frontal (HITS $M = -0.79$, $SE = 0.47$, CR $M = -1.6$, $SE = 0.47$, $p < .001$) and central electrodes (HITS $M = -0.46$, $SE = 0.28$, CR $M = -1.19$, $SE = 0.24$, $p < .001$), but did not differ at parietal localizations (HIT $M = 2.77$, $SE = .49$ and CR $M = 2.96$, $SE = .44$, $p = .2$). The interaction between lateralization and response category was also significant, $F(1.9, 36.4) = 29.22$, $p < .001$. Post-hoc tests showed that the amplitude of HITS compared to CR was more positive only in the case of the middle electrodes (HIT $M = 1.03$, $SE = 0.35$, CR $M = -0.24$, $SE = 0.32$, $p < .001$), but did not differ in the case of the left or the right lateral electrodes (HIT $M = .06$, $SE = .2$ and CR $M = -.004$, $SE = .22$, $p = .44$ for left and HIT $M = .43$, $SE = .18$ and CR $M = .43$, $SE = .22$, $p = .98$ for right). These results indicate the presence of an old/new effect between 1000 and 1200ms. Similarly to the 500-800ms time window, this positivity has a fronto-central and midline maximum.

FALSE MEMORY: FM versus CR

Regarding the first time window corresponding to 300-500ms, a main effect of response category was found $F(1, 19) = 24.33$, $p < .001$ being FM responses more positive with M = 0.36, SE = .01 when compared to CR M = .06, SE = 0.11. Interaction between localization and response category was found $F(2, 38) = 7.71$, $p = .02$ and a follow-up analysis indicated that FM voltages were more positive compared with CR at frontal (FM M = -1.12, SE = 0.43 and CR M = -1.6, SE = 0.47, $p<0.001$) and central sites (FM M = -0.62, SE = 0.27 and CR M = -1.2, SE = 0.24, $p = .002$) but no difference was found at parietal sites (FM M = 2.82 , SE = .44 and CR M = 2.96, SE = .44, $p = .35$). Lateralization interacted with response category $F(1.6, 30.2) = 18.04$, $p < .001$) with posterior post-hoc comparisons indicating that higher voltage for FM corresponded exclusively to middle sites (FM M = 0.6, SE = 0.32 and CR M = -0.24, SE = 0.32, $p < .001$) as no difference was present for left (FM M = -.03, SE = .204 and CR M = -.004, SE = .222, $p = .712$) nor right lateralization (FM M = .507, SE = .204 and CR M = .43, SE = .224, $p = .219$).

In conclusion, from 300-500ms, false recollection presented an old/new ERP effect, with more positive voltages for FM responses when compared to CR. This effect had a fronto-central localization with no lateralization effects but a significant middle difference.

The following 500-800ms time window also presented the main effect of response category $F(1, 19) = 58.26$, $p< .001$, with FM responses presenting significantly higher voltages compared with CR (FM M = 0.62, SE = 0.1 and CR M = 0.23, SE = 0.11, $p < .001$). Interactions were found between localization and response category $F(2, 38) = 8.27$, $p = .001$ with significantly higher voltages for FM compared to CR at frontal (M = -0.51, SE = 0.46 and CR M = -1.12, SE = 0.43, $p = .005$) and central (FM M= 0.82, SE = 0.21 and CR M = 0.001, SE = 0.21, $p<.001$) but no difference found at parietal sites (FM M = 1.55, SE = .52 and CR M = 1.81, SE = .45, $p = .207$). Interaction between response category and lateralization ($F(1.8,35.1)=17.93$; $p<0.001$) showed again higher voltages for FM when compared with CR but only at middle sites (FM M= 1.53, SE = 0.3 and CR M = 0.43, SE = 0.32, $p < .001$), finding equivalent voltages for both response categories at left (FM M = .25, SE = .17 and CR M = .3, SE = .16, $p = .67$) and right localization (FM M = .08, SE = .17 and CR M = -.04, SE = .17, $p = .2$).

At this time window, old/new effects were also present when comparing FM and CR, with higher voltages corresponding to FM responses. This effect had a fronto-central and middle localization.

At the last 1000-1200ms time window, analysis indicated a main effect of response category $F(1, 19) = 13.41$, $p = 0.002$, with higher voltages for FM when compared to CR (FM M = 0.42, SE = 0.1 and CR M = 0.2, SE = 0.1, $p = .002$). Response category and localization showed significant interaction $F(2, 38) = 14.98$, $p< .001$, and follow-up analysis indicated that voltages for FM were more positive when compared with CR at frontal (FM M = 1.5, SE = 0.27 and CR M = 0.72, SE = 0.18, $p = .002$) and central (FM M = 1.52, SE = 0.2 and CR M = 0.89, SE = 0.17, $P < .001$). Later on, FM changed to be more negative at parietal localizations (FM M = -1.74, SE = 0.36 and CR M = -1.01, SE = 0.3, $p = .002$). Lateralization interaction with response category $F(1.8, 35.87) = 6.62$, $p=0.004$ indicated that FM was significantly more negative than CR in the case of left electrode localizations (FM M = 0.1, SE = 0.18 and CR M = 0.44, SE = 0.16, $p = .034$), but more positive at middle and right sites (middle FM M = 0.7, SE = 0.26 and CR M = 0.12, SE = 0.26, $p = .008$; right FM M = 0.47, SE = 0.17 and CR M = 0.03, SE = 0.15, $p = .012$).

In conclusion, at this late time window, a consistent higher voltage for FM responses indicated an old/new effect. Fronto-central areas were associated with this effect. Data indicated a lateralization to the middle-right hemisphere.

COMPARING TRUE VERSUS FALSE MEMORY: HIT-FM

For this analysis, we will consider that HIT will indicate a measure of true memory as opposite to FM that indicates a false memory measure. From 300-500ms the main effect of response category proved that voltage differences were statistically significant $F(1, 19) = 25.6$, $p <.001$ between true and false memory, with higher voltages corresponding to true memory (HIT M = 0.51, SE = 0.11 and FM M = 0.36, SE = 0.1, $p < .001$). Interaction was found between response category and lateralization $F(1.6, 31) = 8.28$, $p = 0.002$, and posterior post-hoc analysis indicated higher voltages for HIT only in the case of middle sites (HIT M = 1.03, SE = 0.35 and FM M = 0.6, SE = 0.32, $p < .001$) but not in the case of left (HIT M = .06, SE = .2 and FM M = -.03, SE = .2, $p = .17$) or right electrode sites (HIT M = .43, SE = .18 and FM M = .51, SE = .2, p

= .39). Localization presented no interactions with response category $F(1.12, 21.3) = 2.12$, $p = .16$).

These results may indicate that true and false memory significantly differed only at middle sites, true responses proving more positive in voltage than false responses.

At 500-800ms time window, true responses were significantly more positive in voltage than false (HIT $M = 0.822$, $SE = 0.1$ and FM $M = 0.62$, $SE = 0.1$, $p < .001$) as indicated by a significant response category main effect $F(1, 19) = 49.72$, $p < .001$. Lateralization and response category significant interaction was found $F(1.8, 34) = 9.98$, $p = .001$, resulting in significantly higher voltages for true when compared to false memory only in the case of middle sites (HIT $M = 2.1$, $SE = 0.32$ and FM $M = 1.53$, $SE = 0.3$, $p < .001$) but no difference in the case of the left (HIT $M = .28$, $SE = .16$ and FM $M = .25$, $SE = .17$, $p = .51$) or right hemisphere was statistically significant (HIT $M = .09$, $SE = .16$ and FM $M = .08$, $SE = .17$, $p = .96$). Localization interaction with response category was not significant $F(1.12, 21.4) = .96$, $p = .394$.

At this time window, true memory showed higher voltages when compared to false memory. This difference was significant only in the case of middle sites, with no localization effect found in this analysis.

At the last time window, from 1000 to 1200ms, main effect of response category was present $F(1, 19) = 4.96$, $p = 0.04$, with significantly higher voltages corresponding to true memory (HIT $M = 0.51$, $SE = 0.1$ and FM $M = 0.42$, $SE = 0.1$, $p = .038$). Lateralization and localization showed no interaction effects with response category ($F(2. 38) = 2.44$, $p = .1$ and $F(1.2, 22.75) = .17$, $p = .73$ respectively).

In conclusion, from 1000 to 1200ms, true and false memory ERP effect showed significantly different voltages. No localization or lateralization effects were present.

ANOTHER FALSE MEMORY MEASURE: FM VERSUS CRL

Based on the idea that new DRM paradigm experiments might provide further inside into the effect of distinctiveness of NEW items in the task, we also compared used CRL as a baseline when responding FM.

In this case, early 300-500ms ERP analysis showed main effect of localization $F(1.3, 24.5) = 23.75$, $p < .001$, finding higher positive voltages at parietal localization ($M = 2.92$, $SE = .46$) when compared to both central ($M = -.7$, $SE = .26$, $p < .001$) and frontal localizations ($M = -1.23$, $SE = .44$, $p < .001$). No further main effects for lateralization $F(2, 38) = 1.36$, $p = .27$ or response category $F(1, 19) = 2.25$, $p = .15$ were found. Interaction effects of response category with localization $F(1.3, 24.3) = 2.68$, $p = .1$ and with lateralization $F(2, 38) = .12$, $p = .89$ were absent.

This data suggested that, apart from a significant positivity at parietal sites as opposite to negativity in the case of fronto-central areas, no other difference was statistically significant.

During 500-800ms time window, data indicated a main effect of response category $F(1, 19) = 14.29$, $p = .001$, with FM presenting significantly higher voltages when compared to CRL ($M = .62$, $SE = .1$ and $M = .44$, $SE = .12$ respectively, $p = .001$). Voltages were more positive in the case of middle electrodes when compared to left (middle $M = 1.31$, $SE = .31$ and left $M = .26$, $SE = .16$, $p = .05$) and right electrodes (right M = .02, SE = .17, p = .002), as lateralization main effect indicated $F(2, 38) = 8.1$, $p = .001$, but no difference was significant when comparing left and right electrodes (M = .26, SE = .16 and M = .02, SE = .17, p = 1). Analysis showed no interactions between response category and lateralization $F(2, 38) = 2.29$, $p = .12$ or localization factors $F(1.4, 26) = 2.13$, $p = .15$.

This data suggested that old/new false memory effect was present, and localization of this effect corresponded to middle electrodes.

For the last 1000-1200ms time window, the only main effect was for localization factor $F(1.4, 26.4) = 27.4$, $p < .001$, indicating a statistically significant negative voltage at parietal sites (M = -1.5, SE = .35) when compared to very positive voltages at central (M = 1.44, SE = .19, $p < .001$) and frontal (M = 1.34, SE = .26, $p < .001$). No response category main effect was present $F(1, 19) = .02$, $p = .9$. Interaction between localization and response category $F(2, 38) = 8.5$, $p = .001$ was found, indicating that differences between voltages of FM and CRL were significantly different at parietal sites with negative voltages for FM (FM M = -1.74, SE = .36 and CRL M = -1.27, SE = .36, $p < .001$), and also FM showing positive voltages at frontal sites (FM M = 1.48, SE = .27 and CRL M = 1.2, SE = .26, p = 0.05), but no difference was found at central sites (FM M = 1.52, SE = .2 and CRL M = 1.36, SE = .2, p = .2). Interaction between lateralization and response category was also present $F(2, 38) = 3.93$, $p = .028$, suggesting a bilateral distribution of significantly higher voltages for FM when compared to CRL at right electrodes (FM M = .47, SE = .17 and CRL M = .04, SE = .17, p = .016) and significantly higher voltages of CRL when compared to FM at left electrodes (FM M = .1, SE = .18 and CRL M = .45, SE = .18, p = .043). No differences were present in the case of middle electrodes between response categories (FM M = .69, SE = .26 and CRL M = .8, SE = .28, p = .59).

At this time window, no difference in voltage was found between FM and CRL, but a fronto-central localization showed positive voltages when compared to negative voltages in the case of parietal localizations. FM voltages were more positive than CRL at frontal sites but they were more negative when parietal localizations were analysed. A similar pattern was present when comparing FM and CRL in terms of lateralization: FM showed higher voltages at right electrodes but lower mean voltages at left electrodes when compared to CRL.

3.5 Summary

VFMT 1.0 is a new false memory task. With this experiment, we aimed to replicate previously true and false memory ERP effects using this new task.

Early 300-500ms old/new effects consisted in higher voltages corresponding to HIT and FM responses when compared to CR. VFMT 1.0 replicated the old/new ERP effect for both HIT and FM at fronto-central and middle-line localizations. When comparing true and false recognition at this time window, true recognition voltage was significantly higher than false recognition at middle sites. When comparing FM and CRL as a false memory measure, analysis showed no voltage difference between these two categories at this time window, where the only main effect was related with a fronto-central localization of the lowest voltage as opposite to significantly higher voltages at parietal sites.

Posterior 500 to 800ms showed the existence of old/new effect for both true and false memory, being consistently associated with higher voltages for HIT and FM when compared to CR. Localization of this effect, nevertheless, was fronto-central in contraposition with classically parietal-posterior localization of it in previous literature. When comparing true and false recognition, higher voltages corresponded to true recognition and middle sites. Results found an old/new effect at middle electrodes when comparing FM and CRL.

Late time window 1000-1200 ms also presented old/new effects. For HIT was fronto-central and middle localized, whilst for FM was fronto-central and middle-right localized. True and false recognition were significantly different in voltage (i.e. HIT were more positive than FM) but equivalent in terms of localization and lateralization. When comparing FM and CRL, FM voltages were more positive than CRL at frontal sites and right electrodes.

3.6 Discussion

VFMT1.0 was introduced at this point as a new technique to study false memory. It used a single scene at study phase, which offered a different approach for all previous studies based on lists (words, pictures, sounds…). It was designed as a short-term memory task in line with previous works that already proved this design is reliable for the study of false memory (Chen, Voss, & Guo, 2012), with immediate recognition task right after encoding as participants did not perform any interference task. We engaged explicit learning-memory procedures as we explained to participants that they were asked to study everything that was in the scene because they would be asked about it afterwards. Nevertheless, the task succeeded in creating a very reasonable number of

HITS and FM to be used in further experiments, in line with the results extracted from short-term memory tasks with verbal (Atkins & Reuter-Lorenz, 2008; H. Chen, Voss, & Guo, 2012; Flegal, Atkins, & Reuter-Lorenz, 2010; Urbach et al., 2005) and numeric material (Pesta, Sanders, & Murphy, 2001).

Behavioural results indicated that our task raised a satisfactory number of hits and lures in line with previous experiments. Our averaged 77.93% for HITS, although slightly below performance compared to some of the previous literature results (88.6% (Nessler et al., 2004); 87.27% (Nessler & Mecklinger, 2003); 80.6% (Wiese & Daum, 2006)) is in line with other classic studies of false memories (75% (Gonsalves & Paller, 2000); 77.8% (Nessler et al., 2001); 74% (Geng et al., 2007)) and clearly improved percentages of some other previous experiments (63% (Duzel et al., 1997); 53% (Curran et al., 2001). Percentage of FM responses for VFMT was 50.4%, higher than previous experiments on DRM-like paradigms (Beato et al., 2012; J. C. Chen et al., 2008; Curran, 2000; Nessler & Mecklinger, 2003; Nessler et al., 2004; Urbach et al., 2005; Wiese & Daum, 2006), a figure proving lower compared to those obtained in other studies (H. Chen et al., 2012; Curran et al., 2001; Fabiani, Stadler, & Wessels, 2000; Geng et al., 2007) yet in line with others (Duzel et al., 1997).

We hypothesized that these differences regarding previous works in the literature laid on the assumption that VFMT engaged a semantic processing of information at encoding and test (see chapter 2 of this thesis for a review on this point), and following the explanations about how false memories are biased by association mechanisms (Ayers & Reder, 1998; Collins & Loftus, 1975; Rhodes & Anastasi, 2000; Underwood, 1965). This can be linked to a Dual Process approach (Yonelinas, 2002) to explain how semantic-strength may influence familiarity and recollection processes in a false memory task.

Regarding response time, previous episodic memory studies found that recognition response times were faster for HITS (Curran, 1999; Herron & Rugg, 2003; Rugg & Allan, 2000) but in the case of false memory experimental designs results are not conclusive. Some studies found HITS as the fastest responses (Nessler et al., 2004) but other authors found that CR responses were significantly faster than HIT (Nessler et al., 2001) because participants noticed they did not belong to the targeted semantic category in the task. In our experiment, the fastest response times corresponded to HITS followed by CR and FM (being FM only 4ms longer than CR). Longer response times corresponded to FA, followed 20ms later by CRL. Our results are in line with behavioural experiments completed by Atkins & Reuter-Lorenz, who observed that in their false memory task, response time corresponding to a lured item (i.e. FM) was almost 100ms longer than responses to correct rejections of lure items (i.e. CRL), indicating that healthy participants responded faster to items of which they were more certain of being correct, such as HITS and CR items (Atkins & Reuter-Lorenz, 2008). Nessler also proved differences in response time in their experiment using two different delay retention intervals (i.e. 40 and 80 seconds-delay), showing the short delay waas significantly faster (Nessler & Mecklinger, 2003). On the other hand, response time based on our experiment was longer compared to previous DRM-like ERP experiments (Fabiani, Stadler, & Wessels, 2000; Geng et al., 2007), in line with times presented by Nessler (Nessler et al., 2001; Nessler et al., 2004).

Results from our experiment must be carefully compared to the few previous experiments that utilized pictures at encoding in a false memory task, because design differences may distinctively affect results. Reviewing some of the most similar experiments to our VFMT in the literature, Miller & Gazzaniga´s one changed from using visual stimuli at encoding to read-out-loud lists of words at recognition in their only behavioural experiment on an equivalent visual-to-verbal modality change present in Koustaal experiments with young and older adults (Koutstaal et al., 1998; Schacter et al., 1997). Another very similar work that specifically designed a DRM task with only pictorial material (Baioui et al., 2012) did not collect any ERP information but psychophysiological measures such as skin conductance, respiration rate, heart rate and finger pulse, intentionally based on the Concealed Information Test (CIT) (see (Verschuere et al., 2011) and their recognition task items were exactly the same ones presented at study scene (i.e. digitally processed to be cut and used from there). In our experiment, modality of presentation was kept constant between encoding and test and the items presented at recognition task were prototypical images.

Semantic processing account addressed that using pictures compared to words may have a differential role in memory retrieval, suggesting that words droved a deeper and more elaborated and conceptual processing compared to pictures (Weldon & Roediger, 1987; Weldon, Roediger, & Challis, 1989). There are some experiments that stressed the fact that visual modality may affect false memory rates, specially related with false memory retrieval (Foley, Foy, Schlemmer, & Belser-Ehrlich, 2010). A series of experiments done by Foley and collaborators supported this idea: when lures were visually presented as pictures, false memories rates were smaller at all ages, dropping from 68 to 30% of false recollection (Foley et al., 2010). As a result of several experiments related to this matter, Foley and collaborators suggested what they named imaginal activation hypothesis. This hypothesis described how when an item is presented, a broad and spontaneous activation takes place at encoding such as related thoughts, episodic related events, image-based thoughts, etc. If those elements are reactivated at recall, some participants could miss-report those items processed as such at encoding, producing false recollection (Foley & Foy, 2008; Foley, Foley, Scheye, & Bonacci, 2007; Foley et al., 2010). All this work from Foley was based on how likely using different modalities of item presentation would engage the spontaneous process of generating visual cues associated that can be re-activated at test and bias a higher proportion false memory production.

Our VFMT1.0, even though exclusively based on visual material, did not use the very same pictures from encoding to test, suggesting that this may produce different a reactivation response in our participants, not solely based on imaginal reactivation effect but also on a semantic-categorical relationship.

We suggest that our results might be explained based on a combination of two theories, i.e. familiarity process from Dual Process Theory plus corroboration mechanism based on Monitoring account. Familiarity of critical lures might bias participants towards a memory searching to corroborate details about those lures. Those details might be borrowed from actually presented items and bound together to the false memory trace (Lampinen, Neuschatz, & Payne, 1999).

Another important aspect to discuss here is the short-term characteristic of our task compared to classic long-term false memory tasks in previous studies (Curran et al., 2001; Duzel et al., 1997; Nessler et al., 2004; Smith et al., 2003). Few investigations appeared with this very short-term delay design between encoding and testing. Chen and collaborators used only three seconds delay (H. Chen et al., 2012), explaining that ERP differences found on N400 familiarity effect between short-term and long-term DRM paradigms may be attributed to distinct cognitive processes. In long-term false memory designs, subjects may produce false memories based on a monitoring failure caused by semantic/conceptual activation of the lure at encoding, whereas short-term false memory designs may be based on a semantic/conceptual priming effect due to that covert activation of the lure during study.

Our results suggested the same fronto-central activity with minimal topographic distinctions and therefore, equivalent familiarity-based processes active for true and false memory at this very early time. At later 500-700ms, Chen and colleagues found a late positive component signal (LPC) for TM only but not for FM, indicating how TM specifically retrieve sensorial information presumably through re-activation processes that were not present on FM, in line with the Sensory Reactivation Hypothesis (Schacter & Slotnick, 2004). Our data reported significant differences in voltage between TM and FM, and showed a very similar fronto-central location of activity for both. At the time related with monitoring rather than activation processes (1000ms onwards), old/new effects were present for both true and false memory, but in different locations: fronto-central and middline located for TM whilst being fronto-central and middle-right located for FM. Differences in voltage between TM and FM were found at this time, being HIT more positive than FM but equivalent in localization and lateralization.

Chen and colleagues concluded that short-term false memory procedure was based on semantic priming (i.e. as indicated by FN400 effect) together with a deficiency on detail retrieval which is present for true memory (i.e. reflected on LCP-like ERP components) and with a less efficient retrieval monitoring (i.e. indicated by ERP components from 700ms onwards). Unfortunately, significant differences in task design (i.e. Chen's task was verbal material and focused on studying priming effect using repetitive presentation of lures) raise some methodological difficulties and comparisons made between these two studies must be achieved with precaution.

To further understand if short-term tasks may influence differently on false memory production, some authors suggested that short study-test retention intervals might be responsible for better recognition rates and a lower false recognition number of responses (Urbach et al., 2005). An alternative explanation based on the Dual Process Theory offered by Hintzman & Curran indicated that, in the case of a fast-responding recognition task, equivalent to our VFMT1.0 response setting, the familiarity process was responsible for discrimination between HITS and CR and would produce an increase of positive responses to FM. On the contrary, when slow responding was allowed to participants, recollection processes would counteract familiarity bias to produce false recollections, helping to discriminate better between HITS and FM (Hintzman & Curran, 1994). In our case, true memory was not affected by short-term recognition design, showing familiarity and recollection ERP effects. On the other hand, FM also showed old/new effect at this time window, being FM voltage more positive when compared to CR. On top of this, true memory voltage at this time window was higher when compared to false memory voltage, suggesting that familiarity process was present in both TM and FM but voltages were higher when considering TM.

As discussed previously at chapter 2 of this thesis, not giving any explicit information about the lured nature of the VFMT to participants may also have had a possible effect on false memory retrieval. In this case, instructions given to participants did not introduce any explicit explanation about the existence of items that were semantically related but not present at study scene. Nevertheless, and after informal chatting with participants after the completion of the task, these spontaneously explained how, after a few trials, became aware of the existence of items that could appear at test because of their semantic relatedness with the context of the scene at study but might not appear in that scene at all. Participants also commented that, after various trials, they decided to adopt a decision-process strategy to respond in those occasions, changing from being liberal and responding yes under any suspect item or, in the other extreme, not responding yes unless being completely sure in a more conservative response style. This information was not coded in our experiment but was collected informally from all our participants. There was no clear influence of the repercussions of this information in the global false memory production in our task, reaching a total of false memories of 50.4% as previously commented, in line with previous conclusions.

ERP signatures corresponding to true and false recollection found in this experiment offered different information compared to previous works on false memory and DRM-like paradigm using ERP designs. It must be said that, the majority of these experiments utilized a different experimental design compared to this VFMT used in this particular case, changing some of the modality of stimuli from encoding to tests (J. C. Chen et al., 2008; Curran et al., 2001), using words instead of pictures (Beato et al., 2012; H. Chen et al., 2012; Curran et al., 2001; Duzel et al., 1997; Nessler et al., 2004; Urbach et al., 2005) or focusing on how item-based information influenced false retrieval regarding perceptual (Herron & Rugg, 2003; Johansson, Stenberg, Lindgren, & Rosén, 2002; Speer & Curran, 2007) or categorical characteristics (Curran, 2000; Geng et al., 2007; Nessler et al., 2001; Nessler & Mecklinger, 2003; Swick, Senkfor, & Van Petten, 2006). Nevertheless, these studies mainly agreed on identifying three main ERP patterns accounting for memory retrieval: a mid-frontal early old/new effect, a left-parietal 500-800ms old/new effect and a later right-frontal old/new effect occurring at the end of the epoch.

We identified old/new effects (defined as HIT voltages being more positive compared to CR voltages) according to previous works starting early from 300ms and lasting almost to the end of the epoch. Localization was different from the classic pattern: instead of finding what has been described as the mid-frontal FN400 old/new effect at early time window from 300 to 500ms, data showed fronto-central old/new effect. Instead of the previous left-parietal activity from 500 to 800ms found previously in the literature, our data proved that old/new effect was strongly present at this time but in central locations. And for the late 1000 to 1200ms time window our data agreed with previous works found right-frontal topography of activation for this old/new effect. We hypothesized three reasons, aforementioned in this chapter, which might explain these ERP differences: semantic encoding, modality of stimuli utilized and delay between encoding and test. The first two are interrelated in a sense, as Paivio stated when explaining that pictures were superior to words in memory retrieval tasks as they can evoke both verbal and image codes, making easier any later recall because of this double and deeper encoding representation (Paivio, 1971). This explanation, together with levels of processing (Craik & Lockhart, 1972; Rhodes & Anastasi, 2000) and associative models (Ayers & Reder, 1998; Collins & Loftus, 1975; Underwood, 1965) addressed the bilateral influence of picture superiority and semantic encoding bias of memory retrieval. Related with contextual/semantic encoding, Paller also suggested that at early timing, mid-frontal old/new effect may be related with conceptual priming, defined as the effect of repeated access to semantic, rather than perceptual, representations (Paller, Voss, & Boehm, 2007). This concept is not clear in the literature as that ERP effect sometimes is not shown with semantic material (Yovel & Paller, 2004) in line with our results; some other times also appeared in the case of non-semantically related items at recognition task (Curran, Tanaka, & Weiskopf, 2002; Groh-Bordin, Zimmer, & Ecker, 2006). Regarding how visual modality may affect ERP results, it has been suggested that lateralization of old/new effect may depend upon the stimuli material, being more left-lateralized when words are utilized (Curran, 2000) and more right-oriented when pictures are used at recognition task (Burgess & Gruzelier, 1997).

Under a different perspective, a work comparing classic memory-retrieval experiments and DRM-like paradigm designs considered that, to be fair with false memory retrieval study, if HIT-CR is the measure of true memory old/new effect, we should consider FM-CRL as a measure of false memory old/new effect (Nessler et al., 2004). If we follow this suggestion and analyse FM versus CRL, data showed negative voltages at fronto-central sites but no difference between these two response categories at 300-500ms time window. At 500-800ms data showed significantly higher voltages for FM when compared to CRL at middle electrodes. The last time window of analysis, 1000-1200ms, revealed that FM voltages were more positive when compared to CRL at frontal sites and right electrodes. In summary, no clear ERP differences were present in our study at early time, suggesting no familiarity process involvement for this false memory measure as we predicted. Nevertheless, clear old/new effect was present at recognition interval from 500-800ms located at middle electrodes and later on, from 1000-1200ms but with a right-frontal localization.

We are aware that the design of our task did not allow us to control some variables that might influence our results to some extent. One of these aspects was the length of our scenes, presented at screen to be studied for 12 seconds. This set up was designed to allow participants to better remember and process deep enough to obtain a semantic gist of the scene, based on the semantic-encoding engagement of our task. Despite, this presentation length might produce behaviours that could interfere with our study aims. Firstly, that allowed participants to “look around” the scene, creating a possible amount of eye-movement interferences at ERP recoding system. This might have proved a problem if we had been interested in ERP signals at study phase, but as long as our main target was to analyse ERP signals at recollection, we consider that this possible interference had no real impact on our results. On the other hand, giving such long time to encode a learning item might offer the possibility to participants for engaging any mnemonic strategy to better encode it. This is not necessarily an issue for our aim, but we assume that in some cases this strategy might have been related with any type of “language-based” translation that we could not control and that it could affect one of our premises: a language-free design for our task. Nevertheless, as we did not quantitatively measure this possible interference, we cannot conclude how strongly this might have contaminated a language-free encoding scenario. In conclusion, none of these two consequences of a long-time encoding presentation could have been controlled in our design, but we considered that their impact for our experimental purposes were minimal.

TM AND FM ERP COMPARISON

A secondary objective of this experiment was to bring new data into the discussion related to whether an ERP signal related with a true memory recollection is different to a false memory ERP signal. In the literature there are works defending both versions. On the one hand, studies concluding that false memory is different to true memory in terms of ERP signal found differences in late post-retrieval evaluation processes related with right-frontal activity over 1000 to 1200ms (Curran et al., 2001); differences at frontal locations between true and false memory with picture stimuli (Goldmann et al., 2003); failing to find an early mid-frontal 300-500ms effect for false recognition when encoding strategies were focused on item-based characteristics, indicating the lack of feeling of familiarity for those item-based words (Nessler et al., 2001); and finding no frontal late effect for false memory present for true memory when retention intervals were manipulated (Nessler & Mecklinger, 2003). On the other hand, other studies found no differences between true and false recollection, when items were randomly presented at test (Duzel et al., 1997; Johnson et al., 1997); same ERP signals at recognition-based time range from 500 to 800ms (Goldmann et al., 2003; Nessler et al., 2001), may be explained as the influence of using distinct modalities for study and test which could affect item-specific recollection processes (Curran et al., 2001; Nessler et al., 2001; Nessler & Mecklinger, 2003); when encoding focused on conceptual similarities (Nessler et al., 2001). Results obtained indicated that although significant differences were found between true and false recollection from 300 to 800ms, they consisted mainly of voltage differences between TM and FM measures (i.e. HIT-CR presented higher positive voltages when compared to FM-C) as topographies of ERP activity were consistently related with middle electrodes for both. TM was different in voltage from FM but equivalent in localization from 1000-1200ms.

Compilation of all this information allowed us to conclude that our VFMT1.0 was a task able to produce old/new ERP effects for true memory and false memory, but we offered some differences to previous experiments, possibly due to differences in the task´s design. Neural correlates accounting true recollection processes for healthy participants were similarly distributed to neural substrates responsible for false recognition of items in a false memory task, with a main central topography for the classic old/new effect and a similar location but a difference in voltage amplitude for false recollection effect from 300 to 800ms.

Chapter 4: Adapting the Task to Patients: Version VFMT2.0

4.1 Overview

VFMT1.0 proved to be a reliable false memory task to study neural correlates of true and false memory retrieval, behaviourally and with ERP designed experiments. Nevertheless, when approaching the study of neural correlates with patients with neurological impairment of memory, there are some aspects that must be considered. Korsakoff syndrome patients typically present an amnesic profile as a clinical feature, and to ensure their better performance on this false memory task, some changes were designed on the previously utilized VFMT1.0. Once those changes were applied, we assessed the new VFMT2.0 version behaviourally to confirm its reliability on true and false memory production in amnesic patients.

4.2 Rationale: changes made to VFMT 1.0

Implicating amnesic patients in the study of false memory is not new in the literature (Dalla Barba, 1993; Melo et al., 1999; Schacter et al., 1997; Schacter, Curran, Galluccio, Milberg, & Bates, 1996; Van Damme & D'Ydewalle, 2009a; Van Damme & D'Ydewalle, 2010b). Having amnesia is a challenge when basic memory processes are under study. However, amnesia influence might be attenuated when experimenters plan memory task design accordingly.

In the case of our experiment with Korsakoff syndrome patients, we must first clarify that our aim was not to produce a therapeutic environment where patients may improve their memory performance. Our target was to design a false memory task that could be completed, to the utmost of their capacity, by amnesic patients despite their amnesia in order to collect information about their cognitive processing of true and false memories. We considered that there were mainly three important points to consider in order to adapt the task to amnesic patients with neurological impairment. We aimed to adapt the difficulty of the task by shortening the learning scenario and testing memory immediately after learning; to give extra help if required by the patient to ensure that they remember and understand the task all the time; and to offer a comfortable experimental environment to avoid any behavioural interference in our laboratory setting. A more detailed explanation of these three points is given below.

The first change applied to the task was to make it more immediate in terms of learning and recollection. VFMT1.0 offered three scenes in a raw to be learnt and a recognition block of 45 items was applied right after. In contrast, we reduced learning to only one scene which was inmediatelly tested at recognition phase. VFMT 1.0 used relaxation times to allow experimenters to check participant execution, to keep them motivated and to record any comment or solve any complaints that might have arisen during the task. As for patient performance, those relaxation times gave evaluators the opportunity to briefly remind them about instructions, to give patients positive feedback on their performance and maintain them focused and collaborative on the task.

