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Dejä vu and Recognition Memory in Temporal Lobe Epilepsy

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Déjà vu and Recognition Memory in Temporal Lobe Epilepsy

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ABSTRACT

Déjà vu is a uniquely curious experience with which many of us are familiar. The experience can be so transient and unpredictable that it typically subsides, just as quickly as it appeared, before one can engage in any meaningful introspective evaluation. At the core of the experience is an impression of familiarity that co-exists with the feeling that it is inappropriate. Currently, there is no consensus among researchers about which theory can best account for the cognitive and neural mechanisms that underlie the experience. The goal of the current study was to examine déjà vu in temporal-lobe epilepsy (TLE) within the framework of the cognitive dual process-model of recognition memory that distinguishes between familiarity and recollection. It was reasoned that TLE patients with déjà vu should also experience deficits in recognition memory inter-ictally and that the exact nature of these deficits might offer insight into the cognitive mechanisms underlying the pathological, subjective experience of déjà vu associated with their seizures. The particular hypothesis tested was that the memory impairments in TLE patients with déjà vu are selective or most pronounced in the domain of familiarity assessment. Toward this end, two experimental recognition memory tasks derived from the cognitive neuroscience literature were administered to patients with unilateral or bilateral seizure origin. In general, converging evidence from the two tasks administered suggests that unilateral TLE patients with déjà vu do indeed have selective familiarity impairments and intact recollection. However, in bilateral cases deficits were found to be broader and included impairments in recollection as well. Inaccurate feelings of familiarity may represent the functional consequence of seizure activity in a region of the MTL critical for assessing feelings of familiarity. Further, these data hint that the cognitive process responsible for identifying the inappropriateness of the sense of

familiarity during déjà vu may not be recollection, as previously suggested in the literature. Together, the present findings suggest that probing the cognitive correlates of déjà vu in TLE inter-ictally can advance our understanding of mechanisms involved in déjà vu at a time when experimental paradigms to elicit the experience in the cognitive laboratory are still missing.

Keywords: Déjà vu, Epilepsy, Recognition Memory, Familiarity, Recollection, Dual Process Model, Medial Temporal Lobes, Perirhinal Cortex, Hippocampus, Amygdala.

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TABLE OF CONTENTS

CERTIFICATE OF EXAMINATION....ii

ABSTRACT....iii

ACKNOLEDGEMENTS....v

TABLE OF CONTENTS....vi

LIST OF TABLES....vii

LIST OF FIGURES....viii

LIST OF APPENDICES....ix

1. Introduction 1
2. What is Déjà vu? 4
   - 2.1. Déjà vu In Healthy Individuals 5
   - 2.2. Déjà vu in Temporal Lobe Epilepsy 6
   - 2.3. Déjà vu localization in TLE 11
3. The Functional Role of the MTL 17
   - 3.1. The MTL and Recognition Memory 19
   - 3.2. Recognition Memory and TLE 22
4. Déjà vu and the Dual Process Model of Recognition Memory 25
5. The Current Study 27
6. Methods 29
   - 6.1. Participants 29
   - 6.2 Questionnaire: Déjà vu Experiences in Temporal Lobe Epilepsy 36
     - 6.2.1 Materials 36
   - 6.3 Experimental Task: Remember-Know 37
     - 6.3.1 Materials 37
     - 6.3.2 Procedures 37
   - 6.4 Experimental Task: Exclusion Task 42
     - 6.4.1 Materials 42
     - 6.4.2 Procedures 42
7. Results 46
   - 7.1 Anecdotal Observations and Questionnaire: Déjà vu Experiences in Temporal Lobe Epilepsy 47
   - 7.2 Experimental Task: Remember-Know 48
   - 7.3 Experimental Task: Exclusion Task 54
8. Discussion 59

References 68

Appendices....77

Curriculum Vitae....97

LIST OF TABLES

Table	Description	Page
1	Patient and Control Demographic Data	30
2	Patient Clinical Characteristics	32
3	Patient Neuropsychological Data	34
4	Modal Response Options Characterizing Déjà vu	49

LIST OF FIGURES

Figure	Description	Page
1	Schematic Diagram of the Remember-Know procedure	41
2	Schematic Diagram of the Exclusion Task	45
3	The mean performance of each group on the measure of overall recognition (d'). Error bars indicate the SEM.	50
4	The mean performance of each group on the measure of familiarity (d'). Error bars indicate the SEM.	52
5	The mean performance of each group on the measure of recollection (proportion of hits – false alarms). Error bars indicate the SEM.	53
6	The normalized (z) recollection and familiarity estimates for bilateral and unilateral patients. Error bars indicate the SEM.	55
7	The mean performance of each group on the measure of accurately identifying old items (proportion of hits – false alarms). Error bars indicate the SEM.	56
8	The mean proportion of false alarms to repeated new items from studied categories for each group across each lags. Error bars indicate the SEM.	58

LIST OF APPENDICES

Appendix	Description	Page
A	Déjà vu Screening Questionnaire	77
B	Déjà vu Questionnaire	79
C	Ethics approval and Letter of Information	87

1. Introduction

Déjà vu is a uniquely curious experience with which many of us are familiar. It is defined as 'any subjectively inappropriate impression of familiarity of a present experience with an undefined past' (Neppe, 1983a). The experience can be so transient and unpredictable that it may subside, just as quickly as it appeared, before one can engage in any meaningful introspective evaluation of the unusual feeling. For this reason it is useful to begin with an illustrative example that captures the discord at the core of déjà vu. Say, for example, you were traveling to New York City for the first time. You are strolling through Central Park and as you approach the first of its 36 unique bridges you are suddenly struck with a strong impression of having already visited that spot in spite of the fact that you have never even been in New York City before. Perhaps, you may engage in a search through your mental catalogue of personal experiences in an effort to reconcile this disconnect between your subjective impression of prior occurrence and your objective knowledge of its true novelty. It is this most apparent inconsistency that renders déjà vu such a strikingly bizarre experience. Its puzzling nature and seeming ubiquity has been referred to by many novelists including Tolstoy in *War and Peace* (1859), Dostoevsky in *The Idiot* (1868), and Heller in *Catch-22* (1955), and has even been the inspiration for blockbuster movies.

Beyond popular fiction déjà vu has fascinated philosophers, neurologists, and psychologists for several centuries. In an empirical research context, the experience has been examined with at least two very different approaches. The first approach is questionnaire based and focuses on the incidence, frequency, situational factors, and various phenomenological aspects of the déjà vu state in healthy individuals (Brown,

2003). Data of this sort are typically obtained in retrospective accounts (Neppe, 1983b; Sno, Schalken, de Jonghe, & Koeter, 1994) and less frequently prospective reports (Sno & Draaisma, 1993). This line of research has been integral in documenting the frequency of déjà vu in relation to demographic factors, personality, and other aspects of psychological functioning. However it is not, by itself, a body of empirical data with which tenable hypotheses about the cognitive underpinnings of the experience can be tested. Thus, questionnaire-based research is inherently limited because, unlike the experimental paradigms used in cognitive psychology and cognitive neuroscience, it does not control or manipulate factors critical for revealing the cognitive processes of déjà vu. The second approach is neurologically-based and addresses déjà vu experiences that are bound to clinical syndromes in neurological patient populations. This neurological approach has been employed most extensively in epilepsy and has clearly been useful for clinical purposes, such as classification of the seizure disorder and prediction of treatment outcome. However, it can also serve as an empirical foundation to develop cognitive neuroscience theories of déjà vu, specifically with respect to the neuroanatomical basis of the experience.

Data from the questionnaire and neurologically-based approaches have engendered many theoretical accounts of déjà vu, some more speculative than others, that have been classified into three broad categories: psychodynamic, perceptual, and mnemonic. Psychodynamic theories, initially proposed by Freud (1995), suggest that déjà vu is triggered by the perception of a situation that approximates a suppressed fantasy. A second line of psychodynamic theories posits that the experience is actually a manifestation of residual dreams (Zuger, 1966). These theories are afforded little merit in

today's empirical climate and are of historical significance only. There are various perceptual accounts of déjà vu but at their core these theories are grounded in the assertion that it is a momentary lapse of normal perceptual processing that produces the experience. For example, one such theory suggests that, instead of both cerebral hemispheres receiving visual input in synchrony, there is a delay in the transmission to one hemisphere resulting in the duplicate processing of identical stimuli (Weinand et al., 1994). Mnemonic theories of déjà vu purport that some acute lapse in normal memory function can account for the experience whereby one does not consciously identify a previously encountered situation as old.

Currently there is no consensus among researchers about which specific theory, or even which broader domain of theories, can best account for the cognitive and neural mechanisms that underlie the experience. However, a combination of the neurological approach with experimental tasks derived from cognitive psychology may allow researchers to advance a theory of déjà vu that finds broad, empirically supported acceptance even in the absence of suitable methodologies to elicit déjà vu in the healthy brain and mind. The current research project is an attempt to take this route and elucidate the cognitive mechanisms of déjà vu in individuals suffering from epilepsy with a new experimental approach that is grounded in the cognitive neuroscience of memory. Current cognitive memory models will be used to formulate and test a specific hypothesis about the nature of potential memory deficits that are correlated with the déjà vu experience in these individuals

2. What is Déjà vu?

Literally, déjà vu translates from French into 'already seen' in English. Yet, it took well over 100 years, and upward of 50 attempts, from the time the term déjà vu was first used (Boirac, 1876) until it was afforded a widely accepted definition based on work by Neppe (1983a; see Brown, 2004). .Each word of Neppe's (1983a) definition of déjà vu, 'any subjectively inappropriate impression of familiarity of a present experience with an undefined past', was deliberately selected and therefore warrants further examination. The word 'any' implies that the experience can occur in both clinical or healthy states and that it is not necessarily a manifestation of some, or any, neural pathology (Wild, 2005). To be 'subjectively inappropriate' one must simultaneously identify a situation as having been previously experienced yet at the same time know that it has not. The term 'impression of familiarity' implies that the individual has a sense of prior occurrence, which in most instances is quite striking. This sense of prior occurrence is not merely a subtle notion. Rather, many individuals report a vivid impression of familiarity accompanied by a strong sense of confidence (Spatt, 2002). Lastly, the term 'undefined past' may take the form of a failure to identify the source of the familiarity or objective knowledge of having never truly experienced the present situation. To be sure, the critical elements of the experience from a phenomenological subjective and from an observer's perspective are the 'subjective inappropriateness' and the 'impression of familiarity'. It is the simultaneous occurrence of these divergent memory states that makes the experience so unique and remarkable.

2.1. Déjà vu In Healthy Individuals

As a notoriously unpredictable phenomenon, not readily amenable to experimental reproduction, research on déjà vu requires creative and novel approaches in order to enter the empirical domain of cognitive neuroscience. However, only recently promising efforts have emerged towards this end (Moulin, 2005, 2008; Bartolomei, 2004; Brown, 2008).As mentioned previously, what information has been garnered about déjà vu in healthy individuals to date has come almost exclusively from questionnaire-based research. The focus of such questionnaires is to define the content, frequency, physical state, and psychological reactions associated with the déjà vu experience. The questionnaire approach has been implemented by many researchers over the past century and, despite various methodological flaws (Harper, 1969; Neppe, 1983b; Gaynard, 1992; Sno et al., 1994), has yielded a large volume of surprisingly consistent data that speaks to demographic factors and psychological states related to the experience. Perhaps the most consistent finding across studies is that the frequency and incidence of déjà vu experiences declines with age (Richardson & Winokur, 1967; Brauer, Harrow, & Tucker, 1970). Also, one important study (Neppe, 1983b) that address various quantitative and qualitative characteristics of déjà vu revealed that the experience only lasts a few seconds, is accompanied by surprised affect, and occurs primarily in reference to an entire visual scene as opposed to people, objects, or activities.

Beyond the lack of experimental control that is inherent to the questionnaire approach, other qualifications are necessary because of the manner in which this type of research has been conducted. The most obvious is that retrospective designs require that participants remember very brief moments in time that may have occurred months or

even years ago. A second limitation of the questionnaire approach has been that the queries are frequently made within the context of investigations of paranormal phenomena (e.g. telepathy), leading to potential biases in sampling and reported self-perception of the experience.

2.2. Déjà vu In Temporal Lobe Epilepsy

It is well established in the neurological literature that a subset of epilepsy patients show a high and consistent incidence of déjà vu experiences as part of their seizures. Epilepsy is a chronic neurological condition of the brain characterized by an enduring propensity to generate epileptic seizures, and by its neurobiological, cognitive, psychological and social consequences (Engel et al., 2007). Epileptic seizures are defined as the transient occurrence of specific symptoms due to abnormally excessive or synchronous activity in the brain. The symptoms can include disturbances in consciousness, cognition, and motor activity. The time during which a seizure occurs is referred to as the ictal period and behaviour and neural activity can be monitored during this period, intra-ictally, or between ictal events, inter-ictally (Engel et al., 2007).