The second modification made to VFMT 1.0 was to offer amnesic partcipants any extra help required to ensure they were always encoding and producing memory retrieval to the best of their capacity. Patient episodic amnesia might interfere with their capacity to remember instructions for the task or response requirements, hence experimenters gave them any required feedback to keep them on track. In some cases, it was necessary for the experimenter or caregiver to stay inside the testing room with the patient to facilitate his/her participation with repeated reminders and instructions on first trials or just keep him/her calm and confident. When ERP settings were applied (i.e.

experiment comparing ERP between patients and healthy controls that will be described in Chapter 5 of this thesis), only the experimenter was allowed to inside the Faraday room, being extremely careful neither to interfere with patient performance nor the EEG recording signal.

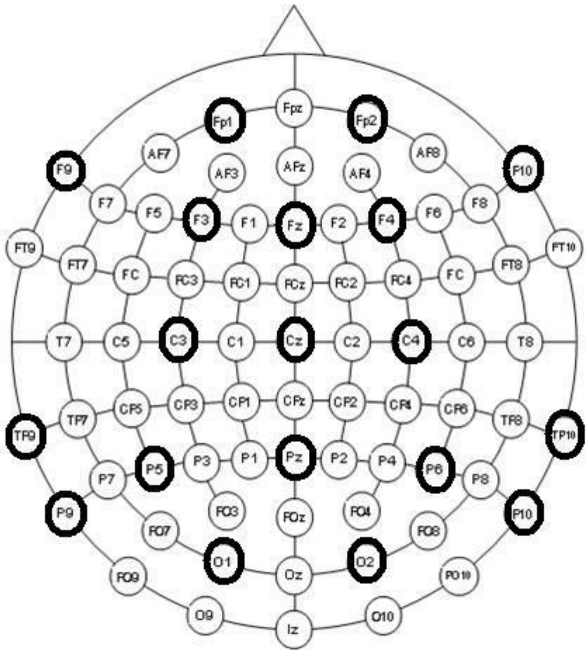

Figure 12 Electrodes selected for VFMT2.0 version with amnesic patients and healthy controls.

The last change applied to VMFT1.0 was focused on offering a comfortable setting to patients and consisted on simplifying the EEG data recollection using 20 electrodes instead of 64 (see Figure 12). This decision was based on the necessity of a faster and easier pre-study scenario that minimizes any discomfort to patients during channel connection process. Experimenters selected these electrodes based on expertise, on previously described important electrodes in ERP false memory paradigms, and with the aim to balance electrical characteristics of the recording set.

In addition to these three modifications, we also followed NHS Ethics Committee requirements to avoid any circumstances that may frustrate a neurological patient in an experimental setting.

Under these specific experimental circumstances, and using a new visual false memory task (VMFT 2.0 for the following) we aimed to explanatorily study true and false memory production in amnesic Korsakoff syndrome patients. Our first hypothesis was that patients would produce a numberof true memories above chance performance (i.e. more than 50% of hits). A second hypothesis suggested that false memories would also be produced by patients above chance performance (i.e. more than 50% of hit responses to lured items). These two results would offer data on the suitability of this VFMT2.0 to be used as false memory task with brain injured patients.

4.3 Rationale: why to target Korsakoff syndrome patients

We offered a complete description of the characteristics of this disease in chapter 1 of this thesis. Briefly, we described it as a disease associating severe anterograde memory impairment compared with other cognitive functions caused by a nutritional deficiency of thiamine. It was of interest to our research for several reasons. The first was that the neurological compromise of KS was almost restricted to mammillary bodies, mammillothalamic tract, fornix, and anterior thalamic nuclei degeneration together with frontal-lobe atrophy and did not implicate MTL structures, which historically have been the focus of studies on learning and memory retrieval. Secondly, KS patients do not frequently show severe cognitive impairment with dementia criteria and other cognitive abilities are unaffected, which allows us to engage them in cognitive testing to study their neuropsychological performance on a false memory task without the interference of cognitive decline. Another important reason was related with the fact that, as a clinical characteristic of this syndrome, confabulations are frequent in these patients. Far from being an inconvenient, we thought it might be an advantage, as it may allow us to study false recollection phenomenon on a sample where we may maximize previously presented performance on false induction of memories.

KS patients were targeted for this investigation as their neurological disorder is an interesting combination of two features: an episodic memory impairment with preservation of overall intelligence, no associated dementia and a tendency to confabulate as a sign of this disease. This was a neurological impairment that allowed experimenters to approach a biological state where false production of memories is present, in this case, in the form of confabulations; and it also made it possible to engage amnesic patients in EEG procedures as their cognitive general status was preserved enough to understand and collaborate in the research.

As previously reviewed at introduction section of this thesis, experimental results presented in the literature showed a pattern of response for this type of amnesic patients. Schacter, based on the previously stated idea considering that amnesic patients will produce more false alarms compared with controls (Cermak et al., 1973) described two opposite hypothesis regarding KS patients´performance on a DRM task: a) if amnesic produced more false alarms, they will produce more false memories than controls; b) because false memories in DRM tasks depends on remembering semantic information about the list, amnesic patients will produce less false memory due to their memory impairment. His experiment proved that amnesic produced more false alarms to lured items than to new (i.e. more FM than FA) suggesting that an associative component guided their recollection. He also discussed that by augmenting the number of associates in a task we can manipulate false memory production in amnesic participants, influencing them to produce less false memories due to their episodic memory impairment (Schacter et al., 1996). He also suggested that in task where a repetition of study-test setting is used, KS patients might present an increased sensibility to the gist, creating a strong representation of semantic gist that increases their FM production (Schacter et al., 1998). A common point can be found in these two experiments: for Schacter and colleagues, it was clear that amnesic patients will produce less true memory responses when compared to healthy participants, due to the episodic memory impairment which is characteristic of this neurological disease.

Based in these results, we aim to find that KS patients of our sample will produce higher number of false memories compared to control group, due to their episodic memory impairment.

4.4 Material and Methods

4.4.1 Participants

A sample of a completely new group of neurological patients was recruited at Dukeries Healthcare, a specialist residential care home at Worksop (Nottinghamshire) for people with Alcohol Related Brain Injury (ARBI) such as Korsakoff's Syndrome. Experimenters contacted Ms. Karen East, Care Services Manager at Victoria House, one of the United Kingdom's only centres specifically designed to care for people with ARBI. We explained our aim, made our request to collaborate with them, presented our project and proposed that professionals would work with them on their premises. Specific ethical approval from the England NHS Ethical Committee was requested and approved by Yorkshire and the Humber – Bradford and South Yorkshire NHS Research

Ethics Committee (REC) based on our original Ethical Approval from Wales NHS REC.

General practitioners or medical professionals from NHS hospitals of that area originally transferred these patients to Victoria House based on a diagnosis of ARBI. No detailed neuropsychological assessment was carried out at the care home, only a cognitive screening at arrival to determine the degree of cognitive impairment in order to plan their assistance in the house. Bot information sheet and consent form (see Appendix Chapter 4) were offered to patients in order to obtain their consent. Two sessions were planned with each patient: the first for neuropscyhological assessment and the second for VFMT2.0 administration.

The experimenter completed a battery of neuropsychological cognitive tests to ensure that the patient cognitive deficit was not compatible with dementia (DSM-IV criteria) and that memory impairment was present in all of them (for a detailled description of this battery of tests, see following sections in this chapter). A total of 12 patients was recruited but data from two of them was rejected because in one case, his cognitive impairment did not permit him to complete the neuropsychological evaluation and for the other, it was impossible to perform the VFMT2.0 (this case is nevertheless presented for neuropsychological findings here). A final number of 10 brain injured participants performed our VFMT 2.0 version without EEG recording. They were offered at the end of the testing session a Debrief sheet and any questions were personally answered (see Appendix Chapter 4).

Our patient sample were mainly female (40% male), all right handed and with an age mean of 50 years (range 42-61, SD=5.77). All participants had followed at least primary level education. The same venue was used for all, a quiet and undisturbed meeting room at Victoria House, where they were tested individually.

4.4.2 Stimuli

The same stimuli from VFMT 1.0 were used but changes were made in block distribution. During the previous experiment with healthy participants, a block was designed to contain three scenes to be studied and 45 items to be tested at recognition phase. Here, only one scene was to be studied and its 15 items were immediately presented at recognition phase. Blocks are distributed in five sets of five with the same self-paced relaxation periods between them (see Figure 13 for details in the comparison between the two VFMT versions). See **Figure 14** for the detailed study-test phase response categories.

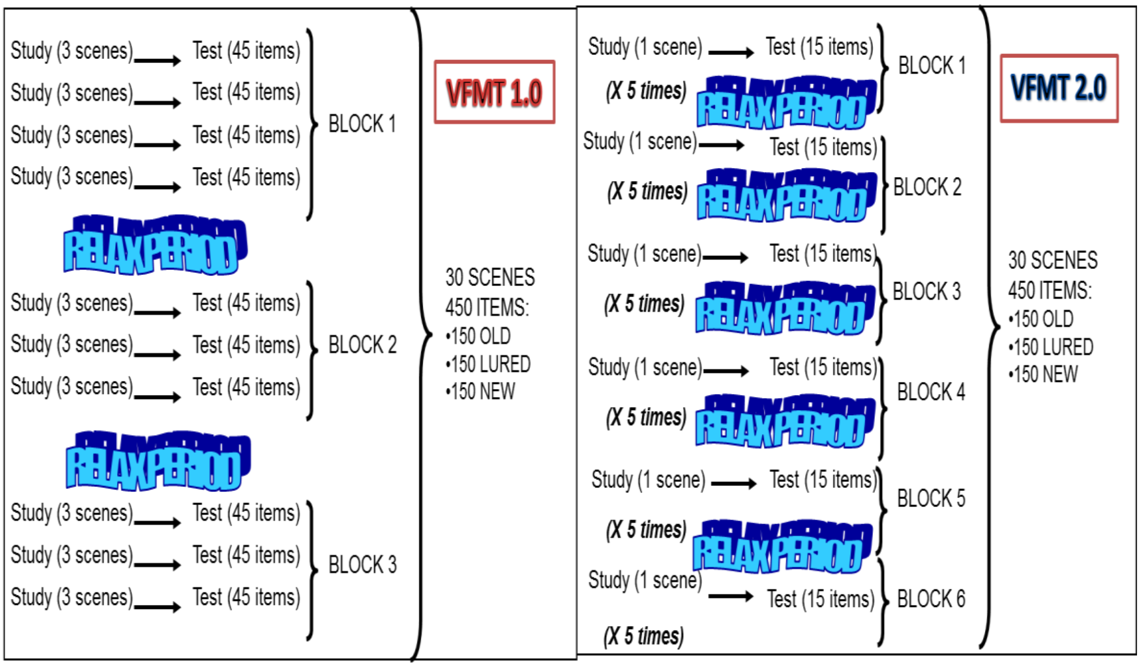

Figure 13 Block design description for VFMT 2.0 with a reminder about detailed description for VFMT 1.0. Note that new design keeps constant the same number of scenes and items tested but with a different distribution: a single scene is studied each trial and only its 15 associated items (5 old, 5 lured and 5 new) are tested immediately after. A block here is composed by doing that study-test trial five times, testing 5 scenes on each block.

4.3.3 Procedure

The same procedure described for VFMT 1.0 was applied here, but no EEG recording was administrated. The only difference regarding the VFMT1.0 procedure was that,on some occasions, the patients required the physical presence of their carers to avoid behavioural agitation.

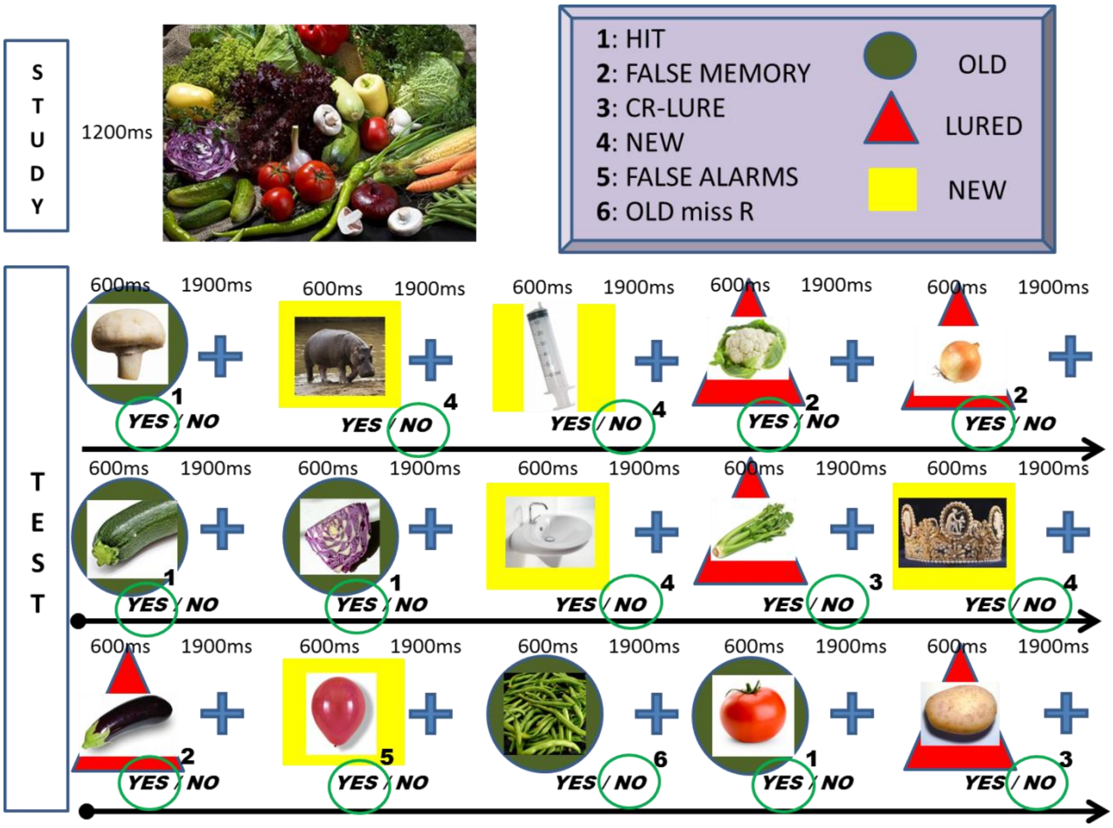

Figure 14: VFMT 2.0 Study-test trial. Schematic view simulating participant´s responses on a recognition trial, with specification on how categories of response were coded. Depending on participant´s response (circled in green) item were considered as follows: HIT when an item was old and was responded as "yes"; OLD miss R if they did not remember it and was responded as "no"; FALSE MEMORY (FM) when a lured item was responded as "yes"; CORRECT REJECTION OF A LURE (CRL) when a lured item was responded as "no"; FALSE ALARM (FA) was coded when a "yes" response was given to a new item and a "no" response was coded as a CORRECT REJECTION TO A NEW (NEW). For this scene, only the associated 5 old (indicated with green circles) and 5 lured items (inside red triangles), mixed with 5 new random items (inside a yellow square) from scenes not selected to be studied are tested. Notice that, as previously explained to participants, items used at test are not exactly the same from the studied scene, to avoid any perceptual or implicit effect.

4.4.4 Neuropsychological Battery

A compendium of tests was selected to evaluate cognitive functions with special focus on three main aspects: learning and episodic memory retrieval (visual and verbal modalities), working memory and executive functions. The description of each test follows:

- Addenbrook´s Cognitive Examination (ACE): this test included items from Mini Mental State Examination (MMSE) and expands that screening with more items reinforcing assessment of language, viso-spatial abilities, episodic memory, naming, verbal fluency and viso-constructive performance. Maximum score of 100 corresponded to normality. A cut-off score below 88 gives 94% sensitivity and 89% specificity for a cognitive status compatible with dementia level. Specificity rise up to 100% using a cut-off score below 82, being sensitivity percentage of 84% in that case (Mathuranath, Nestor, Berrios, Rakowicz, & Hodges, 2000).

- California Verbal Learning Test, version II (CVLT-II): this is one of the classic list-of-words tests to evaluate learning and episodic verbal memory recollection. It included a learning set of 16 words (list A) belonging to four semantic categories (vegetables, animals, ways of transport and furniture). Learning is evaluated after five learning trials with free recall for each, and after that, an interference list B is applied in the same manner. Inmediatelly after free recall of list B, evaluator will ask again for a short term memory recollection of list A first as a free recall and later after giving category cues to participants. After an interval of approximately 20 minutes, long term memory recollection under the same conditions (free and cued recall) is performed. The last trial was a recognition task where the participant must respond yes-no to a set of words including words from list A, from list B and completely new items.(Delis, Kramer, Kaplan, & Ober, 2000).

- Rey Osterrieth Complex Figure (ROCF): this test primarily offers a score related to visual memory but also gives some qualitative information about viso-constructive abilities and executive functions such as planning, organization strategies and perseverative behaviour. An abstract drawing with no semantic meaning must be copied by participant. Short term recollection was asked after a few minutes and long term performance was also collected after 20 minutes. Regular colour changes during participant performance help examiner to check temporary track performance in order to analyse executive abilities (Osterrieth, 1944).

- Trail Making Test (TMT): this task has two parts. TMT-A (only numbers) requires the participant to draw a line that links together all the numbers displayed on a paper in ascending order, as fast as they can and with no errors.This is a measure of speed of processing, focused and sustained attention. The second part is TMT-B (numbers and letters), and it adds the requirement to alternate between numbers and letters; therefore, aspects of shifting attention and working memory were evaluated (Reitan, 1992).

- Digit Span, from Weschler Memory Scale (WMS): a string of numbers is given verbally out loud to the participant, who has to repeat the same sequence of numbers exactly as given. This task has two trials: one with the repetition in the same order (forward digit span) and a second one repeating from the last number to the first (backwards digit span). The verbal working memory is evaluated here, especially with the backwards task. Information regarding short term memory capacity is also given by the total amount of numbers remembered at forward task (Wechsler, 1987).

- Corsi Blocks, from Weschler Memory Scale (WMS): this is the visual working memory task correspondent to Digit Span. Here, a set of blocks spatially fixed on a wooden board is used. The examiner indicates a sequence of blocks with his/her finger that participant must replicate, in the same spatial order (forward) or in reverse (backward). In this case, the viso-spatial working memory component is evaluated.

- Verbal fluency task (COWAT): participant is asked to produce words for 60 seconds starting with a given letter (F, A and S) with the following rules: production does not allow proper names, numbers or changes made to a previously produced word. The same procedure is repeated giving categorical cues to participant (animals).

4.4.5 Neuropsychological profile of patients

In Table 5 we show the results of the neuropsychological testing from nine of our ten patients who later performed VMFT 2.0 (neuropsychological results from one patient were lost in the records).

Results from evaluation showed how only four of our patients scored as impaired in screening basic test (i.e. MMSE), this number being higher when an extensive screening test was applied (eight out of 12 were rated as cognitively impaired). Learning and retrieval from memory was equally affected for verbal and visual material in this sample. Ten out of twelve patients achieved an impaired score when short-term retrieval of the ROCF was requested, even though their visospatial abilities were not that compromised. As for verbal material, a clear impairment of retrieval information, even if freely conduced or induced by offering semantic cues to patients, can be seen at Table 5. Performance was not significantly repetitive, only for three out of 12 patients, but it was clearly intrusive, producing in 10 of the patients a high number of intrusions in recall and also in 9 of the patients a high number of false positives at recognition task. Lastly, for four patients learning was compromised as their recognition score was below the normal range, but for the others, their memory performance improved when the recognition trial was offered, suggesting a spared capability of new learning but with compromised retrieval strategies.

No attentional impairment was present (see TMT A and B scores at Table 5). As for executive function measures (i.e. working memory capacity scores from WMS digits and corsi cubes, and COWAT fluency task), a majority of the patients in this sample performed normally.

Table 5

Neuropsychological data from memory and executive functions assessment

Cognitive tasks		PATIENTS											
		1	2	3	4	5	6	7	8	9	10	11	12
MMSE (/30)		25	26	30	23	27	30	23	28	25	23	22	26
ACE (/100)		79	71	91	70	78	82	73	87	85	67	73	65
CLVT													
	Free recall A5	-4,00	-2,00	-3,50	-2,50	-2,50	-2,00	-3,50	-2,50	-1,00	-5,00	-4,50	-2,00
	Free recall B	-1,50	-2,00	-1,50	-1,00	-2,00	-0,50	-1,50	-1,50	0,00	-2,00	-2,00	-2,50
	Short delay free recall	-4,00	-2,00	-4,50	-2,50	-3,00	-3,50	-3,00	-3,00	-1,00	-0,35	-3,50	-2,00
	Short delay cued recall	-4,00	-1,50	-3,50	-3,00	-3,00	-3,00	-3,50	-2,00	-1,00	-2,50	-4,00	-2,00
	Long delay free recall	-5,00	-1,50	-5,00	-3,00	-2,50	-3,50	-3,00	-2,00	-1,50	-5,00	-4,00	-2,00
	Long delay cued recall	-4,00	-1,50	-4,00	-2,50	-2,50	-3,00	-3,00	-1,00	-1,50	-3,50	-3,50	-1,00
	Repetitions	-2,50	0,00	-0,50	1,00	-0,50	0,50	-0,50	0,50	2,00	-1,00	-1,00	2,50
	Intrusions Total	5,00	0,00	1,00	4,50	3,00	2,00	5,00	2,50	3,00	1,50	3,50	1,50
	Recognition	-2,50	-1,00	-0,50	-0,50	1,00	-2,50	-2,00	-0,50	1,00	-0,50	-5,00	-0,50
	False positives	5,00	0,50	4,00	2,00	5,00	1,00	4,00	4,00	2,50	1,50	0,00	2,50
ROCF													
	Copy	-2,33	0,00	0,05	-2,00	-0,67	1,00	-0,33	0,00	1,00	-2,00	-1,00	-2,00
	Short delay memory	-2,33	-2,33	-1,99	-1,67	-2,33	-1,67	-1,00	-1,67	-0,67	-2,33	-2,33	-1,67
TMT													
	A	0,67	-1,00	1,14	0,00	1,00	0,00	-0,67	1,33	0,00	-2,00	-0,33	-2,67
	B	-1,33	0,00	0,00	-0,67	0,00	0,67	0,67	0,67	0,00	-1,33	0,67	-2,67
WMS													
	Digit span total forward (max)	6,00	6,00	8,00	7,00	6,00	7,00	6,00	7,00	6,00	4,00	6,00	4,00
	Digit span total backwards (max)	3,00	4,00	5,00	3,00	5,00	5,00	4,00	3,00	5,00	2,00	3,00	3,00
CORSI BLOCKS													
	Direct (max)	4,00	4,00	6,00	4,00	6,00	5,00	5,00	4,00	4,00	3,00	6,00	n.a.
	Backwards (max)	4,00	5,00	6,00	2,00	4,00	4,00	5,00	6,00	3,00	3,00	5,00	n.a.
COWAT													
	F+A+S	1	0	0,67	-2,00	0,00	-0,33	0,33	0,00	0,33	0,33	-1,00	-1,33
	Animals	-0,43	-0,05	-0,80	-1,10	-0,80	0,10	-2,10	3,20	0,40	-2,60	-0,90	-2,10

Note: All scores are Zscores but the ones from WMS and Corsi Blocks, which correspond to the length of the series. MMSE: Mini Mental State Examination; ACE: Addenbrooks Cognitive Examination; CLVT: California Learning Verbal Test; ROCF: Rey Osterrieth Complex Figure; TMT: Trail Making Test; WMS: Wechsler Memory Scale; *COWAT: Controlled oral word association test (FAS)*. The shadowed data correspond to scores 1.5 times under the mean. As some of the performance scores that are related with impaired execution at some subtest are positive instead of negative scores, and with the aim to clarify the most, * describes scores that have been changed from positive to negative sign or vice versa to ensure the direction of pathological performance into a negative score in all cases.

4.4.6 Statistical analysis

Behavioural results were analysed using t-test and considering α= .05. One way ANOVA was executed to analyse differences on response production along blocks in the task.

4.5 Results

We analysed whether patient performance appeared to be different all along our 6 testing blocks (see Table 6 for details) due perhaps to fatigue or to any cognitive difficulty such as attentional interference (i.e. starting a new task) or working memory problems (i.e. any possible failure to remember instructions). We described participant learning curve during each of 6 testing blocks for correct old items (i.e. HITS), yes responses to lured items(i.e. FM), yes responses to new items (i.e. FA), correct rejections of new items (i.e. CR) and correct rejections of lured items (i.e.CRL) as main response categories to compare.

One Way ANOVA analysis, with Block as a factor, resulted in no significant effect of block number on response performance. Therefore, data suggests participants achieved the same efficacy through all blocks. Hence there was no influence from external condioners such as fatigue or other cognitive interferences which might have effected their memory performance along blocks. A detailed description on percentages of accuracy, means and standard deviation along different blocks and response categories is displayed in Table 6.

Table 6

Patients´ performance in each response category and testing block.

	HITS			**FM**			**CRL**			**CR**			**FA**		
	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD	%	Mean	SD
B1[1]	59.6	14.9	4.9	46.8	11.7	6.7	39.6	9.9	6.3	78.8	19.9	4.2	1.8	2.7	2.3
B2	63.2	15.8	5.4	49.6	12.4	5.3	36.4	9.1	5.9	8.8	20.2	7.1	6.4	1.6	1.3
B3	64.8	16.2	4.8	64.8	16.2	5.5	3.4	7.6	5.0	9.8	20.3	7.6	4.8	1.2	1.6
B4	61.6	15.4	5.4	52.8	13.2	4.6	42.8	10.7	4.5	86.8	21.7	2.2	1.8	2.7	1.9
B5	65.6	16.4	5.1	61.2	15.1	6.4	36.4	9.1	7.0	88.8	22.2	1.6	8.8	2.2	1.2
B6	66.8	16.7	5.7	56.0	14.0	6.6	39.2	9.8	6.8	89.6	22.4	1.3	8.4	2.1	1.0
T	**63.6**	**15.9**	**5.1**	**55.2**	**13.8**	**5.8**	**37.5**	**9.4**	**5.8**	**85.9**	**21.1**	**4.7**	**8.3**	**2.1**	**1.6**

Note: [1] B corresponds to Block number and T to total values from all blocks. % corresponds to accuracy percentage, SD to standard deviation. FM refers to false memory responses, CRL to correct rejections of lured items, CR to correct rejections of new items and FA to false alarms.

Behavioural results from VFMT2.0 performance by our patients are displayed in detail in *Figure 15*. The new version of the task allowed patients to produce a total of 55.2% of false memories and a total number of false alarms of only 8.33%. Considering results obtained in our healthy population in VFMT1.0 at 50.4% of FM and 7.5% of FA (see Chapter 3 of this thesis for more details), data suggested that our VFMT2.0 produced an equivalent rate of true and false recollection as first version of the task, which may support its use with ERP experimental design. A last analysis comparing HIT versus FA production indicated significant differences between these two response categories ($t(59) = 20.03$, $p < .001$), suggesting that participant performance is not based on chance responses but on their own mnemonic effort.

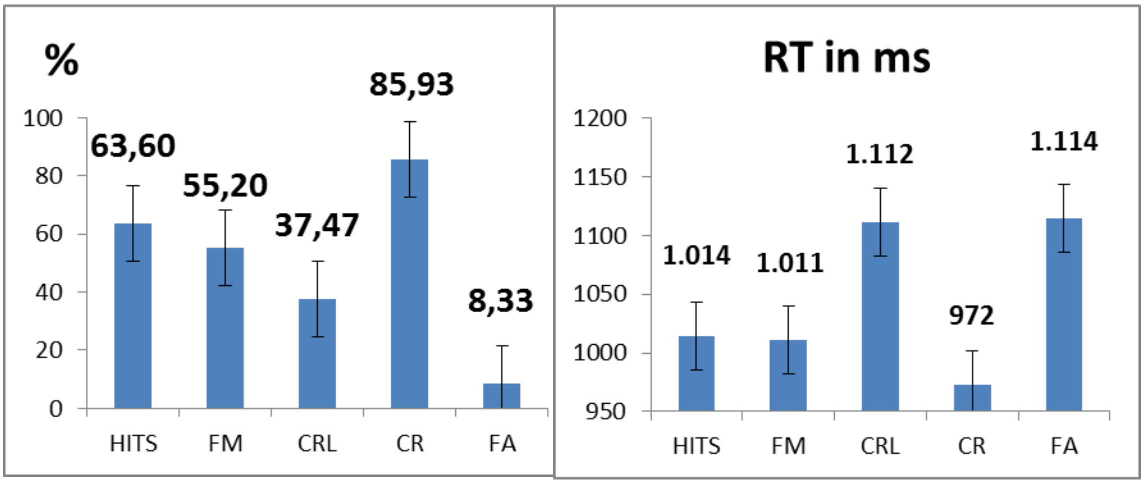

Figure 15 Descriptive data: percentages of responses on the left and response time on the right.

Response time data showed that patients responded faster to CR and FM (this last response was only 4 seconds faster than HITS). It took them longer to respond when items required them to correctly reject a lured item and to produce a false alarm (see *Figure 15*).

4.6 Summary

After a neuropsychological evaluation, amnesic impairment was present for all participants in this sample neurologically diagnosed as KS.

The new VFMT-2.0 version proved to be effective in false memory production when amnesic patients are recruited, producing a total of 55.2% of lured items identified as false memories, very similar to false memory percentage found with VFMT 1.0 in healthy participants. It was also a good general memory task because, although their episodic memory impairment interfered with the total numbert of hits on the memory task (63.6%), this percentage was above chance performance. Also, a high number of correct rejections together with a low number of false alarms indicated that this new version is useful to evaluate memory and false memory performance in alcohol related brain injury patients.

4.7 Discussion

It was expected that amnesic patients would produce a lesser number of correct HITS when compared to a healthy population with the VFMT1.0 version, due to patients´ characteristic episodic memory impairment. However, and despite this episodic memory deficit, patient capability to produce false memory under VFMT2.0 version experimental manipulation of contextual information was possible on an equivalent percentage as the former VFMT1.0 rates (i.e. 55.2% by patients with VFMT2.0 compared to 50.4% by healthy students on VFMT1.0).

Even though analysis of response percentages between blocks suggested no differences between them, we are aware that we cannot directly relate this with a null effect of fatigue, attentional interference or to a specific cause as we can only guess what might be the process underlying their performance. Nevertheless, independently of which cognitive or enviromental factor might be interfering with their response, data suggested there was no effect in their performance between blocks.

It can be argued that the results from these two versions of the false memory task (i.e. VFMT1.0 and VFMT2.0) present design differences that may render direct comparison difficult as to false memory (and true memory) production. In addition, we are aware that due to an easier design (i.e. VFMT2.0 only-one-scene encoding design and inmediate recognition test) may boost accuracy rates of true recognition in healthy participants and arguably decrease false memory production under similar premises. A pilot study on a healthy population of a similar age range as in this patient sample would have been necessary to test this aspect more accurately. However, this will be approached in the following chapter of this thesis, where VFMT2.0 will be administered to a different sample of amnesic patients and to age-matched controls under EEG laboratory conditions.

It must be noted that the aim to develop this VFMT2.0 was not to improve memory performance in amnesic population but to pursue experimental conditions that allow sufficient memory processes to produce false recognition even in an episodic memory impairment deficit scenario. Repeated reminders, easier encoding and testing trials with only one scene instead of three and constant support to patients during the task were planned to avoid interference of other cognitive factors that may interfere with memory such as attentional overload, immediate memory problems that might not allow patients to easily assimilate test instructions and/or behavioural disturbances due to non-ecological experimental conditions. Controlling these possible interferences was necessary when pursuing amnesic patients´ best memory performance.

The results presented in this chapter indicate how patients produced a reliable number of false memories all through the blocks thus confirming their ability to successfully perform this task despite their episodic memory impairment.

Chapter 5: False Memory in Brain Injured Patients

5.1 Overview

The main purpose of this chapter is to study false memory in amnesic patients. As previously described in Chapter 1 of this thesis, various experiments were performed to study this phenomenon in amnesic patients, and more specifically, some of them utilized DRM paradigm tasks to do so. As our VFMT2.0 was originally based on DRM paradigm premises of semantic relatedness between encoded information and critical lures, we will focus on results obtained from this type of task in amnesic patients.

In this chapter, we develop an ERP experiment with the new version of VFMT2.0 for the first time and whereby we compare healthy controls and amnesic patients. We aimed to administer VFMT2.0 in a sample of amnesic patients and an age-matched control group. We analysed ERP characteristics for true and false memory of each group separately, to finally compare performance of patients versus VFMT2.0.

5.2 Introduction

ERP memory effects have been extensively described in the literature. The classic old/new memory effect, reported in initial ERP experiments, was defined as a parietal-left peak activity at 400-800ms with more positive-going voltages elicited by correctly classified as old items compared with those elicited by correctly classified as new (Sanquist, Rohrbaugh, Syndulko, & Lindsley, 1980; Warren, 1980) and have been supported by a large amount of posterior event-related potentials (ERP) experiments on false memories (Curran et al., 2001; Duzel et al., 1997; Nessler et al., 2001). This effect takes place usually around 400 to 800ms, being topographically and functionally different from other EEG effects which occur at the same timing (such as stimulus probability and response confidence). This effect is associated with recollection processes according to Dual Process Theory (Brainerd & Reyna, 2001; Yonelinas, 2002).

A second classic memory effect was described by Curran as a consistent left-superior-anterior 300-500ms N400-like component, more negative for new than for old items and named as FN400 (Curran, 2000). This effect is associated with familiarity processes according to Dual Process Theory account.

Regarding false memory ERP effects, previous experiments in the literature described a left-parietal 400-800ms component more positive for hits than lures and new items (Allan, Wilding, & Rugg, 1998). Based on the premise that comparing correct responses to old items and correctly rejected items (i.e. the old/new effect) is paramount to retrieving episodic details, Chen and collaborators, hypothesized that this ERP effect must be more positive for hits than lures (H. Chen et al., 2012). Furthermore, the amplitude of this old/new effect, which they named as late positive component (LPC), was proved in their experiment to be no greater for falsely endorsed critical lures (i.e. CRL) than for correct rejections of new items. LPC should not be present for FM. It has also been studied with amnesic patients (diencephalon or MTL damaged) to whom this component is more positive for HITS than for FM (Curran, 2000).

A last old/new memory effect was described on late timing activity, from 800 to 1500ms after presentation of the stimuli. It was named as the right frontal late effect and is characterized by a greater voltage of HIT responses compared to CR over right-frontal hemisphere peaking at 600-1900ms (Allan et al., 1998).

Previous experiments in the literature covering different approaches to the study of false memory in a healthy population are reviewed in Chapter 3 of this thesis. We also reviewed controversial results in the literature regarding whether or not the ERP signal corresponding to true memory differs from the one associated to false memory production. This will be approached here again with a slightly different false memory task (i.e. VFMT 2.0).

To briefly summarize results in the literature (for a more extensive description, see chapter 3), we can say that some experiments found no differences in ERP characteristics corresponding to true and false memory processes. The first study that approached this was performed by Duzel and colleagues (Duzel et al., 1997) using a DRM-like task with words. They found ERP old/new effect at fronto-central localizations associated with “knowing” responses from 300-600ms, a parietal effect also related with “remember” responses from 600-100ms and finally, a right-frontal effect associated with remember and know responses. However, those effects were similar for TM and FM. Later, Curran and collaborators recovered Duzel´s task but changing from visually presented to auditory presented material at study (Curran et al., 2001). Authors found that old/new right-frontal ERP activity from 1000-1500ms that appeared to be similar to lure/new effect for good performers (and was absent for poor performers) was not indicative of effort or retrieval success previously associated with frontal lobes as they do not differ between TM and FM. They suggested that this right-frontal late effect was related with evaluation processes. A study from Nessler and colleagues found that, when encoding is category-based, no frontal ERP late differences were found between true and false memory (Nessler et al., 2001). More recently, Atkins & Reuter-Lorenz (Atkins & Reuter-Lorenz, 2011) suggested the existence of a common neural representation of “oldness” related with both true and false recognition in both long and short-term false memory tasks. They also found some overlaps regarding neural correlates for true and false memory: for true memory, a higher activity of left fusiform gyrus accounting for an increase of perceptual processing is present when compared to false memory activity, and it may help to distinguish between true and false (Slotnick & Schacter, 2004).

But on the other hand, some experiments exposed indications of ERP differences between true and false memories. Johnson and collaborators found differences between TM and FM at broad frontal-parietal areas from 775-1500ms, only when test items were condition-blocked (and not randomly mixed like in most behavioural experiments). (Johnson et al., 1997). More recently, Chen and colleagues quantified that late fronto-parietal effect from 800ms onwards can distinguish TM from FM. Greater amplitude corresponded to TM, intermediate amplitude to FM and lower amplitude to new items. This was related with a more effective post-retrieval monitoring process for TM compared to FM (H. Chen et al., 2012). Differences between TM and FM were found in experiments using visual modality of item presentation at both encoding and test related with FN400 early ERP signal (Curran, 1999; M. Rugg et al., 1998; M. D. Rugg et al., 1998). Nessler and colleagues compared a classic memory task against a false memory DRM paradigm task also found differences in ERP voltages at parietal sites (400-700ms): HITS were more positive than CR at classic paradigms but showed no difference at false memory paradigm. Using a DRM task, Wiese & Daum concluded that ERP corresponding to HITS and FM were similar at parietal sites from 400-700ms but presented differences at frontal electrodes localizations, being present for true but not false memory at that same time window (Wiese & Daum, 2006).

Frontal differences on ERP components have been reported on several studies: using a DRM paradigm task (Wiese & Daum, 2006), with pictorical stimuli (Goldmann et al., 2003) and with item-based encoding strategies experimental designs (Nessler et al., 2001). Early 300-500ms fronto-median ERP effect for false memory was absent when participants focused on item-specific information during study phase, reflecting a lack of familiarity feeling for those (Nessler et al., 2001). When manipulating retention interval, ERP differences were found between true and false memory regarding early frontal effect, present for true but absent for false recognition in the long delay trial (Nessler & Mecklinger, 2003). From the anatomical point of view, fMRI studies reflected how left parahipocampal gyrus was selectively activated when a true memory was retrieved and not for a false memory in both short and long-term retention intervals. Increase of activation at right VLPFC was also associated to true memory, accounting for the inhibition control needed to respond (Atkins & Reuter-Lorenz, 2011).

It has been suggested that both true and false memory measured with HITS and FM responses might be based on similar cognitive processes. Nessler and Mecklinger suggested three reasons to explain that: a) because lure rates are equal or even higher than old rates on DRM paradigm-like experiments; b) in experiments rating response confidence, similar rates were found for old and lured responses (H. L. 3. Roediger & McDermott, 1995); and c) no differences were found in remember/know judgements when comparing old and lured responses (Nessler & Mecklinger, 2003). Along these lines, a recent study on mice concluded that the same neural areas are engaged in false and true memories. Ramirez and collaborators, based on previous studies that identified the hippocampus as the neuronal target activated for both false and correct memories (Cabeza, Rao, Wagner, Mayer, & Schacter, 2001), created an animal model to investigate specific areas from the hippocampus involved in false and genuine memory creation (Ramirez et al., 2013). They speculated that some memories are falsely created because of internally driven retrieval of previously memories that are then associated with concurrent external and significant information. All these results may be indicating that both, true and false memory, are processed by the same neural structures, but no further explanation is given to whether those areas behave in the same way for both types of memories.

It is worth presenting here studies that approached a true and false memory analysis with a new perspective. Classically, true memory was studied in ERP experiments as a result of the comparison between HITS and CR and false memory was analysed as a comparison between FM and CR (Curran, 2000; Friedman & Trott, 2000). Nevertheless, following experiments considered some other combinations in order to analyse different aspects of true and false memory.

Good versus Poor performers experiments carried out by Curran and colleagues analysed a late frontal effect from 1000-1500ms and found that CRL responses were more voltage-positive than CR and equal to FM responses for Good group of participants, but no differences found for Poor group (Curran et al., 2001). Chen and collaborators specifically analysed in their DRM study CRL responses (H. Chen et al., 2012). They used it as a baseline condition of FM against which to compare true memory. They define false memory as *"incorrect memory decisions for related lures as compared to correct memory decisions for the same stimulus category"* (p 5). They explain the influence of the oddball effect present at P300, resulting from the high dissimilarity between CRL compared to FA. They suggested that *"using unrelated lures as the baseline condition would introduce a stimulus confound that would obscure ERP correlates of false recognition. In contrast, by comparing false alarms to correct rejections for related lures, we were able to isolate the neural processing events associated specifically with the experiences of false recognition for some related lures and of correct recognition (rejection) for other related lures"* (p 6). They compared HITS and FM against CRL throughout their experiment, as they considered it enable to compare true memory and false memory fairly.

Another experiment formulating a new way to approach true and false memory in an ERP experimental context was introduced by Nessler and colleagues (Nessler et al., 2004). Classic memory paradigm using OLD-NEW effect find that OLD-CRL might be the equivalent effect in false memory paradigms ,as CR items in false memory tasks are very distinctive regarding categorical and semantic relation with HIT and therefore, their ERP components would be rather different from NEW items in classic experiments (i.e. OLD and NEW both belonged to the same category in classic experiments). In Wieser & Daum's study using DRM classic 24 word lists test, they analysed ERP difference waves between HIT-FM, FM-CRL and FM-CR study (Wiese & Daum, 2006). Topographical maps of these difference waves indicated that for HIT-FM there was an important positivity for HITS starting approximately from 550ms and lasting 150ms at frontal electrodes; a widespread positivity between 550-750ms was present for HIT-NEW; LURE-CR of a lure showed more positivity at left posterior locations from 450-700ms for LURES; and finally, when comparing LURE-NEW from 650-750ms, a higher positivity for LURES over left posterior regions was found. Statistical analysis confirmed these data: similar old/new effects at parietal P5 site were present for LURES and HITS, in the case of frontal and central electrodes this old/new effect appeared for true but not for false recognition.

Another study analysed the fact that CRL takes longer response times compared to CR, indicating that semantic relatedness with contextual information at encoding required additional processes to reach an accurate response causing that increment of response time (Atkins & Reuter-Lorenz, 2008). This may happen because of two main reasons: first, the familiarity-based proactive interference effect (Jonides, Smith, Marshuetz, Koeppe, & Reuter-Lorenz, 1998); and second, the source memory (Johnson et al., 1993) dealing with the decision of whether a memory was actually presented or just strongly associated to the source.

The only study, to our knowledge, designed as an ERP experiment completed on alcoholic patients was performed by Pfefferbaum and collaborators (Pfefferbaum, Rosenbloom, & Ford, 1987) involving alcoholic participants who had been abstinent for a period of at least 10-62 days. No specific clinical description was offered to match the Korsakoff syndrome for this sample and memory task was not DRM-like. Patients showed changes at P300 respect to control participants during a visual material of a go-no go task: their latency was smaller for the Go trial but not for the NO-go compared to controls. Also a tendency on P300 latency was present, being later for alcoholics on the Go trial but not for the NO-go trial compared to controls. Authors concluded that P300 changes are present in alcoholic patients being consistent with previous findings of the same effects for other diseases causing cognitive impairment.

The aim of this chapter is multiple. First, we aim to prove our VFMT2.0 in an amnesic population to study false memory production in a sample or KS patients. Based on what has been previously found in the literature, we expect them to be able to produce false memories in a semantically related induced environment, as we hypothesize that they would be able to process semantic information successfully. Moreover, we expect them to produce, as compared to healthy controls, a fewer number of HITS and a higher number of FM based on that premise. This might be due to patients´ ability to process the gist of the scene and use it at recognition task. This fact, together with their possible impairment on executive function and monitoring processes, will produce a high number of false recognition trials. We expect that the failure of the monitoring process will also be present regarding response time in patients: they might engage some sort of monitoring process but it will not succeed to effectively check their response according to episodic memory processes, therefore, response time for CRL and FM will be longer compared to HITS and CR, as these last two would not implicate any decision-monitoring processes.

We also aim to study neuropsychological and neuroimage characteristics of this amnesic population, willing to match previous research regarding the constant presence of episodic memory impairment together with a variable affectation of executive functions. From the neuroimage, we aim to find information related with the impairment of certain structures in this type of neurological disease: the mammillary bodies, the thalamus and the mammillothalamic tract. Using a high-resolution MRI scan we expect to find alterations of those structures in our sample of KS patients.

Regarding the ERP analysis, we have several hypotheses regarding our two different groups. For the group of healthy participants, we expect to find similar results compared to those obtained in our previous experiment depicted in chapter 3 of this thesis: when studying true memory, we will find a clear mid-frontal old/new effect present at early time window at frontal localizations, together with a later 500-800ms old/new effect and a late 1000-1200ms positive voltages at right-frontal localizations of the scalp. Regarding false memory, early 300-500ms mid-frontal positivity for FM will be present, a mid-frontal higher voltages for FM will be present from 500-800ms and finally, a fronto-central and right lateralized effect from 1000-1200ms will show higher voltages for FM when compared to CR. When comparing true and false memory, we expect to find higher voltages corresponding to TM when compared to FM measures at all time windows of interest.

When studying a patients´ group, our hypotheses about their ERP profiles cannot be based upon previous literature findings, as no previous study has been made using a DRM-like paradigm and ERP techniques. Based on the hypothesis that patients can process semantic information and might find some difficulties in post-retrieval monitoring processes, we hypothesize that we will find ERP old/new effects corresponding to familiarity-based 300-500 early effects similar to control participants. Regarding recollection-based ERP signatures at 500-800ms, we expect to find differences when compared to controls due to their amnesic problems, but still aim to find old/new differences regarding response voltages. Late 1000-1200ms ERP signal will also produce different voltages for HITS when compared to CR but differences regarding FM and CR will also be present. For this group of patients, we expect to find no ERP differences when comparing true and false memories, as we hypothesize that both memories will be based upon the same process of gist recollection whereby monitoring processes will not allow patients to distinguish between them.

When comparing patients versus controls, we expect to find differences regarding ERP signatures for true and false memories, that will follow post-retrieval and recollection processes.

5.3 Material and Methods

5.3.1Participants

A total of 26 participants were recruited for this experiment, divided in two groups: patients and controls.

In the first one, 13 participants were diagnosed by and recruited under the supervision of a consultant neurologist. They met diagnostic criteria of neurological disease that compromised memory but were not compatible with dementia (henceforth the definition of "patients"). Data from one patient was dismissed because he was unable to finish the task. Mean age for this group was 57 years old, with 12 male and 1 female patients. Diagnosis was compatible with Korsakoff syndrome for 9 of them, the other 4 were compatible with amnesic syndrome of different aetiology (diencephalic damage). They did not participate in the adaptation of the task assigned to amnesic patients described in chapter 5 of this thesis.

In the second group, 13 age-matched healthy controls participated in the study (denominated as "controls"). They were required to have no previous neurological disease and normal or corrected to normal vision. Mean age for this group was 59 years old and an equivalent rate of male and females compared to patients group were recruited (11 and 2 respectively). Control participants were volunteers from the University Community Panel, and some others collaborated thanks to word of mouth.

The same procedure at EEG laboratory was employed for both groups. No differences were found regarding age or sex between groups (see Table 7 for details).

Table 7
Descriptive data related to age from both groups.

	PATIENTS	CONTROLS
N	12	13
Age range	49-67	46-68
Mean age	57.25	59.39
SD	5.41	6.71
Mean Error	1.56	1.86

5.3.2 Stimuli

The same materials described in Chapter 3 were utilized.

5.3.3 Procedure

Testing sessions were completed individually. Evaluators gave participants detailed information about the experiment and a consent form to read and sign so as to complete the task. The experiment was approved by the School of Psychology's Ethic Committee, at Bangor University and the local NHS' Research Ethics Committee of Wales.

All 12 patients completed a neuropsychological assessment (commented in Chapter 4 of this thesis), performance on VFMT 2.0 with an EEG recording and MRI scanning session.

5.3.4 EEG Recording and ERP methods

Some minor changes to the original VFMT1.0 EEG session were applied to adapt the VFMT to patients´ capability (see Chapter 5 for details on EEG setting modifications). Recording was taken from 21 electrodes (i.e. IO1, Fp1, Fp2, F9, F3, Fz, F4, F10, FCz, C3, Cz, C4, TP9, TP10, P9, P5, Pz, P6, P10, O1 and O2). After ERP signals were base-lined and corrected with respect to 200ms pre-stimulus recording interval and digitally band-pass filtered at 0.1 to 35Hz, data was corrected for ocular interferences and averaged to reference electrode (FCz) to minimize the effect of reference-site activity and estimate topography data of electrical fields of interest in our experiment.

During the performance of our VFMT 2.0, a recording of our participants´ electrical brain activity was collected for all responses given. Same response categories depicted in chapter 3 of this thesis were coded by our EEG system.

Eye-movement artefacts were removed from data either manually after visual inspection of the trials and automatically using eye-movement EEG information previously registered for each participant (see chapter 3 for details). Considering that the EEG recording was a rather strange environment for patients and the fact that they were not used to taking part in a research project, EEG data contained more artefacts compared to control participants, whom were more familiar with this type of setting as these usually collaborated with University research. We expected that, after cleaning EEG trials from artefacts, we might end up with a lower number of trials for patients when compared to controls and wanted to analyse the impact on the final number of trials available for ERP analysis. We performed an independent sample t-test with groups as a grouping variable and response categories as independent variables.

We found that the number of trials resulting after ICA and manual removal were statistically different in the number of trials for HIT responses when comparing patients and controls ($t(23) = -3.84$, $p = .001$, with a higher number of trials for control group (patients M = 74.1, S = 29.97 and control M = 109, S = 12.9). Those differences were also significant when comparing the number of trials used for CR responses t(23) = -3.3, p = .003 (patients M = 92.75, S = 25 and controls M = 118.15, S = 11.7). No difference was found when comparing the number of final trials for FM t(23) = -1.44, p = .17 (patients M = 58.6, S = 29.5 and controls M = 74.3, S = 25.3) and CRL t(23) = .25, p = .81 (patients M = 60.25, S = 18.5 and controls M = 58.2, S = 23).

To analyse ERP signals we opted to focus on collapsed time as previous works suggested (Addante, Ranganath, Olichney, & Yonelinas, 2012; Curran & Friedman, 2004; Curran et al., 2001; Wilding & Rugg, 1997). On this occasion, we included the following time windows of interest: 300 to 500ms, 500 to 800ms, 800 to 1000ms, 1000 to 1200ms and 1200 to 1500ms. We included all electrodes for statistical analysis, not selecting electrodes as we did in the VFMT1.0 experiment (see chapter 3) because of the small number of electrodes included in this design.

We will divide the following analysis into two steps: first, we will consider behavioural results in each group that we will compare at the end; and secondly, we will describe results obtained via the ERP experiment for each memory effect, detailing first control participants´ execution, followed by patients´ group results and finally we will provide a comparison between those two groups.

5.3.5 Statistical Analysis

Two tailed t-test comparisons were applied separately to analyse paired response categories within each group (i.e. HITS versus CR, FM versus CR, etc.). When comparison between true and false memory was approached for each group, two independent factors ANOVA analysis were conducted. The final analysis, regarding patients and controls analysis of both true and false memory was performed with ANOVA. Details of each of these analyses will be offered in each section. α value was set to .05.

5.4 Results

5.4.1 Neuropsychological results

These 12 patients were neuropshychologically assessed with the same battery of cognitive tests described previously in chapter 4 of this thesis. See Table 8 for detailed scores and test utilized.

Data showed that all of them presented consistent memory impairment mainly related with verbal material. Only patient number 45 presented preserved scores in verbal memory test (i.e. CLVT-II) regarding learning and recall since his memory failure was caused by a high number of intrusions at free recall and false positives at recognition task.

Attentional performance measured with TMT was preserved but for patient 47, which performance was interfered by speed: patient´s performance produced no errors but time was above normal limits for his age.

Results on executive function were heterogeneous. Some patients presented a working memory impairment related with verbal material, being the visuospatial sketchpad generally better preserved. Regarding verbal fluency, only two patients presented problems with generating words using a phonetic cue and only one using a categorical cue.

Table 8:
Neuropsychological data from memory and executive functions assessment.

Cognitive tasks	PATIENTS								
	44	45	46	47	48	49	50	51	52
MMSE (/30)	24	27	25	21	27	26	19	27	20
ACE (/100)	66	76	86	65	73	87	63	81	69
CLVT									
Free recall A5	-2	-1	-1	-4	-2.5	-2.5	-3.5	-2	-2
Free recall B	-1.5	-1	-3.5	-2.5	-1	0	-1.5	-1.5	-2
Short delay free recall	-2.5	-0.5	-1.5	-3.5	-2	-3	-4	-2	-2.5
Short delay cued recall	-3.5	0	-1	-4	-1	-2.5	-3	-2	-3
Long delay free recall	-3	-1	-2	-4	-1	-4	-3.5	-2.5	-3
Long delay cued recall	-3.5	-1	-2.5	-3	-1.5	-2.5	-4	-1.5	-3.5
Repetitions	- 1.5*	0	0	-0.5	-2*	-0.5	0.5	-1	0
Intrusions Free Recall	-2.5*	-1*	-1*	0	-2*	-5*	1	-2.5*	-1.5*
Intrusions Cued Recall	-5*	-4.5*	-4*	-5*	-5*	-5*	-4.5*	-5*	0.5
Recognition	-2	0	1	-1	-1.5	-1	-5	1	-1.5
False positives	-2.5*	-2.5*	-3*	-5*	1	-4*	-1.5*	-4*	-2.5*
ROCF									
Copy	-0.33	-1.33	-1.33	-1	-2	-0.67	-1.65	-1.33	1.33
Short delay memory	-2.33	-0.33	-0.67	-2.33	-2	-0.67	-2.33	-2.33	-2.33
TMT									
A	0.67	-0.33	0.33	-2.67	1.67	0.67	-0.33	-0.33	-1.33
B	-0.67	0.33	1.33	-1.33	-0.33	0.67	-0.33	-0.67	0
WMS									
Digit span total forward (max)	4	8	8	5	5	6	5	6	7
Digit span total backwards (max)	4	9	5	4	4	6	3	4	7
CORSI BLOCKS									
Direct (max)	5	6	6	3	4	7	5	5	4
Backwards (max)	5	5	4	2	4	6	5	5	5
COWAT									
F+A+S	-1.67	0.33	1.33	-1	-0.33	2.67	-2.67	-1	-0.33
Animals	-2.33	0	0.67	-0.33	0	1.33	-1	0	-1.33

Note: All scores are Zscores but the ones from WMS and Corsi Blocks, which correspond to the length of the series. MMSE: Mini Mental State Examination; ACE: Addenbrooks Cognitive Examination; CLVT: California Learning Verbal Test; ROCF: Rey Osterrieth Complex Figure; TMT: Trail Making Test; WMS: Wechsler Memory Scale; *COWAT: Controlled oral word association test (FAS)*. The shadowed data correspond to scores 1.5 times under the mean. As some of the performance scores that are related with impaired execution at some subtest are positive instead of negative scores, and with the aim to clarify the most, * describes scores that have been changed from a positive to negative sign or vice versa to ensure the direction of pathological performance into a negative score in all cases.

5.4.2 Neuroimage results

From the neuroimage point of view, only four of our patients were tested using MRI techniques to study brain structures associated with KS characteristic impairment and with memory processing. The reason why not all of our 12 patients participated was that, for some of them, it was not possible to travel to our University venues for scanning sessions. Nevertheless, we offer data about neuroimaging findings for four of our patients, whom gave their oral and written consent to participate in a study of the imaging features of KS. The research protocol was approved by both Bangor University and NHS Ethics Committees. In accordance with the Data Protection Act 1998, all of the patients' details were anonymized and scans de-identified. We re-named those four patients as 44, 45, 46 and 47 for analysis purposes.

High field and resolution T1-weighted MRI scans were obtained. High resolution T1-weighted images were generated with a Philips 3T Achieva (Best, Netherlands) scanner at Bangor University for each of the four KS patients with the following imaging parameters of interest: FOV (field of view) = 240 mm; number of excitations (NEX) = 2; in plane resolution = 0.7 x 0.7 mm; 185 slices; slice thickness = 0.7 mm; TR (repetition time) = 8.40 s; TE (echo time) =3.80 ms; flip angle = 8^{o}; SENSE factor = 2; axial oblique acquisition angle.

For all Korsakoff patients, the ventro-dorsal diameter of the mammillary bodies (MB) was measured. Regions of interests in the mammillary body, superior colliculus and head of the caudate nucleus (See Figure 3 for examples) were manually traced in each hemisphere using Analyze 8.0, and their mean intensity value computed.

The MB was shrunken in all four patients and two (45 and 47), had central gliosis of the MB. Demyelization of mamillothalamic tract (MTT) was observed in 3 patients. (See *Figure 16*). In one (Patient 46) the entire extent of the MTT was demyelinated and hypointense; in two (Patients 45 and 47) only the distal portion of the MMT was degenerated, with preserved myelinisation of the MTT through the hypothalamus. Gliotic lesions in the anterior nucleus of the thalamus were seen in two patients (Patients 46 and 47). Figure 17 shows enlarged images highlighting the key findings in two patients: central gliosis of the MB and terminal degeneration of the MTT.

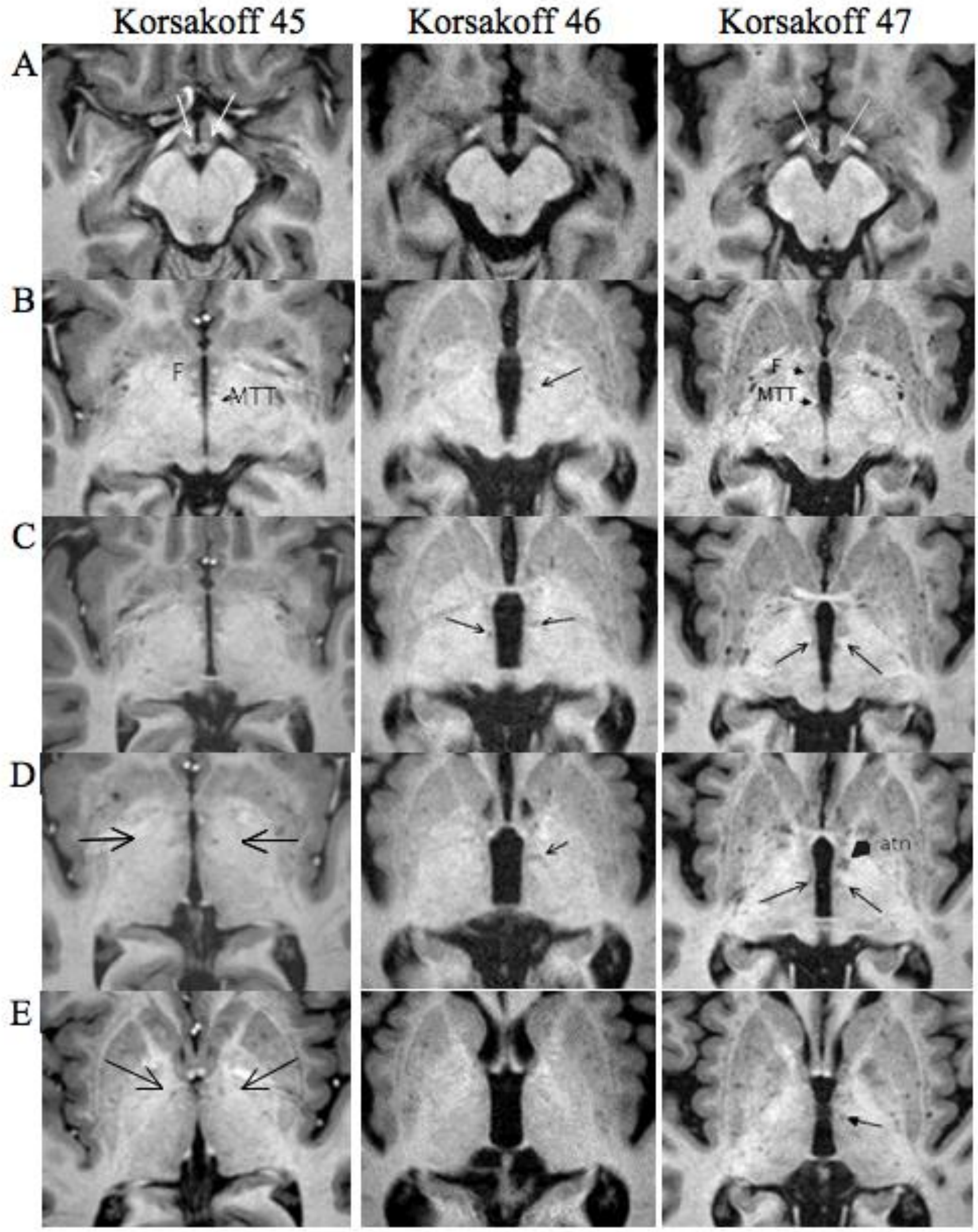

Figure 16: Central hypo-intensity (gliosis) of the mammillary bodies is seen in Korsakoff 45 and 47, and gliosis in the anterior thalamic nucleus is evident in Korsakoff 47 (heavy arrowhead in slice D). Myelination of the MTT is absent throughout the full extent of the MTT bilaterally in Korsakoff 46; instead, punctate hypo-intensity indicating degeneration of the tract is seen in several sections (arrows). Preserved myelination is seen in the proximal MTT of Korsakoff 45 and 47 (slices B and C); but there is demyelination and degeneration of the distal MTT (slice D & E). In particular, note punctate hypo-intensities at the termination of the MTT in the anterior thalamic nucleus in Korsakoff 45 (arrows in slice E).

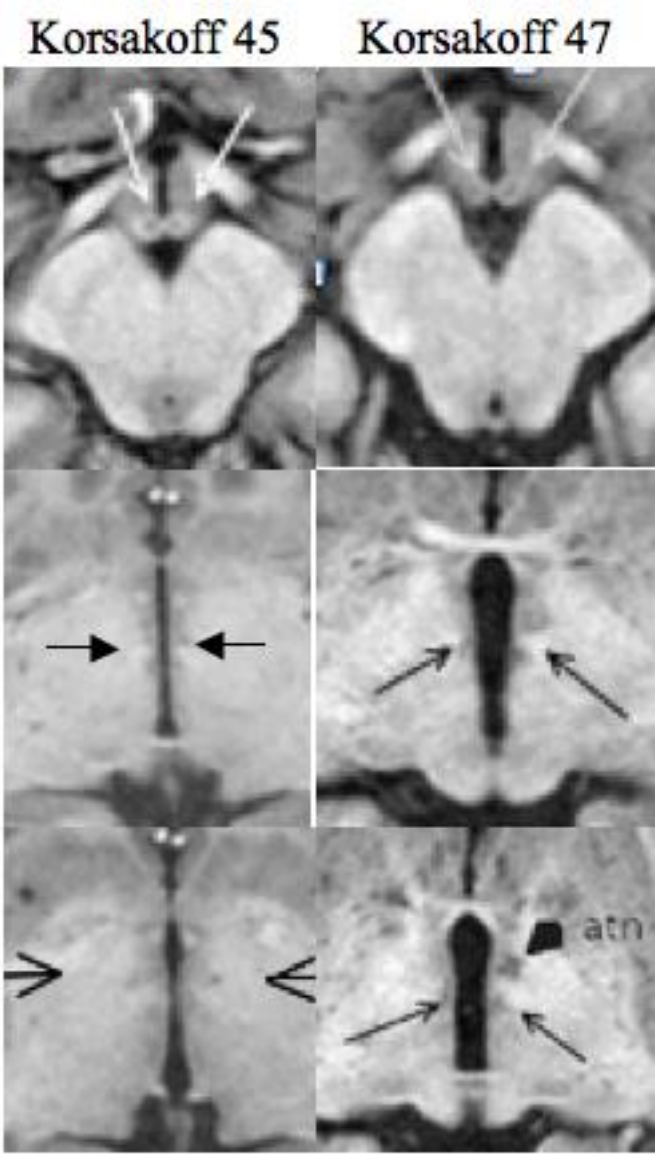

Figure 17: Enlarged images from Figure 16 demonstrating central gliosis of the MB and terminal degeneration of the MTT.

5.4.3 Behavioural results

For the purposes of this analysis, we only took into account a number of trials for each response category where participants actually responded. This means that we did not focus on those trials during which participants missed the response, due to eventually a lack of time or any type of distraction. Nevertheless, and in order to offer complete numbers for each response category, we indicate percentage figures of missed responses together with yes and no responses for each item category at Figure 18. Regarding time analysis, we excluded missed responses, and calculated mean times only for yes or no responded items.

When analysing each group separately, data showed that healthy control group performance in VFMT 2.0 produced a high rate for hits and a very low percentage of false alarms. Significant statistic differences were found when comparing control participants´ performance for old(yes) and old(miss) ($t(12) = 17.87$; $p < .001$) as well as for correct rejections (i.e. new(no)) and false alarms to new (i.e. new(yes)) items ($t(12) = 46.98$; $p < .001$), confirming that a memory effect was present. Nevertheless, no difference was found when comparing yes and no responses to lured items during the memory task. A clear difference in response percentage was found for the control group regarding their performance on hits for old and hits for lured items ($t(12) = 6.6$; $p < .001$) with a higher accuracy for old(yes). Regarding incorrect responses in our memory task (i.e. respond “no” to an old item and respond “yes” to a new item) we found a significant difference ($t(12) = 4.57$; $p = .001$), being more frequent for our control participants to mistakenly forget about hits than positively respond to a false alarm. An expected difference was found comparing false alarms to new items versus correct rejections to lured items, the latter proving usually more frequent due to their semantic relationship with the studied items ($t(12) = 6.54$; $p < .001$). Interestingly, when comparing incorrect responses which had a strong semantic relationship with previous studied items (i.e. as missed response to an old and correct rejection of a lure), a very strong difference is found ($t(12) = -6.52$; $p < .001$) with a higher percentage of response for the latter. A false memory effect was also proven as percentage of false memories (i.e. positive responses to a lure) was significantly higher compared with the percentage of false alarms with regards to new items ($t(12) = 10.51$, $p < .001$) (See Figure 18 for percentage figures of response in the control group).

On the other hand, when analysing these behavioural indices in the patients' group, no difference regarding the percentage of response when comparing positive and negative responses to lured items was present, as control participants showed. In general, patients had a similar response percentage pattern compared to controls, but their significant differences were not that important. This is the case when comparing hits versus miss responses to old ($t(11) = 2.64$; $p = .23$); hits versus false memories ($t(11) = 3.37$; $p = .006$); correct rejections of a lure versus false alarms ($t(11) = 3.41$; $p = .006$) and old miss compared with correct rejections to a lured item ($t(11) = -3.14$; $p = .009$). The memory effect therefore was also present in the case of the patients group, just like the false memory effect together with a significantly higher percentage of false memories compared to false alarms ($t(11) = 5.086$, $p < .001$) (See Figure 18 for details on percentages obtained from the patients´ group).