Of particular interest for the current research is the subset of epilepsy patients who experience déjà vu as an experiential manifestation of their seizures in temporal-lobe epilepsy (TLE). TLE refers to the repeated occurrence of epileptic seizures with an origin in the temporal lobes. These TLE seizures may occur bilaterally or be confined to a single cerebral hemisphere and it is possible for the seizure activity to generalize to brain regions outside of the temporal lobes. The déjà vu experience in TLE occurs intra-ictally and is symptomatic of the aura of simple and complex partial seizures (SPS and

CPS; Engel et al., 2007). A seizure is classified as a partial seizure if it has a focal onset. SPSs are partial seizures during which consciousness is preserved during the ictal event. CPSs are partial seizures that result in impaired or lost consciousness during the ictal event. Critically, during a CPS consciousness may be retained or only slightly clouded prior to the ictal period indicating that the individual is typically able to subsequently recall their subjective state in the moments preceding a seizure (Engel et al., 2007). The aura, the period during which some TLE patients report déjà vu, is a sudden experience of strangeness overcoming consciousness that indicates the beginning of a partial seizure. In and of itself it is a type of simple partial seizure and may occur with or without progression to a more serious ictal event, such as a CPS (Johanson, Valli, Revonsuo, & Wedlund, 2008).

Reports about the incidence rate of déjà vu in TLE vary between studies. Gloor et al. (1982) suggested that 11-48% of intractable TLE patients experience déjà vu at the onset of their complex partial seizures while Weinand et al. (1994), have reported this number to be only 1.3%. The discrepancy in incidence reports is likely attributable to inconsistent operational definitions of déjà vu between studies and sampling criteria, specifically whether the sample is limited to TLE patients with pharmacologically resistant (i.e., intractable) epilepsy or not. It has been noted that individuals with intractable epilepsy have a higher incidence of déjà vu than patients whose TLE is alleviated by medication (Brown, 2004). Regardless, a number of TLE patients do experience déjà vu intra-ictally and these individuals represent a unique population that can be tested to gain new insight into neural and cognitive mechanisms of déjà vu based on the observation of associated, persistent inter-ictal abnormalities.

Research on déjà vu in TLE has a rich history as an ancillary to clinically relevant investigations. The primary objective of this research has been to identify the region of ictal origin and to localize the subsequent seizure activity. However, the data can be useful from a basic-science perspective as well in terms of answering questions about the neural mechanisms involved in déjà vu and about associated behavioral and cognitive manifestations. In modern clinical settings an extraordinarily detailed evaluation is made to determine if a given TLE patient will benefit from neurosurgical intervention or if their seizures are best controlled by medication. Modern evaluations invariably include neuropsychological testing of cognitive functions, a detailed analysis of the behavioural manifestations of the seizures, magnetic resonance imaging (MRI), and surface electroencephalograms (EEG). An EEG records electrical activity of the brain. It is obtained by placing a series of electrodes on the scalp that detect changes in voltage over time. The technique is clinically useful for broadly localizing seizure activity. However it does not provide the fine grained spatial resolution that enables the clinician to precisely identify the location of the ictal origin (Luck, 2005). If seizures are not adequately managed with medication it may be necessary to consider surgical alternatives that can minimize the frequency and severity of ictal events. When this is the case a second, more invasive, electrophysiological recording technique called stereotaxicelectroencephalography (SEEG), which shares the temporal resolution of EEG but has the added benefit of more precise spatial resolution, may be employed. A consideration of this methodology is important for the question at hand because research using SEEG in TLE has been critical towards revealing the neuroanatomical mechanisms underlying déjà vu. In addition to recording electrical activity for the purpose of

localizing seizure activity, clinicians can use SEEG electrodes to stimulate neural tissue at the contact points in an effort to elicit epileptic seizure discharges for diagnostic purposes. Although invasive and limited to clinical populations, these stimulations are perhaps the only method known to elicit déjà vu experiences experimentally.

Due to conductance limitations inherently bound to conventional scalp electrodes SEEG monitoring is particularly important when attempting to do precise localization of seizures originating in medial regions of the temporal lobes. The procedure requires the implantation of multiple contact intra-cerebral electrodes using a standard Talairach stereotactic frame (Bartolomei et al., 2002). The precise location of the electrode contact points can be confirmed with CT scans after they are implanted. Upon removal further confirmation may take the form of MR images that clearly identify the tract traversed by the electrodes. The contact points are selected for diagnostic purposes, not with the intent to test any hypotheses beyond what is clinically relevant. However, researchers can explore the nature of déjà vu experiences in the context of SEEG implementations because the electrodes are located in regions that, when electrically stimulated, may evoke déjà vu experiences. It is these fortuitous circumstances that have yielded the most relevant data on déjà vu in TLE populations.

Before reviewing the literature from this neurological approach in TLE patients there is an important methodological issue that warrants clarification. Perhaps the most problematic shortcoming in the déjà vu literature on epilepsy is the reliance upon poorly constructed operational definitions of the experience. The research that is rooted in clinical settings is often confusing with respect to whether déjà vu has been distinguished from other, similar experiential phenomenon that can accompany TLE seizures. The term

'experiential phenomena' was introduced by Penfield (1954) and refers to mnemonic phenomena that are evoked by electrical stimulation of the cortex or that occur spontaneously during seizure discharges. These experiential phenomena reflect subjective experiences, sometimes episodic instances from the personal past, which have compelling immediacy. Consistent with the broad definition of experiential phenomena, Gloor (1990) noted that they may also include memory experiences of various types. One type relates to the actual recall of a past event or a situation. A second type concerns triggered feelings of familiarity. However, déjà vu is only one of a multitude of experiential phenomena that may or may not differ in theoretically meaningful ways. In the clinical literature, experiential phenomena including jamais vu, flashbacks, and the dreamy state are frequently grouped together into a broadly defined category of déjà vu or pathological impressions of familiarity. Jamais vu, the opposite of déjà vu, refers to a state that is characterized as an inappropriate sense of unfamiliarity. That is to say, it refers to a situation or setting that has been encountered before, and is recognized as such, but lacks the familiarity that should be present as a result. Flashbacks can be visual hallucinations that leave the individual with the sense that they are immersed in the midst of a prior experience. The 'dreamy state', first described by Jackson (1898), is an altered state of consciousness consisting of memory like hallucinations, and/or a feeling of familiarity that occurs in the context of electrical stimulation during neurosurgery. The dreamy state is a broad term that traditionally encompasses various experiential phenomena including déjà vu, jamais vu, flashbacks, and hallucinations (Wild, 2005). It is not entirely clear whether all of these terms refer to distinct phenomenological experiences. Unfortunately, they are sometimes used synonymously and with

inconsistent definitions across reports. This situation can make interpreting and comparing of data across studies challenging; differences in operational definition present challenges when researchers attempt to amalgamate findings and aim to generate theories upon which future empirical endeavors can be based. Nevertheless, despite these limitations, the neurologically based literature does offer a surprisingly consistent picture concerning the neuroanatomical basis of déjà vu and abnormal feelings of familiarity that points to promising, potentially important overlap with the cognitive neuroscience literature of recognition memory. Given the state of the neurological literature, for the purpose of the following review, the term déjà vu will be used loosely, without implying the stringent definition developed by Neppe (1983a).

2.3. Déjà vu Localization in TLE

For over 70 years the clinical goal of intra-operative stimulations, EEG recording, and SEEG stimulations has been to localize the ictal origin region of TLE patients. These investigations have sought to identify the lateralization (right or left) of seizures that are accompanied by déjà vu, whether they originate in lateral temporal lobe or medial temporal lobe (MTL) regions, and whether they can be linked to more specific temporal lobe structures. The lateralizing and localizing value of déjà vu in epilepsy has been greatly debated (Penfield, 1958; Mullan & Penfield, 1959; Penfield & Perrot, 1963; Penfield & Mathieson, 1974; Halgren, Babb, & Crandall, 1978; Gloor et al., 1982). Whether it is of practical clinical significance with respect to seizure classification, diagnosis, or treatment outcome remains a matter of discussion.

The first effort toward localizing déjà vu came from Penfield who electrically stimulated neural tissue in conscious TLE patients undergoing surgical resections, lesionectomies, or lobectomies in an effort to ameliorate intractable epilepsy. Penfield (1938) first discovered that experiential phenomena, including déjà vu, could be reproduced intra-operatively by electrical stimulation of the temporal lobes, but virtually never by stimulation applied to other regions of the cortex, in epileptic patients. Subsequent investigations (Penfield, 1958) implementing lateral temporal stimulations yielded 'illusions of familiarity' in 10 of 11 patients who experienced déjà vu at the onset of their seizures outside of the surgical context. Stimulations of patients who did not experience déjà vu as a manifestation of their seizures did not elicit any mnemonic responses. Penfield and Perrot (1963), having refined their stimulation procedures, reported that déjà vu was evoked by electrical stimulations of the superior temporal gyrus in 7.7% (n = 520) of TLE cases, and very rarely from MTL stimulations. Similar stimulations in temporal regions of 612 individuals with non-temporal lobe epilepsy did not evoke a single déjà vu experience.

Subsequent research (Halgren et al., 1978; Gloor et al., 1982; Bancaud, Brunet-Bourgin, Chauvel, & Halgren, 1994; Bartolomei et al., 2002; Vignal, Maillard, McGonigal, & Chauvel, 2007) has been based on more refined stimulation techniques in attempts to determine how TLE seizure activity can elicit experiential phenomena including déjà vu. Halgren, Walter, Cherlow, and Crandall (1978), taking advantage of SEEG pre-surgical evaluations reported the results of stimulation of the amygdala and hippocampus, two MTL structures, in 36 TLE patients. However, no lateral temporal lobe stimulations were administered for comparison. Of the 36 patients, 19 indicated that

they experienced déjà vu during the aura of spontaneously occurring seizures, although caution must be taken because an operational definition is not provided. Stimulations of the amygdala and hippocampus elicited déjà vu in 18 of the 19 who experienced it regularly with their seizures. Interestingly, déjà vu was rarely evoked unless the stimulations resulted in widespread potentials and after discharges that reached beyond the hippocampus and amygdala. Further, the response was not elicited consistently after repeated stimulations with identical parameters to the same cortical locations. The authors concluded that only widespread disruptions of MTL activity evoke déjà vu and do so with low reproducibility. However, lateral temporal lobe activity, similar to that reported by Penfield, cannot be definitively ruled out.

Gloor et al. (1982) used SEEG depth electrodes to stimulate the MTL and lateral temporal lobes in 35 TLE patients, 4 of which experienced déjà vu regularly with their seizures. Of the 4 TLE patients with déjà vu virtually all experiential responses were obtained by stimulation of the MTL and limbic structures and rarely from stimulation of the lateral temporal lobes. In order to avoid biases, a comparable number of stimulations were administered at each site. In particular the amygdala yielded the highest incidence of experiential phenomena. The propensity for amygdaloid stimulation to be effective in evoking experiential phenomena could not be explained by spreading activation as the majority of the positive responses were not associated with an after discharge, or only an after discharge that was locally confined to the amygdala. Stimulation of the amygdala elicited two responses: affective and experiential. The affective response was not particularly surprising but that stimulation of the amygdala resulted in mnemonic experiences, including déjà vu, was unexpected. To reconcile these data with Penfield

and Perrot's (1963), the authors re-examined the stimulation protocols used in the earlier investigations. In doing so they concluded that the small number of experiential phenomena evoked by Penfield and Perrot's MTL stimulations was a result of a methodological bias. That is, the lateral temporal lobes were stimulated considerably more frequently than the MTL. This research is of particular importance because it localized déjà vu, as it is currently defined, to the MTL.

In an effort to reconcile conflicting results from Penfield and Perrot (1963) and Gloor et al. (1982), Bancaud, Brunet-Bourgin, Chauvel, and Halgren (1994) examined both spontaneous and evoked experiential phenomena using SEEG in both MTL and lateral temporal lobe structures. All patients (n = 16) reported experiential phenomena, including déjà vu or vivid memory based hallucinations, at the onset of their seizures. The authors examined the relative ease with which experiential phenomena could be evoked across structures and recorded the spread of activation during spontaneous instances of such phenomena. To this end a total of 145 electrodes were implanted (107 right hemisphere) and 57 experiential phenomena (43 electrically induced, 9 spontaneously occurring, and five chemically induced) were studied. The patients provided extensive verbal accounts of the phenomena. For example, in response to a stimulation of the anterior hippocampus a patient reported: "the impression of having already done what I am in the process of doing; it seems to me I have already lived through the entire situation; with a feeling of strangeness" (Bancaud et al., 1994, p. 79). Another patient, describing a spontaneous experiential phenomenon in response to a seizure involving the left amygdala, hippocampus, parahippocampal gyrus, and superior temporal gyrus, reported: "I started by seeing the buildings next to our house, then while

looking at the light I saw some changing scene - a scene with trees and fields, but no people" (p. 78). These accounts are typical of experiential phenomena but only the first one comes close to meeting the currently accepted cognitive definition of déjà vu (Neppe 1983a). By contrast, the second one may be considered a visual hallucination. Nevertheless, the electrophysiological data from the patients who reported any such experiential phenomena always implicated the anterior hippocampus and less frequently the amygdala and lateral temporal cortex. Gil-Nagel & Risinger (1997), using surface EEG, have also localized the seizure activity of TLE patients with déjà vu to the anterior MTL, but to adjacent neocortical regions in the parahippocampal gyrus, rather than to the hippocampus itself. Concerning laterality, Weinand et al. (1994), using subdural EEG monitoring techniques, reported that in six of eight patients (75%) ictal déjà vu originated in the right MTL. Similarly, van Paesschen, King, Duncan, and Connelly (2001), using surface EEG, reported that the large majority of TLE patients with déjà vu (73%) experienced seizures that originated in the right hemisphere. Together, this research suggests that déjà vu is most often, although not exclusively, associated with right MTL seizure activity.