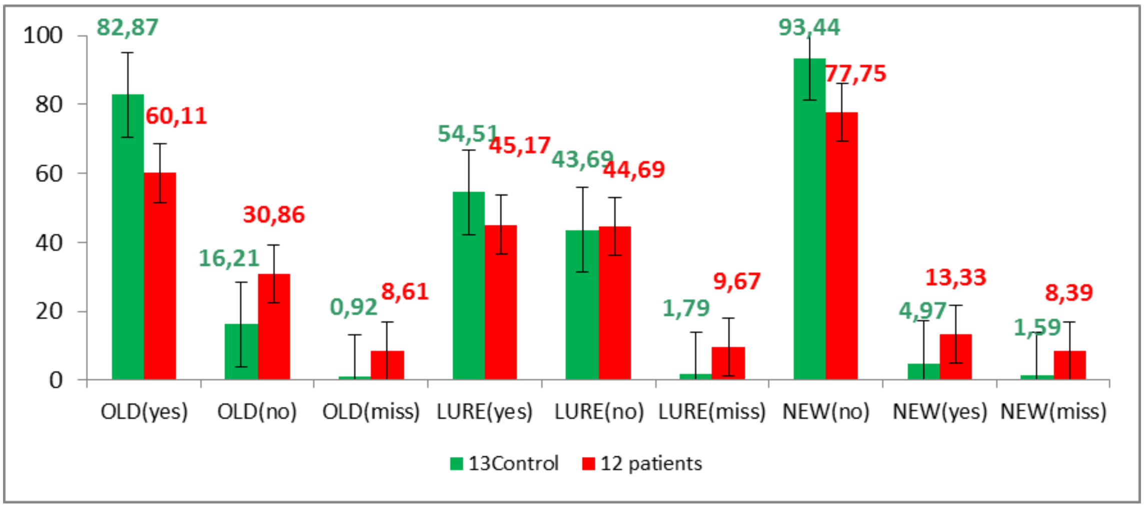

Figure 18: Percentages of response for patients and controls. X axis corresponds to type of item and response given by participants, including when no response was produced (i.e. miss). Error bars correspond to standard error.

Response time performance for control group showed faster responses to old hits when compared to miss responses to old ($t(12) = -7.08$; $p < .001$), as well as in the case of false memory responses compared to correct rejections of lured items ($t(12) = -6.54$; $p < .001$). Participants were faster to correctly reject new items an provide positive responses to old and lured items, indicating that performance was faster when participant felt sure about the correct response. In the case of incorrect responses (i.e. misses to hits, false alarms and correct rejections of lures) they showed a longer response time. Faster response times were present for hits compared to false memories ($t(12) = -3.77$; $p = .003$) and also faster for false alarms compared to correct rejections of lured items ($t(12) = 4.02$; $p = .002$). No significant difference regarding the response time was found when comparing hits with correct rejections for new items (see Figure 19 for control group data).

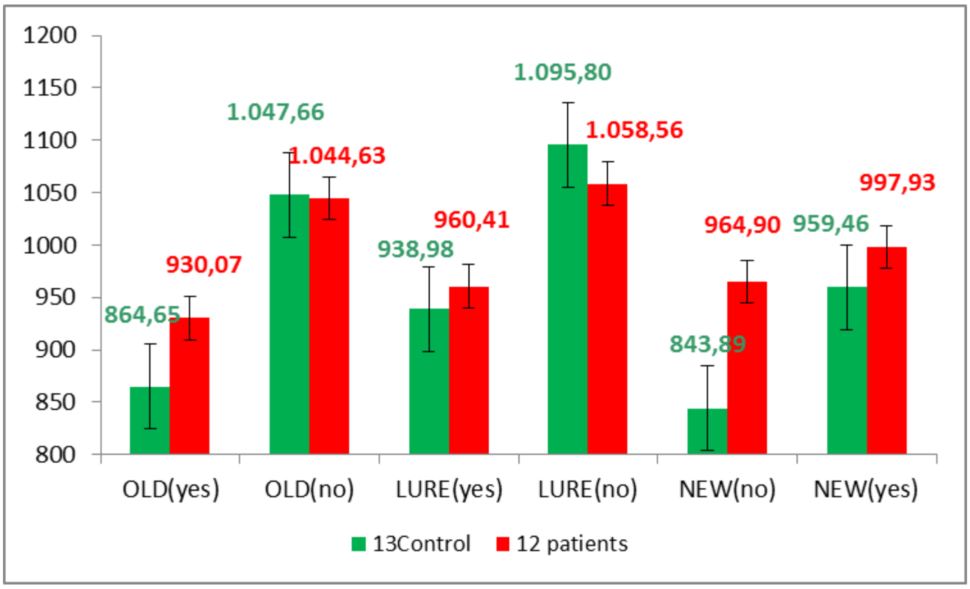

Figure 19: Mean repose time in milliseconds for each response category and group. Horizontal axis indicates item type and response between brackets. Error bars display standard errors.

These results might indicate how control participants' responses were faster presumably because of their certainty of response, with a gradient timing arguably related to semantic content from not having any semantic relationship (i.e. correct rejections), to be clearly related and having a clear memory about the item being present (i.e. hit), followed by being semantically related and having a strong feeling of being presented before (i.e. false memory).

When analysing patients' response times, we faced a peculiar fact: no difference proved significant within this group. Regarding speed, patients presented a slightly different pattern compared to controls, proving faster when responding to hits, followed by false memories and finally to correct rejections to new. It is interesting to observe that, related to new items, patients did not show a clear difference in favour of correct rejections compared to false alarms.

In general, patients showed a significantly worse performance with less correct responses and more incorrect responses compared to control participants involved in our task. No differences were found related to response time.

When comparing patients versus controls in terms of behavioural data, significant differences were found only for HITS, with a clear higher percentage for controls compared to patients ($t(12.58) = -3.34$, $p = .006$) and for CR ($t(11.7) = -2.88$, $p = .014$) with the opposite pattern (see Figure 18 for details on response percentages). No other significant difference was observed in any other response category, neither in relation with reaction times between patients and controls (depicted on Figure 19).

5.4.4 ERP

We describe in detail data related to each group separately. We describe first grand averaged waves for each response category to later analyse differences waves related to both true and false recollection processes independently first, and one against the other at the end.

In a last section of this chapter, we will compare ERP performance on true and false recollection between the two groups: patients against control participants.

5.4.4.1Control group

Visual inspection of grand averaged waves for midsagittal electrodes of our control group is displayed in Figure 20. As data shows, differences are present on several of the time windows with a “stepped-like” distribution of voltages for each response category in the case of the central electrodes.

A two-tailed paired t-test analysis comparing averaged voltages for HITS and CR showed significant differences at Fz, FCz and Cz from 300-500ms ($t(12)=4.084$; $p=.002$; $t(12)=2.988$; $p=.011$; $t(12)=2.951$; $p=.012$ respectively). For the time window corresponding to 500-800ms, only Fz showed a significant difference comparing those abovementioned conditions ($t(12)= 2.581$; $p=.024$). In the time from 1000-1200ms, Fz and FCz presented significant differences ($t(12)=3.012$; $p=.011$ and $t(12)=2.165$;$p=.05$ respectively).

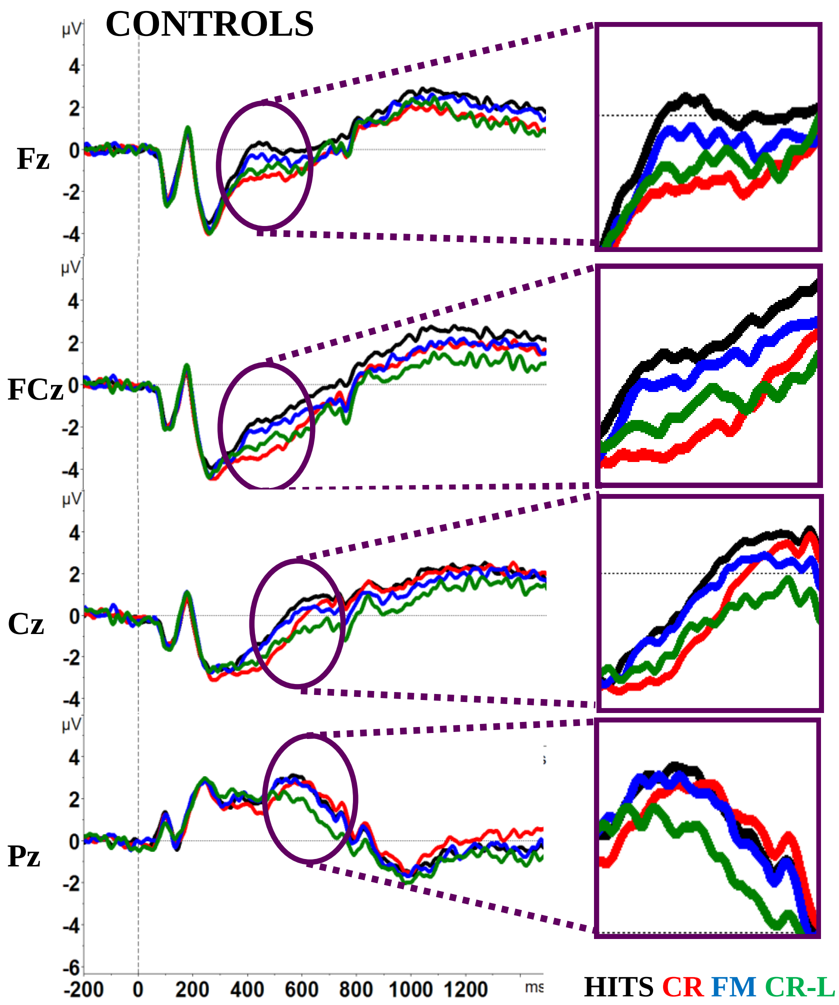

Figure 20 Grand averaged waves for our four main response categories on central electrodes. Milliseconds are displayed at X axis and microvolts at Y.

When grand averages corresponding to HITS were compared with the ones corresponding to FM at these central electrodes, data showed that from 300-500ms, both were significantly different on Fz only (t(12)=3.581; p=.004). In the time from 500-800ms, differences between HITS and FM were found at FCz, Cz and Fz (t(12)=2.189;p=.049; t(12)=2.187; p=.049 and t(12)=2.413; p=.033 respectively). No significant differences were present from 1000 to 1200ms.

In conclusion, when comparing voltages corresponding to HITS versus CR, frontal areas appeared as significantly different, proving centrally located at very early

300-500ms to change into a right-frontal localization until the very last time window, from 1200-1500ms where significant differences returned to fronto-central electrodes again. When HITS are compared with FM, fronto-central electrodes showed the highest statistical difference from early timing till 1000ms.

TRUE MEMORY

In a context of a memory experiment and in order to certify validity of the test, a measure is required. This measure is based on the premise that the signal related to hits of the task and the signal related to correct rejections cannot be the same, and therefore, a subtraction of those two signals must result in a difference. In the context of an ERP experiment, a difference wave is calculated to subtract ERP voltages related to CR from voltages related to HITS. This difference wave takes into account the real activity that is specific to memory retrieval processes.

We also considered a second index of true recollection previously utilized in the literature: the HIT-FM effect. This difference wave compares mean voltages of FM from HIT. This comparison faces together two different response decisions: one for HITS, whereby participant was certain that the item was old and that response was correct; and the second one for FM whereby, even though the participant thought that the item were present, it was not, but semantic relatedness with the theme of the studied scene was high. This might be considered a true memory measure.

HITS-CR effect

When analysis of 13 control participants' performance on VFMT 2.0 was completed on a 100ms time window basis (See Figure 21 for topographic view, Figure 22 for difference waves) data showed that voltage of this difference wave reached the highest positive pick at F4 ($t(12)=3.277$; $p=.007$) but showing also significant differences on Fz, Fp2 and C4 at the time from 300 to 400ms. This right-frontal localization of significant electrodes was kept from 400-500ms it was and spread to central electrodes, including Cz, Fz, Fp2, F4, C4 and peaking at FCz ($t(12)=4.056$; $p=.001$). The central tendency remained for the following 500 to 600ms time window, with significant differences found at Fp2, Fz, F4, FCz and C4, being the highest difference at Cz ($t(12)=3.833$; $p=.002$). From 600 to 700ms a bilateral situation was present, with the highest voltage for this difference wave found at F4 (i.e. 0.93 microvolts) but statistically significant differences were found at Fp2 but more significantly at F9 ($t(12)=3.42$; $p=.005$). For the next 100ms, data showed the same significant electrodes (i.e. F9, F4 and Fp2) but on this occasion, peak voltage and statistical significance both corresponded to Fp2 ($t(12)=2.978$; $p=.012$) describing a right-frontal derivation of this HIT-CR effect. It remained right-frontal for the following 800 to 900ms showing significant differences for F4 but being higher at Fp2 ($t(12)=3.021$;$p=.011$). From here onwards, data showed a right frontal maximum difference peaking at F4 from 900 to 1000ms ($t(12)=4.017$; $p=.002$) with also significant differences in the case of F9, Fp2 and Fz; again F4 from 1000 to 1100ms ($t(12)= 3.589$; $p=.004$) with F9, Fz, FCz and Fp2 as also statistical significant electrodes; highest significance for F4 ($t(12)=3.03$;$p=.01$) from 1100-1200ms with also Fp2 and Fz; the highest difference from 1200 to 1300ms corresponds to F4 ($t(12)=2.632$; $p=.022$) with only Fz as significant electrode to be added; and finally, from 1300 to 1400ms, F4 was again the electrode with the highest difference ($t(12)=2.644$; $p=.021$) with Fz and Fp2 frontal electrodes proving also significant. This consistent right-frontal tendency on this true memory effect turned out into central localizations at the last time window, from 1400 to 1500 ms, showing Fp2 and F4 as significant electrodes but peaking with the highest statistical difference at Fz ($t(12)=3.618$; $p=.004$).

When time windows were collapsed, control participants´ data showed that from 300 to 500ms significant differences between voltages for HITS and CR signals appeared at central (Fz, FCz and Cz) and right electrodes (Fp2, F4 and C4), proving more significance at Fz ($t(12)=4.084$; $p=.002$). From 500 to 800ms differences are more frontally displayed, with Fp2, Fz and F4 proving significant difference and with Fp2 as the most significant ($t(12)=3.085$;$p=.009$. During the next 200ms, from 800-1000ms, the same scenario was observed, adding F9 to the aforementioned positive electrodes of previous time window, and with Fp2 ($t(12)=3.587$; $p=.004$) as the most significantly different electrode. From 1000 to 1200ms significant positive electrodes were F9, Fz, Pp2 and F4, with peak of significance on F4 ($t(12)=3.381$;$p=.005$). During the last collapsed time period, from 1200 to 1500, data showed positive significant differences on Fz, Fp2 and F4, Fz ($t(12)=2.837$; $p=.015$) proving more significant. See Figure 21 for a detailed topographic view.

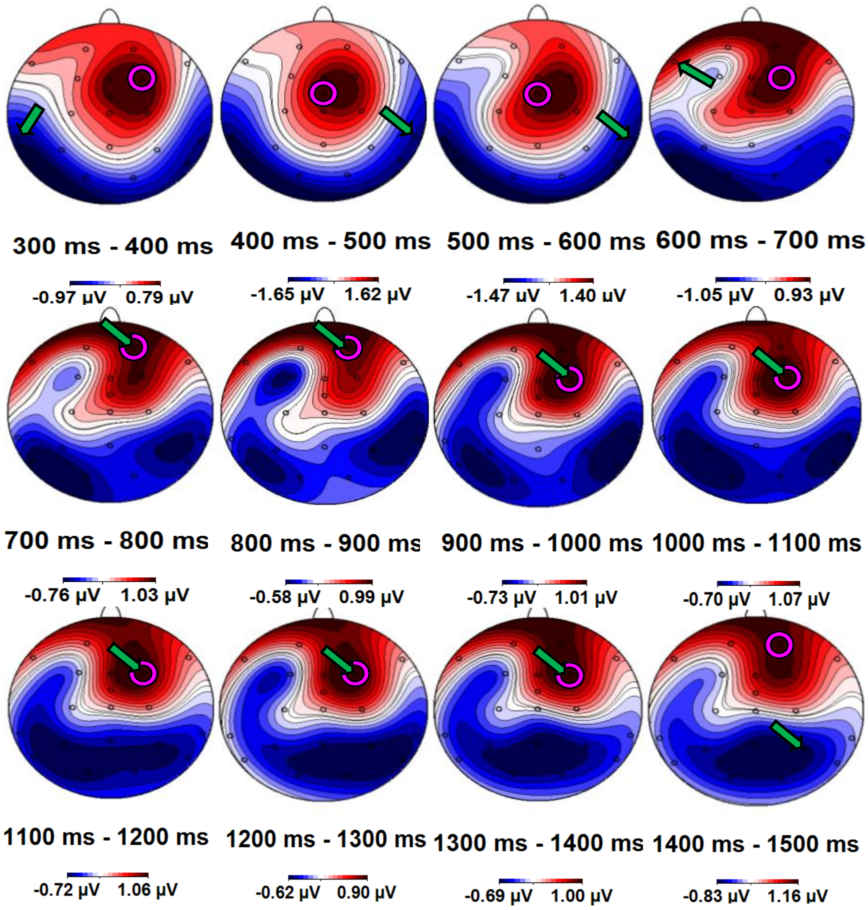

Figure 21 Mapping view of the control group's performance. Voltages correspond to a HIT-CR difference wave. The pink circle indicates the electrode with the maximum voltage and the green arrow points to the electrode with the highest p value after t-test. Electrodes were depicted in Chapter 4.

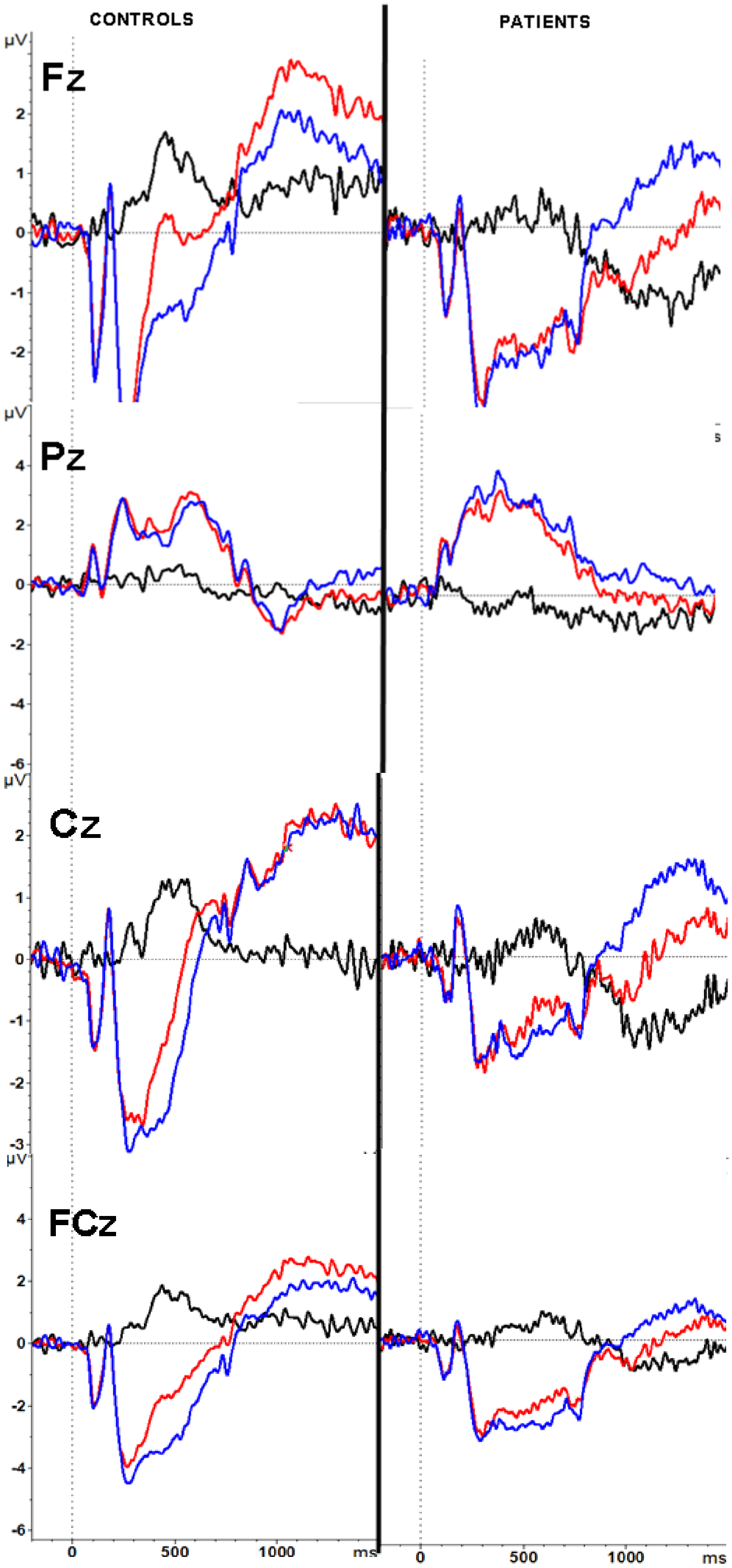

Figure 22 Difference wave from the HIT-CR memory effect. Difference wave is represented by a black line, HIT by a red line and CR by a blue line. Milliseconds are displayed at X axis and microvolts at Y.

In conclusion, when analysing the HIT-CR effect on our control sample (see Figure 23), significant differences appeared in early times at fronto-central electrodes, these changed into a more right-frontal localization for the following 500ms. This was followed by a more lateralized right frontal activity from 1000 to 1200ms and changed back to fronto-central electrodes at the last 300ms interval.

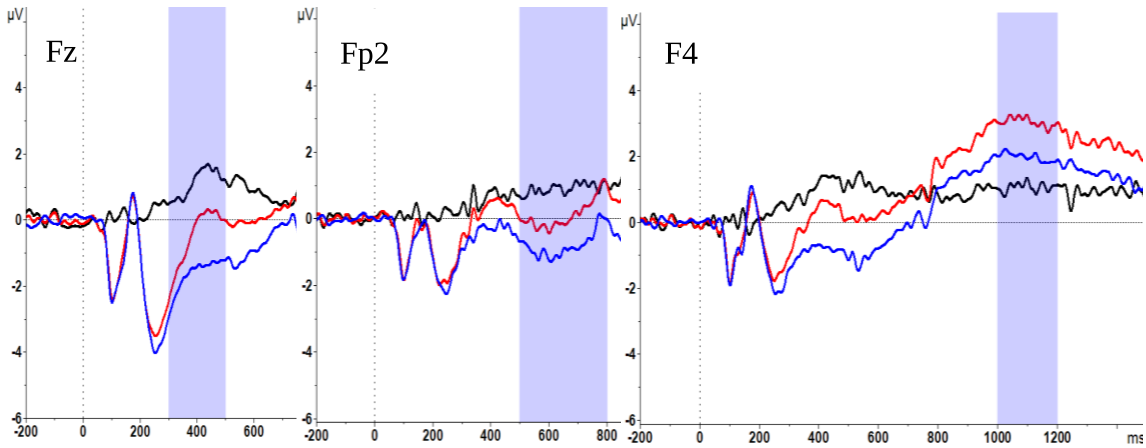

Figure 23 Control group HIT-CR difference wave for the highest significant electrodes on each collapsed time window. The red line corresponds to hits, the blue line to correct rejections and the black line displays their difference. The highlighted vertical area corresponds to collapsed time windows, i.e., 300-500, 500-800 and 1000-1200ms.

HIT-FM effect

The comparison between FM voltage and HIT voltage corresponds to the HIT-FM effect. On this occasion, we only analyse responses whereby the participants feel certain abou them regardless of whether they are correct or not. In both cases, FM and HIT responses are positive responses to the question “was this item present at study?” The only real difference between a HIT and an FM response is our experimental manipulation, i.e. the semantic relationship of lured items with the theme of the studied scene albeit not being present at study. The result of this subtraction is considered a true memory indicator.

Control participants´ differences appeared early in time, at 300ms and continued until 500ms at Fz electrode ($t(12)=2.796$;$p=.016$ from 300-400ms and $t(12)=2.921$: $p=.013$ from 400-500ms) (see **Figure 24**). No differences between HITS and FM were found from 500-600ms but Fz was the electrode with the maximum voltage ($t(12)=2.016$; $p=.067$, n.s.). A broader number of electrodes proved significant from 600-700ms including FCz and Cz and being maximal at Fz ($t(12)=2.691$; $p=.02$). Differences continued to be related with middle line electrodes such us Cz from 700-800ms, but proving more significantly different at FCz ($t(12)=2.079$; $p=.019$). At the following time windows no significant differences between HITS and FM were found, but when considering the highest voltage of all electrodes, data showed that from 800-900ms it corresponded to FCz ($t(12)=1.897$; $p=.082$ n.s.), from 900-1000ms it proved related to Cz ($t(12)=2.089$; $p=.059$ n.s.), from 1000-1100ms it was present at Cz ($t(12)=2.032$; $p=.065$) and a peak was found at FCz from 1100-1200ms ($t(12)=1.282$; $p=.224$). A change with regards to localization was present for the following 1200-1300 and 1300-1400ms, from central to left posterior sites with the highest voltage difference present at P9 electrode ($t(12)=1.557$; $p=.145$ and $t(12)=.998$; $p=.342$ respectively for both time windows) but getting no statistical significant difference. At the last time window, FCz reached the highest voltage again but with no statistically significant difference between HIT and FM ($t(12)=1.124$; $p=.283$).

When collapsing time windows, our control participants showed that HIT-FM comparison was significantly different from 300-500ms only at Fz ($t(12)=3.587$; $p=.004$). For the following 500-800ms time, Fz was the electrode with the highest significant difference (t(12)=2.413; p=.033) together with another two, FCz and Cz. No significant differences were found for the rest of time windows, but were close to significance at FCz from 800-1000ms (t(12)=2.023; p=.066).

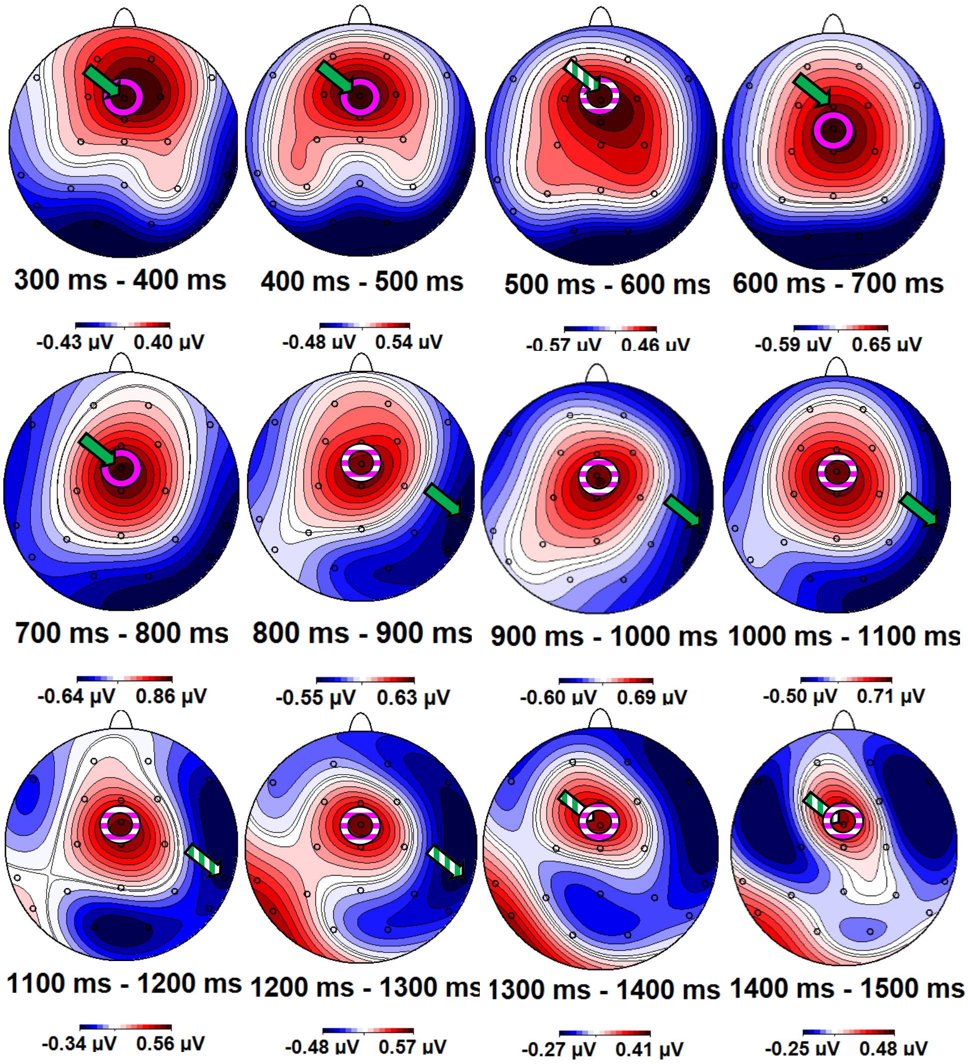

Figure 24 Mapping view of the control group´s performance. Voltages correspond to the HIT-FM difference wave. The pink circle indicates the electrode with the maximum voltage and the green arrow points to the electrode with the highest p value after t-test. Stripped indicators correspond to electrodes with p>.05 on t-test.

In conclusion, for this HIT-FM effect, a significant fronto-central activity was present from early times and remained at these locations until 800ms. No significant differences were found for the rest of the time windows, despite a central distribution of the electrodes showing the highest voltage for this difference wave.

FALSE MEMORY

Based on the same premise from the previous HIT-CR effect, we consider the FM-CR effect as a measure of false memory. We assume that comparing the ERP signal related to positive responses to a lured item (i.e. false memories) with the ERP signal related to correct rejection, this will give us information related to pure false retrieval. These positive responses to critical lures cannot be considered true memories because they were not present at study but participants will consider them as such because of their semantic relationship with the theme of the studied scene. This FM-CR effect has been described in the literature as the false memory effect.

Significant differences between amplitudes related to false memories compared with correct rejections appeared in our data from 300 to 400ms only at C4 electrode ($t(12)=2.462$; $p=.03$). A broader range of significant electrodes, including Fz, FCz, Cz, F4 and C4 became significant for this FM-CR comparison from 400 to 500ms, with a maximal significance peak at FCz ($t(12)=4.894$;$p<.001$). From 500 to 600ms data showed no significant difference at any electrode, being FCz the closest to significance ($t(12)=2.123$;$p=.055$). The activity changed into the left side for the following 300ms, with F9 as significant electrode from 600-700ms ($t(12)=2.645$;$p=.021$) and 700-800ms ($t(12)=2.397$;$p=.034$) but reaching no significance from 800-900ms ($t(12)=1.917$; $p=.079$). For the following 900 to 1000ms, F9 appeared as significantly different but the highest difference corresponded to Fp2 ($t(12)=2.418$; $p=.032$). From 1000-1100ms significance was found at F9, Fp2 and F4, showing the highest significance difference at F4 ($t(12)=2.718$; $p=.019$) from 1100 to 1200ms, F9 and Fp2 electrodes were significantly different and the maximum difference at this time appeared at F4 ($t(12)=2.671$; $p=.02$). The higher significant difference between FM and CR voltages was present at F4 from 1200-1300ms (t(12)=2.65; p=.021) with also Fp2 showing significant differences at this same period of time. The highest significance changed into Fp2 from 1300 to 1400ms (t(12)=2.511; p=.027) to return again at F4 for the very last time window, from 1400 to 1500ms (t(12)=2.657; p=.021).

Analysing collapsed time windows, data showed that from 300 to 500ms significant electrodes for this FM-CR effect were Fcz, Cz, F4 and C4, with a peak on FCz (t(12)=3.78; p=.003). Only one electrode appeared significant from 500 to 800ms, F9 (t(12)=2.249; p=.044), almost reaching significance also from 800 to 1000ms (t(12)=2.156; p=.052). The scenario changed to the right side from 1000 to 1200ms, with significant electrodes being Fp2 and F4, with the highest difference (t(12)=2.86; p=.01) and stayed right-frontal on the very last 1200 to 1500ms time window, with again a significance peak on F4 (t(12)=2.642; p=.021).

In conclusion, for this FM-CR effect in control participants, significant differences were found at early timing in fronto-central electrodes, to change into left-frontal electrodes from 500 to 100ms and changing again to right-frontal electrodes till the end of our time analysis.