Bartolomei et al. (2002) conducted the most recent and perhaps most convincing research implementing SEEG stimulation intended to explore déjà vu. The objective of their experiments was to further examine the role of more specific MTL structures in the genesis of déjà vu. They stimulated the amygdala, as identified by Gloor et al. (1982), the anterior hippocampus as implicated by Bancaud et al. (1994), and the rhinal cortices (both perirhinal and entorhinal cortices) on the grounds that they had recently been implicated by cognitive neuroscience research as regions critical for sensations of

familiarity (Brown & Aggleton, 2001, see full discussion below). A total of 24 patients were selected based upon the criteria that they had SEEG electrode placements that sampled the amygdala, hippocampus, and rhinal cortices. A total of 280 stimulations were included in their analyses: 146 in the rhinal cortices (83 in entorhinal cortex; 63 in perirhinal cortex), 46 in the anterior hippocampus, and 89 in the amygdala. The stimulation intensity did not differ across sites. The stimulations of the rhinal cortices yielded déjà vu in 16 stimulations (11% of the stimulations) in seven different patients (30% of the patients) compared to the amygdala in one patient (2.2 % of stimulations) and the anterior hippocampus in another patient (2.1% of the stimulations). Further examination of the rhinal cortices revealed that déjà vu was evoked statistically more frequently in entorhinal cortex and that the reminiscence of detailed scenes was evoked more frequently in perirhinal cortex. This study advanced the localization of déjà vu in epilepsy even further by identifying a more specific MTL region, namely the rhinal cortices, that is critical for the genesis of the experience. However, even in this study the criteria employed to classify a reported experience as déjà vu did not follow the strict definition advanced by Neppe (1983a)

Taken together, data from EEG, SEEG recording, and SEEG stimulation studies most consistently implicate the MTL in the genesis of déjà vu in TLE, with a suggestion that perirhinal and entorhinal cortex are at the core. However, some conflicting results are clearly present in the literature and remain insufficiently understood. Moreover, it should not be overlooked that clinical studies, in particular those based on stimulation, cannot be conducted with the methodological rigor that would be desired from an experimental-psychology perspective. Nevertheless, these data are also intriguing because they relate in

meaningful ways to a broader body of cognitive neuroscience research in healthy individuals and neurological patients with other disorders. In this literature, recognition memory of prior occurrence has been linked to MTL functioning with a wide variety of experimental approaches. Examining this literature in the context of investigations aimed at increasing our understanding of déjà vu promises to offer important additional insight.

3. The Functional Role of the MTL

Beginning with Scoville and Milner's (1957) seminal work on patient HM, neuropsychological research has firmly established the link between long term declarative memory and the MTL. Declarative memory is the capacity for the conscious recovery of facts and personally experienced events (Milner, Squire, & Kandel, 1998). To treat intractable epilepsy, HM underwent a bilateral resection of his MTL and subsequently suffered from profound anterograde amnesia. Anterograde amnesia, as a result of a neurological condition, refers to a deficit in forming new declarative long term memory representations. For example, HM was unable to learn new word pairs or recognize people that he encountered after the resection while his ability to remember events that had taken place prior to surgery remained relatively intact. While the impairment in forming new memories is the hallmark of anterograde amnesia there are three other characteristics that have been noted in research starting with the initial investigations in HM. The first is that the impairment is multimodal, i.e., declarative memory for information is affected regardless of sensory modality and material type (Milner, 1972; Squire, 2004). Another characteristic typical of MTL damage is that immediate, or short term, memory, such as processing assessed with digit span, remains

broadly intact (Squire, 2004; Milner, Squire, & Kandel, 1998; but see Ranganath & Blumenfeld, 2005, for a different view). Finally, the memory impairment is present despite intact perceptual and intellectual functioning (Squire, Stark, & Clark, 2004; but see Buckley, Wilson, & Gaffan, 2005). Notably, much of what is known about the MTL and declarative memory has been gained from investigations in TLE patients who underwent surgical resections of temporal structures for the treatment of epilepsy.

In response to the findings in patient HM, several researchers worked to develop animal models in non-human primates and rats that would mirror the memory impairments seen in humans with MTL lesions. Zola-Morgan, Squire, and Mishkin (1983) were successful in identifying such a deficit in non-human primates with bilateral MTL lesions. Such lesions impaired performance on recognition memory tasks in a manner consistent with HM and other cases of anterograde amnesia. Recognition memory is declarative in nature and refers to the ability to recognize prior occurrence, i.e., to note that a stimulus or situation has been encountered before (Squire et al, 2004; Yonelinas, 2002; Eichenbaum et al., 2007). It was this line of animal-lesion research that first identified the anatomical components of the MTL memory system with more precision: the hippocampus proper and the adjacent entorhinal cortex, perirhinal cortex, and parahippocampal cortex (Squire and Zola-Morgan, 1991).

More recently, neuroimaging researchers have examined the role of the MTL in declarative memory of healthy individuals. Functional MRI (fMRI) has demonstrated that activity in the MTL is correlated with successful encoding and recognition memory performance for words, pictures, and associations (Squire, Wixted, & Clark, 2007; Diana, Yonelinas, & Ranganath, 2007).

Taken together the evidence is clear that at the very least the MTL forms a critical node or bottleneck in a declarative memory system. However, there is still much to be resolved about the functional contributions of the MTL. Specifically, one issue of contention pertains to whether there is a division of labour (i.e., functional specialization) within the MTL concerning different aspects of recognition memory.

3.1. The MTL and Recognition Memory

Recognition memory is required to distinguish between old (i.e., previously encountered) and new information whether it be a person you see in a restaurant or a picture you see each night on your bedroom wall. One can distinguish between previously encountered and new stimuli on the basis of familiarity or recollection, the two processes that support recognition (Yonelinas, 2002). The first process, familiarity, supports recognition without the retrieval of any contextual information and can vary in strength from a weak intuition to a strong sense of belief that the current stimulus has been previously encountered. The second process, recollection, involves the detailed recovery of contextual, associative details about the episode in which a stimulus was encountered (Eichenbaum et al., 2007). It is worth providing an example to illustrate the distinction between familiarity and recollection: It is quite common to encounter a person whom we have met on a previous occasion. Upon seeing this individual one of three episodic experiences may happen: we may recollect having met them, they may seem familiar, or recognition memory fails and we do not remember the initial encounter at all. To recollect the individual is to recall specific details about the circumstances under which they were previously encountered such as where you were and what you

discussed. In another instance, upon encountering a person for a second time, they may only seem familiar to you. You know that you have met them before but cannot recall any specific details as in the recollective experience. This feeling of "your face looks familiar, but I can't remember your name" is a common phenomenon experienced by many (Mandler, 1991). Alternatively, the recognition memory system may fail and you would not be able to say that you have met the person previously. There are several cognitive-neuroscience accounts of recognition memory that address the functional role of the MTL with respect to familiarity and recollection.

One prominent class of recognition memory theories considers the distinction between familiarity and recollection to be quantitative in nature and to reflect the strength of the memory signal (Squire et al., 2007). By this account all MTL structures are equally important for both recollection and familiarity. Another influential account of familiarity and recollection emphasizes qualitative differences (Eichenbaum, Otto, & Cohen 1992; Aggleton & Brown, 1999; Yonelinas, 2002, Eichenbaum, 2007). Such models are based on the notion that these processes are functionally distinct, independent, and supported by distinct MTL structures. That is to say, there are qualitative differences between recollection and familiarity in cognitive terms and in the way these processes are supported by MTL structures.

Brown and Aggleton (2001) were among the first to propose that the hippocampus and perirhinal cortex form the neuroanatomical substrates of the two processes in the MTL. In this influential proposition it is the hippocampus that is critical for recollection and perirhinal cortex that supports the independent assessment of familiarity. Based on this model hypotheses can be derived and tested in patients with

selective MTL damage. Patients with damage limited to the hippocampus should exhibit deficits in recollection with spared familiarity. By contrast, patients with damage limited to perirhinal cortex should exhibit deficits in familiarity while recollection should remain intact.

Recent research has attempted to test these hypotheses. When the recognition memory of patients with selective hippocampal damage was tested it has been found that some of these individuals have recollection impairments but preserved familiarity. This finding has been reported across a variety of paradigms including Remember-Know experiments and studies focused on the Receiver Operating Characteristics (ROC) of recognition judgments (Eichenbaum et al., 2007). For example, Aggleton et al. (2005) reported such selective recollection impairments with both methodological approaches in a single case study of an individual with hippocampal atrophy caused by meningitis. However, the literature presents some inconsistencies in that recognition impairments in patients with selective hippocampal damage are not always limited to recollection (Squire, Stark, & Clark, 2004). Accordingly, the cognitive neuroscience models of recognition memory that map both processes onto separate structures remain contentious.

Dissociating the functional role of perirhinal cortex from the hippocampus, by way of a true double dissociation has proven to be a particularly strong challenge. The problem lies in the nature of the MTL damage that is typically seen in naturally occurring lesions; perirhinal cortex is rarely damaged selectively. However, recently, Bowles et al. (2007) investigated the recognition memory performance of patient NB who underwent an anterior temporal lobe resection that included large aspects of perirhinal cortex but spared the hippocampus. NB presented with intractable TLE caused by a ganglioglioma

in the left amygdala in close proximity to perirhinal cortex. Her primary seizure type was complex partial and it was accompanied by déjà vu pre-surgically. To treat her epilepsy, NB underwent a unilateral (left) lesionectomy that targeted the amygdala, perirhinal cortex, and entorhinal cortex but spared the hippocampus and parahippocampal cortex. Anterior lateral temporal lobe structures were also included in the resection. NB's recognition memory was tested post-surgically in four different experiments with three different verbal paradigms to probe recollection and familiarity. Her performance consistently indicated intact recollection abilities and impaired familiarity. For example, she showed impairments in a Remember-Know recognition task that directly required her to reflect on the subjective nature of her recognition experience by indicating whether it was one of recollection, with contextual details, or based on feelings of familiarity (Tulving 1985). The case of NB is significant in that it is the only instance of a selective familiarity deficit associated with a focal temporal lobe lesion in the literature so far. The case is of great theoretical importance for dual process models of recognition memory as it is fully in line with Brown and Aggleton's (2001) proposition.

3.2. Recognition Memory and TLE

Given the integral role of the MTL in declarative memory it is perhaps not surprising that repeated seizure activity in this region can have lasting structural and functional effects that are deleterious to recognition memory performance (Hermann et al., 2006). A neuropathological condition associated with epilepsy, and frequently with memory deficits, is neural atrophy in the MTL, which can occur as a result of excitotoxicity produced by excessive electrical activity occurring during epileptic seizure

discharges (Moran, Lemieux, Kitchen, Fish, & Shorvan, 2001). Atrophy of this sort has been coined mesial temporal sclerosis (MTS) and can be the cause or result of TLE. Volumetric analyses of MTL tissue based on detailed structural MR images have revealed that MTS can affect both the hippocampus and surrounding entorhinal and perirhinal cortex (Jack et al., 1992; O'Brien, Bowden, Bardenhagen, Cook, 2003). A consideration of the empirical literature at large suggests that regions that are frequently and repeatedly subject to ictal events are also be subject to the concomitant memory problems (Helmstaedter, 2002; Saling, 2009). Whether MTS in different MTL regions is associated with different types of recognition impairments, however, remains unclear. Declarative memory impairments are generally subtler in pre-surgical cases than post-surgically. Anterograde amnesia is a rare post-operative consequence of unilateral temporal lobe resections and, when present, may reflect undetected bilateral MTL damage pre-surgically (Saling, 2009). In fact it has been suggested that there are no instances of post-operative amnesia following unilateral resection when MRI evidence indicates that a patient's contralateral temporal lobe was normal pre-surgically (Baxendale, 2008). It would appear as though the MTL memory system is rather resilient across the two hemispheres as bilateral MTL damage results in more profound memory deficits than unilateral damage.

The nature of the pre-surgical deficits that have been observed in TLE patients is often material specific. It has been demonstrated that left medial TLE is most consistently associated with verbal memory deficits and that right medial TLE is most consistently associated with non-verbal memory deficits (Moscovitch & McAndrews, 2002; Giovagnoli, Casazza, & Avanzini, 1995). Gleissner, Helmstaedter, and Elger

(1998) examined preoperative right TLE patients and found that they had impaired visual recognition memory on standard neuropsychological tests as reflected in their retention of non-verbal materials. Curiously, however, successful recognition of scenes has been suggested to recruit both the right and the left MTLs in research on post-surgical TLE, likely because some of the information contained in scenes can be verbalized whereas other aspects cannot (Pigott & Milner, 1993). Material specificity aside, a review by Helmstaedter (2002) concluded that patients with medial TLE have deficits relative to age matched controls in recognition memory and that these deficits may be progressive.

More to the point of the current investigation, Moscovitch and McAndrews (2002) examined recollection and familiarity in unilateral TLE patients using the Remember-Know paradigm with verbal and non-verbal stimuli. They tested the hypothesis that recollection may reflect conceptual processing mediated by the left hemisphere whereas familiarity is based on the fluency of processing mediated by the right hemisphere. If so, patients with left-lateralized TLE would be expected to have disproportionately impaired recollection regardless of stimulus material. By contrast, patients with right-lateralized TLE would have disproportionately impaired familiarity irrespective of material. The stimuli employed were faces and words, which were studied under conditions that promoted conceptual or perceptual processing. The results revealed that, contrary to the authors' hypotheses, the deficits were material rather than process specific. Left TLE patients exhibited impaired recollection for verbal material and right TLE patients showed impaired recollection for non-verbal material. Importantly, familiarity-based responses were not affected by TLE under any of the experimental conditions. To my knowledge, with the exception of case NB (discussed previously), no

single patient or patient group with documented MTL lesions has been reported to exhibit selective familiarity deficits. The deficits that have been reported are either global recognition deficits that affect both processes (e.g., Yonelinas et al., 2002) or selective recollection deficits (e.g., Aggleton et al., 2005; Mayes et al., 2004). It is worth noting, however, that for memory related research in TLE, patients have typically not been selected according to the presence or absence of déjà vu or other experiential phenomena.

In addition to NB's post-surgical familiarity deficit, at least one recent case study (Bujarski & Sperling, 2008) has demonstrated that feelings of familiarity can be altered by focal epilepsy. A young woman being evaluated in an epilepsy clinic experienced acute, post-ictal hyperfamiliarity. After experiencing acute CPSs, the patient reported strong feelings of familiarity for people or photographs that she had never met or seen before. On clinical neuropsychological tests of face recognition, she showed signs of impairment. Interestingly, after the seizures were medically controlled the sensation of familiarity for faces abated. The patient's ictal EEG recordings revealed that the seizures were originating in the anterior temporal lobes bilaterally. While this case does not meet criteria to be considered déjà vu, given that no subjective sense of inappropriateness accompanied her hyperfamiliarity, it provides additional suggestive evidence that the disruption of recognition processes associated with TLE may be familiarity specific.

4. Déjà vu and the Dual Process Model of Recognition Memory

That the region whose stimulation can lead to instances of déjà vu in TLE is also the region critical for distinguishing between previously encountered and novel situations on the basis of familiarity reflects an intuitively appealing link between both phenomena.

The seizure profile of case NB, which included the presence of déjà vu experiences in association with her CPSs pre-surgically, is also consistent with the evidence localizing evoked déjà vu to the rhinal cortices. In addition, these findings support Gloor's (1990) proposal that experiential phenomena elicited by temporal lobe seizures or stimulation are positive expressions of the functions of the temporal lobe and do not reflect ictal interference or paralysis of these functions.

An explanatory theory of déjà vu that is consistent with the experience of TLE patients such as NB in both spontaneous and evoked episodes has been proposed by Spatt (2002). He suggested that déjà vu is the result of false activation of connections between MTL memory structures and neocortical areas involved in the perception of the immediate environment. The false activation of perirhinal cortex presumably results in an inappropriate labeling of the current situation as familiar. The unaffected hippocampus, perhaps together with frontal lobe structures, may produce the concurrent subjective sense of inappropriateness of the familiarity experience. The false activation that occurs during intra-ictal déjà vu would likely be due to seizure activity. Thus, in such an account eliciting stimulus is not required.

O'Connor and Moulin (2008) reported the case of MH that directly addresses the notion that déjà vu is an interpretive state resulting from neural activity that generates stimulus non-specific feelings of familiarity. MH began experiencing CPSs subsequent to recovering from encephalitis at the age of 33. Prior to the onset of his epilepsy MH had never experienced déjà vu but it became a prominent phenomenological feature of his seizures lasting as long as one minute. The experience frightened MH and in an effort to alleviate the sensation he would consciously shift his focus of attention, hoping to

discover something that did not seem eerily familiar. However MH's efforts invariably failed, and the sensation of inappropriate familiarity would "follow his line of vision and hearing" (O'Connor & Moulin, 2008, p. 145). This eloquent account of a falsely generalized feeling of familiarity suggests that the experience is not bound to any single stimulus or environmental element. Rather, the experience may reflect a top-down interpretive state, whereby feelings of familiarity are assigned to the immediate environment despite the individual's knowledge that this cannot be true.

5. The Current Study

The goal of the current study is to examine déjà vu in TLE within the framework of the dual process model of recognition memory. The objective is to elucidate the cognitive mechanisms underlying déjà vu associated with TLE. The case of NB (Bowles et al., 2007) and compelling neurological evidence from stimulation studies in TLE has implicated perirhinal cortex as a region closely associated with intra-ictal déjà vu. Further, it is known that epilepsy is associated with lasting inter-ictal recognition memory deficits. These deficits are thought to originate from structural and functional changes related to ictal activity (Hermann et al., 2006). As noted, one such change is MTS, which has been documented in the perirhinal cortex of some TLE patients (O'Brien et al., 2003). In the current study, therefore, I propose that TLE patients with déjà vu should also experience deficits in recognition memory inter-ictally and that the exact nature of these deficits might offer insight into the cognitive mechanisms underlying the pathological, subjective experience of déjà vu associated with their seizures. More specifically, I hypothesize that the memory impairments in TLE patients

with déjà vu are selective or most pronounced, in the domain of familiarity assessment. At the same time, the nature of déjà vu is such that the individual can identify the inappropriateness of the familiarity suggesting that, at least initially in the course of the seizure, the processes that operate to identify this inappropriateness are intact. The hippocampus may serve this function by way of recollection. If so, one might expect the functional integrity of the hippocampus to remain relatively intact. Accordingly, TLE patients with déjà vu may have damage that is more severe or limited to perirhinal cortex with a relatively intact hippocampus. Such a pattern of pathology may produce a familiarity deficit that is selective and consistent with the one observed in NB post-surgically.

In the current thesis, the specified account will be tested behaviourally with two recognition memory paradigms in TLE patients with documented déjà vu. Visual scenes will be used as stimuli in both experimental tasks for two reasons: First, most subjective reports indicate that déjà vu occurs in reference to an entire scene, rather than towards individual objects or people (Brown, 2004). Second, unlike verbal material, scene recognition is sensitive to lesions or damage in both temporal lobes (Pigott & Milner, 1993). Given that déjà vu has been associated with seizure foci in the right as well as in the left temporal lobe, scenes thus can be considered a particularly promising stimulus class to probe the contributions of both hemispheres to potential deficits in familiarity assessment.

Two complementary experimental paradigms were selected from established cognitive neuroscience research; they address recognition memory from slightly different perspectives. A Remember-Know paradigm, first developed by Tulving (1985), will be

employed to assess overall recognition performance and to gain insight into the subjective experiences of recollection and familiarity. The task is such that quantitative estimates of familiarity and recollection performance can be derived and compared between groups. A second experimental task, a so-called exclusion task developed by Jacoby and Jennings (1997), will be used to explore how familiarity and recollection contribute to recognition when placed in opposition. In doing so we can determine how, if present, a selective deficit influences the typical interplay between familiarity and recollection.

6. Methods

6.1 Participants

A total of 10 patients with intractable temporal lobe epilepsy completed two experimental tasks. Demographic information for each patient is presented in Table 1. The patients were selected according to the criteria that each had TLE and experienced déjà vu, as defined by Neppe (1983a), at the onset of their seizures. Each patient was recruited from the epilepsy monitoring unit in the London Health Sciences Centre (LHSC) where they were being evaluated to explore treatment options. Potential candidates were flagged by an LHSC clinician based on an unstructured interview addressing the presence of déjà vu as a seizure symptom and a willingness to participate in research. To determine whether they satisfied the inclusion criteria of déjà vu, according to Neppe's (1983a) definition, all candidates completed an initial screening questionnaire about their intra-ictal experiences.

Table 1

Demographic Data

Patient	Sex	Age (years)	Education (years)
Bilateral Patients			
1071	F	19	12
1072	M	20	10
1073	F	48	14
1076	M	21	12
Mean		27.00	12.0
SD		14.02	1.63
Unilateral Patients			
1075	M	35	19
1077	F	22	12
1078	M	26	11
1079	F	42	15
1080	F	22	11
1081	F	21	16
Mean		28.00	14.00
SD		8.60	3.22
Healthy Controls			
Mean		27.25	13.35
SD		10.69	2.45
Range		18-52	10-20

The screening questionnaire consists of four items selected from a larger questionnaire on déjà vu experiences in epilepsy, which is described in more detail below. Refer to Appendix A for the complete screening questionnaire. A prerequisite for inclusion were answers on two of these questions that verified that each patient's experiential phenomena had both features at the core of the déjà vu experience: a sense of familiarity and knowledge that it is inappropriate (questions number 1 and 2 respectively).

If the screening questionnaire confirmed that a patient's experiential phenomenon was consistent with déjà vu, their clinical evaluation was considered to verify that a diagnosis of TLE could be made. The diagnosis, and seizure classification, was made by an epileptologist using ictal EEG recordings, clinical MRI scans, and the behavioural manifestations of the seizures observed in the epilepsy monitoring unit at the LHSC. Although not an explicit inclusion criterion, TLE could be further classified as CPSs in all individuals who participated in this study. Six patients had unilateral and four had bilateral mesial temporal lobe seizure origin. Further details of clinical classification are presented in Table 2. In addition to their detailed neurological examinations, all TLE patients completed a neuropsychological evaluation administered by an LHSC neuropsychologist. The evaluation of neuropsychological functioning occurred in the relevant domains of overall intelligence (Wechsler Abbreviated Scale of Intelligence, 1999), episodic memory (Wechsler Memory Scale, 1997; California Verbal Learning Test, 2000), and semantic memory (Boston Naming Task, 1976; Animal Naming Task).

Table 2

Patient clinical characteristics

Patient	Duration of epilepsy	Laterality	MTS [A]	Medication
1071	11 months	Bilateral	No	Lamotrigine
1072	14 months	Bilateral	Bilateral	Lamotrigine
1073	4 years	Bilateral	No	Tegretol
1075	27 years	Left	No	Lamotrigine
1076	8 years	Bilateral	Bilateral	Tegretol
1077	5 years	Right	Right	Dilantin
1078	5 years	Right	Right	Tegretol
1079	12 years	Right	No	Lamotrigine
1080	6 years	Left	No	Tegretol
1081	10 months	Right	Right	Dilantin

[A] Mesial Temporal Sclerosis

The resulting neuropsychological performance indices are presented in Table 3. A multivariate analysis of variance (MANOVA) was conducted to determine whether the unilateral and bilateral patients differed significantly in any regard. The MANOVA revealed no significant differences with respect to age, level of education, duration of epilepsy, or any neuropsychological index, $\Lambda = .073$, *ns*. Clinical practice deems neuropsychological functioning impaired when performance is two standard deviations below the mean on normative data. Using this criterion, neither the mean for the unilateral nor the bilateral patient groups were in the impaired range. However, as Table 3 indicates, one bilateral patient did have an impairment in delayed visual memory and both left-lateralized, unilateral patients were impaired on measures of semantic memory.

A second group, consisting of 20 (11 females, 9 males) healthy control participants, completed the same experimental tasks as the TLE patients. The demographics of the control participants are presented in Table 1. The controls were recruited from the patients' families (i.e., siblings), the psychology undergraduate participant pool, and the broader communities of London and Windsor, Ontario. These individuals were selected on a yoked basis with the goal of obtaining two corresponding controls for each patient that are matched with respect to age (+/- 4 years), sex, and years of education (+/- 2 years). A MANOVA confirmed that there were no significant differences between the patients and controls with respect to age or education, $\Lambda = .16$, *ns*. Control participants were also screened for the absence of previous neurological problems including epilepsy and a history of concussions.

Table 3

Patient neuropsychological data

Bilateral Patient	WASI [A] (full scale)	WMS [B] (Verbal Immediate)	WMS (Verbal Delayed)	WMS (Visual Immediate)	WMS (Visual Delayed)
1071	108	108	117	112	109
1072	109	99	105	98	100
1073	96	99	97	84	81
1076	-	80	86	71	68*
Mean	104.3	96.5	101.3	91.3	89.5
SD	7.23	11.8	13.1	17.7	18.5
Unilateral Patient					
1075	113	111	108	127	112
1077	112	130	117	100	103
1078	98	92	99	78	78
1079	83	92	92	115	81
1080	88	97	89	91	84
1081	123	120	120	94	81
Mean	102.8	107.0	104.1	100.8	89.8
SD	15.7	15.9	12.9	17.61	14.1

[A] Wechsler Abbreviated Scale of Intelligence: mean = 100, SD = 15
[B] Wechsler Memory Scale – Third Edition: mean = 100, SD = 15
* Clinically meaningful impairment
** continued on next page

Table 3 (continued)

Patient neuropsychological data

Patient	CVLT [C] Recognition Discrimination	Semantic Fluency	Boston Naming
Bilateral			
1071	45	80	37
1072	55	49	54
1073	50	53	45
1076	-	32	32
Mean	50.0	53.5	42.0
SD	5.0	19.8	9.6
Unilateral			
1075	40	29*	30*
1077	60	41	52
1078	50	40	42
1079	50	32	31
1080	45	17*	30*
1081	50	73	50
Mean	49.2	38.7	39.2
SD	6.6	18.9	9.3

Standardized t-scores: mean = 50, SD = 10

[C] California Verbal Learning Test – Second Edition

* Clinically meaningful impairment

Data from two individuals (participant 1079 and 1081) were excluded from all analyses in one of the experimental tasks, the Exclusion task which is described in more detail below, due to a failure to understand the instructions in one case and technical problems in another. The control participants corresponding to these patients were also removed from the corresponding analyses.

Informed consent was obtained from all of the research participants. The research protocol was approved by the Health Sciences Research Ethics Board at the LHSC. Refer to Appendix C for the ethics approval form, complete letter of information, and consent form. Questions or concerns regarding the rights of the participants were addressed prior to obtaining consent and participants were made aware that they could withdraw from testing at any point during the experiments and that their data would be removed upon request any time after completion.