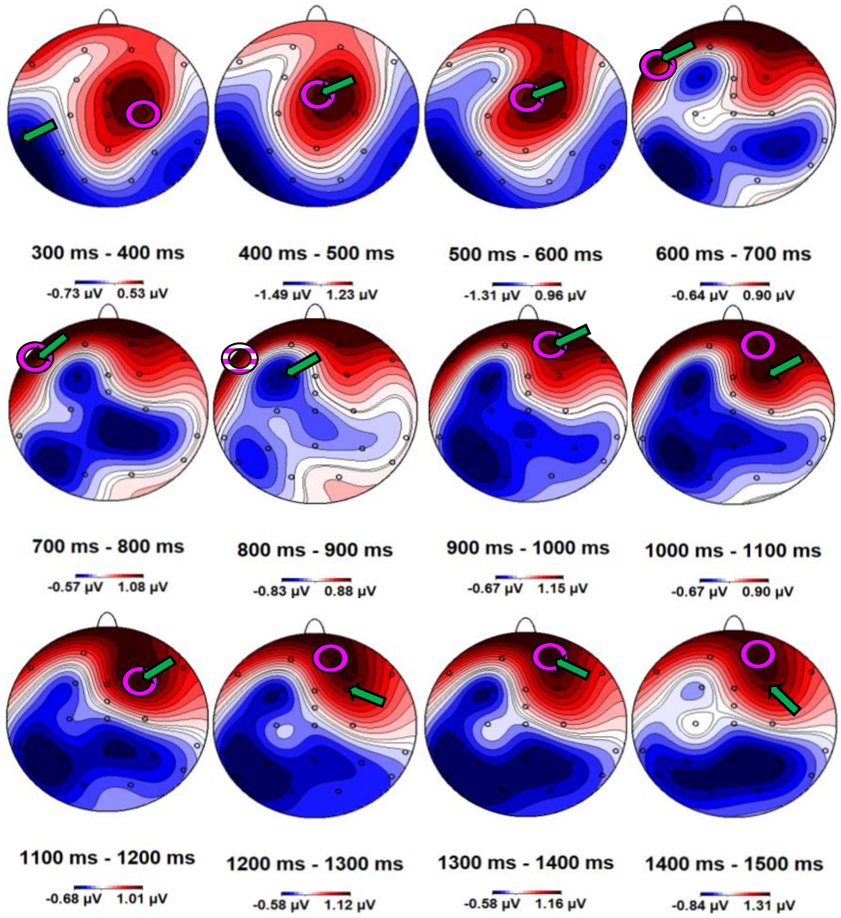

Figure 25 Mapping view of the control group´s performance. Voltages correspond to a HIT-CR difference wave. The pink circle indicates the electrode with the maximum voltage and the green arrow points to the electrode with the highest p value after t-test. Stripped indicators correspond to electrodes with p>.05 on t-test. For details of electrodes, see chapter 2.

COMPARING TRUE VERSUS FALSE MEMORY IN THE CONTROL GROUP

After depicting ERP characteristics of true and false memory signals in the control group, our aim is to study any possible difference between those two memory effects within this group, in continuation with previous works in this field. For inspection of difference waves corresponding to true versus false recognition, see Figures 5 and 6 from Appendix Chapter 5.

ANOVA with type of memory (i.e. HIT-CR for true memory (TM) and FM-CR for false memory (FM)) and locations regarding topographic distribution of interest (Fz, F4, FCz, Cz, C4 and FP2) as factors and voltage as a dependent variable were run for each time window. The selected electrodes were Fp2, Fz, F4, F9, FCz, Cz and C4. This election was based on the previous analysis, including only the electrodes that proved to be significantly different in any of both comparisons (i.e. HIT-CR and/or FM-CR).

For the first 300-500ms time window, a significant effect of type of memory was observed ($F(1,12)= 5.09$, $p=.044$), with a higher estimated mean for TM compared to FM (0.939, SE=0.256 and 0.669, SE=0.256 respectively), but no effect on localization neither interaction between those two factors was identified. At the following 500-800ms time window, no significant effect was found for type of memory or electrodes but there was a significant interaction ($F(5,70) = 2.722$, $p = .028$). Posterior contrasts indicated that differences regarding both types of memories were related to fronto-central electrodes compared with left-frontal sites (Fz against F9 ($F(1,12)=8.17$,$p=.014$) and Cz against F9 (F1,12)=5.14, $p=.043$). No effects or interactions were found from 800 to 1000ms at analyzed locations (F9, FP2, Fz and F4). Regarding the following 1000-1200ms time window, localization showed a significant effect $F(4,48)=5.07$, $p=.054$ when considering F9, FP2, Fz, F4 and Cz electrodes. Posterior contrasts indicated that specific differences corresponded to higher voltages at right-frontal electrodes compared to central (FP2 M = .940, SE=.287; F4 M = .989, SE=.294 and Cz M = -.106, SE=.396) ($F(1,12)=4.578$, $p=.054$ and $F(1,12)=6.8$, $p=.023$ respectively). No effect or interaction was found for the last time window 1200-1500ms (electrodes of analysis Fp2, Fz, F4 and F9).

In conclusion, healthy control participants showed voltage differences between types of memory early in time but these disappeared later on. Localization of activation was significantly fronto-central from 500-800ms and right-frontal from 1000-1200ms. Topographic distribution corresponding to this analysis can be found in Figure 26.

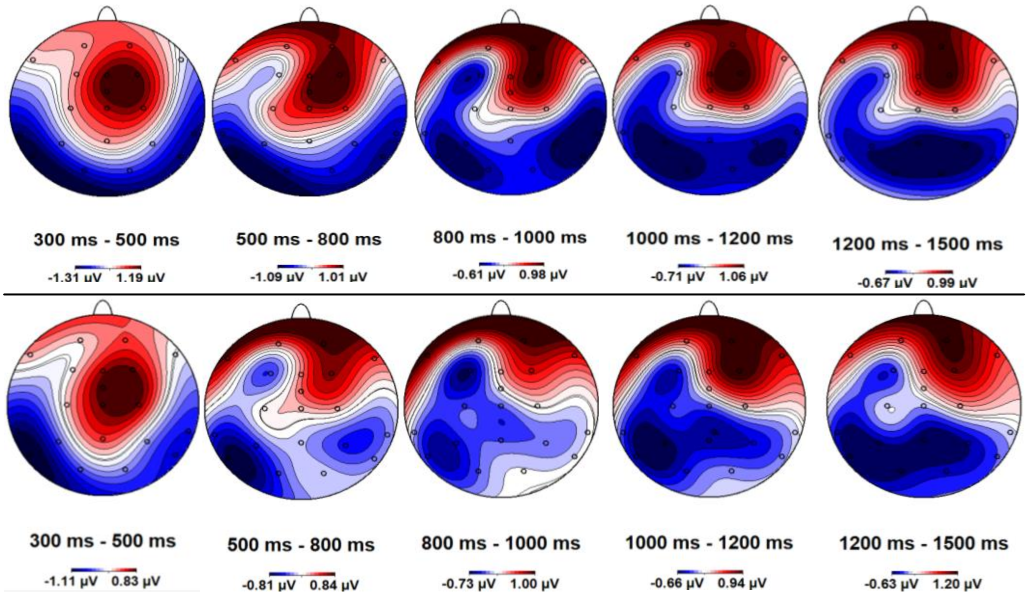

Figure 26 Topographic distribution of voltages for HIT-CR (top) and FM-CR (bottom) corresponding to collapsed time windows for the control group.

5.4.4.2 Patients Group

In the following section we will analyse indexes corresponding with true and false memory in our sample of amnesic patients.

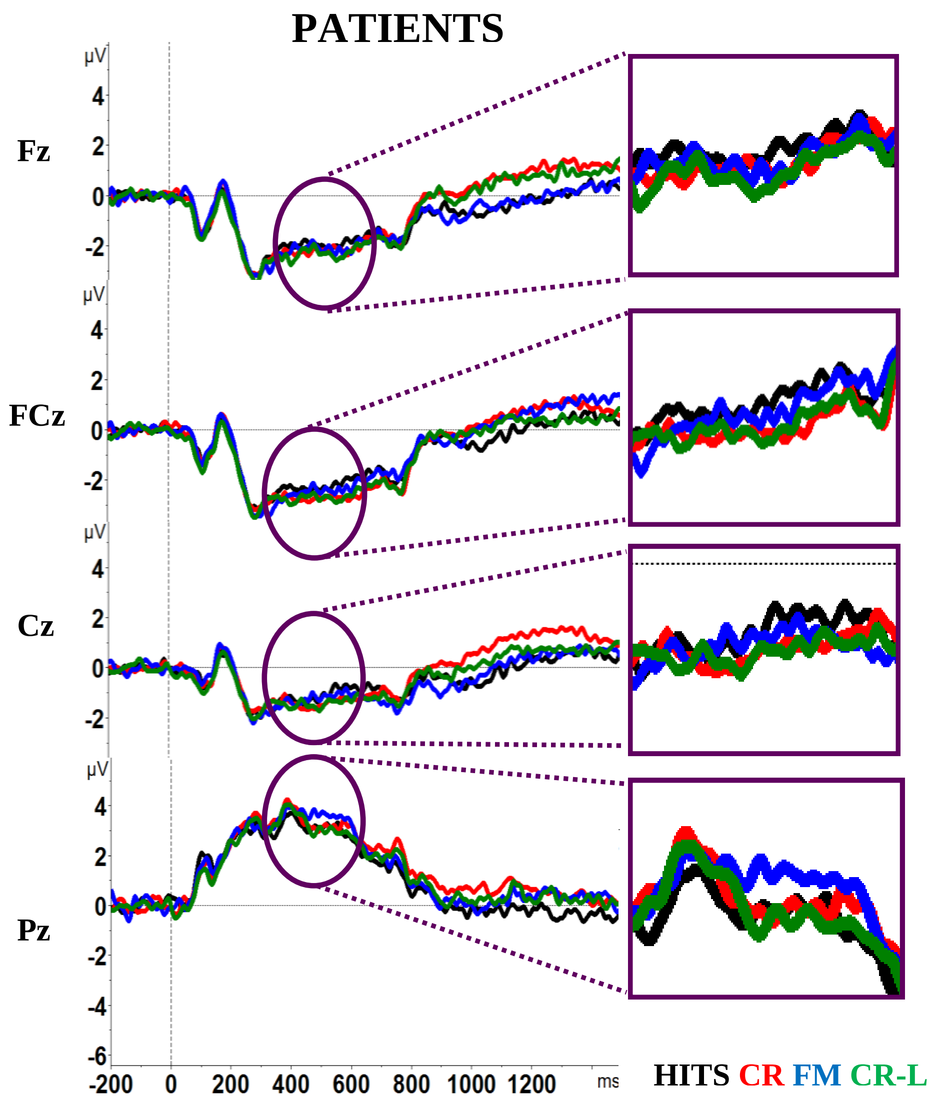

Figure 27: Grand averages for patients groups on midsagittal electrodes and for our main response categories.

A different scenario from what control participants produced was present when visual inspection of patients´ averaged waves for each response category was analysed.

As Figure 27 shows, no big differences were appreciable at midsagittal electrodes until late timing, from 800ms onwards approximately. It is interesting to note how at Fz, CR and CR-L showed a very similar voltage whereas FM and HITS present similar lower voltage. No other important differences are present at visual inspection.

If we analyse in detail how averaged waves corresponding to our response categories behaved in our patients´ group, the data showed that on the classical HIT versus CR difference wave a consistent significant difference was found at left-frontal F9 electrode from 300 to 1200ms. From that time, until the end of the epoch, a negative signal on fronto-central electrode Fz was observed (we will analyse in more detail this memory effect in following sections of this chapter).

The difference wave resulted from comparing FM to CR, interestingly showed the same pattern, except for the last 1200-1500ms time window where significant differences were present at bilateral-occipital electrodes.

A heterogeneous pattern with no significant differences was found when comparing HITS to FM waves from 300-500, with F10 and TP10 as closer to significant electrodes. From 500-800ms there was a clear significance at right-frontal F4 electrode. From 800-1000ms a significant electrode was located at left-prefrontal Fp1. A change in lateralization of the significant electrode to a right-parietal site at P10 was observed from a 1000-1200ms time window.

Regarding the last comparison, between CRL and FM, no electrode reached statistical significance until the very last 1200-1500ms time window, localized at P9.

1.1.1.1 TRUE MEMORY

As we depicted with control participants, two indexes will be analysed to study true memory effect; they are described in the following sections.

HIT-CR effect

From 300 to 400ms onwards differences between these two response categories appeared on a left-frontal localization, at Fp1 and F9, with the highest significance at F9 ($t(11)=3.275$; $p=.007$). This F9 electrode did not reach significance on the following 400 to 500ms time window. F9 appeared again as the electrode with a higher significant difference along the following time windows (500-600ms with $t(11)=3.392$; $p=.006$; 600-700ms with $t(11)=2.877$; $p=.015$; 700-800ms with $t(11)=3.098$; $p=.01$; 800-900ms with $t(11)=3.391$; $p=.007$; 900-1000ms with $t(11)=3.699$; $p=.004$; 1000-1100ms with $t(11)=3.71$; $p=.003$ and from 1100-1200ms with $t(11)=3.271$; $p=.007$), sharing also significance with FCz and F4 from 600-700ms and with TP9 and P9 from 1000-1200ms. It is at that time, from 1200 to 1300ms when significance changed into posterior sites to P9 till the end of our time windows ($t(11)=2.609$; $p=.024$ from 1200-1300ms; $t(11)=2.229$; $p=.048$ from 1300-1400ms and not significant from 1400-1500ms, but with the highest p value $t(11)= 1.477$; $p=.168$).

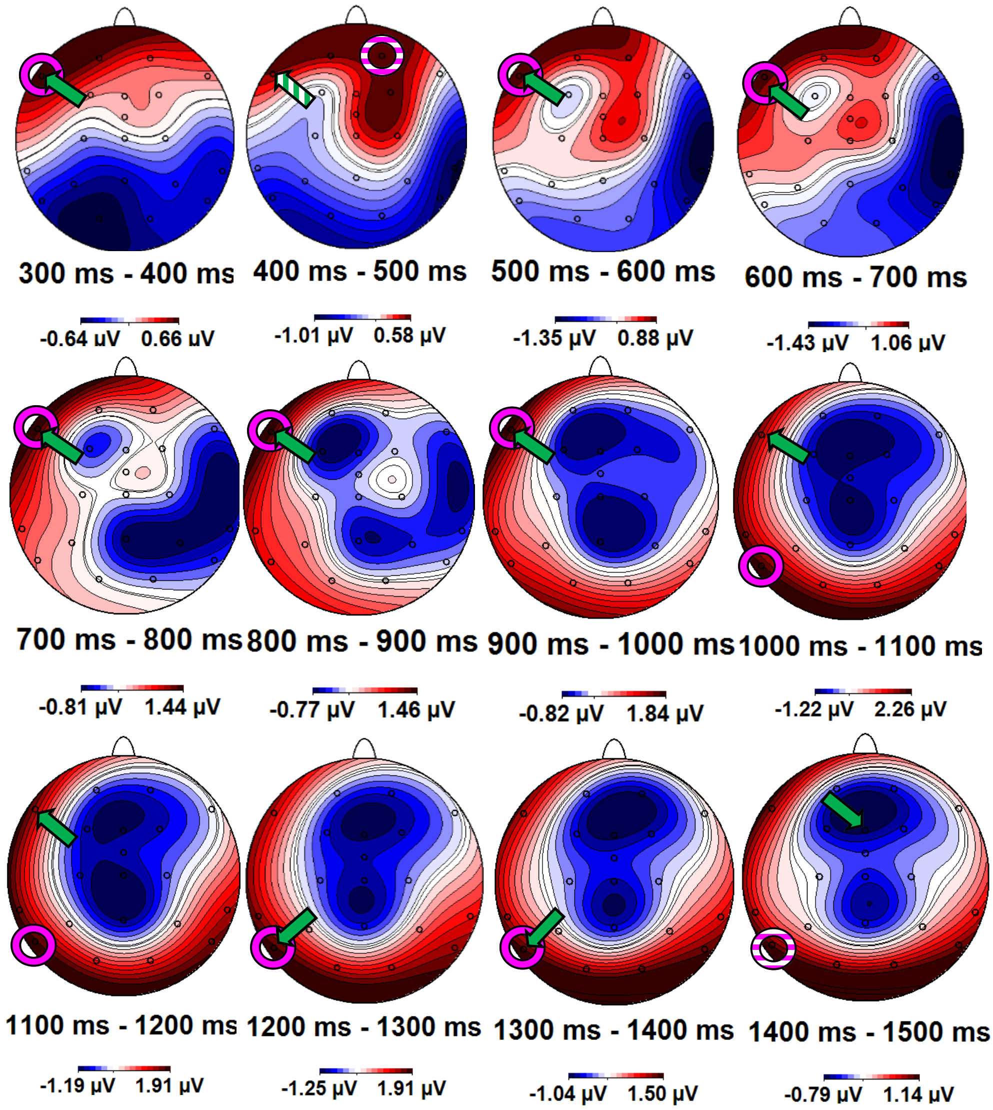

Figure 28: Mapping views of the difference wave HIT-CR in our sample of patients. The pink circle indicates the electrode with the maximum voltage and the green arrow points to the electrode with the highest p value after t-test. Strapped electrode indicators account for p>.05 but closer to statistic significant values.

When time windows are analysed in a collapsed manner, data showed the same tendency as described beforehand. A clear left-frontal localization of the highest significant differences appeared focused on the F9 electrode from 300-500ms ($t(11)=2.543$; $p=.027$), from 500 to 800ms ($t(11)=3.212$; $p=.008$), from 800 to 1000ms ($t(11)=3.602$; $p=.004$) and 1000-1200ms ($t(11)=3.543$; $p=.005$). The shift into left-posterior areas is present from 1200 to 1500ms, with the highest difference found at P9 electrode ($t(11)=2.171$; $p=.05$).

HITS-FM effect

When subtracting the signal related to lured items from the old signal, the general outcome showed that there were no big differences between them along the majority of times for the patients group. To describe this effect in detail, data showed how from 300-400ms significant differences were found at F4 ($t(11)=2.160$; $p=.05$) not reaching any significance on the following 200ms at any electrode but presenting the highest voltage at F4, which was finally significant from 600-700ms ($t(11)=2.787$; $p=.018$). Except from 900-1000ms, where Fp1 reached significance ($t(11)=2.570$; $p=.026$), no other difference was found. The electrodes that showed the highest p values for that difference were distributed broadly over the skull (i.e. Fp1 from 700-800ms; F4 from 800-900ms; TP9 from 1000-1100ms; P10 from 1100-1200ms; Fp1 from 1200-1400ms and C3 from 1400-1500ms).

For collapsed time windows, a very similar scenario was observed, with no differences found from 300-500ms, with a right-frontal localization of significant differences at F4 from 500-800ms ($t(11)=2.204$; $p=.05$) changing into left-frontal from 800-1000ms (Fp1 with $t(11)=2.345$; $p=.039$). A posterior non-significant localization were present from 1000-1200ms, with a voltage peak located at P10 ($t(11)=1.623$; $p=.133$) to convert again into a left-frontal non-significant peak at Fp1($t(11)=1.201$; $p=.255$).

1.1.1.2 FALSE MEMORY

The FM-CR difference wave was analysed here. No significant differences were found in the case of this difference wave from 300 to 400ms, F9 proving nevertheless the electrode with the highest voltage at this time ($t(11)=1.532$; $p=.154$). A negative sign for this difference wave was present from 400 to 500ms, with TP10 as the only significant electrode ($t(11)= -3.489$; $p=.005$). It is from 500ms to 900ms when F9 appeared as the only significant electrode (500-600ms with $t(11)=2.236$; $p=.047$; 600-700ms with $t(11)=2.337$; $p=.04$; 700-800ms with $t(11)=2.706$; $p=.02$ and 800-900ms with $t(11)=2.895$; $p=.015$ respectively). A posterior site of significance started to be present from 900-1000ms onwards at P9, being F9 remaining the electrode with the highest significant difference from 900-1000ms ($t(11)3.726$; $p=.003$), from 1000-1100ms ($t(11)=3.787$; $p=.003$) and 1100-1200ms ($t(11)=3.085$; $p=.01$) but changing into P9 from 1200-1300ms time window ($t(11)=2.910$; $p=.014$). For the last time windows, no significant differences were found but, nevertheless, a clear posterior localization of the highest voltages was present (i.e. O2 with $t(11)=2.125$; $p=.057$ from 1300-1400ms and O2 with $t(11)=1.813$; $p=.097$ from 1400-1500ms).

With this constant pattern present when analysing time windows of 100ms, no big changes were expected when analysing collapsed time windows. No significant difference between FM and CR voltages was reached for a 300-500ms timing, with F9 as the electrode with the highest voltage but with not statistic significant difference. This same F9 electrode appeared as significant for the next time windows (500-800ms with $t(11)=2.636$; $p=.023$; 800-1000ms with $t(11)=3.269$; $p=.007$ and 1000-1200ms with $t(11)=3.439$; $p=.006$ respectively) until the last time window, from 1200-1500ms, where no significances were found but a tendency to significance was observed in the case of right-posterior sites (i.e. O2 with $t(11)=1952$; $p=.077$).

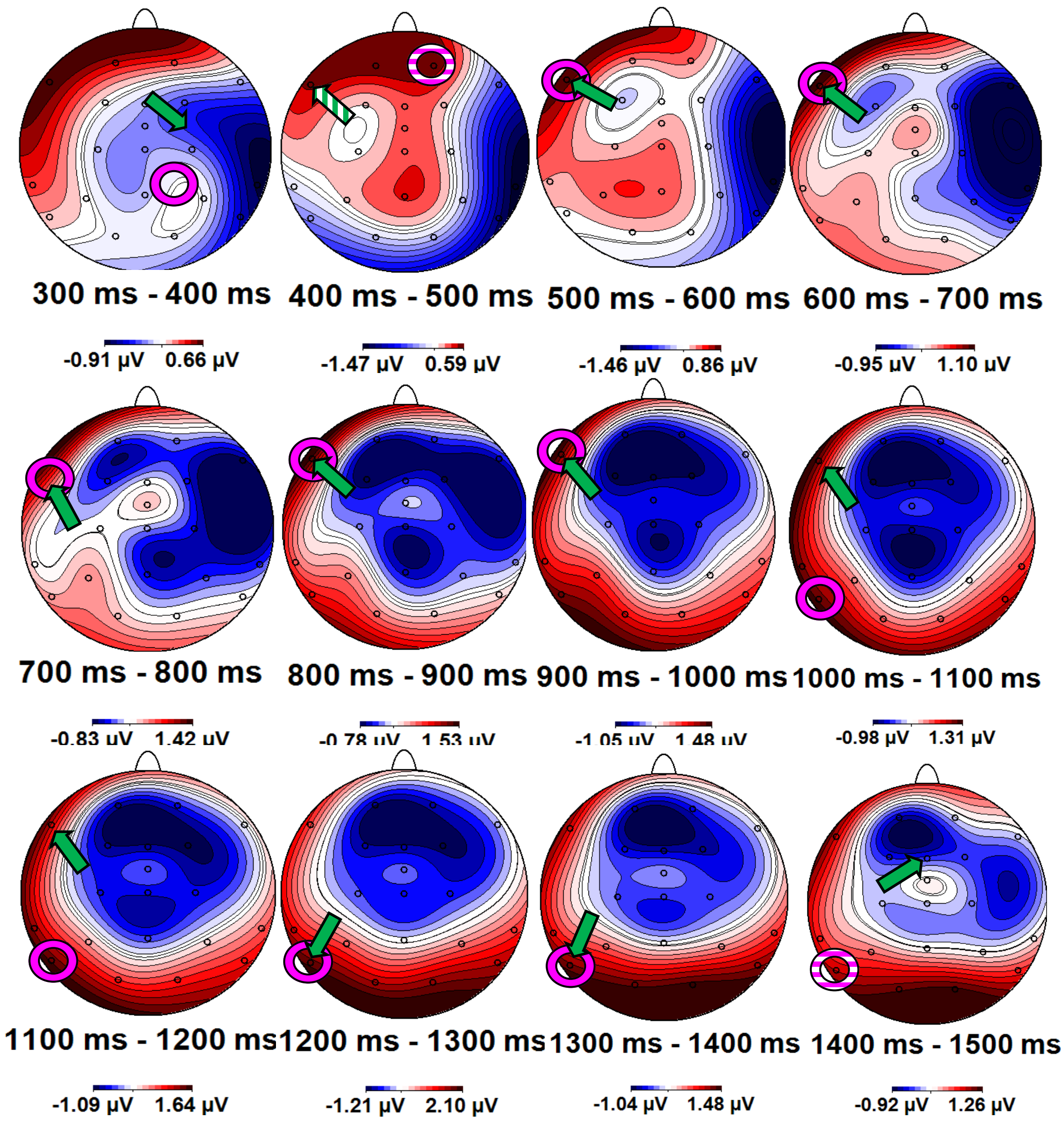

Figure 29: Mapping views of patients´ group performance. Voltages correspond to an FM-CR difference wave. The pink circle indicates the electrode with the maximum voltage and the green arrow points to the electrode with the highest p value after t-test. Stripped indicators correspond to electrodes with p>.05 in t-test.

1.1.1.3 COMPARING TRUE AND FALSE MEMORY IN PATIENTS

Table 9 specifies electrodes included in our analysis. These electrodes corresponded to those with a higher statistic significant difference when two responses were compared (i.e. HIT versus CR and FM versus CR). This table gives information about both patients and control groups and about each time window of interest. Data related to the control group has been already analysed previously in this section. In this case, we want to focus only on the amnesic patients´ group. When checking the electrode that was significantly different in the case of each memory effect and for each time window, the reader can easily appreciate from this Table 9 that patients consistently showed F9 as the electrode with the highest significance in all time windows except in the last one. From 1200 to 1500 ms, a significant electrode for true memory was Fz but it reached no significance for false recollection.

Table 9

Electrodes with the most significant difference on each difference wave for each time window.

ms	300-500		500-800		800-1000		1000-1200		1200-1500	
	Cont	Pat	Cont	Pat	Cont	Pat	Cont	Pat	Cont	Pat
HIT-CR	TP10	F9	Fp2	F9	Fp2	F9	F4	F9	P6	Fz
FM-CR	FCz	*F9**	F9	F9	F9	F9	F4	F9	F4	*O1**

Note Cont: Control sample; Pat: patients. * indicates p>.05

Nevertheless, the same ANOVA run with control participants was applied comparing localization of electrodes and types of memory for the patients group. The first significant effect of localization was found at 800-1000ms time window $F(1.4,15.8)=5.155$, $p=.027$. Greenhouse-Geisser correction was applied after sphericity violation was confirmed by Mauchly's test (χ^2 (5)=19.589, p=.002). This effect was indicating that at this time, F9 electrode corresponding to left-frontal sites presented the highest voltage (M = 1.558, SE=.440) compared with right-frontal electrodes (M = -0.629, SE=.656) ($F(1,11)=4.517$, $p=.057$). The same conclusion can be addressed on the following 1000-1200ms time window, where effect of localization was found $F(1.84,20.2)=6.712$, $p=.007$, Greenhouse-Geisser correction due to violation of sphericity assumption (χ^2 (9)=26.81, p=.002). Again, lateralization of positive voltages to left-frontal F9 electrode (M= 1.428 SE=.375) compared to central electrode Cz (M= -

1.077, SE=.432) was identified in patients. This left-frontal localization of the activity was still present at the last time window, where a localization effect was found $F(1.6,17.61)=4.189$, $p=.04$, Greenhouse-Geisser's correction was applied after Mauchly's sphericity test concluded lack of sphericity assumption ($\chi^2(5)=16.159$, $p=.007$).

In conclusion, patients processed both types of memory differently only early on in time, while showing the same localization later on until the end of the epoch on a clearly left-frontal lateralized placement. Amnesic patients seem to activate true and false recollection processes in very similar locations in the brain (see also Figure 30 for details on topographic distribution of both memory effects).

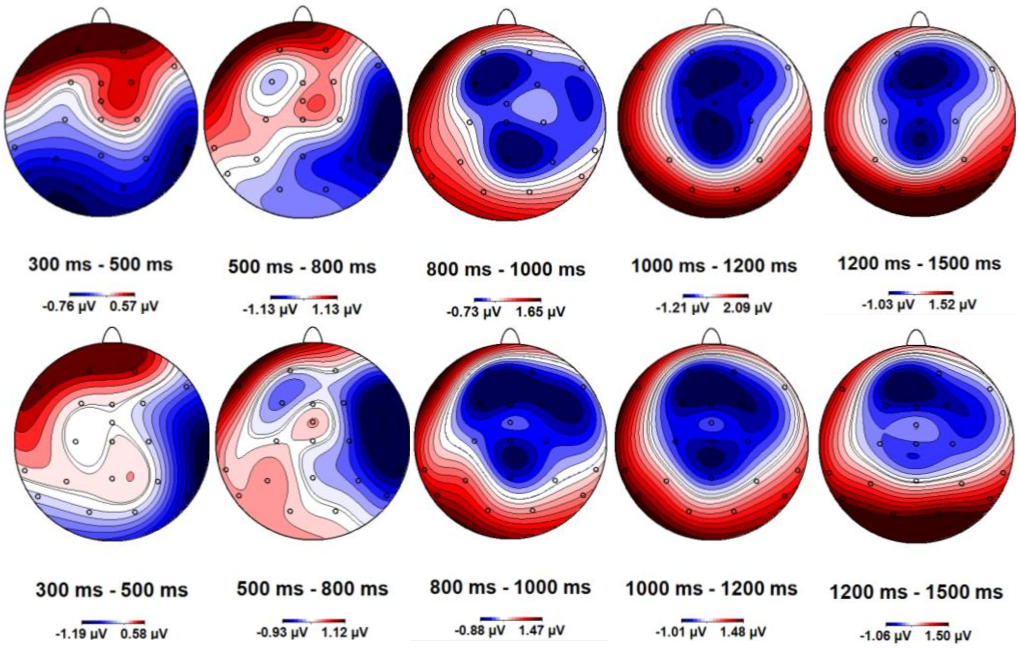

Figure 30: Topographic distribution of voltages for HIT-CR (top) and FM-CR (bottom) corresponding to collapsed time windows for patients.

5.4.4.3Comparing Patients versus Controls

So far, the data showed how neural correlates implicated in processing true and false recognition seemed to be related in amnesic neurological patients and in their age-matched healthy controls as independent groups. However our interest was in analysing whether there is any differential ERP pattern when these two samples are compared directly. Table 10displays the electrodes where maximum significance for difference waves on each group was calculated in 100ms time windows. The table shows the first differences and similarities between groups´ performances which we will analyse in detail below.

Table 10
Results from statistical analysis of difference waves for our two groups of participants.

	HIT-CR		FM-CR	
ms	control	patients	control	patients
300-400	F4	F9	C4	*F9*
400-500	Fz	TP10	FCz	TP10
500-600	Cz	F9	FCz	TP10
600-700	F9	F9	**F9**	**F9**
700-800	Fp2	F9	**F9**	**F9**
800-900	Fp2	F9	***F9***	**F9**
900-1000	F4	F9	Fp2	F9
1000-1100	F4	F9	F4	F9
1100-1200	F4	F9	F4	F9
1200-1300	F4	P9	F4	P9
1300-1400	F4	P9	Fp2	*O1*
1400-1500	Fz	Fz	F4	*O2*

Note: Cursive values correspond to electrodes that did not reach statistical significance but were the closer to p=.05. Note how for FM-CR difference, and along 500 to 900ms, both groups showed the same localization. CR: correct rejection; FM: false memory.

In order to carry out a comparison of the memory effects between patients and controls, we calculated a new variable resulting from the subtraction of two mean averages corresponding to the specific response categories To compare true memory (TM), in this case, mean voltage in CR responses was subtracted from the mean voltage in HIT responses, resulting in a measure of voltage allowing us to compare true memory effect directly between patients and controls. The same calculation was applied for FM-CR to obtain a measure of false memory (FM).

Topographic distribution of voltage activity for true and false memory defined as the abovementioned HIT-CR and FM-CR respectively can be seen in Figure 31 and Figure 32.

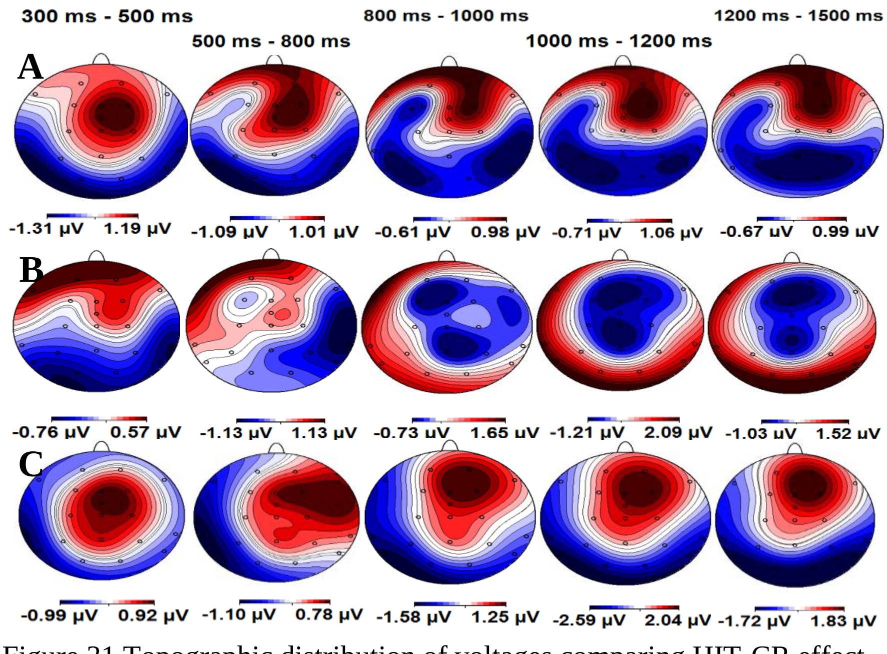

Figure 31 Topographic distribution of voltages comparing HIT-CR effect. A: control participants; B: patients; C: subtraction of HIT-CR from controls minus HIT-CR from patients.

The ANOVA was calculated to study differences between groups regarding true and false memory effects. To do so, we utilized the same recalculated variables as we used in ANOVA comparisons for each group (i.e. TM resulting from HIT minus CR voltages and FM from FM minus CR voltages). We included the following factors: group as between subjects factor (X2 patients and controls), memory effect (X2 TM and FM) and electrodes (X6 F9, Fz, F4, Cz, C4 and FCz). We only focused on the interaction effect between group and memory effect, which might help us explain differences between groups and types of memory.