6.2 Questionnaire: Déjà vu Experiences in Temporal Lobe Epilepsy

6.2.1 Materials

Prior to completing the experimental tasks all TLE patients provided a subjective account of their intra-ictal déjà vu experiences. However, because spontaneous subjective reports vary in thoroughness and detail between patients, we developed and employed a formal assessment tool based loosely on Sno et al.'s (1994) Inventory for Déjà vu Experiences Assessment (IDEA). The questionnaire was modified and tailored to specifically address déjà vu experiences in the context of TLE. Further, questions making reference to paranormal phenomena were removed and questions were modified and expanded so as to differentiate between intra- and inter-ictal déjà vu. The compete

questionnaire consists of 17 questions, some open-ended and some with a rating scale, that address the cognitive components of the experience, the frequency with which it occurs, the psychological and emotional states that accompany it, and environmental factors associated with déjà vu. It took approximately 15 minutes to complete the questionnaire. The goal of the questionnaire was to characterize various quantitative and qualitative aspects of the experience in a formal manner. Refer to Appendix B for the complete questionnaire.

6.3 Experimental Task: Remember-Know

6.3.1 Materials

Stimuli for the Remember-Know task were pictures of indoor scenes, all with an emotionally neutral valence (500 x 375 pixels). A total of 170 pictures, drawn from three different categories of indoor scenes (57 living rooms, 57 bedrooms, and 56 kitchens), were used. The scenes were restricted to only three categories to ensure that the discrimination task was challenging as humans generally have good scene memory (Standing, Conezio, & Haber, 1970). The stimuli were presented and controlled by a laptop computer and participants' responses were recorded with a numbered response box.

6.3.2 Procedures

The Remember-Know procedure is a recognition memory paradigm with three discrete stages: study, delay, and test. Prior to beginning the study stage five practice trials were presented in order to familiarize participants with the encoding task and the

timing of each trial. After the practice trials participants were given an opportunity to have any questions answered before proceeding, or to complete the practice trials again if necessary. During the study stage, participants were presented with 80 indoor scenes from all three categories, presented centrally on a white background, in a randomly generated order. The series was presented sequentially whereby each picture was displayed for 2250 ms before being replaced by a fixation cross, which remained on screen for 2750 ms. The participants were given an incidental encoding task, which required that they estimate the wealth of the owner of each room. The wealth judgments were entirely subjective with no objectively correct answers and could be made at any point after a stimulus appeared and before the subsequent one was presented. This encoding task ensured that participants remained engaged and evaluated the entire scene at a semantic processing level (Manns et al., 2003), and was introduced to prevent participants from engaging in idiosyncratic learning strategies. If a response was not given in the allotted time they were encouraged to move on to the next item and adjust their response time accordingly.

The test stage of the experiment commenced after a five-minute delay during which participants worked on an unrelated distracter task that involved solving a word search puzzle. After the delay all participants were given detailed instructions, adapted from established paradigms (Rajaram, 1993), for the test session. They were first told that half of the test items would be old, half would be new, and that their objective was to discriminate between them based on their memory from the study session. Responses were made in a two step manner: for each item an 'old/new' judgment was made followed by a 'remember/know' judgment for items endorsed as 'old'. To minimize

guessing they were instructed to endorse an item as 'old' only if they were reasonably certain that they had previously encountered it. To distinguish between an appropriate 'remember' and 'know' response participants were told that they might recognize a picture as a result of experiencing a memory that was directly related to the episode in which they were first exposed, in which case they should respond 'remember', or that they might recognize that a picture had been previously encountered based on feelings of familiarity, in which case they should respond 'know'.

The participants were told that 'remember' experiences could result from a specific memory bound to the initial exposure of a picture, such as recalling specific perceptual details, or that it may be an arbitrary association such as a thought or emotion that occurred in response to a specific item during the study stage. In this manner it was emphasized that 'remember' responses require a specific memory pertaining to the initial episode of encountering a specific picture (i.e., recollection). Finally, participants were instructed to verbally justify remember responses to ensure that they understood the response and to minimize any biases (Rotello et al., 1995). They were also told that 'know' experiences are familiarity based and occur in the absence of specific memories of contextual detail. Importantly, it was explained that the distinction between appropriate 'remember' and 'know' responses is based on the experience that the individual would have upon seeing the item and is independent of confidence. A cue card summarizing the distinction between remember and know responses remained visible throughout the test stage and participants were encouraged to ask for further clarification if required at any point.

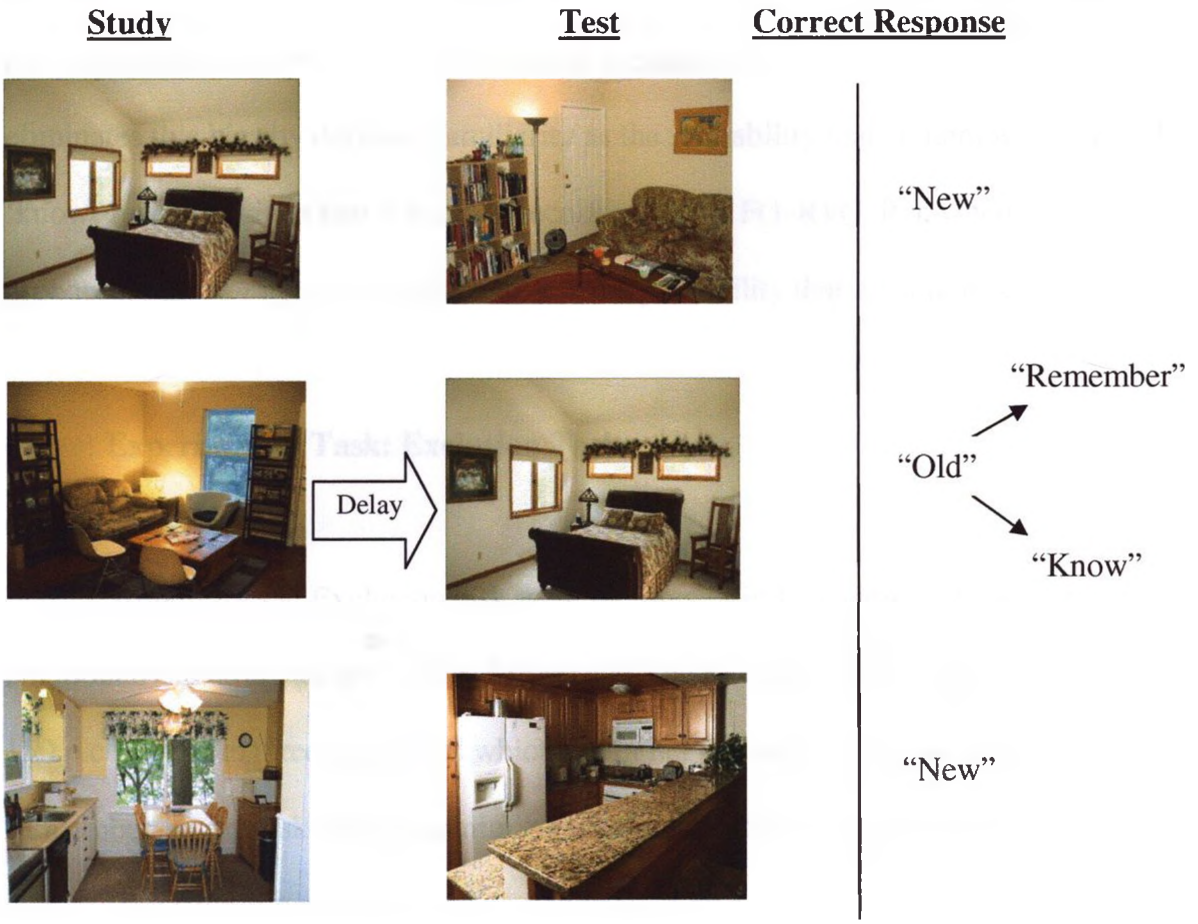
Like the study stage, the test stage was preceded by a practice session in which five new pictures were presented along with the five items from the practice session that preceded the study phase. If the participant appeared to understand the instructions the test commenced. If the participant was not using the 'remember/know' responses appropriately the instructions were administered a second time and more elaborate clarification was provided. In the test stage participants were presented with 160 pictures sequentially. Eighty of these pictures had been presented in the study stage and 80 were new, meaning they were not presented during the study stage. Unlike the study stage, the task in the test stage was self paced. A schematic diagram of the Remember-Know procedure is presented in Figure 1.

To determine how well participants discriminated between previously studied and new scenes, a measure of overall recognition memory performance will be calculated with the discriminability index d' based on signal detection theory (Snodgrass & Corwin, 1988). The discriminability index d' measures accuracy independent of response bias and incorporates the hit rate (calling an old item 'old') and the false alarm rate (calling a new item 'old').

In addition to the overall ability to discriminate between old and new stimuli, separate estimates of recollection and familiarity will be derived based on Yonelinas' (2002) dual process model of recognition memory. The recollection estimate represents the 'remember' hit rate minus the 'remember' false alarm rate. The familiarity estimate, familiarity d', is based on the 'know' hit rate and the 'know' false alarm rate and is calculated with a correction for independence between recollection and familiarity. The correction is necessary because, within the dual process models, some recollection

Figure 1.

Schematic diagram of the Remember-Know procedure.



responses co-occur with a sense of familiarity whereas others do not. However, the nature of the Remember-Know task is such that the participant only uses the 'know' response when an item is familiar but not recollected. Therefore, if left uncorrected, know responses do not provide an unbiased measure of familiarity. The correction eliminates this bias by defining familiarity as the probability that an item will received a 'know' response given that it was not recollected [F = F(1-R)/(1-R)], where F = the probability that an item is familiar and R = the probability that an item is recollected.

6.4 Experimental Task: Exclusion Task

6.4.1 Materials

Stimuli for the Exclusion task were pictures of indoor scenes, all with an emotionally neutral valence (500 x 375 pixels).The Exclusion task employed a total of 150 pictures from three categories which are rather distinct from those used in the Remember-Know task so as to minimize interference (62 offices, 62 restaurants, and 26 stores). The stimuli were presented and controlled by a laptop computer and participants' responses were recorded with a numbered response box.

6.42 Procedures

Like the Remember-Know procedure, the Exclusion task is a recognition memory paradigm in which participants are exposed to a list of stimuli, in a study session, and subsequently asked to discriminate between old and new items in a test session. Prior to beginning the study session, practice trials were presented in order to familiarize participants with the encoding task and the timing of each trial. After the practice trials

participants were given an opportunity to have any questions answered before proceeding, or to complete the practice trials again if necessary.

The study session consisted of 72 images, from two of the three categories (offices and restaurants), presented on a white background in a randomly generated order. The series was presented sequentially whereby each picture was displayed for 2250 ms before being replaced by a fixation cross which remained visible for 2750 ms. As in the Remember-Know task, participants were given incidental encoding instructions that required a wealth judgment. Participants were also able to respond at any point after the presentation of an image and before the next one appeared. If a response was not given in the allotted time they were encouraged to move on to the next item and adjust their response time accordingly.

The test stage of the experiment began after a five-minute delay during which participants worked on an unrelated distracter task. After the delay, all participants were given detailed instructions for the test session. Their objective was to discriminate between old and new images. They were told that they would see a second series of scenes and that half of the scenes would be old and half new. The old scenes were the 36 offices and 36 restaurants that were studied. The new scenes consisted of 24 offices, 24 restaurants, and 24 stores. Participants were not told that one third of the new scenes would be from a category that was not previously studied. It was also made explicit that each of the 72 new scenes would be repeated one time each and that these items are to be treated as new, on both the first and second presentation. Only images that were studied, but not those that were repeated in the test session, should be endorsed as old. The new items were repeated after lags of 4, 18, or 48 intervening items for a total of eight items