For the first time window, 300-500ms, a significant interaction effect was found for group and memory effect: control participants presented consistently higher voltages when compared to patients in true memory $F(1,23) = 4.27$, $p = .05$ and false memory $F(1,23) = 4.43$, $p = .046$ (control for TM $M = .87$; $SE = .2$ and FM $M = .64$; $SE = .2$ and patients TM $M = .28$; $SE = .2$ and FM $M = .06$, $SE= .2$). The interaction effect was present between group and electrode $F(5,115) = 2.46$, $p = .037$, showing the fact that control presented higher voltages at central electrodes Cz and FCz when compared to patients (Cz for control $M = .73$, $SE=.23$ and patients $M = .05$, $SE = .24$; FCz for control $M = 1.01$, $SE = .26$ and patients $M = .16$,$SE = .27$).

From a 500-800ms time window, no significant interactions were found between group and memory effect $F(1,23) = .16$, $p = .7$ or group and electrode $F(5,115) = 1.36$, $p = .25$.

The following time window from 800-1000ms presented no interactions of significance between group and neither memory effect $F(1,23) = .05$, $p = .82$ or electrodes $F(5,115) = 1.64$, $p = .16$.

From 1000 to 1200ms data showed predominance of higher voltages for control group related with both memory effects when compared with patients. Higher voltages for true memory corresponded to control group $F(1,23) = 8.27$, $p = .009$ (control $M = .62$, $SE=.27$ and patients $M = -.51$, $SE = .28$) and the same happened with false memory $F(1,23) = 4.84$, $p = .04$ (control $M = .38$, $SE = .25$ and patients $M = -.42$, $SE = .26$). These differences in voltage corresponded to electrodes Fz and F4: the control group had significantly higher voltages than patients $F(1,23) = 9.59$, $p = .005$ and $F(1,23) = 9.53$, $p = .005$ respectively (control Fz $M = .74$, $SE = .41$ and F4 $M = .99$, $SE = .44$ and patients Fz $M = -1.1$, $SE = .43$ and F4 $M = -.98$, $SE = .46$).

The last time window presented an interaction effect in the case of true memory $F(1,23) = 5.83$, $p=.024$ only, showing that the control group reached higher voltages ($M = .50$, $SE = .25$) when compared to patients ($M = -.38$, $SE = .26$). Interaction with electrode was also present $F(5,115) =2.3$, $p = .05$ and differences between patients and controls were again present only at frontal electrodes with higher voltages for controls (Fz control $M = .69$, $SE = .37$ and patients $M =-1$, $SE = .39$ and F4 control $M = .94$, $SE = .4$ and patients $M = -.79$, $SE= .42$).

In conclusion, when comparing our two groups, differences between true and false memories reflected consistently that control participants reached higher voltages when compared to patients. This aspect can be found from 300-500ms for both memory effects but disappeared until later on, from 1000-1200ms onwards. At the last time window, from 1200-1500ms onwards this difference was only present for true memory effect, but not for false memory.

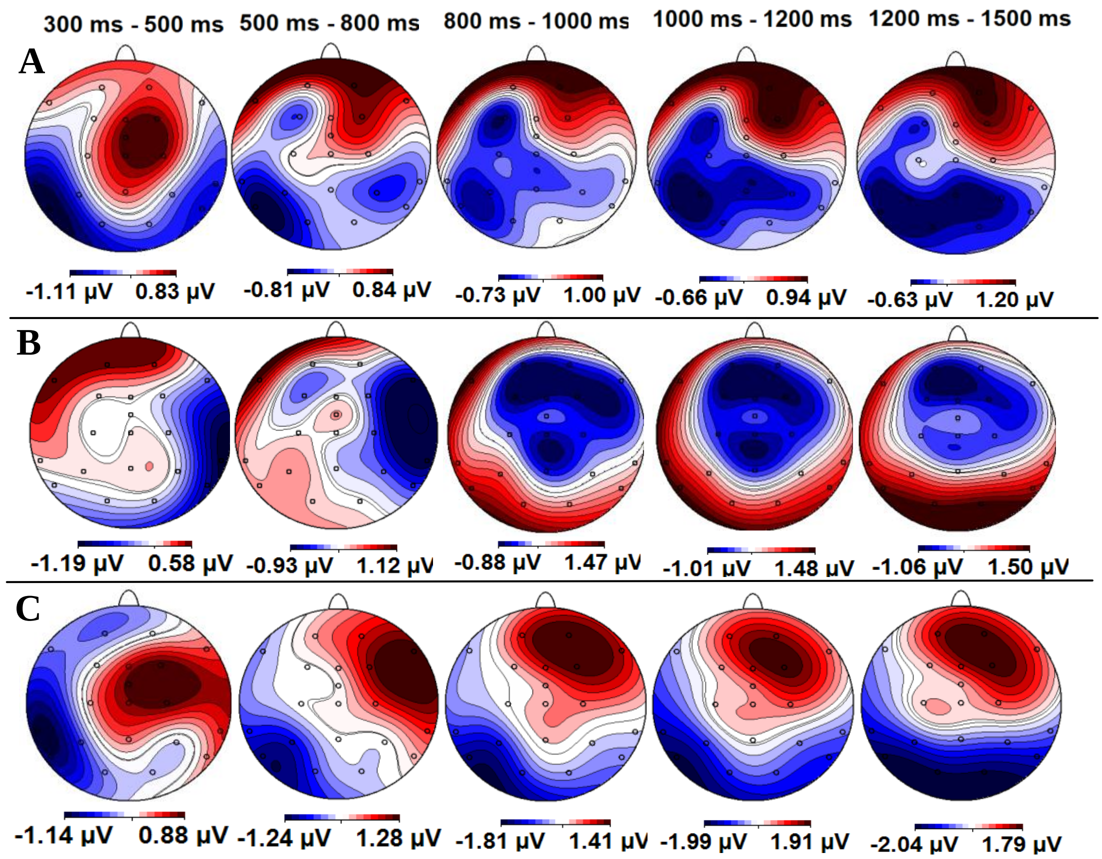

Figure 32 Topographic distribution of voltages comparing FM-CR effect. A: control participants; B: patients; C: subtraction of FM-CR from controls minus FM-CR from patients.

5.5Conclusions

In this chapter we utilized the adapted version of VFMT2.0 with a sample of amnesic patients in an ERP experimental design and compared their performance with age-matched healthy control participants.

5.5.1 Control group

Behavioural results replicated previously confirmed data described in Chapter 3 concerning the validity of VFMT as a useful true and false memory task. In this second version, high accuracy for hits was achieved by control participants, with a higher percentage compared with VFMT1.0 (82.87% compared to 77.97%). False memory responses were produced above chance.

Regarding ERP analysis, higher voltages for HITS compared to CR were found at fronto-central electrodes from 300 to 500ms. The following time period, between 500 and 1200ms, showed that higher voltages corresponded to right-frontal electrodes up to the very last time window, from 1200-1500ms, where voltages for HITS were higher compared to CR at fronto-central sites. HIT voltages were higher than FM at fronto-central electrodes from 300 to 1000ms. FM-CR effect consisted in higher voltages for FM compared to CR at fronto-central areas from 300 to 500ms, changing later to left-frontal electrodes from 500 to 100ms and changing again to become right-frontal up to the end of our time analysis. Finally, if we compare FM against CR-L condition in the control group the only significant difference is found from 1000-1200ms at left-frontal electrodes, with a higher voltage corresponding to CR-L.

When difference waves were analysed, the control group showed higher voltages for true (i.e. HIT-CR) versus false (i.e.FM-CR) memory effects only at the very early 300-500ms time window. The same electrodes and voltages for both memory effects were present at the following time windows (fronto-central from 500-800ms and right-frontal from 1000-1200ms).

5.5.2 Amnesic group

When the patient group results were analysed, a constant left-frontal localization of electrodes with higher voltages for HITS for almost the complete duration of the epoch (from 300 to 1200ms) was found when compared to CR. HITS versus FM showed no significant difference. FM versus CR showed significant differences with higher voltages for FM at left-frontal localizations all through the time windows. No significant differences were found for patients when FM and CRL were compared.

When comparing difference waves corresponding to HIT-CR versus FM-CR, the patient group showed consistent left-frontal electrode significance, regardless of the type of memory through the entire duration.

Neural correlates engaged in processing both true and false memories in amnesic patients appeared to rely on the activity of similar electrodes as for control participants, and implicated in false memory processing for the period of time from 500 to 1000ms (i.e. left-frontal areas, F9 electrode).

5.5.3Comparing Groups

Behaviourally, differences were found between the groups in terms of accuracy of response regarding signal detection theory. However, we found no differences at all between and within these two samples as to false memory percentage. Reaction time to each response category showed no significant differences between patients and controls, but a slightly different pattern was observed: the control group presented the fastest response to CR, followed by HIT, FM, FA and CRL; whereas for the patient group the fastest response corresponded to HIT, followed by FM, CR, FA and CRL. Neural substrate accounting true and false memory production was found different when amnesic patients' and control participants' ERP activity was analysed. Nevertheless, differing from healthy controls, patients with amnesia seem to base their memory performance on the same neurological structures regardless whether true or falsely recollected.

5.6 Discussion

With this experiment we wanted to study true and false memory using our VFMT2.0 and recording EEG signal during performance. To do it so, we targeted KS patients as the amnesic sample and we assessed them from the neuropsychological and neuroimage aspects. Cognition in this neurological disease has been described as heterogeneous, being part of a continuum from spared cognition to dementia compatible diagnosis (Parsons, 1998; Victor et al., 1989). In our sample of 12 KS patients, data suggested a consistent amnesic profile for either verbal or visual material among them, with a variable degree of executive function impairment.

Neuroimage data collected here in some of our patients was to determine whether high-resolution MRI could be used to identify lesions in subcortical structures belonging to circuits affected in KS. In three out of four patients with KS, we observed diagnostic neuroradiological abnormalities not reported previously. First, central gliosis of the mammillary bodies (MB) was present bilaterally in two patients, indicating that MRI can demonstrate one of the established pathological hallmarks of the disease. Secondly, degeneration of the mammillothalamic tract (MMT) was observed in three patients. To our knowledge, the latter finding is a novel observation that has no precedent in reports of the pathological changes associated with WKS.

In two of the three patients, the degeneration appeared to be restricted to the distal MTT. MTT degeneration did not seem to be related to visible gliosis in the MB. Complete MTT degeneration was present in a patient with no evidence of central gliosis of the MB; whereas central gliosis of the MB was present in both patients with distal MTT degeneration. Given the proximal sparing of the MTT in two patients, and the observed dissociation between MB central gliosis and terminal MTT degeneration, it seems unlikely that the demyelization and hypointensities seen in the MTT represent Wallerian degeneration secondary to neuronal loss in the MB. The selective degeneration of the distal MTT is consistent with a dying-back axonopathy (Conforti, Adalbert, & Coleman, 2007; Spencer & Schaumburg, 1977), and suggests that this mechanism may contribute to the pathogenesis of the disease independently from the well-established nuclear lesions found in the MB and thalamus.

The current observations suggest that high resolution MRI may aid the clinical diagnosis of KS. In the future, greater availability of high resolution MRI may help to mitigate the underestimation of the incidence of this disease that is potentially preventable and that can be iatrogenic, as in the case of Patient 46 reported here who was administered intravenous glucose without parenteral thiamine.

Future research could provide a better understanding of the neuropsychological heterogeneity of Korsakoff syndrome by correlating intensity measurements in thalamic nuclei with the pattern of neuropsychological performance of large samples of Korsakoff patients.

Regarding behavioural results in this experiment, response time (RT) analysis in classic episodic memory experiments indicated that RT were faster for hits (Curran, 1999; Herron & Rugg, 2003; M. D. Rugg & Allan, 2000) but on false memory experimental designs, results are not conclusive. Some studies found HITS were the fastest responses (Nessler et al., 2004) but others found that NEW responses were significantly faster than OLD (Nessler et al., 2001) because participants noticed they did not belong to the semantic category targeted in the task. In our experiments, VFMT1.0

(see chapter 3 of this thesis) presented faster response times for hits (n=20, mean age of 29; M=942.28ms) compared with correct rejections to new items (M=1006.23ms), whereas for the VFMT2.0 version of the task, involving shorter encoding-to-test intervals, RT were slightly faster for correct rejections of new items compared with older adults in the experiment described in this chapter (n=13; mean age of 59; M=843.89 and M=864.65 respectively).

A different approach by Atkins and Reuter-Lorenz suggested that CRL takes a longer RT than NEW, and that is the base for their semantic interference hypothesis (SI). When response requires the engagement of control processes to ensure memory accuracy, this might slow down responses. What is more, fMRI studies indicated that left mid-ventrolateral prefrontal cortex (L VLPFC) is more active for CRL compared with NEW responses, and it has been suggested that this cerebral structure plays an important role in post-semantic retrieval processes that help to select between semantic competitors (Atkins & Reuter-Lorenz, 2011). Our data reported a faster RT for both patients and controls for NEW compared to CRL, supporting the hypothesis of implicated decision processes in correct rejections of semantically related lures regardless of episodic memory impairment.

One of the main objectives of this chapter is to analyse true and false memory processes in the amnesic population. Previous studies reviewed how episodic memory is impaired in brain injured patients but only some focused on the DRM paradigm performance in KS patients (Schacter et al., 1997; Schacter et al., 1998; Schacter et al., 1996; Van Damme & D'Ydewalle, 2009a; Van Damme & D'Ydewalle, 2009b; Van Damme & D'Ydewalle, 2010a; Van Damme & D'Ydewalle, 2010b). None of them offered any ERP performance. They mainly concluded that KS patients produced less false memories compared with controls, and their explanation was dichotomized into two main branches: a deficit in encoding and retrieving the gist of semantic context and a failure of retrieval strategies.

As for the suggestion of a lack of capacity to encode and/or retrieve semantic gist of the learnt material, Schacter and collaborators produced several experiments in order to study this aspect in detail. In the first (Schacter et al., 1996) and also in reviewing previous works in the same area (Cermak et al., 1973; Verfaellie & Treadwell, 1993), Schacter and colleagues designed this first study on false memory with amnesic patients using the DRM task. They wanted to investigate on the one hand whether false memory production might depend on remembering the gist of the list, therefore amnesic patients would produce less false memories compared with controls; or on the other hand, they would produce more false alarms than controls as patients are prone to produce false alarms. False memory rates for patients on a recognition task were 59% compared to 84% for controls. These rates were lower when free recall task was applied (i.e. 29% of lures for patients and 33% for controls). We should comment here that one of the conclusions from the authors of this experiment is that patients would produce less false memories compared to controls, but considering the excessive rate of false memories that control participants achieved on this task, this conclusion should be taken cautiously.

In contrast with the account on the problems in semantic processing, other authors presented their own conclusions. For instance, Cermak (Cermak et al., 1973) suggested that KS patients were able to process semantic features spontaneously but they could not utilize them to improve their performance until prompted by the examiner. This may suggest that encoding semantic features is not an impaired process in KS but executive functions required to use that strategy to improve performance may. Even when considering response time on a DRM task it can be concluded that semantic relationship existed in that a correct rejection of a lured item takes longer than the correct rejection of a probe not semantically related (i.e. CR) (Atkins & Reuter-Lorenz, 2008),as described in our experiments (response time for CRL of 1058.56ms compared to 997.93ms for CR in the patient group).

As for the second branch of the explanation on why KS patients produced fewer false memories, authors such as Van Damme defended that it might be related to an impaired retrieval process influencing false memory production. He demonstrated that KS patient ability to encode semantic context was sufficient as priming tasks proved and that patients may access that semantic information without the need to make it conscious (Van Damme & D'Ydewalle, 2009a; Van Damme & D'Ydewalle, 2010b) and pointed out that the main reason to produce false memories would be a problem in strategic retrieval of information (Van Damme & D'Ydewalle, 2010a).

The premise of all of these studies was not in consonance with our data, as with VFMT2.0 no decrease in false memory production in the patient group was found compared with controls; on the contrary, rates showed an equivalent. In an attempt to find reasons to explain this difference considering previous literature, we suggest that our VFMT2.0 offers a memory testing frame that may engage different processes such as gist generation, activation of related schemas of studied information or familiarity. Another factor may be related with a higher engagement of semantic relationship between studied and tested material, presumably engaging deeper or easier gist formation that may guide participants to a later false memory production due to a failure in monitoring their accuracy of responses.

We describe here a persistent left-frontal ERP positivity in the patient group and discussion about this point should be carried out. Positive voltages at frontal areas of the scalp might be related with eye-movements, biasing positive voltages either to the right or to the left hemispheres depending on eyesight direction. Eye-movement might have influenced ERP frontal signal but we cannot be certain. We trust that ICA eye-movement correction removed the majority of artefacts related with eye-movements and no technical process was available to measure any possible tendency of patients to direct their eyesight to the left side of the screen during recognition task. It seems difficult to justify that all the patients would produce a similar pattern of eye-movement as a group, generating consistent left-frontal positivity in their ERP not present in the control group. Eye-movement directed to the left side of the screen can influence left-frontal positivity, but in our experiment it is difficult to prove. However in future experiments we suggest to utilizing high-resolution eye-tracking techniques to investigate a possible contribution of eye-movement artefacts to the ERP signal in this population.

Working with patients in a EEG setting can be challenging and expectations on getting a higher number of artefacts at testing sessions compared to control participants is a real matter to consider in order to avoid any data biasing. In addition to the ICA removal of eye-movement artefacts, experimenters also visually inspected the resulting number of trials after ICA in order to remove any important voltage variation that might interfere with a clear EEG signal. The sum of those two filters resulted in a lower total number of HIT and CR trials for patients compared with the control group, but there was no difference in the number of trials used for ERP analysis for FM or CRL categories of response. This might arguably allow us to suggest that, regarding the aim of studying false memory in these two groups, the number of valid trials for ERP analysis might not be interfering with it.

In spite of this, ERP data from the present experiment gave important information regarding neural correlates of true and false memory. When control participants were analysed under dual process terminology, familiarity processes involved in true and false memory retrieval were the same and fronto-centrally located. On the contrary, process of true and false memories differed during the period implicated in recollection (i.e. 500 to 100ms) being right-frontally related for true memory and left-frontal for false memory. When dual process account suggested monitoring processes may take place (i.e. late timing from 1000ms onwards), voltage for true memory was related with electrodes at right-frontal locations to change later on to fronto-central areas, whereas false memory voltage appeared at right-frontal electrodes from 1000ms until the end of the epoch. We may suggest that false memories may require longer monitoring processes compared with true memories, possibly because a HIT produces a stronger recollection effect and therefore requires less posterior monitoring of response whereas a false memory may need longer checking.

This suggestion is on the line of that Wilding & Rugg presented on their ERP study on DRM task. They found two ERP patterns related to HITS, different in terms of time and topography, one being phasic and larger at left-parietal localizations; and the other being sustained and right-frontal located. Only the first was present on ERP for NEW responses. They explained that HITS required retrieving some contextual information not needed for NEW items, that being the reason why the two ERP signals were present for HITS (Wilding & Rugg, 1997).

Similarly, in the Curran and colleagues good-versus-poor experiment (Curran et al., 2001) a right-frontal late 1000-1500ms effect amplitude was present for both true and false memory for Good performers but not for Poor performers. Authors questioned whether this right-frontal effect could be related with effort or retrieval success or with a post-retrieval evaluation process. Their analysis considered previous results indicating that frontal monitoring processes may be required to respond to a familiar item but are not needed when the participant is completely sure about the response (Henson, Shallice, & Dolan, 1999), together with their own results indicating that retrieval effort did not differentiate true and false memory as both ERP signals were equivalent. Curran finally concluded that right-frontal effect reflected a post-retrieval evaluation process that allowed Good performers to distinguish better between true and false memories when compared with Poor performers.

Following this same conclusion, our ERP data may suggest that for patient performance on both true and false memory, no successful post-retrieval evaluation process was present as no right-frontal activation appeared at any point. A note must be made as to the lateralization of the effects. In our results, activity related with true memory was related with electrodes in the right hemisphere whereas for patients, this activity was related with electrodes in the left hemisphere. One explanation might be related with what has been suggested regarding the use of different stimuli material and its effect on the lateralization of old/new effect: it was left-lateralized when using words (Curran, 2000) and more right-oriented when pictures are used for the recognition task (Burgess & Gruzelier, 1997). In line with this and with our ERP results, an fMRI study on deception indicated that left-prefrontal cortex was activated during “pretending to know” responses (i.e. participants were asked to lie and respond even when they did not know the response) on both true and false memory performance (Abe et al., 2008). However, considering possible differences in localization of activity due to the use of a new false memory task, and the inaccuracy of ERP techniques to localize cognition-involved brain structures, this must be evaluated further in the future.

Interesting information was found in this experiment when comparing true and false memory effects between our two experimental groups. In this case, data showed that control group consistently reached higher voltages when those differences were present. That was at the time window from 300-500ms for both true and false memory effects, but it disappeared when recollection processes were on charge (i.e. from 500-800ms) to return again from 1000-1200ms. These results might suggest that, patients and control participants´ voltages for both true and false memories were equivalent at the time where recollection process is taking place, but they present differences when familiarity and monitoring processes are active. We acknowledge that these results are very difficult to explain and we have not any previous study comparing ERP signals between these two groups. We suggest that further investigation is needed to replicate these results and to go deeper into the study of these differences presented here.

To resume, VFMT2.0 was a useful task to study true and false memory under ERP techniques in both healthy and KS patients. For healthy controls the only difference between true and false memory was found from early 300 to 500ms where true memory presented higher voltages compared with false memories. Distribution of the activity suggested different neural substrates for these two memory effects, with different localization of the electrodes on timings from 500 to 800ms (right-frontal for true memory and left-frontal for false memory). Controversially, the KS patient group presented a consistent activity pattern along both true and false memory effects and for almost the entire duration of analysis. Electric activity was localized at left-frontal sites, the same as the healthy controls activated when false memory was processed from 500 to 800ms.

In spite of the fact that no differences in false memory production between patients and controls were found behaviourally, ERP techniques could help to identify differences in voltage corresponding to each memory effect and for each group. This is the first time where ERP data of true and false memory production is offered comparing KS patients performance against age-matched controls. We suggest that monitoring and executive processes may play a role in distinctive false memory processing for KS patients compared with controls.

Chapter 6: General Discussion

Every chapter of this thesis comprises its own discussion section where the most important points and their specific issues are commented. Nevertheless, a general discussion section is appropriate and will allow us to gather together all the information gained in all our experiments and described in each chapter of this thesis.

6.1 A New Task

In Chapter 1 Introduction, we exposed our general aims. One was to create a new false memory task. Authors have been strongly focused on the DRM paradigm task to produce experiments, perhaps because it was one of the first experimental settings that demonstrated its validity to produce false memories in a controlled laboratory environment. Its value cannot be denied but with the new experimental contribution that followed that first Roediger & McDermott experiment, new approaches seemed to be required. One of the claims was related to the need for tasks more related to the real world than to artificial laboratory conditions. That was in our mind when designing VFMT. We presented a single visual scene with a thematic context at encoding as a modality that people usually confront in a daily basis. We consider that in their routine they may engage in episodic memory recollection based on visual information in a learning-retrieval context where semantic relationship and associative learning are frequent. The constructive nature of our memory system, the ability to activate similar schemas to properly make a decision on whether an event was previously experienced or not, relies on real day-to-day basis processes when using the approach suggested by VFMT. However, as previously commented upon in the discussion section of chapter 2, we could not control whether visual processing was exclusively engaged by participants under our experimental condition. It might be possible that each participant on their own decision would have processed stimuli under their own better-performance strategies, changing visual material into verbal modality to better encode or retrieve at test.

The increment of semantic relation between what is studied and what needs to be retrieved is one of the objectives of our new false memory task, previously described in chapter 2. We followed the suggestion offered by Schacter regarding the possibility of influencing false memory production in amnesic patients by manipulating the number of associates to a lure (Schacter et al., 1996): as the number of associates increases, healthy participants might produce more false memories but amnesic patients were predicted to decrease their rate due to their difficulty in remembering the general gist of a learning list. The retention of associative or semantic information was suggested by the authors as necessary for a DRM task and amnesic patients, because their episodic memory problem will not retain that contextual information and therefore will produce more false alarms and less true and false memories (Schacter et al., 1997; Schacter et al., 1996). Our results indicated that, when semantic relatedness and number of associates were increased using five critical lures for each scene studied, false memory production rate was above chance and similar in percentage in both patients and controls.

A second aim was to design a task with a lower influence of language in encoding and retrieval processes, presenting a different false memory task to be utilized in different countries and at different educational levels as well as producing an alternative to the DRM task which could be used to investigate further into false memory research from a different point of view (i.e. with a different design and using EEG techniques).

And finally, a third objective was to design a false memory task where items at encoding already had a semantic relation, thus facilitating associative and gist-generation processes which influence posterior false memory production.

6.2 Behavioural results

As was pointed out in the discussion in chapter 2, our new tasks lack of association norms that might offer information on how strongly those semantic relations we aimed to engage were actually produced for each scene and item used in our task. A previous study with healthy participants should had been made in order to rate how likely our scenes were to suggest a thematic context. This experiment would allow us to improve our selection of the scenes according to their ability to produce and associate a semantic context and thus a stronger contextual link between encoded and retrieved material.

Because of the reasons already described in chapter 5 of this thesis, we tested two versions of the VFMT. The first aspect we want to consider here is a comparison of the two healthy control samples who performed the VFMT. The differences in response percentages of VFMT2.0 compared to the previous experiment using VFMT 1.0 in healthy students are obvious. The percentage of HITS was higher for the second version (i.e. 82.87%) compared to the first (77.97%) but this difference was not statistically significant $t(31) = -1.76$, $p = .09$ (VFMT1.0 M =116.95, se = 12.65 and VFMT2.0 M = 124.31, SE = 10.03). Moreover, no differences were found between the two versions of the task as to the number of FM responses $t(31) = -.66$, $p = .51$ (VFMT1.0 M = 75.6, SE = 24.3 and VFMT2.0 M = 81.8, se = 28.7) or FA responses $t(31) = 1.7$, $p= .1$ (VFTM1.0 M = 11.3, SE = 7.2 and VFMT2.0 M = 7.5, SE = 4.7). This result suggests that, even when experimental design reduced the number of scenes to be encoded at study, both true and false memory performance remained equivalent in our two versions of the task.

Nevertheless, and arguably due to the different size of both samples (i.e. VFMT1.0 with 20 participants and VFMT2.0 with only 13), we could suggest that difference in HIT responses between our two versions of the task, although not being significant now, might reflect a tendency to reach significance with a bigger sample. This would be in the line of previous studies that demonstrated that participants produced a higher HIT rate in a DRM paradigm experiment where participants performed the recognition task just 45seconds after encoding each list, filling this small time gap with letter-string match-to-sample task. Clear differences on HIT rate between different recognition delays were present (i.e. short and long delay), with higher percentage of HITS for the short-term performance of recognition task (Urbach et al., 2005).

Another reason why we hypothesize that the HIT rate may be incremented in our second version of the task could be that participants were asked to study only one scene at the time for VFMT2.0 compared to the requirement of three scenes in a row for VFMT1.0. This memory effort may require less attentional resources and therefore, may produce higher HIT rates. Also, age information regarding our two healthy participant samples supports the fact that the second version of the task was easier for healthy participants. Despite the age difference (mean age of 29 years old for VFMT1.0 and 59 years old for VFMT2.0), older participants still produced a higher number of hits, taking clear advantage of easier memory conditions. Age, it has been suggested, may represent an interference factor when discrimination between true and false memory was required (Balota et al., 1999; Kensinger & Schacter, 1999) but in our data it did not produce a decrement on true memory in the older sample compared with the younger. However, age differences on false memory production require further investigation.

Regarding false memory, we already showed that no differences were found between these two versions of the task: VFMT 1.0 reached 50.4% of false memories and VFMT2.0 54.51% for healthy participants. This might be suggest that even the task seemed to be easier in terms of true memory requirement while false memory was not significantly affected by short-term delay testing conditions. This result is in line with previous studies that proved how false recollection is possible in testing conditions with only seconds between encoding and test (Atkins & Reuter-Lorenz, 2008; H. Chen et al., 2012) and utilizing different modalities of stimuli such as numbers (Pesta, Sanders, & Murphy, 2001). The Nessler and Mecklinger study on the influence of different retention delays may not be directly applied to our results here as their suggested timings of 40 and 80 seconds were still longer than our immediate testing condition and their false memory rates on a DRM-like task were lower than ours (17.72% of lures for 40 seconds delay and 21.33% lures for 80 seconds delay) (Nessler & Mecklinger, 2003). Nevertheless, Nessler´s explanation on how delay may influence false memory production must be considered here. We introduce a little twist on the main point made by Nessler and Mecklinger, questioning how learning time may influence false memory. Long learning intervals (i.e. in our case studying 3 scenes in a row at VFMT1.0, 12 seconds each scene) may produce less accurate true memory than short learning intervals (i.e. only one scene at VFMT2.0) but produced no changes on false memory production. This point, however, should be experimentally designed for corroboration in the future. Regarding amnesic patients, delay on testing showed that interfere with retrieval in free recall conditions but had no effect on true memory if cues were offered to KS patients (Cermak et al., 1973).

What is important is that the percentages of false memories produced by patients and controls in VFMT2.0 were equivalent; therefore, no discrimination between the groups was possible regarding behavioural measures. However, as we will comment in the following sections, ERP signatures allowed experimenters to find differential features that may be utilized to distinguish between true and false memory in the brain.

6.3 ERP for True Memory

The first aspect to comment on is that our VFMT did not meet previous descriptions of true and false memory components in the literature. The equivalent FN400 old/new effect was not so frontal but centrally located in VFMT1.0 in healthy controls, whereas activity at VFMT2.0 for controls was fronto-central from 300 to 500ms. Regarding classic parietal old/new effect, our data from 500 to 800 ms. presented a very different location, being central at VFMT1.0 and right-frontal at VFMT2.0. We suggest that this difference may lie in two possible explanations. First, this change in localization of activity may be related to the fact that localization of old/new effects could change depending on the modality of stimuli used, as previously corroborated by studies with faces compared with using objects or words (MacKenzie & Donaldson, 2007). The majority of the studies on the DRM paradigm utilized words in a visual or auditory presentation but VFMT was designed with visual scenes. A second possibility we address here is related to the important implication of executive function in memory retrieval and decision making required to responding to VFMT2.0 compared with VFMT1.0. As explained above, short-term characteristics of testing conditions for the second version of the test may implicate a higher role of executive function instead of memory processes in order to accurately respond. The amount of information to be remembered was lower for VFMT2.0 and participant responses needed to be accurate and fast, with attentional processes and generation of strategies to optimize performance being implicated in this case. Under these conditions, we arguably suggest that participants may rely on creating a strategy to respond, and management of the gist of each scene may help them to decide. In addition, as testing items were not exactly the same as those present in the study scene, participants may store them in a semantic manner that may help them to create a schema to be used at recognition task, in the line of suggested fuzzy trace account (Brainerd & Reyna, 2001).

It is worth commenting that, despite having no quantitative measure of it, examiners asked participants after performing the task regarding their feeling of accuracy, and whether they utilized any strategy to respond better to the task. Informal reports from healthy participants in both versions of the task matched in one aspect: they usually came across a strategy that helped them to respond after several study-test trials. Characteristics regarding choosing liberal or conservative response criteria changed across participants. This also connects with theories that explain the importance of monitoring processes in memory retrieval, which will be further commented on the following section of this chapter on false memory.

The relation between response style and frontal lesion was offered by Melo and colleagues who concluded that damage to the right-frontal lobe was associated with a liberal response bias facilitating an increase in false alarms at memory tasks. When DRM tasks were applied, right-frontal injured patients increased their false alarm rate

(Melo et al., 1999). Data on this aspect could not be fully analysed in this thesis, but may result in interesting research in the future.

When version 1.0 and 2.0 of VFMT were compared in healthy individuals, data showed that ERP old/new effects were found despite changes in task design. Healthy participants showed central activity for true memory in both versions, being fronto-central for VFMT2.0 at the time window where familiarity processes are suggested to take place by dual process theory. We hypothesize that short-term delay characteristic of the VFTM2.0 may produce a different sense of familiarity in healthy participants and that might be the reason why ERP activity is driven to fronto-central electrodes in our second version of the task. S further research will be required to disentangle this point as this explanation should be taken with precaution due to a possible speculative value.

Timing corresponding to 500-800ms presented showed different patterns for our two versions of the task in healthy participants. This time window, which is associated with ERP signals related to recollection process by dual process theory, presented a right-frontal ERP activity for version 2.0 and central electrodes presented higher voltages for version 1.0. Although difficult to interpret, we suggest that this difference may be related to a higher engagement of executive functions in the second version of the task, linked with generation of a strategy for better performance.

In the last time window of analysis, from 1000-1200ms, where monitoring processes had been suggested, activity of these two versions of the task showed no differences. Nevertheless, the absence of difference does not mean the similarity of the processes taking place at that time; hence, we must be cautious and not generate any conclusion on the monitoring processes implicated in both versions of the task.

We found a striking result regarding ERP signatures in healthy participants corresponding to versions 1.0 and 2.0 of VFMT. True memory seemed to be equivalent (despite differences in voltage) in location compared to false memories in version 1.0 whereas for version 2.0 important differences regarding lateralization of a consistent frontal activity appeared when comparing true versus false memory. The first thing to underline here is that the difference between central activity in VFMT1.0 and frontal activity (either left or right) for VFMT2.0 may suggest that characteristics related to short-term delay application of the task and less learning material at study implicated higher frontal activity. This activity was right-sided when true memory was processed and left-sided when false memory was processed. In the literature it has been suggested that right frontal activity is associated with post-retrieval evaluation processes and results in better differentiating FM from HITS (Curran et al., 2001). In other words, the better you distinguish between true and false memory, the higher the ERP activity at right-frontal areas according to Curran and colleagues.

Our ERP experiment on amnesic patients revealed new information on how brain injured patients with episodic memory problems processed and produced true memories. Previous literature on fMRI and ERP experiments declared how important medial temporal lobe and prefrontal cortex structures are for episodic memory retrieval. But the interesting point of this thesis is that we study true memory in amnesic patients diagnosed as KS, with no major implication of these cortical structures but mainly subcortical damage on mammillary bodies, thalamic nuclei and connective white matter structures such as mammillothalamic tract and fornix as we described at Chapter 4. The neuropsychological characteristics of this sample corroborated episodic memory impairment in our patients, with a general profile of memory deficit compared with executive function that was mainly preserved.

6.4 ERP for False Memory

The neuropsychological profile of our sample confirmed episodic memory impairment but generally preserved executive functioning abilities. This was important as it allowed us to disentangle between episodic memory impairment and executive functions involvement in memory retrieval. Given these cognitive characteristics, we found that amnesic patient ERP signal corresponding to true memory presented differences with their age-matched controls' ERP signals. Almost constant activity for true memory responses was present at left-frontal sites of the scalp nearly during the entire EEG recording, changing to left-parietal electrodes at the last 200ms of the period. This ERP activity associated with true memory and, hence, neural correlates that accounted for it were different from that showed by control participants' ERP data. The implications of this difference were given in the Discussion section of Chapter 5. We selected KS patients with an amnesic cognitive profile but generally spared executive functions that might allow them post-retrieval monitoring or strategy generation at recognition task. We would expect to find that ERP signals related with memory-based processes (i.e. familiarity and recollection processes according to dual process theory) for KS patients would present differences with their age-matched controls, but no differences would appear at the late monitoring ERP signal.6.4

When comparing the false memory ERP signal in healthy participants in the two VFMT versions, we found that early 300 to 500ms showed no difference in localization; familiarity process seemed to be unaffected by a shorter testing delay. Nevertheless, important differences were found regarding timing between 500 and 1000ms. For healthy participants and from 500 to 800ms (i.e. recollection process time according to dual process theory) the same fronto-central activity presented at previous 300-500ms was observed for VFMT1.0, changing to right-frontal areas from 800 to 1000ms. On the other hand, VFMT2.0 for healthy controls showed left-frontal consistent localization from 500 to 1000ms. This is an interesting phenomenon but is difficult to explain. Differences between these two versions of the task produced equivalent HIT and FM rates in healthy controls. Moreover, ERP differences were found according to where ERP activity was present: right-frontal and fronto-central electrodes for version 1.0 compared to left-frontal electrodes for version 2.0. If we review the literature, we find that left-frontal activity had been associated with interference-resolution processes under conflict of response scenario (Atkins & Reuter-Lorenz, 2011). Atkins and Reuter-Lorenz found in an fMRI experiment that left ventro-lateral-prefrontal cortex (L-VLPFC, Broadmann Area 45) activity was higher when a lure was correctly rejected compared to production of a false alarm. Authors concluded that this L-VLPFC region had a role in interference resolution, showing higher activity when interference at response is higher. On the other hand, authors explained the activity of this L-VLPFC as a region that "calculates" an index of interference that may be utilized by other brain regions to support memory accuracy processes. Atkins and Reuter-Lorenz´s data pointed to the second explanation; being the left dorso-lateral prefrontal cortex the area that may be in charge of determining if interference found at L-VLPFC can be solved and false memory can be reduced into a more accurate memory performance. We suggest following this explanation to frame future research on the implication of lateralization in false memory production, with the precaution needed when ERP techniques are utilized, as direct inference of anatomical localization of the electrical source cannot be done.

The study of false memory is not only the analysis of encoding strategies, as some authors focused on in their experiments (Rhodes & Anastasi, 2000; Underwood, 1965). As important is the analysis of executive functions implicated in retrieval processes such as monitoring of performance and use of strategies for retrieval. Following this assumption are experiments introduced by Miller and Woldford (M. B. Miller & Wolford, 1999) previously commented at chapter 5. Our data were following this line, as we looked with interest into the influence of executive function and monitoring processes in false memory production, as previously suggested by authors such as Atkins, who proposed that the interference control process is an important aspect in avoiding false memory production (Atkins & Reuter-Lorenz, 2011). Eventually, we may arguably suggest that differences found between amnesic patients and controls may rely on executive management of memory retrieval, an aspect previously suggested in the literature under the source monitoring account (Johnson et al., 1993) and commented on in the discussion section of Chapter 5.

We also maintain the importance of creating a gist of the information to retrieve, a mechanism that may drive healthy participants to produce false memories due to their spared ability to create a well-organized semantic representation of the contextual information in the scenes, as Schacter suggested (Schacter et al., 1998). Healthy participants would match items presented at recognition task with the gist representation built at encoding, and this scenario helps them to respond positively to lured items, with a strong sense of familiarity. Schacter suggested that amnesic patients could not produce that gist and this, together with their impairment to access explicit recollection of features from memory, would result in lower FM production (Schacter et al., 1998). In the case of amnesic patients, results from this thesis suggested their ability to generate a gist of the encoded information, in line with previous studies maintaining that amnesic patients can code semantic information, but they only use it involuntary and automatically, resulting in a retrieval deficit when an effort or controlled recollection strategy is required (Van Damme & D'Ydewalle, 2008). Nevertheless, controversy is still present in the literature regarding which is the process that most influences false memory production in amnesic: is it an encoding problem or is it an impaired retrieval ability? Further research is needed to answer this question.

We already reviewed in a previous discussion the literature on whether using pictures instead of words may change ERP reflection of memory processing. Attempts have been made to demonstrate what has been defined as picture superiority effect. This theory states that memory of pictures is better than of words (Embree, Budson, & Ally, 2012) and three main theories supporting this were proposed in support (Ally, 2012): a)dual-coding account that explains how pictures can be processed deeper as they may evoke both verbal and image codes, whereas words only evoke verbal codes thus making a later recall task easier because of this double, stronger encoding representation (Paivio, 1971); b) distinctiveness account: pictures offer more distinctive features at encoding than words and that makes their recall easier (Nelson, Reed, & Walling, 1976); and c) semantic processing account: this effect is the result of a deeper and more elaborated and conceptual processing driven by pictures instead of words (Weldon & Roediger, 1987; Weldon, Roediger, & Challis, 1989).

As an alternative explanation, Foley and collaborators produced several studies focused on how modality of stimuli presentation may affect false recognition. Some of their experiments stressed the fact that visual modality may affect false memory rates (Foley & Foy, 2008; Foley et al., 2007; Foley et al., 2010). All his work was based on how likely the use different modalities of item presentation would be in engaging the spontaneous process of generating visual cues associated with them that can be re-activated at test and bias a higher proportion false memory production. For this author, using only pictures at encoding would increase false memories as they re-activate visual cues at test and influence monitoring processes based on the distinctiveness of materials. This supports our decision to select visual stimuli in the design of our false memory task, as it was suggested as a useful presentation modality when false memory production was targeted.

6.4 Future Research

We are aware that the research presented in this thesis shows some weaknesses. We will discuss them in more detail and suggest future aspects to be considered in subsequent investigations in this field.

The first and most important is the size of our patient sample that may render the interpretation of our data difficult. Intuitively, it is easy to consider that 12 patients was not a large cohort, and further calculations of sample-size requirements confirmed this point. To calculate sample size we used an automatic calculator (G*Power 3.1 free version). We established a t-test comparison of one dependent variable (i.e. mean voltage for each electrode) in our two independent samples (i.e. patients and controls). Parameters were set as follows: we specified a two-tailed analysis, with a medium effect size d of 0.5, and probability of 0.05 and power estimated of 80%. We introduced mean and standard deviation of one electrode for each group into the calculator (i.e. mean voltage for F3 electrode and CR response: control group M =-0.71, SE = 2.1; patients M = -1.7, SE = 1.8). These calculations indicated that the total sample size should be 128 participants, 64 for each group, to attain statistically significant results in 80% of the number of times we theoretically performed the study under these conditions (i.e. power level of analysis of 0.8). In our experiment reaching such a large sample was impossible for different reasons, one of them related with the difficulty in finding such a high number of KS patients in our geographic area. Despite this statistical precaution that should be taken when interpreting our data, the results from this experiment offer new information related with a research field not explored before using the same techniques as in our experiment. The actual ERP data collected from amnesic patients during a false memory task newly designed for the purposes of memory-processes study might offer preliminary data from which further investigations could be undertaken.

A second point to be improved in further investigations might be related to the fact that our experimental design could be improved by including two features, present in previous literature, which could offer more detailed information about the memory process. On the one hand, free recall task after encoding phase may produce interesting data regarding spontaneous utilization of strategies, differential behavioural percentages of both true and false memory and indices that may help to disentangle whether encoding or retrieval process is mainly involved on false memory production. However, despite its value, we are aware that performing a free recall task and later a recognition task may alter posterior production of both true and false memory.

On the other hand, producing a remember-know judgement task may also be interesting. In our defence, we did not utilize it because we anticipated the complexity resulting from demanding two responses (i.e. yes/no response and remember/know task) and the high involvement of working memory in this task, both being sufficient reasons for rejection when amnesic patients are the target sample.

As for neuropsychological characteristics of KS patients, a consideration to be taken into account in future investigations may result from the definition of the two main groups to be compared using VFMT. One group should present episodic memory as main cognitive impairment and a second group with patients who also presented dysexecutive syndrome as well. That may allow dissociating the involvement of these two cognitive functions in true and false memory in KS patients, and correlate it with their characteristically impaired anatomical structures (i.e. mammillary bodies, anterior thalamic nuclei and connection structures such as mammillothalamic tract and fornix), timidly approached here in Chapter 5 but definitely in need of more research.

This research compared different response category measures to study true and false memories using ERP techniques. The existence of significant differences when comparing voltage corresponding to correct rejection of a lure and correct rejection of a new item may offer an alternative index to study false memory. Moreover, other indexes of false memory studied here such as correct rejection of a lure compared with false memory may also be considered as a false memory index. This analysis was possible in this research thanks to the high number of critical lures corresponding to each studied scene and had not been achieved previously in the literature as rates were low and did not allow ERP processing.

As we discussed at chapter 5, results regarding the comparison of true and false memory between our two groups of patients and controls offered some quite difficult data to be interpreted. We consider that more investigation using this technique and improving weaknesses of this study should be done in order to better interpret these aspects.

Interesting future research in this field may implicate the option of recording ERP data not only at recognition but also at encoding phase, as previously presented in the literature. Results from previous studies on the DRM task with healthy participants showed how differential ERP features for subsequently remembered items appeared before the memory task was executed (Friedman & Trott, 2000; Paller, Kutas, & Mayes, 1987; Urbach et al., 2005). Replicating this data using this VFMT task in a study in amnesic patients may generate valuable data to explain false memory process.

A very recent investigation field emerged and promises the production of important results. Brain connectivity study will certainly offer data on how neural structures are related in time using advanced MRI techniques and which structures may have a decisive role in false memory.

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Appendices

Appendix Chapter 2

Depict of scenes and items at Pilot experiment

Scene	Old items	Lure items
Wedding carriage	Carriage, bouquet, tiara, bridal veil, bow tie	Coachman, necklace, rings, bracelet, cufflinks
Animal group	Elephant, giraffe, rabbit, zebra, lion	Eagle, hippo, monkey, panther, rhino
Airplane cabin	Flight attendant, luggage compartment, airplane seats, airplane table, airplane tv	seat light, window, emergency exit, seat belt, crew seat
barbeque	Barbeque, red plate, raw meat, tongs, cooking glove	Apron, hamburger, beer, coal, ribs
Basketball game	Score board, ceiling lights, training shorts, t-shirt, basketball court	Basketball net, basketball, spectator stand, headband, basketball uniform
Bathroom	Bathtub, shower, sink, towels, toilet	Bathrobe, bidet, toilet brush, mirror, toilet roll
Beach	Sand, shore, deck chair, bikini, swimmer	Swimming costume, beach umbrella, swimming ring, sun lotion, beach towel
Bedroom	Mattress, duvet, rug, chair, bedspread	Bedside table, lamp, pillow, slippers, dressing table
Chemical analysis	White coat, latex gloves, pipette stand, beaker, chemical bottle	Glass funnel, Erlenmeyer flask, microscope, mortar/pestle, pipette
Blood sample	Yellow antiseptic bottle, tourniquet, sharps disposal, storage box, patient	Sample tube, cotton swabs, syringe, BP tester, needle
Boat in water	Boat, buoy, ladder, sea water, ropes	Anchor, gangway, mast, rudder, lifejacket
boxing	Boxing gloves, boxing shorts, referee, white boxer, black boxer	Boxing ring, face protector, ring corner, gumshield, ring ropes
Food on plates	Green grapes, orange juice, toast, ham, cheese	Boiled eggs, butter, teapot, toast holder, coffee
Building construction	Brick, bucket, safety helmet, brick wall, builder	Trowel, cement mixer, wheelbarrow, safety jacket, scaffolding
Bullfighting	Bullring, bull horn, bullfighter shoes, bullfighter jacket, bull	Banderilla, bullring refuge, cape, bullfighter sword, bullfighter hat
Nativity	Awning, king, Mary, camel, baby	Cradle, ornate box, donkey, hay, cherub

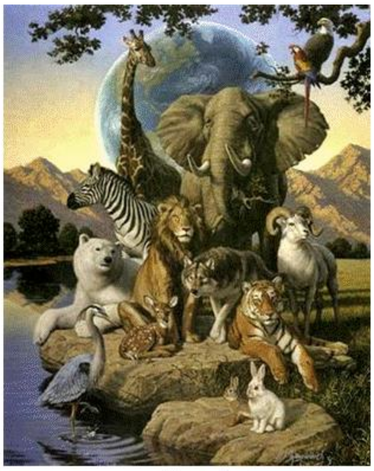
Camping	Canoe, paddle, forest, camping blanket, tent	Camping stove, camping light, anti-mosquito lotion, chair, backpack
Indian pow-wow	Plaited hair, chief, fire, moccasins, headdress	Tomahawk, spear, knife, bow, peace-pipe
Cartoon pirate scene	Crocodile, pirate ship, captain hook, peter pan, pirate shoes	Tinkerbell, hook, cartoon boy, cartoon dwarfs, cartoon girl
Christmas decorations	Tree, presents, tree angel, wrapping paper, tree lights	Guiding star, santa claus, Christmas sweet, sock, red flower
Church scene	Baptismal candle, priest, praying man, stained glass window, priest robes	Pew, crucifix, virgin Mary statue, praying woman, sacred wafer
Classroom	Blackboard, school desk, schoolgirl, teacher, schoolboy	Chalk, teachers desk, school backpack, book, clothes hooks
Riot	Police helmet, shield, demonstrators, rubbish container, photographer	Police car, loudspeaker, truncheon, police van, protest banner
Dentist	Drill etc. rack, mask, dentist, latex gloves, chair lamp	Mouth x-ray, dentist pliers, dentist hook, dentist chair, dentist mirror
People in car	Road map, car seats, rear-view mirror, steering wheel, a/c grille	Gearstick, handbrake, satnav, radio, rev counter
Wild-west items on table	Sheriff badge, bullets, playing cards, gun, pocket watch	Cowboy hat, spurs, holster, hipflask, cowboy tie
Cartoon farmyard	Goat, chicken, horse, sheep, sunflower	Tractor, cow, farmer, pig, windmill
Football	Football field, goalkeeper gloves, goal, goalkeeper, football shoes	Football, umpire flag, whistle, football referee, crossbar
Fruit stand	Black grapes, mango, loquat, fig, cherries	Blueberries, pomegranate, banana, pineapple, pear
Flamenco girls	Fan, necklace, earrings, flamenco dress, hair flower	Castanets, flamenco comb, white spots on red backing, flamenco shoes, flamenco shawl
Hairdresser	Sink, stand hair drier, hair products, dresser tray, hair dresser seat	Comb, brush, handheld hairdryer, curler, hair clasp
Hospital ward	Privacy curtain, hospital bed, side table, clipboard, hospital sheets	Bed rail, I/V kit, I/V stand, oxygen dials, ECG monitor
Musicians playing	Music stand, drums, piano, trombone, violin	Clarinet, drumstick, guitar, music score, microphone
Ensemble of cartoon characters	Palace, Buzz lightyear, mouse, bear, cowboy	Shreck, mickey mouse, child, masked girl, one-eyed animal
Kitchen	Extractor fan, glass container, ladle, tap, washing machine	Dishwasher, kitchen sink, frying pan, fridge, microwave
Lounge	Wooden chair, stand lamp, cowskin rug, pottery, curtains	Table, sofa, window, cushion, magazine rack

Army scene	Military- tent, helmet, jacket, trousers, cap	Army boots, rifle bullets, waistcoat, army radio, rifle
Man in office	Desk lamp, diary, newspaper, desk phone, tie	Pc screen, pencil holder, hole punch, executive chair, office tray
Park	Girl resting, fountain, bench, lake, bicycle	Squirrel, runner, duck, dog, walkers
Flower stand	Daisy, fern, poppy, rose, blue flower	White flower, small blue flowers, red/white flowers, red/black flower, orange flower
Sewing	Sewing machine wheel, machine needle mechanism, scissors, fabrics, sewing machine	Tape measure, threads, thimble, hand sewing needle, pins
Nuns skiing	Ski boot, nuns, snow covered tree, ski sticks, ski slope	Skis, ski goggles, ski trousers, ski suit, balaclava
Boys studying	Calculator, notebook, book pile, student	Post its, paperclip, pencil sharpener, marker, pencil case
Tennis	Female tennis player, court, net, racket, tennis shoes	Tennis ball, referee chair, male tennis player, wrist band, skirt
Underwater	Fish, view of water, wetsuit tops, seaweed, skate	Flippers, snorkel, swimming suit, oxygen cylinder, underwater camera

Detail of Scenes and Items Utilized at Encoding and Recognition Test

OLD

1. Elephant
2. Giraffe
3. Rabbit
4. Zebra
5. Lion



LURES

1. Eagle
2. Hippopotamus
3. Monkey
4. Panther
5. Rhinoceros










OLD

1. Airplain lamp
2. Airplain window
3. Emergency exit
4. Airplain sit belt
5. Crew sit

LURES

1. Flight attendant
2. Luggage compartiment
3. Plain sit
4. Plain table
5. Airplain Tv screen










OLD

1. Barbecue
2. Red plate
3. Steak
4. Tongs
5. Cooking glove

LURES

1. Arpron
2. Hamburger
3. Beer
4. Coal
5. ribs







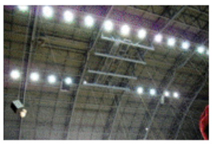



OLD

1. Score board
2. Ceiling lights
3. Training shorts
4. T-shirt
5. Basket court

LURES

1. Basket
2. Basketball
3. Stands
4. headband
5. Basketball uniform







OLD

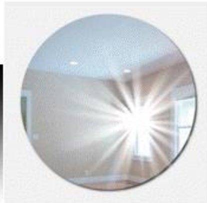
1. Bathtube
2. Shower
3. Sink
4. Towels
5. Toilet

LURES

1. Bathrobe
2. Bidet
3. Toilet brush
4. Mirror
5. Toilet roll







OLD

1. Sand
2. Shore
3. Deck chair
4. Bikini
5. swimmer

LURES

1. Swimming costume
2. Beach umbrella
3. Rubber ring
4. Sun lotion
5. Beach towel










OLD

1. Mattress
2. Duvet
3. Rug
4. Chair
5. bedspread

LURES

1. Night table
2. Lamp
3. Pillow
4. Slippers
5. Dressing table










OLD

1. White coat
2. Latex gloves
3. Pippette stand
4. Lab glass
5. Chemical bottle

LURES

1. Lab funnel
2. Lab glass
3. Microscope
4. Lab morter
5. pippette







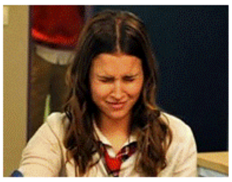



OLD

1. Betadine
2. Tourniquet
3. Phonendoscope
4. White coat
5. patient

LURES

1. Blood sample tube
2. Cotton
3. Syringe
4. Blood preasure tester
5. Needle

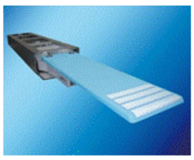


OLD

1. Boat
2. Buoy
3. Boat stairs
4. Sea water
5. Boat ropes

LURES

1. Anchor
2. gangway
3. Mast
4. rudder
5. Safety jacket



OLD

1. Boxing gloves
2. Boxing shorts
3. Boxing referee
4. Boxer
5. Black boxer torso

LURES

1. Boxing ring
2. Face protector
3. Boxing ring corner
4. Teeth protector
5. Ring ropes







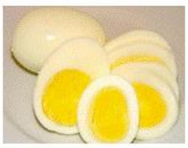

OLD

1. Green grapes
2. Orange juice
3. Toast
4. Ham
5. Cheese

LURES

1. Boiled eggs
2. Butter
3. Teapot
4. Toast holder
5. coffee







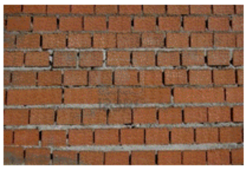

OLD

1. Brick
2. Bucket
3. Safety helmet
4. Brick wall
5. builder

LURES

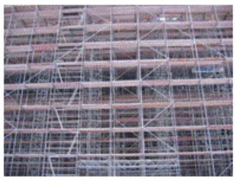
1. Trowel
2. Cement mixer
3. wheelbarrow
4. Builders safety jacket
5. scafolding







OLD

1. bullring
2. Bull horn
3. Bullfighter shoes
4. Bullfighter outfit
5. bull

LURES

1. Banderilla
2. Refuge in bullring
3. Cape
4. Bullfighter sword
5. Bullfighter´s hat



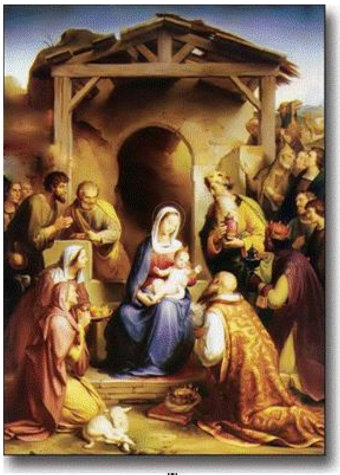






OLD

1. Café chair
2. Café table
3. Troley
4. White wine glass
5. Bottle rack



LURES

1. Mug
2. Waiter tray
3. Coke bottle
4. Waiter
5. Caffe stand










OLD

1. Antimosquito lotion
2. Canoa
3. Tree
4. Blanquet
5. Tent

LURES

1. Camping stove
2. Camping light
3. Sleeping bag
4. Camping chair
5. Camping backpack










OLD

1. wing mirror
2. Wheel
3. Car light
4. radiator
5. Car door handle

LURES

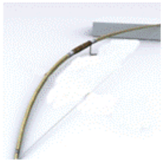
1. Registration number
2. Car sit
3. Windscreen wippers
4. Rear-view mirror
5. mudguard











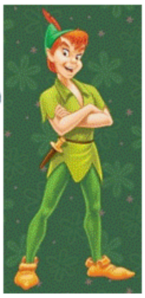
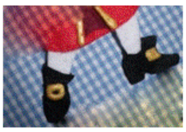

OLD

1. Crocodile
2. Pirate ship
3. Captain Hook
4. Peter Pan
5. Pirata shoes

LURES

1. Tinkerbell
2. Hook
3. Jhon
4. Lost boys
5. Mary






OLD

1. Christmas tree
2. Presents
3. Christmas tree angel
4. Wraping paper
5. Christmas tree lights

LURES

1. Guiding star
2. Santa Claus
3. Christmas sweet
4. Christmas sock
5. Christmas flower










OLD

1. Baptismal candle
2. Priest
3. Praying man
4. Stain glass window
5. Priest suit

LURES

1. Church pew
2. Crucifix
3. Virgin Mary statue
4. Praying woman
5. Sacred host










OLD

1. Blackboard
2. School desk
3. School girl
4. Teacher
5. School boy

LURES

1. Chalk
2. Teacher desk
3. School backpack
4. Book
5. Clothes hooks









OLD

1. Police helmet
2. Police shield
3. Demonstrators
4. container
5. photographer

LURES

1. Police car
2. loudspeaker
3. truncheon
4. Police van
5. banner





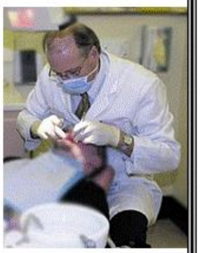

OLD

1. Dentist chair tools
2. mask
3. Dentist
4. Latex gloves
5. Dentist chair lamp

LURES

1. X-ray from mouth
2. Dentist pliers
3. Dentist hook
4. Dentist chair
5. Dentist mirror










OLD

1. Road map
2. Car chairs
3. Rear-view mirror
4. Steering wheel
5. A/C grille

LURES

1. gearbox
2. handbrake
3. SatNav
4. Radio
5. Rev counter










OLD

1. Sheriff plack
2. Bullets
3. Pocker cards
4. Gun
5. Pocket watch

LURES

1. Cowboy hat
2. spurs
3. holster
4. hipflask
5. Cowbow tie









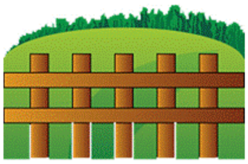
OLD

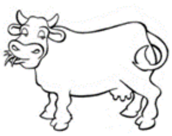
1. Goat
2. Chicken
3. Horse
4. Sheep
5. sunflower

LURES

1. Tractor
2. Cow
3. Farmer
4. Pig
5. Windmill




OLD

1. Football court
2. Goalkeeper gloves
3. goal
4. Goalkeeper
5. Football shoes

LURES

1. Football
2. flag
3. Whistle
4. Referee
5. crossbar










OLD

1. Black grapes
2. Mango
3. loquat
4. Fig
5. cherries

LURES

1. Blueberries
2. Granate
3. Banana
4. Pineapple
5. pear










OLD

1. fan
2. Necklace
3. Earings
4. Flamenca dress
5. Hair flower

LURES

1. castanets
2. Flamenca comb
3. Spots
4. Flamenca shoes
5. Flamenca shawl










OLD

1. Hair dresser sink
2. Stand hair dryer
3. Hair products
4. Hair dresser tray
5. Hair dresser sit

LURES

1. comb
2. brush
3. Hairdryer
4. curler
5. Hair pin









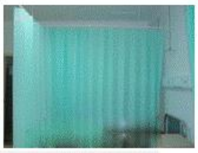


OLD

1. Hospital courtain
2. Hospital bed
3. Hospital side table
4. Hospital anamnesis board
5. Hospital bed sheets

LURES

1. Bed banister
2. I/V
3. I/V stand
4. Oxigen controllers
5. ECG monitor










OLD

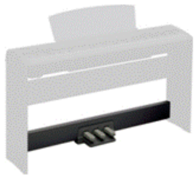
1. Stand
2. drums
3. Piano
4. trombone
5. violin

LURES

1. Clarinet
2. drumstick
3. Guitar
4. Music score
5. microphone







OLD

1. m

LURES

1. m

OLD

1. Fan
2. Counterpad
3. ladle
4. Tap
5. Washing machine

LURES

1. Dishwasher
2. Kitchen sink
3. Frypan
4. Fridge
5. microwave

OLD

1. Wooden chair
2. Stand lamp
3. Cow carpet
4. Pottery
5. Curtains

LURES

1. Table
2. Sofa
3. Window
4. Cushion
5. Magacine rack










OLD

1. Military tent
2. Military helmet
3. Military jacket
4. Military trousers
5. Military hat

LURES

1. Military boots
2. Bullets
3. Military waistcoat
4. Military radio
5. Submachine gun










OLD

1. Desk lamp
2. Office desk
3. Pen
4. Office phone
5. tie

LURES

1. Pc monitor
2. Pencil tin
3. Hole puncher
4. Executive chair
5. Office tray







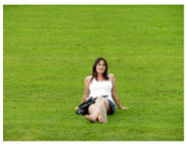



OLD

1. People resting on the grass
2. Lake fountain
3. Bench
4. Lake water
5. tree

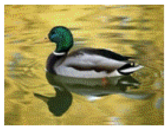
LURES

1. squirrel
2. Park runner
3. Duck
4. Dog
5. People walking







OLD

1. Medals
2. Cycling jersey
3. Cycling shoes
4. Cyclist
5. culotte

LURES

1. Winner´s flowers
2. Cycling hat
3. Podium
4. Trophy
5. Cicling helmet







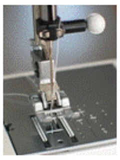



OLD

1. Sewing machine wheel
2. Pisatelas
3. Scissors
4. Fabrics
5. Sewing machine

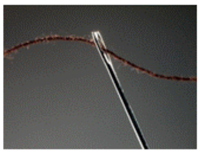
LURES

1. Tape measure
2. thread
3. thimble
4. Sewing needle
5. Sewing pins






OLD

1. Skiing boot
2. Nuns
3. Snowed tree
4. Skiing sticks
5. Snow court

LURES

1. Skies
2. Sking googles
3. Skiing trousers
4. Skiing suit
5. balaclava










OLD

1. Calculator
2. Notebook
3. Books
4. Pencil
5. student

LURES

1. Post it
2. Clip
3. Pencil sharpener
4. Edding
5. Pencil case







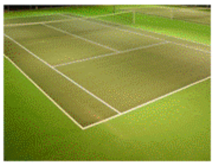



OLD

1. Woman tennis player
2. Tennis court
3. Tennis net
4. Racket
5. Tennis shoes

LURES

1. Tennis ball
2. Tennis referee chair
3. Man tennis player
4. Wrist bandage
5. Tennis skirt







OLD

1. Fish
2. Water under the sea
3. Neopren
4. Seaweed
5. skate

LURES

1. flippers
2. Snorkle
3. Swiming suit
4. Diving oxigen cylinder
5. Underwater camera










Information Sheet

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COLLEGE OF HEALTH & BEHAVIOURAL SCIENCES

YSGOL SEICOLEG
SCHOOL OF PSYCHOLOGY

PRIFYSGOL
BANGOR
UNIVERSITY

Information Sheet

Welcome to our lab and many thanks for volunteering to participate in our investigation. Before taking part in this research, please read the following information regarding the study, and also carefully read and sign the consent form.

In this study, we will show you pictures or scenes on a computer screen, and we will test your knowledge for them. It is important that you can see them well, so please make sure that you wear glasses or contact lenses if you normally do so. Your responses will be measured via button presses on a keyboard.

The whole study will last a maximum of 1 hour, and you will receive £6 or course/print credits for your participation. As your participation is voluntary, you can withdraw from the experiment at any time and for any reason without penalty. All data obtained is treated with complete confidentiality and in full anonymity.

Before we will commence with the study, please feel free to ask any questions about the study that you might have.

Any complaints concerning the conduct of this research should be addressed to Mr. Hefin Francis, School Manager, School of Psychology, Bangor University, Gwynedd, LL57 2AS

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Registered charity number: 1141565

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Version 3 (23/9/2011)

Consent Form

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COLLEGE OF HEALTH & BEHAVIOURAL SCIENCES

YSGOL SEICOLEG
SCHOOL OF PSYCHOLOGY

School of Psychology, Bangor University
Informed Consent Form

PRIFYSGOL BANGOR UNIVERSITY

Name and position of investigators:
Dr. Stephan Boehm – Lecturer
Mark Roberts – Research Officer
Yolanda Higueras, Christian Valt and Oren Poliva – PhD students
Paul Horwitz and Maida Toumaian – Masters Students

This is to certify that I, ………………………………………………, hereby agree to participate as a volunteer in a scientific investigation as an authorised part of the research ventures within the School of Psychology at Bangor University under the supervision of Dr. Stephan Boehm.

I understand that when I am willing to participate and choose not to withdraw, then I will be expected to participate actively.

The investigation and my part in the investigation have been fully explained to me by one of the investigators listed above and I understand his/her explanation. The procedures of this investigation and their risks have been answered to my satisfaction.

I understand that I am free not to answer specific items or questions in interviews or on questionnaires.

I understand that all data will be stored, analysed and published in a completely confidential manner with regard to my identity, and that I am free to withdraw my consent and terminate my participation at any time and for any reason without penalty.

I understand that I will receive a debriefing sheet about the aims of the research project at the end of the experiment, and that I may request a summary of the results of this study. I know of no medical condition, which may cause adverse effects to me if I participate in this experiment.

Signed ______________________________ Date ________________

I, the undersigned, have fully explained the investigation to the above individual.