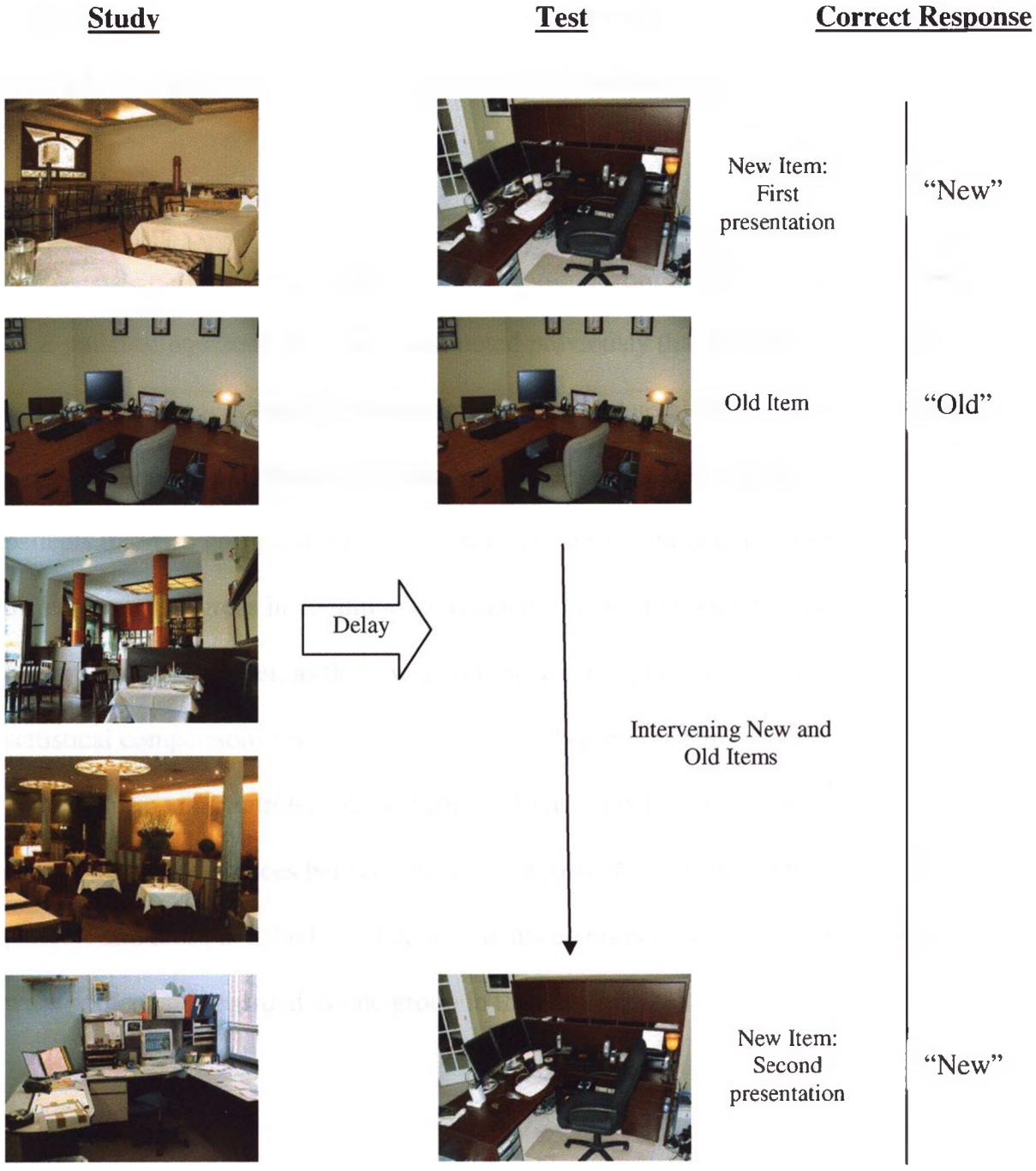
from each of three categories being repeated at each lag. A schematic diagram of the Exclusion task is presented in Figure 2.

This design places familiarity and recollection in opposition by forcing participants to reject repeated new items on the basis of recollection, despite the fact that those items would be familiar. To be more specific, each studied item would be familiar based on its presentation during the study session. By contrast, each repeated new item would be familiar because it had been presented 4, 18, or 48 items prior in the test session. If one fails to identify the source of that familiarity, through a lack of recollection that it has already been presented in the test session, a repeated item can be expected to be endorsed as old on the grounds that it seems familiar. In other words, successful performance on the task requires avoiding false alarm responses to repeated items based on a recollection of the source. In such a design, performance can be examined with respect to old items correctly identified as such, the susceptibility to mistakenly call repeated new items 'old', and how the latter changes with varying numbers of intervening items.

Performance on discriminating between old and new items, on their first presentation, reflects both recollection and familiarity processing. At this level of analysis the exclusion task does not discriminate between recollection and familiarity-based responses. However, correctly rejecting the repeated new items reflects a pure measure of recollection, where a relative propensity toward false alarms is indicative of a recollection deficit. This rationale holds for items from studied categories only, as some repeated items were from a category that was not studied. Performance on repeated new items from the unstudied category (stores) can be based on the recovery of gist that does

Figure 2.

Schematic diagram of the exclusion task.



not require a detailed, item-based recollection. An increased false alarm rate for unstudied items would suggest that the recollective process is not even operating at the level of gist. Note that the Exclusion task, by itself, does not provide a separate estimate of familiarity processing. Familiarity and recollection can only be separated indirectly through a comparison of performance for the various item types.

7. Results

All analyses were conducted on three groups: unilateral TLE patients, bilateral TLE patients, and controls. It has been noted previously that bilateral TLE can result in broader and more profound memory deficits than unilateral TLE (e.g., Guerreiro, Jones-Gotman, Andermann, Bastos, & Cendes, 2001). Therefore, by separating the TLE patients into two groups, it was hoped that analyses would remain sensitive to potential differences or degrees in cognitive impairments associated with déjà vu in unilateral or bilateral TLE. However, as there were no specific predictions towards this end, the statistical comparisons for the experimental tasks presented are between the unilateral patient group and controls, and between the bilateral patient group and controls. Because no significant differences between the control participants matched to the unilateral patients and those matched to bilateral patients emerged, $\Lambda = .22$, all control participants were pooled and regarded as one group in these analyses.

7.1 Anecdotal Observations and Questionnaire: Déjà vu Experiences in Temporal Lobe Epilepsy

Prior to completing the questionnaire, all TLE patients provided a detailed, informal account of their subjective experience during intra-ictal déjà vu. When asked open-ended questions, many participants struggled to provide a coherent description of their subjective experiences beyond a statement such as 'It just feels like I've done this before even though I haven't'. However, some patients were able to provide rather eloquent introspective descriptions of their intra-ictal déjà vu that offer valuable insight towards revealing the cognitive mechanisms underlying the experience. For example, one patient reported the following: "It's highly visual – not the entire situation or setting but specific objects or even people. They will suddenly become very familiar. There isn't a progression from vaguely to highly familiar. It's just 'PING' highly familiar. It's initially object specific but when I focus my attention on something else it too becomes familiar. I will even search the room for something that isn't familiar but everything seems so." A second individual's description captures the inappropriateness of the familiarity that characterizes the déjà vu experience, "Things feel familiar. I'll be in a room, this room for example, that I've never been in before but if I have a seizure I feel like I've been here before – and wait a minute – I've never been here, this is new." Notably, all patients reported that the feeling of familiarity is not bound to any one object throughout the entire experience. Rather, the familiarity persists when their attention shifts from one environmental stimulus to the next. In this manner, these descriptions are consistent with O'Connor and Moulin's (2008) account of patient MH.

Informal, spontaneously generated descriptions of the kind provided are valuable but the extent to which each patient can highlight conceptually important aspects of déjà vu experiences is a limiting factor. The questionnaire offers quantitative and qualitative data in a more organized manner. Due to the extent of the resulting data and their variability across individuals, the responses to the questionnaire will not be reported in their entirety. Rather, data have been consolidated from a selection of questions that aptly illustrate the nature of the déjà vu experiences in this sample. Table 4 presents those specific response options that best characterize the sample (i.e., the response mode) in terms of the proportion of patients that endorsed them. These data reveal that the patients experience déjà vu with the majority of their seizures and that, at the time of testing, most had done so within the last week. Further, the questionnaire revealed that the experience typically lasts only a few seconds, is primarily visual in nature, may be associated with negative affect, and is qualitatively different than normal, inter-ictal déjà vu, which in the majority of cases occurs only a few times per year. Although not assessed with formal statistics, the data in Table 4 and the anecdotal observations hint that there was no apparent difference in the nature of the déjà vu experience between both patient groups.

7.2 Experimental Task: Remember-Know

The results of the Remember-Know task will be presented first. Figure 3 shows the performance of both patient groups (unilateral and bilateral TLE) and healthy control participants on the measure of overall recognition (d'), irrespective of the specific contributions of familiarity and recollection. A one-way analysis of variance (ANOVA) was conducted on the overall d' scores with group as the between-subjects factor in order

Table 4

Modal response options characterizing déjà vu.

Item	Bilateral	Unilateral
Proportion of seizures accompanied by déjà vu.	.75	.73
Déjà vu occurred within the last week *(8).	.75	.67
Déjà vu persists for a few seconds (7).	.75	.83
Déjà vu accompanied by negative affect (11).	.50	.50
Déjà vu is visual in nature (12)	1.0	1.0
Experience déjà vu inter-ictally a few times per year (13).	1.0	.83
Inter-ictal déjà vu is not exact same as intra-ictal (14).	1.0	.83

*Questionnaire item number presented in parentheses

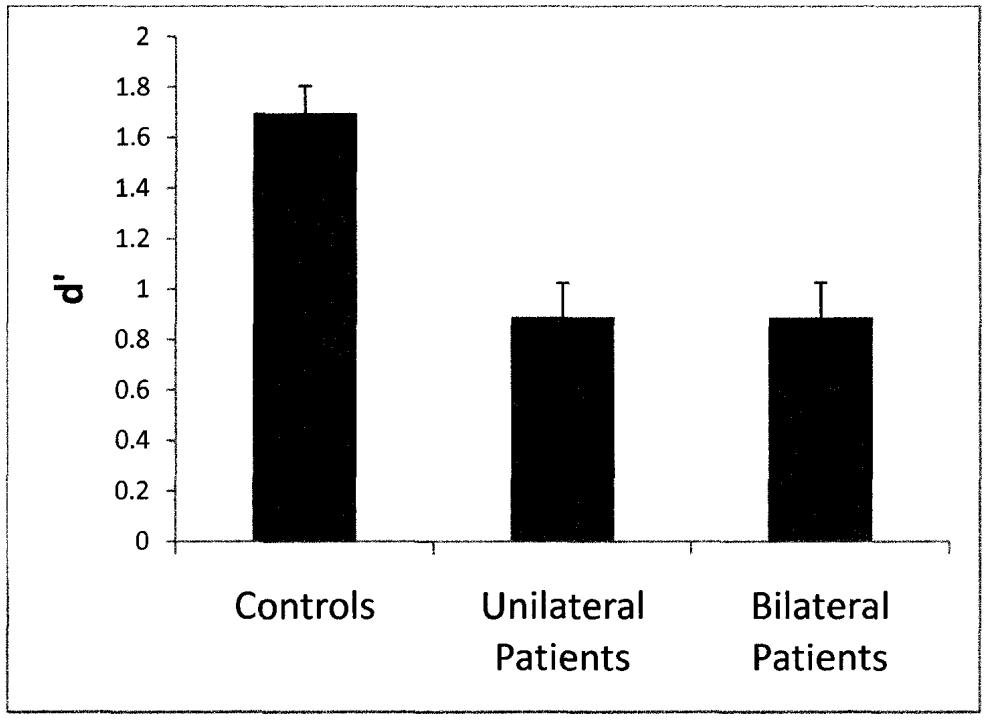


Figure 3. The mean performance of each group on the measure of overall recognition (d'). Error bars indicate the SEM.

to determine whether there was a recognition deficit in the patient groups as compared to healthy controls. The ANOVA revealed a significant difference among the group means, F (2, 27) = 11.69, $p < .01$. Two planned pairwise comparisons were made to compare each patient group individually to the controls. The first comparison revealed that overall d' was impaired in unilateral patients relative to controls, t (24) = -4.04, $p < .01$. The second comparison revealed that the bilateral patients were impaired relative to controls as well, t (22) = -3.46, $p < .01$.

To examine the nature of the recognition memory deficits evident in both patient groups, measures of recollection and familiarity were analyzed. Figure 4 shows the performance for all groups on the measure of familiarity. Estimates of familiarity reflect the discrimination index d' that is based on hits and false alarm rates of 'know' responses, corrected for the frequency of 'remember' responses provided. A one-way ANOVA revealed that there was a significant difference between the group means, F (2, 27) = 12.52, $p < 01$. Pairwise comparisons revealed that both the unilateral, t (24) = -4.56, $p < .01$, and the bilateral, t (22) = -2.95, $p < .01$, groups were impaired relative to controls.

Figure 5 shows the performance of the patient groups and the healthy controls on the measure of recollection. This measure is based on the number of 'remember' responses and is calculated as the proportion of hits minus false alarms for this response category. A one-way ANOVA conducted on the mean recollection scores revealed that there was a significant difference among the groups, F (2, 27) = 3.62, $p < .05$. Planned comparisons revealed that the unilateral patients were not impaired relative to controls,

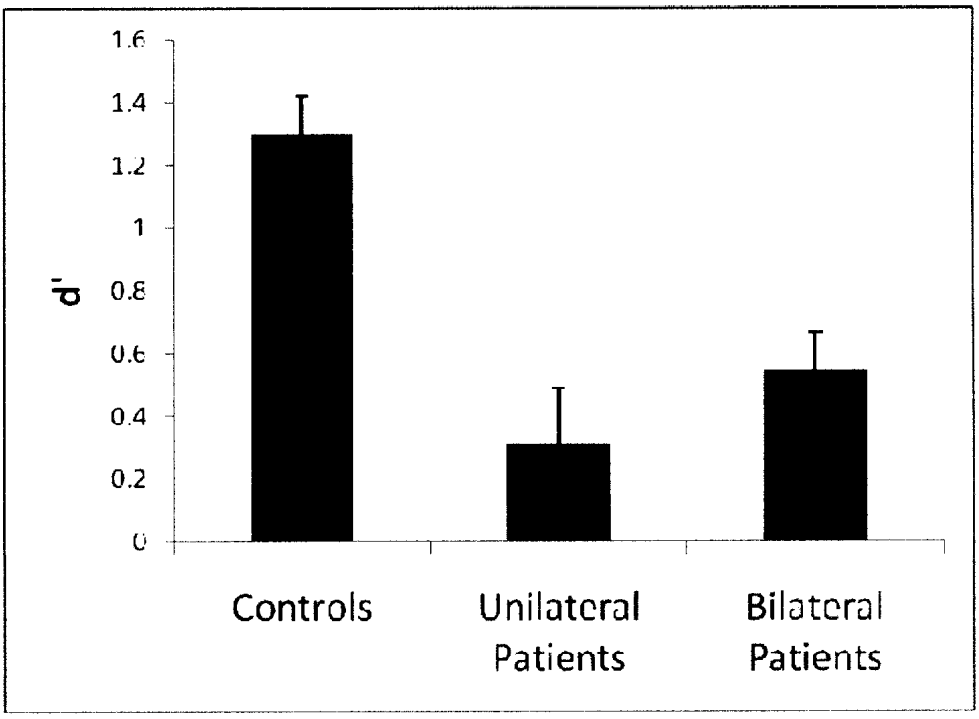


Figure 4. The mean performance of each group on the measure of familiarity (d'). Error bars indicate the SEM.

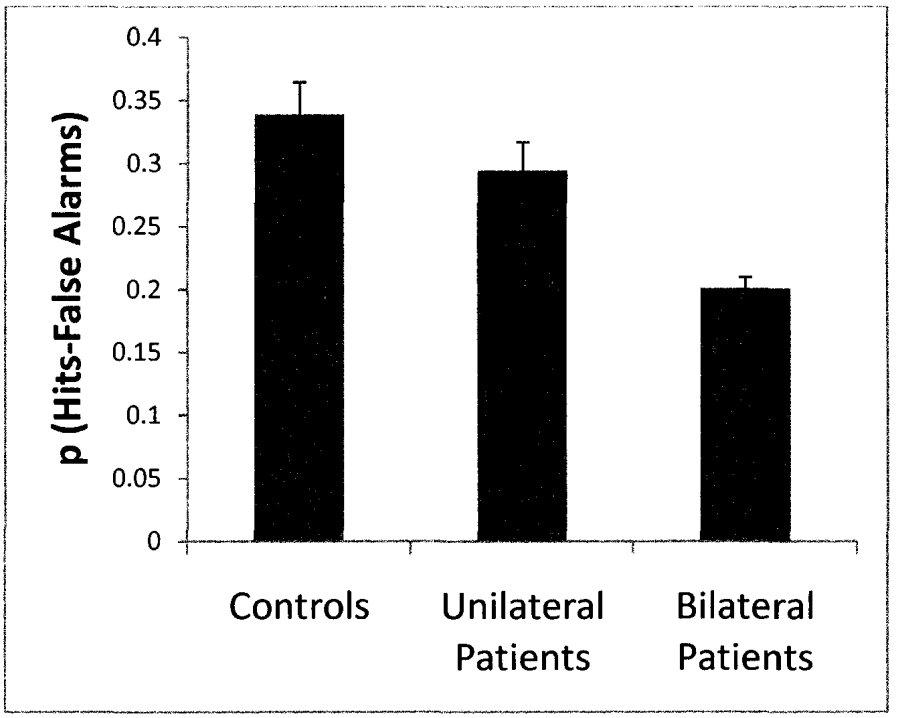


Figure 5. The mean performance of each group on the measure of recollection (proportion of hits – false alarms). Error bars indicate the SEM.

t (24) = -1.02, *ns*, but that the bilateral patients did show a deficit, t (22) = -2.6, $p < .05$.

Because recollection and familiarity estimates are measured with different metrics it is difficult to directly compare the relative contributions of each to the overall recognition deficit observed. Therefore, recollection and familiarity scores for the patient groups were normalized to z-score format in order to allow for direct comparison. Each z-score represents the difference between the patient group means and healthy control means in standard deviation units. The normalized data are presented in Figure 6. A 2-way ANOVA (Group X Recognition Process: familiarity and recollection) was conducted on these z- transformed data to determine how familiarity and recollection deviate from the control participant means in each patient group separately. The ANOVA revealed a significant main effect of Recognition Process, F (1, 16), = 11.01, $p < .01$. The Group X Recognition Response interaction was also significant, F (1, 16), = 5.71, $p <$ .05. Further analyses, implementing a Bonferonni correction, revealed a simple main effect of Recognition Response in the unilateral group, F (1, 16), = 20.37, $p < .01$, but not in the bilateral group, F (1, 16), = .358, *ns*. This result indicates that only familiarity deviates significantly from healthy control means in the unilateral patient group. By contrast, in bilateral patients the measures of recollection and familiarity deviate equally from the means of control participants.

7.3 Experimental Task: Exclusion Task

Figure 7 presents the performance of the patient groups and healthy controls on a measure that considers studied items and non-studied new items that have not been

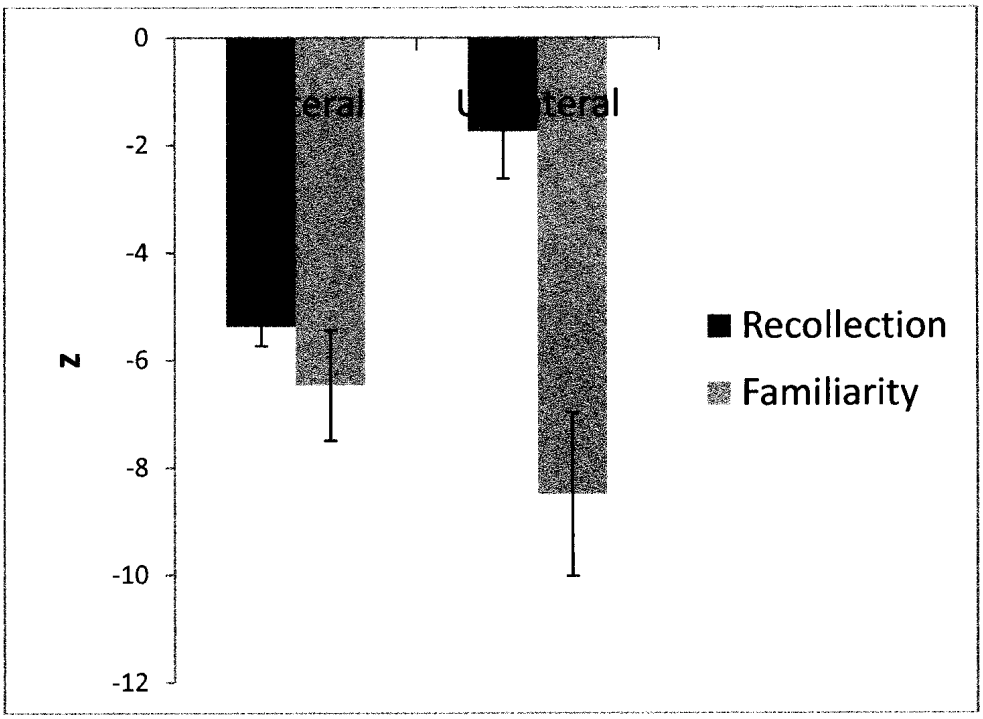


Figure 6. The normalized (z) recollection and familiarity estimates for bilateral and unilateral patients. Error bars indicate the SEM.

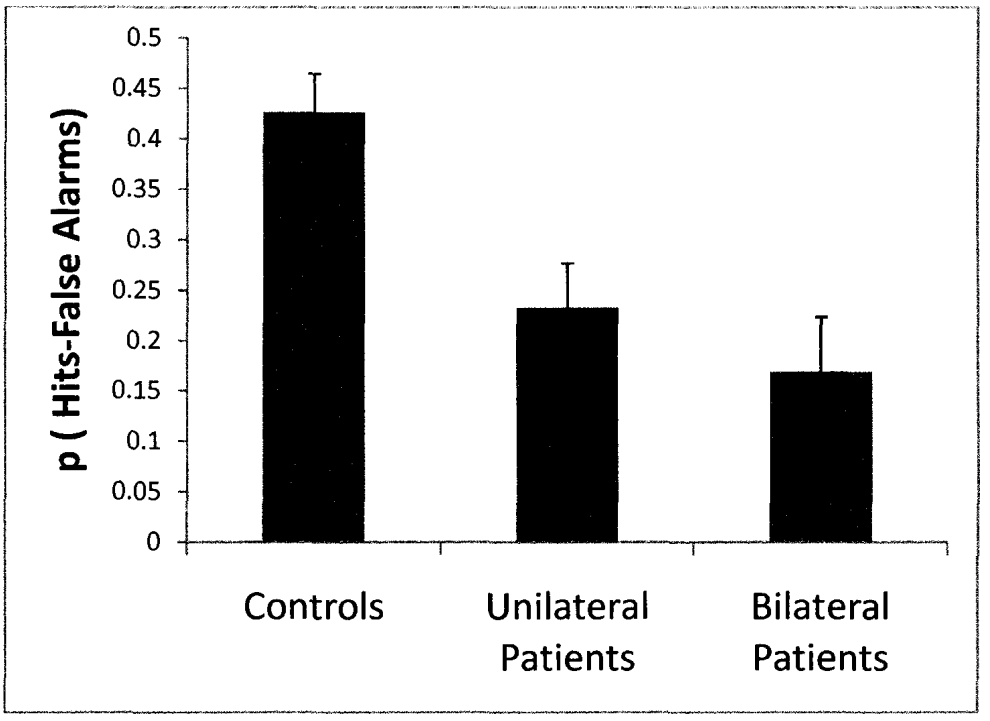


Figure 7. The mean performance of each group on the measure of accurately identifying old items (proportion of hits – false alarms). Error bars indicate the SEM.

repeated yet in the test session. Overall recognition performance is calculated as the proportion of hits (correctly calling old items 'old') minus false alarms (incorrectly calling new items 'old' on their first presentation). This measure reflects an estimate of the combined influence of familiarity and recollection on the ability to discriminate between new and old items. A one-way ANOVA revealed a significant difference between the groups, F (2, 21) = 11.29, $p < .01$. Planned pairwise comparisons showed that both the unilateral, t (18) = -2.33, $p < .05$, and bilateral, t (18) = -3.11, $p < .01$, groups were impaired relative to controls. To probe processes of item-specific recollection, performance on repeated new items from studied categories was examined. On this measure, a larger score reflects an increased tendency to incorrectly endorse repeated new items as coming from the study list. Thus, it reflects the ability to counteract familiarity induced through repeated exposure of novel items at test by way of recollecting that they were on the test but not the study list. The corresponding data are presented in Figure 8. A 2-way (Group X Lag) ANOVA revealed a main effect of lag, F (2, 63) = 15.66, $p < .01$, and Group, F (2, 63) = 7.23, $p < .01$ but no significant interaction F (4, 63) = .393, *ns*. Planned pairwise comparisons showed that the main effect of Group was attributable to the bilateral patients performing worse than the controls, t (58) = -3.77, $p < .01$. The difference between unilateral patients and controls was not significant, t (58) = -.34, *ns*. To examine the ability to counteract familiarity based on retrieval of gist, but without detailed item-specific recollection, an additional analysis focused on data for repeated new items from unstudied categories. Overall, there were few instances of false alarms for these types of items. The corresponding 2-way (Group X Lag)

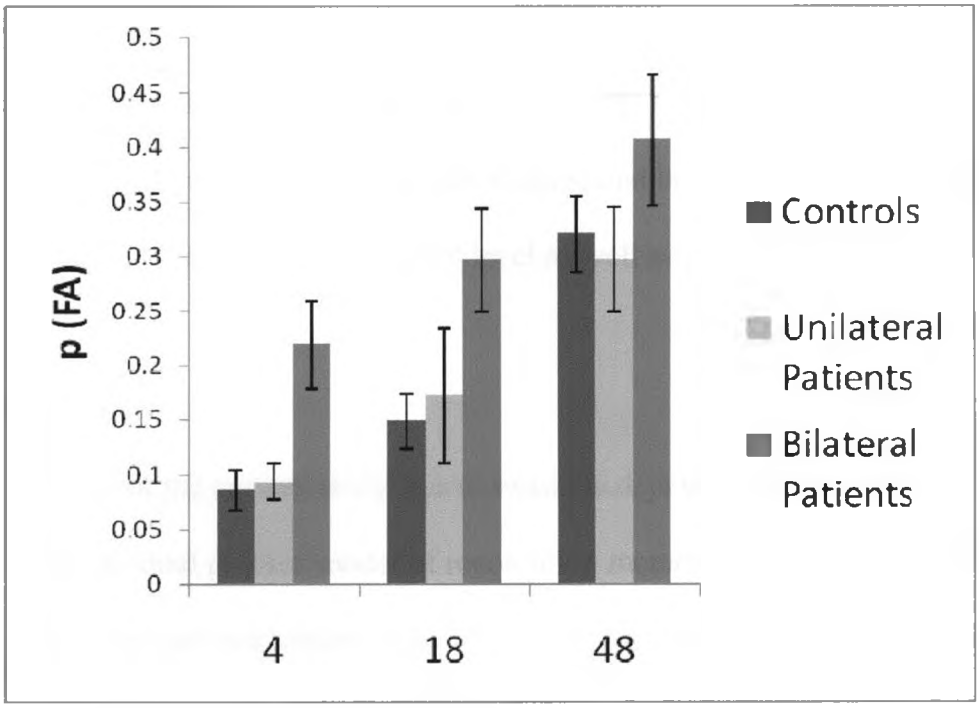


Figure 8. The mean proportion of false alarms to repeated new items from studied categories for each group across each lags. Error bars indicate the SEM.

ANOVA revealed that there were no significant differences across lags, F (2, 21) = .448, *ns*, or between groups, F (2, 21) = .603, *ns*. The Group X Lag interaction was also not significant, F (4, 21) = .183, *ns*. These data suggest that both patient groups were able to reject repeated items at a broad gist-based level as well as control participants.