Signature of Investigator ________________ Date ________________

Any complaints concerning the conduct of this research should be addressed to Mr. Hefin Francis, School Manager, School of Psychology, Bangor University, Gwynedd, LL57 2AS

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Appendix Chapter 3

Information Sheet

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COLLEGE OF HEALTH & BEHAVIOURAL SCIENCES

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SCHOOL OF PSYCHOLOGY

PRIFYSGOL BANGOR UNIVERSITY

PARTICIPANT INFORMATION SHEET

TITLE OF THE STUDY	**Investigation of memory in amnesia.**
INVESTIGATOR'S NAMES	Yolanda Higueras – PhD student. Dr. Stephan Boehm – Lecturer. Prof. Robert Rafal – Consultant neurologist. Professor of Clinical Neuroscience and Neuropsychology.
What is the purpose of the study?	We invite you to take part in our research study to investigate the biology of human memory and how it is impaired in neurological diseases. We will be testing both healthy individuals and patients who have impaired memory due to brain injury. As you have a diagnosed with amnesia, you are a good participant to help us to study how memory processes are impaired in amnesia.
What are the procedures?	If you agree to participate, it may take approximately 2 hours of your time. In that session Yolanda Higueras is going to assess your cognitive abilities with some test that are commonly used by neuropsychologist in clinical practice to evaluate your memory, your planning capacity, your attention skills and your general intelligence. These neuropsychological tests are commonly used in clinical context and will be done in approximately 1 hour. After that, you will be asked to complete another kind of testing that needs a computer to be applied. In this occasion, you will need to answer pressing buttons and the task will be explained carefully to you. This will take another hour approximately.
Are there any risk?	This measure is not painful or dangerous in any way. This procedure is completely safe and commonly used in both clinical and research environments.
What are the benefits?	There are no direct benefits to you for participating in this part of the study. This is not a clinical measure so we would not be able to make a diagnosis based on this. However your participation will be helpful in understanding false memories in both healthy controls and amnesic patients. This may eventually help to tailor cognitive rehabilitation programs for patients with amnesia.
How is	The scientific information obtained from these experiments may be

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Version 4 (23/11/2011)

confidentiality ensured?	published in scientific papers, but your name will not appear in any public document, nor will the results be published in a form which would make it possible for you to be identified. All data may be stored in a private registry and will be anonymized and treated with full confidentiality.
Will I receive compensation?	If you should decide to participate, you will receive £6 per hour.
Do I have a right to refuse or withdraw?	You may refuse to participate without your health care being affected. You may change your mind about being in the study and quit after the study has started, and if you feel, for any reason, uncomfortable, the study will be discontinued. If this happens, we would be thankful to use any result from your collaboration although you quit.
What if I have further questions?	We welcome the opportunity to answer any question you may have about any aspect of this study or your participation in it. You can contact the investigator PhD Yolanda Higueras or any of the leads investigators, Prof. Bob Rafal and Dr. S. Boehm, all of them available at School of Psychology, Bangor University.
What if I have a complaint?	Any complaints concerning the conduct of this research should be addressed to Miss Karen East, Director of ARBI, Dukeries Healthcare Ltd. She will transmit any complaints to Mr. Hefin Francis, School Manager, School of Psychology, Bangor University, Gwynedd, LL57 2AS.

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Consent Form

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COLLEGE OF HEALTH & BEHAVIOURAL SCIENCES

YSGOL SEICOLEG
SCHOOL OF PSYCHOLOGY

PRIFYSGOL BANGOR UNIVERSITY

Informed Consent Form

Name and position of investigators:

Dr. Stephan Boehm	Lecturer
Prof. Robert Rafal	Consultant Neurologist, Professor of Clinical Neuroscience and Neuropsychology
Yolanda Higueras	PhD student

Project: Investigation of memory in amnesia

☐ This is to certify that I, …………………………….……………, hereby agree to participate as a volunteer in a scientific investigation as an authorised part of the research ventures within the School of Psychology at Bangor University under the supervision of Dr. Stephan Boehm.

☐ I understand that when I am willing to participate and choose not to withdraw, then I will be expected to participate actively.

☐ The investigation and my part in the investigation have been fully explained to me by one of the investigators listed above and I understand his/her explanation. The procedures of this investigation and their risks have been answered to my satisfaction.

☐ I understand that I am free not to answer specific items or questions in interviews or on questionnaires.

☐ I understand that all data will be stored in the researcher's database, analyzed and published in a completely confidential manner with regard to my identity. The storage of my data will be only for research purpose and will always keep my personal information confidential.

☐ I am free to withdraw my consent and terminate my participation at any time and for any reason without my medical care or legal rights being affected.

☐ I understand I may request a summary of the results of this study from the investigators.

Signed ______________________________ Date ______________

Name (in capital letters) ____________________________________

I, the undersigned, have fully explained the investigation to the above individual.

Signature of Investigator ______________ Date ______________

Any complaints concerning the conduct of this research should be addressed to Miss Karen East, Director of ARBI, Dukeries Healthcare Ltd. She will transmit any complaints to Mr. Hefin Francis, School Manager, School of Psychology, Bangor University, Gwynedd, LL57 2AS

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Debrief sheet

Debriefing Information

Thank you very much for taking part in our study.

Mental time travel – going back in time to remember events that happened in one's own past – is an important facet of human existence. Often, time travel succeeds, but in some instances, it may fail and produce inaccurate memories. We are particularly interested in these inaccurate memories, and we are using a new way of memory testing to improve the understanding of the basis of memory and how remembering sometimes fails.

Thank you again for your participation in the study.

If you wish to receive more information on this topic, or if you would be interested in the results of this investigation, please contact the lead investigator Yolanda Higueras (pspc09@bangor.ac.uk), or the supervising researcher Dr. Stephan Boehm (s.boehm@bangor.ac.uk).

Version 5 (13/12/2011)

Appendix Chapter 5

Table 11

Descriptive data for Control group corresponding to total number of responses (%) and reaction times (RT)

	Mean		SD		MSE		t		gl		Sig.	
	%	RT	%	RT	%	RT	%	RT	%	RT	%	RT
FM-CRL	16.231	-1568.246	56.996	864.048	15.808	239.644	1.027	-6.544	12	12	0.325	0.000
CR-FA	132.692	-1155.657	10.185	1427.462	2.825	395.907	46.975	-2.919	12	12	0.000	0.013
HIT-FM	42.538	-743.315	23.240	711.538	6.446	197.345	6.600	-3.767	12	12	0.000	0.003
HIT-NEW	-15.846	207.516	13.521	934.517	3.750	259.188	-4.226	0.801	12	12	0.001	0.439
FM-CR	-58.385	950.831	32.212	1013.574	8.934	281.115	-6.535	3.382	12	12	0.000	0.005
CRL-FA	58.077	1363.420	32.032	1223.100	8.884	339.227	6.537	4.019	12	12	0.000	0.002
OLD MISSED-CRL	-41.231	-481.444	22.797	841.444	6.323	233.375	-6.521	-2.063	12	12	0.000	0.061
OLD MISSED-FA	16.846	881.976	13.303	1200.141	3.690	332.859	4.566	2.650	12	12	0.001	0.021

Note SD: standard deviation; MSE: mean standard error; gl: degrees of freedom; Sig: significance.

Table 12

Descriptive data for Patients group corresponding to total number of responses (%) and reaction times (RT)

	Mean		SD		MSE		t		df		Sig.	
	%	RT	%	RT	%	RT	%	RT	%	RT	%	RT
FM-CRL	2.000	-981.501	59.464	1695.915	17.166	489.568	.117	-2.005	11	11	.909	.070
CR-FA	93.750	-330.306	52.624	1945.347	15.191	561.573	6.171	-.588	11	11	.000	.568
HIT-FM	21.833	-303.444	22.457	647.109	6.483	186.804	3.368	-1.624	11	11	.006	.133
HIT-NEW	-25.000	-348.286	37.904	1399.954	10.942	404.132	-2.285	-.862	11	11	.043	.407
FM-CR	-46.833	-44.842	46.591	1706.143	13.450	492.521	-3.482	-.091	11	11	.005	.929
CRL-FA	44.917	606.354	45.596	1986.867	13.162	573.559	3.412	1.057	11	11	.006	.313
OLD MISSED-CRL	-20.250	-139.345	22.308	800.039	6.440	230.951	-3.144	-.603	11	11	.009	.559
OLD MISSED-FA	24.667	467.008	37.886	1878.591	10.937	542.303	2.255	.861	11	11	.045	.408

Note SD: standard deviation; MSE: mean standard error; df: degrees of freedom; Sig: significance

Table 13

Mean voltages corresponding to HIT-CR subtraction, in microvolts for each group and each electrode.

	300-500ms			500-800ms			800-1000ms			1000-1200ms			1200-1500ms		
	CONT	PAT	p	CONT	PAT	p	CONT	PAT	p	CONT	PAT	p	CONT	PAT	p
FP1	0.29	0.56	0.48	0.33	0.44	0.83	0.29	-0.35	0.24	0.40	-0.61	0.11	0.47	-0.40	0.14
FP2	0.63	0.43	0.63	0.92	0.65	0.65	0.98	-0.10	0.041*	0.94	-0.65	0.009*	0.99	-0.70	0.025*
F9	0.20	0.57	0.25	0.47	1.13	0.11	0.66	1.65	0.07	0.49	1.64	0.037*	0.44	1.11	0.30
F3	0.32	0.04	0.31	-0.20	-0.30	0.82	-0.52	-0.73	0.71	-0.33	-0.94	0.29	-0.34	-0.73	0.49
Fz	1.14	0.22	0.017*	0.81	0.09	0.10	0.59	-0.66	0.018*	0.88	-1.16	0.005**	0.80	-1.03	0.002**
F4	1.04	0.37	0.11	0.98	0.20	0.22	0.87	-0.38	0.07	1.06	-0.96	0.007*	0.93	-0.72	0.009*
F10	-0.10	0.16	0.45	0.19	-0.50	0.29	0.20	-0.35	0.38	0.29	-0.30	0.42	0.26	-0.05	0.56
C3	0.28	-0.16	0.20	0.37	0.19	0.79	0.02	-0.06	0.90	-0.04	-0.68	0.24	0.03	-2.77	0.53
Cz	0.78	0.08	0.07	0.59	0.21	0.37	0.09	-0.55	0.23	0.12	-1.21	0.045*	-0.05	-0.84	0.18
C4	0.85	0.14	0.11	0.58	0.05	0.46	0.28	-0.22	0.53	0.41	-0.58	0.22	0.32	-0.30	0.38
TP9	-1.23	-0.24	0.042*	-0.81	0.29	0.06	-0.37	0.72	0.09	-0.45	1.51	0.012*	-0.34	0.92	0.07
TP10	-1.08	-0.76	0.45	-0.82	-1.13	0.59	-0.61	-0.01	0.33	-0.47	1.30	0.06	-0.28	0.91	0.14
P9	-1.31	-0.56	0.16	-1.09	-0.05	0.13	-0.47	1.11	0.049*	-0.50	2.09	0.016*	-0.20	1.52	0.032*
P5	-0.48	-0.42	0.88	0.45	0.10	0.31	-0.45	0.47	0.09	-0.71	0.50	0.039*	-0.56	0.26	0.11
Pz	0.32	-0.32	0.06	-0.03	-0.46	0.41	-0.22	-0.71	0.43	-0.44	-0.91	0.44	-0.68	-0.68	0.99
P6	-0.29	-0.33	0.88	-0.55	-0.80	0.54	-0.57	-0.44	0.76	-0.60	0.25	0.16	-0.67	0.37	0.14
P10	-1.04	-0.59	0.36	-0.86	-0.83	0.96	-0.60	0.15	0.20	-0.63	1.40	0.006*	-0.50	1.15	0.10
FCz	1.19	0.29	0.07	1.01	0.48	0.38	0.70	-0.19	0.14	0.79	-0.78	0.028*	0.56	-0.50	0.12

Note * indicates $p<0.05$ and ** $p<.005$. CONT: control participants; PAT: patients. p: T-test p value resulting from patients versus control mean voltages comparison.

Table 14

Mean voltages corresponding to FM-CR subtraction, in microvolts for each group and each electrode.

	300-500ms			500-800ms			800-1000ms			1000-1200ms			1200-1500ms		
	CONT	PAT	p	CONT	PAT	p	CONT	PAT	p	CONT	PAT	p	CONT	PAT	p
FP1	0.07	0.51	0.36	0.24	-0.20	0.45	0.21	-0.86	0.08	0.34	-0.92	0.043*	0.47	-1.06	0.06
FP2	0.42	0.47	0.95	0.84	0.17	0.34	1.00	-0.40	0.07	0.94	-0.41	0.048*	1.20	-0.31	0.06
F9	0.26	0.58	0.53	0.71	1.12	0.44	0.96	0.96	0.43	0.76	1.21	0.38	0.63	1.03	0.57
F3	0.04	0.05	0.99	-0.48	-0.37	0.82	-0.73	-0.74	0.81	-0.54	-0.84	0.63	-0.47	0.63	0.81
Fz	0.67	0.02	0.18	0.31	-0.01	0.60	0.30	0.30	0.10	0.61	-1.01	0.013*	0.57	-0.98	0.027*
F4	0.68	-0.17	0.09	0.61	-0.45	0.15	0.53	0.53	0.10	0.92	-0.99	0.010*	0.94	-0.85	0.017*
F10	-0.03	-0.38	0.59	0.38	-0.90	0.12	0.56	0.56	0.13	0.64	-0.13	0.23	0.56	-0.29	0.23
C3	0.16	-0.07	0.49	0.12	0.06	0.93	-0.23	-0.23	0.91	-0.24	-0.62	0.60	0.04	-0.47	0.45
Cz	0.68	0.02	0.046*	0.07	-0.07	0.79	-0.41	-0.41	0.50	-0.33	-0.95	0.34	-0.18	-0.70	0.46
C4	0.74	-0.14	0.07	0.24	-0.38	0.44	0.11	0.11	0.52	0.18	-0.64	0.30	0.29	-0.46	0.33
TP9	-1.02	0.13	0.045*	-0.46	-0.02	0.59	-0.22	-0.22	0.45	-0.37	0.91	0.049*	0.52	0.64	0.038*
TP10	-0.62	-1.19	0.23	-0.24	-0.93	0.22	-0.04	-0.04	0.77	-0.05	0.69	0.22	0.00	0.69	0.39
P9	-1.11	-0.17	0.13	-0.81	0.43	0.10	-0.47	-0.47	0.036*	-0.52	1.48	0.007*	-0.54	1.50	0.03*
P5	-0.47	0.08	0.29	-0.47	0.44	0.19	-0.52	0.69	0.07	-0.66	0.47	0.06	-0.58	0.69	0.06
Pz	0.42	0.07	0.41	-0.16	0.00	0.93	-0.30	-0.52	0.73	-0.53	-0.58	0.92	-0.63	0.01	0.22
P6	-0.32	-0.11	0.61	-0.50	-0.39	0.81	-0.33	-0.10	0.68	-0.48	0.10	0.32	-0.55	0.29	0.15
P10	-0.66	-0.86	0.70	-0.29	-0.50	0.73	-0.12	0.36	0.55	-0.27	0.76	0.10	-0.38	0.94	0.08
FCz	0.83	0.03	0.026*	0.36	0.43	0.92	0.04	0.04	0.82	0.16	-0.13	0.71	0.07	0.16	0.91

Note * indicates p<0.05 and ** p<.005. CONT: control participants; PAT: patients. p: T-test p value resulting from patients versus control mean voltages comparison.

CONTROLS

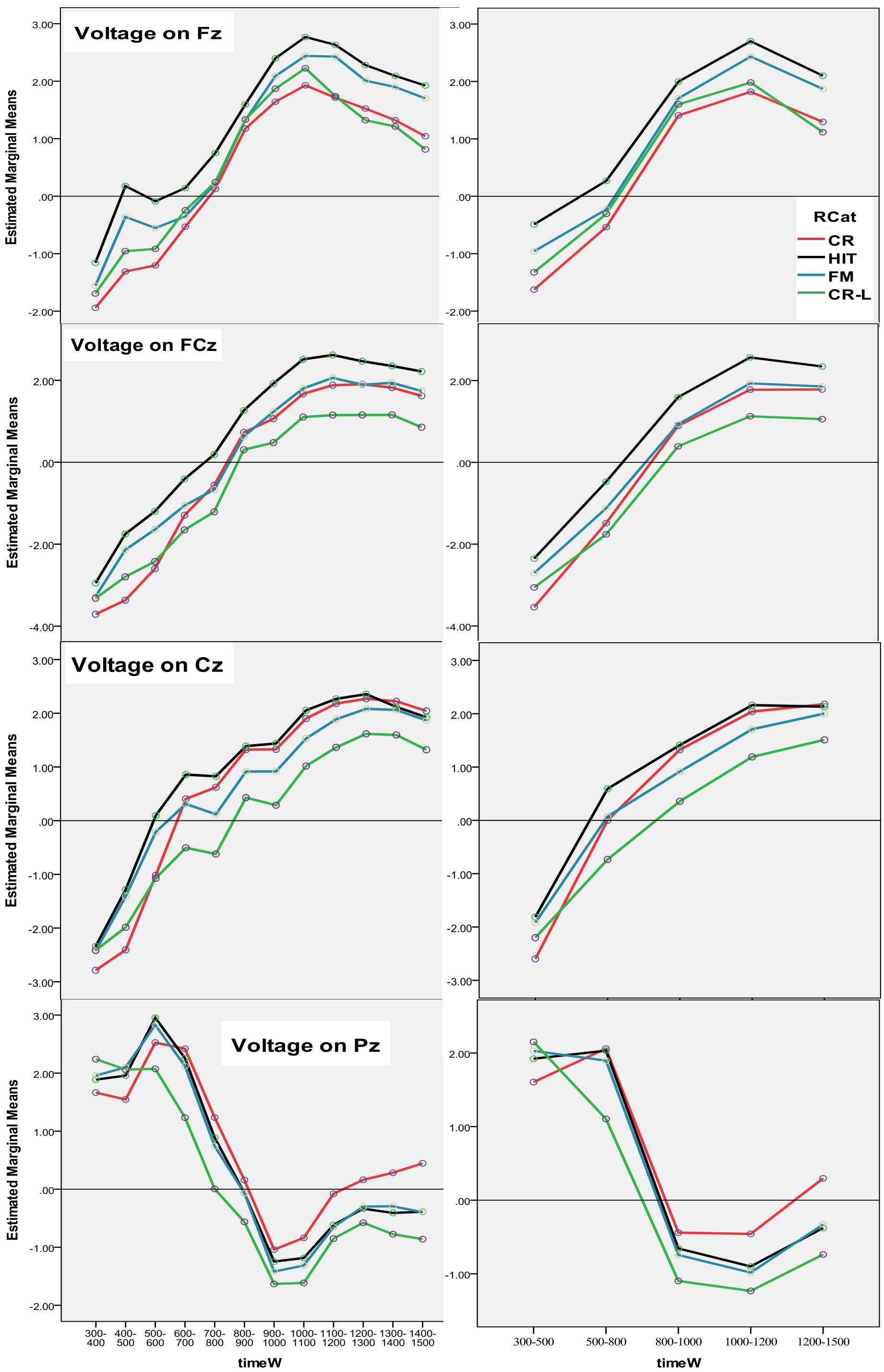

Figure 33 Estimated means for our 4 main response categories on midsagittal electrodes for control participants. Plot on the left side displays mean estimated voltages for every 100ms time windows, starting from 300 to 400ms onwards. Plot on the right side displays collapsed time windows. R Cat: response category; CR: correct rejection; FM: false memory; CR-L: correct rejection to a lure.

PATIENTS

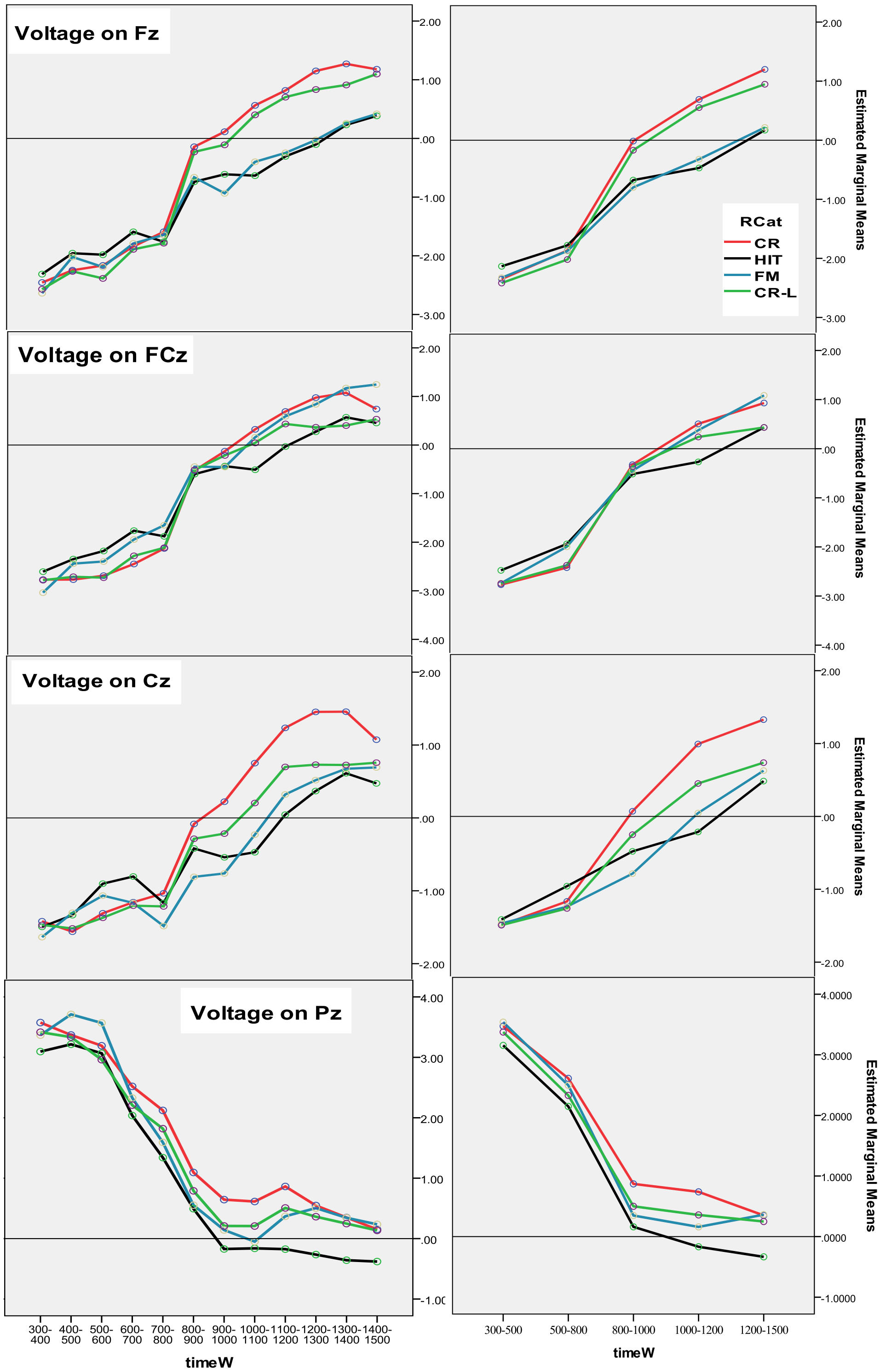

Figure 34: Estimated means for our 4 main response categories on central electrodes for patients. Plot on the left side displays mean estimated voltages for every 100ms time windows, starting from 300 to 400ms onwards. Plot on the right side displays collapsed time windows. R Cat: response categories; CR: correct rejection; FM: false memory; CR-L: correct rejection to a lure.

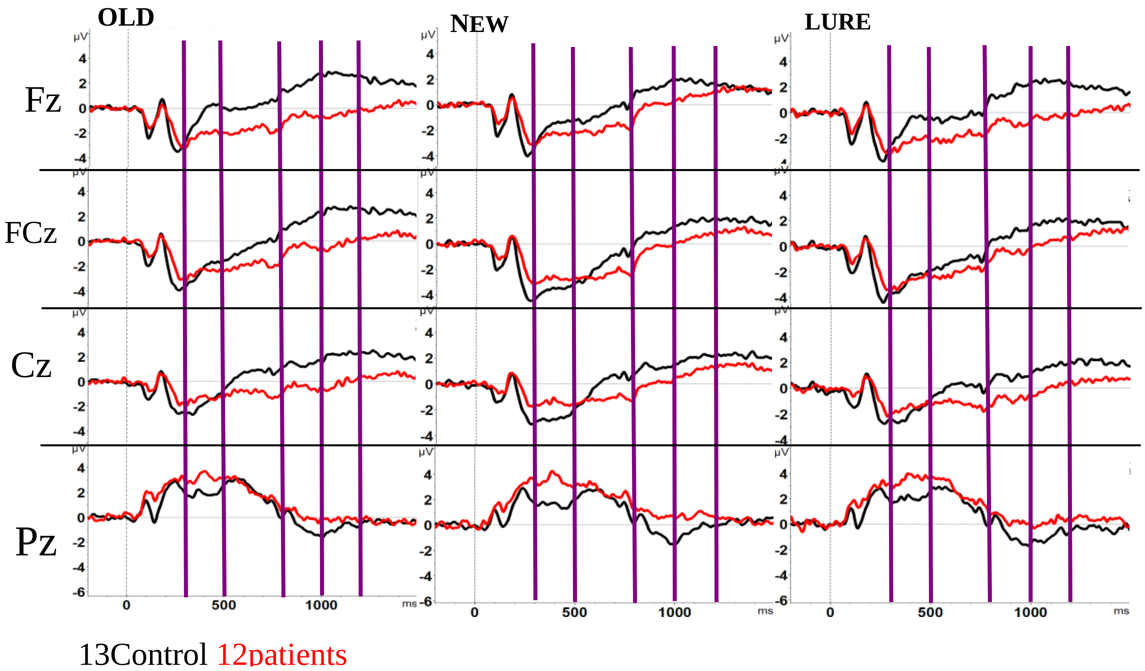

Figure 35 Grand Averaged waves on central electrodes for our four main response categories comparing control participants (black line) and patients (red line). New corresponds to correct rejections, Old to hits, Lured to false memories. Purple vertical lines indicate collapsed time windows of interest, i.e. 300 to 500ms, 500 to 800ms and 1000 to 1200ms.

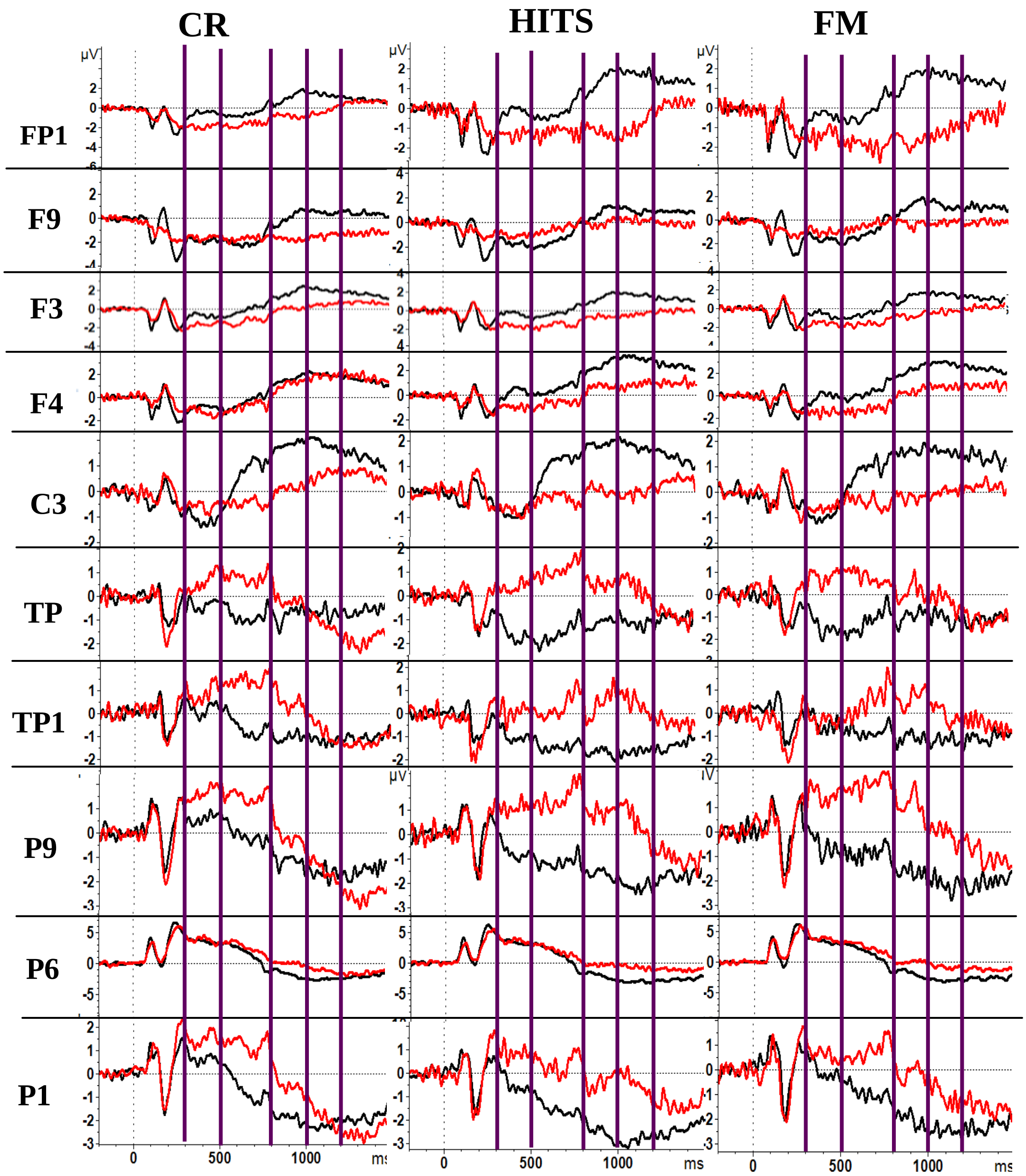

Figure 36 Grand Averaged waves comparison between control group (black line) and patients (red line). Purple lines indicate collapsed time windows of study, i.e. 300 to 500ms, 500 to 800ms and 1000 to 1200ms.

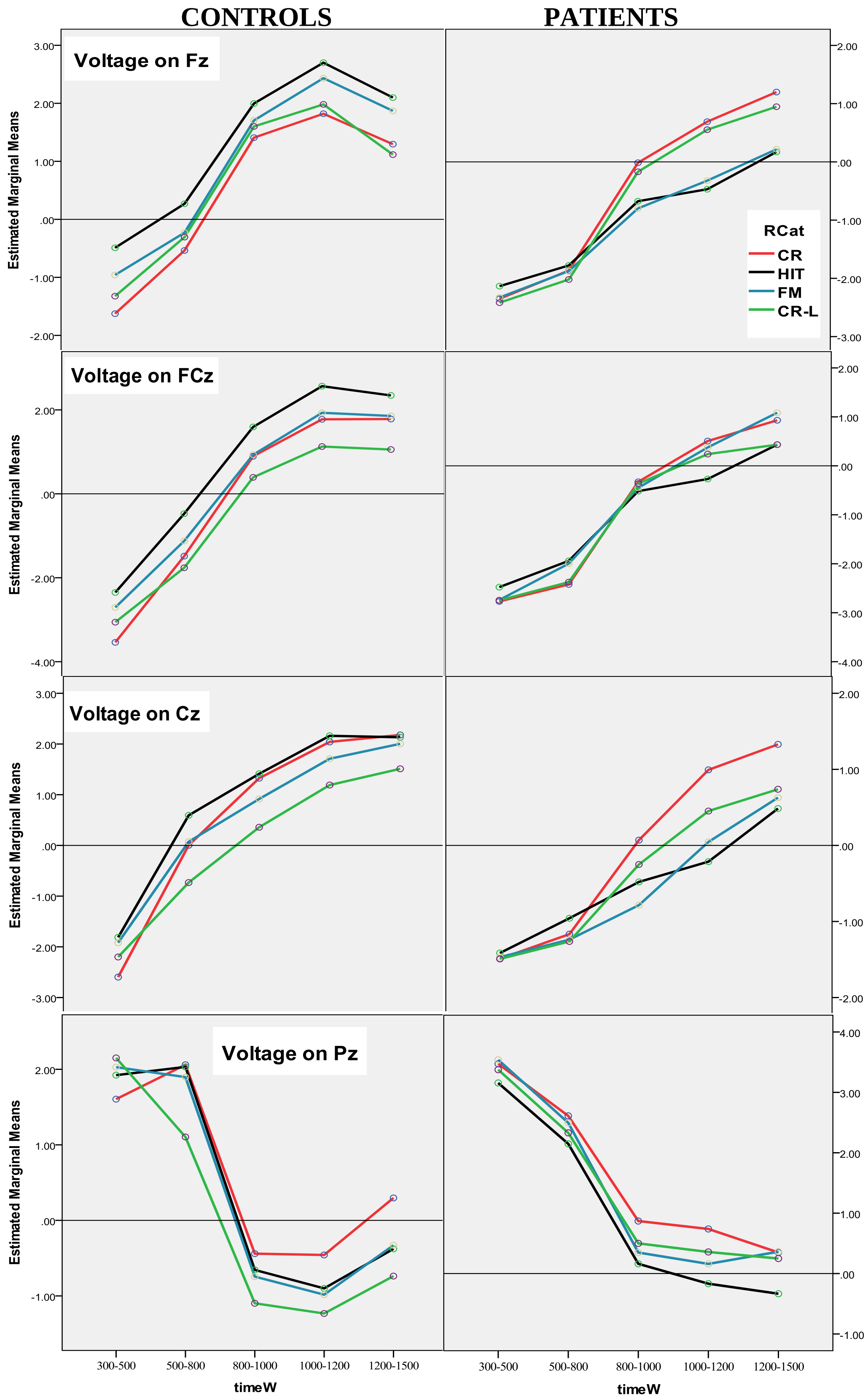

Figure 5: Estimated Means comparison at central electrodes between control participants (on the left) and patients (on the right) for collapsed time windows. CR: correct rejections; FM: false memories; CR-L: correct rejection to a lured.