8. Discussion

The goal of the current study was to examine déjà vu in TLE within the framework of the dual process model of recognition memory. The objective was to elucidate the cognitive mechanisms underlying déjà vu experiences. Toward this end, two experimental tasks were employed to test the hypothesis that TLE patients with déjà vu would have selective, or disproportionate, familiarity deficits that are detectable inter-ictally. In general, converging evidence from the two tasks administered suggests that unilateral TLE patients with déjà vu do indeed have selective familiarity impairments and intact recollection. However, in the bilateral patients, a broader impairment was detected as both familiarity and recollection deficits were observed. These deficits offer interesting additional insight into the cognitive mechanisms of déjà vu.

The first experimental task was a Remember-Know paradigm implemented to determine the extent to which recollection and familiarity contribute toward recognition memory at the level of subjective self report. The results revealed that overall recognition memory, as indexed by overall d', was impaired in both the unilateral and bilateral patients relative to healthy controls. This finding is rather interesting because the neuropsychological evaluations revealed that neither TLE groups had clinically impaired memory. The detection of these deficits suggests that the Remember-Know task

employed in the current study is highly sensitive to recognition memory impairments. While these deficits may not constitute clinically meaningful impairments, as they are currently defined, they do offer important insight from a cognitive neuroscience perspective when combined with a more detailed examination of familiarity and recollection.

Relative to healthy controls, both patient groups were impaired with respect to familiarity. This finding is in line with the hypothesis that TLE patients with déjà vu display familiarity impairments inter-ictally. However, it does not speak to whether these familiarity deficits are selective. To determine whether this is the case we examined recollection performance as well. The corresponding analyses revealed that the unilateral patients did in fact have a selective deficit as recollection, measured based on subjective self-reports, was intact. Further, the familiarity estimates in unilateral patients were significantly lower than the estimates of recollection. By contrast, the bilateral patients, in addition to showing deficits of familiarity, were impaired on the measure of recollection as well. It was also revealed that, in contrast to our predictions, the familiarity deficit in bilateral patients was equal in proportion to the recollection deficit, as revealed by normalized data.

The data from the Exclusion task offer evidence that converges with those obtained with the Remember-Know task. The Exclusion task is based on the process dissociation procedure (Jennings & Jacoby, 1997). The rationale for implementing the Exclusion task was to verify whether any observed familiarity deficits were in fact selective and, if so, to determine how recollection and familiarity interact when one process is not functioning properly. Successful performance on the exclusion task relies

exclusively on recollective processes because one must recollect that the source of the familiarity for repeated items from studied categories is from the test as opposed to the study stage. Critically, unlike the Remember-Know paradigm, the exclusion task does not require introspection to evaluate the nature of the recognition experience. A selective familiarity deficit could be detected in this task if performance on discriminations between old and new items, at their first presentation, were impaired and performance for repeated items, as reflected in correct rejections, were intact. Within such an interpretive framework, the first discrimination reflects both recollection and familiarity-based judgment while the second reflects only recollection.

In the Exclusion task it was found that unilateral patients performed worse than healthy controls with respect to discriminating between old and new items from studied categories presented the first time. Like the data from the Remember-Know task, these data also demonstrate that the unilateral group has difficulty discriminating between old and new items. Further, performance for the repeated items, from both studied and unstudied categories of stimuli, confirmed that detail- and gist-based recollection are in fact intact in the unilateral patients, as they had no more false alarms for these items than controls. Taken together, the results for both measures converge nicely with those from the Remember-Know task indicating that unilateral TLE patients have selective familiarity deficits. Further, this pattern also suggests that the familiarity deficit detected in the Remember-Know task does not simply reflect an inability to introspect and evaluate cognitive memory states.

The bilateral patients also performed worse than healthy controls with respect to discriminating between old and new items from studied categories presented the first

time. However, performance on the repeated items, from studied categories, was also impaired. In fact, the performance of the bilateral patients in this sample was similar to a pattern observed in a sample of elderly individuals (M age = 73.2) known to have recollection deficits (Jennings and Jacoby, 1997). Further, the various repetition lags revealed that bilateral patients have considerable difficulty retaining the source information of an item even after very short intervals (i.e., 4 intervening items). These data converge with those from the Remember-Know task by revealing that bilateral patients do have recollection deficits at the level of item-based detail. However, gist-based recollection was intact in the bilateral patients as indicated by normal performance for repeated items from unstudied categories. Finally, it should be noted that the data from this Exclusion task are also consistent with the notion of a familiarity deficit in bilateral patients, as shown more directly with the Remember-Know task. However, when considered in isolation, the data from the Exclusion task are open to other interpretations in the bilateral group given that the task does not provide a direct measure of familiarity.

Taken together, the data from both experiments in the unilateral patient group supported the hypothesis that déjà vu in TLE is associated with a selective familiarity deficits and intact recollection inter-ictally. To the extent that this inter-ictal deficit is linked to the pathological processes also operating during déjà vu experiences at seizure onset, these findings can be explained within the following scenario: TLE seizures that elicit déjà vu do so by way of falsely engaging processes of familiarity assessment. However, to be a recognized as a true déjà vu experience these feelings of familiarity must be identified as inappropriate. It has been proposed (Spatt, 2002) that recollection

serves to identify this inappropriateness. More precisely, it is the absence of recollection that has been proposed as the cognitive mechanism that signals the inappropriateness of a false familiarity experience in déjà vu. The data from the unilateral TLE patients are consistent with this proposition as recollection abilities were intact as measured by two different experimental paradigms. However, the findings in bilateral patients suggest an alternative, likely more viable account.

With respect to bilateral TLE, it has been demonstrated previously that bilateral as compared to unilateral seizure focus can result in more profound memory deficits (Guerreiro et al., 2001). Further, more generalized seizure propagation may produce broader functional impairments (Mueller et al., 2006). In the case of bilateral TLE patients with déjà vu, the present data from the Remember-Know task do indicate this type of broader impairment, as, unlike in unilateral cases, deficits in both recollection and familiarity were found. The Exclusion task confirmed that the bilateral patients display recollection deficits as indicated by the increased false alarm rate to repeated new items from studied categories as compared to controls. This finding speaks to the processes that may mediate the feelings of inappropriateness in déjà vu. The fact that bilateral patients can identify that the feelings of familiarity are inappropriate, despite not having normally functioning recollection, suggests that recollection may not be the cognitive mechanism responsible for signaling inappropriateness.

It is plausible and intuitively appealing to propose that the identification of inappropriateness, a very fast subjective experience, may not always come about through an exhaustive search process that produces no positive results in terms of a specific recollection. Searching through one's autobiographical memory to recollect a specific

episode can be an effortful, time consuming process. However, the majority of the patients in this study reported that their déjà vu experiences last only a few seconds. It seems unlikely that, within a few brief seconds, one can engage in an exhaustive search of episodic memory that produces a null result with such remarkable confidence and consequences. It is also entirely possible to experience déjà vu in an environment that has been encountered many times previously. For instance, a TLE patient may experience déjà vu at the onset of their seizure despite being in their own bedroom. In such an experience the autobiographical search becomes more complicated because the familiarity is not so easily identified as inappropriate based on some objective knowledge of environmental novelty (i.e., having never visited New York City). Further, it is not uncommon for most people, whether neurologically impaired or not, to experience familiarity in the absence of recollection in everyday life. Yet, we typically do not have a déjà vu experience each time we encounter this isolated sense of familiarity, for example when we meet somebody who seems familiar without any clues as to why.

An alternative cognitive process that may account for the feelings of inappropriateness in déjà vu has primarily been examined in literature examining confabulations in amnesic patients (Gilboa & Moscovitch, 2002; Gilboa et al. 2009). Gilboa, Moscovitch and their colleagues have suggested that the ventromedial prefrontal cortex is involved in processing autobiographical information and specifically supports memory control processes involved in 'feelings of rightness'. This 'feeling of rightness' refers to the ability to quickly appreciate the appropriateness, suitability, and accuracy of a self-generated response in relation to the goals of the memory task at hand. It is possible that, in the context of déjà vu, this rapid prefrontally mediated monitoring

process plays a role in evaluating the veracity of feelings of familiarity that occur in response to a seizure discharge such that a sense of inappropriateness is experienced almost immediately. Based on the observation that patients with impaired recollection can still appreciate the inappropriateness of the sense of familiarity experienced during déjà vu, and considering the fleeting nature of the experience, a 'feeling of rightness' account, although speculative, is certainly appealing. It may be instructive to examine this possibility in future research by evaluating the functional and structural integrity of the regions responsible for 'feelings of rightness' in bilateral patients with déjà vu.

In addition to the behavioural data, the results of the questionnaire and self reports of each patient's intra-ictal déjà vu experience are enlightening toward understanding the subjective experience of the cognitive mechanisms underlying déjà vu. O'Connor and Moulin (2008), after having examined the anecdotal reports of patient MH, have suggested that déjà vu is an interpretive state resulting from neural activity that generates stimulus non-specific feelings of familiarity. MH had indicated that the sense of familiarity central to his déjà vu experience was not bound to any single object or feature of a scene. Rather, the familiarity followed his attention and generalized to everything within the environment. Each of the TLE patients in the current study endorsed the notion that when their attention shifts their sense of familiarity, which they know to be inappropriate, generalizes as opposed to remaining fixed or bound to the initial object or event being attended. These reports are consistent with Spatt's (2002) proposal that déjà vu is the result of false activation of perirhinal cortex which evokes feelings of familiarity. They are also consistent with O'Connor and Moulin's proposal that these feelings of familiarity create a top-down interpretive state whereby stimulus non-specific

familiarity is applicable to whatever environmental stimuli are being actively attended. These phenomenological reports suggest that this non-specific memory state is interpretive and indicative of an overarching cognitive feeling that is applied to, as opposed to caused by, perceptual input are evidence against bottom-up perceptual theories of déjà vu. Perceptually based accounts of déjà vu are largely data driven in that the familiarity experienced is incomplete but not erroneous as the stimulus that elicits the familiarity has in fact been encountered, or processed, previously. That the sense of familiarity persists despite switching ones attentional focus suggests that the familiarity associated with déjà vu is most consistent with a top-down interpretive account that is influenced by higher order cognitive memory.

Beyond the cognitive mechanisms, these data lend themselves to speculation about the neural mechanisms of déjà vu. The behavioural data from the unilateral patients are similar to what was observed in patient NB whose left perirhinal cortex was lesioned while sparing the hippocampus (Bowles et al., 2007). The presence of a selective familiarity deficit suggests that the neural mechanism underlying the familiarity in déjà vu, within the context of TLE, is the positive expression of the functional role of perirhinal cortex. The feelings of familiarity are likely evoked by the onset of seizure activity in, or in close proximity to, perirhinal cortex, which has been identified as critical for the assessment of familiarity (Eichenbaum et al., 2007). However, the current study does not offer the MRI data required to assess the structural integrity of perirhinal cortex and the hippocampus. Further, the amygdala, which is situated adjacent to perirhinal cortex and was also resected in patient NB, has been suggested to play a role in déjà vu previously as well (Gloor, 1982). Therefore, without proper neuroanatomical analyses,

the specific structures in the MTL that produce déjà vu in TLE remain a topic for further investigation.

While the current study provides new evidence suggesting that selective familiarity impairments can be detected in some TLE patients with déjà vu, the data do not reveal directly whether this selective deficit is a behavioural pattern that is unique to those TLE patients who experience déjà vu as part of their seizure profile. To establish this firmly, an additional group of closely matched TLE patients who do not experience intra-ictal déjà vu would have to be tested with the same experimental tasks. However, it is not entirely clear what subgroup of TLE patients would constitute an appropriate control group in this case. Regardless, indirect evidence that speaks to this issue comes from a study by Moscovitch and McAndrews (2002) who reported recognition-memory deficits in unilateral TLE patients that were specific to recollection, rather than specific to familiarity as reported in the current study. The patients studied by Moscovitch and McAndrews were not selected according to the presence of déjà vu. This pattern suggests that the current findings may in fact be unique to unilateral TLE that is associated with déjà vu.

In conclusion, the current study revealed that familiarity deficits accompany déjà vu in both unilateral and bilateral cases of TLE. These deficits may represent the functional consequence of seizure activity in a region of the MTL critical for assessing feelings of familiarity. Further, these data hint that the cognitive process responsible for identifying the inappropriateness of the sense of familiarity during déjà vu may not be recollection. It is possible that a frontally mediated process serves to quickly generate 'feelings of rightness' that are incompatible with the sense of familiarity. On another

level, the present findings suggest that probing the cognitive correlates of déjà vu in TLE inter-ictally can advance our understanding of mechanisms involved in déjà vu at a time when experimental paradigms to elicit the experience in the cognitive laboratory are still missing.

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Appendix A

Screening Questionnaire

Screening Questionnaire for Déjà vu Experiences in Epilepsy

Participant Number: .....

Date: .....

INTRODUCTION

The following questions refer only to the feelings that occur in the context of your epileptic seizures. Specifically, these questions refer to the experiences that precede your seizures.

Please take your time to read each question carefully. If you have any questions or concerns you are welcome to ask.

1. In the moments preceding a seizure do you ever have the feeling that you have experienced the present situation before when in fact you are experiencing it for the first time?

O Never
O Yes, infrequently
O Yes, often
O Yes, always
O Don't know

2. While you have this feeling of *'déjà vu' preceding a seizure*, is it the case that you cannot remember exactly where and when you experienced this strangely familiar situation before?

O Yes
O No, I vaguely remember
O No, I can remember exactly
O Don't know

3. How long does this feeling of *'déjà vu'* preceding a seizure usually last?

O One second or less
O A few seconds
O One minute or several minutes
O Up to one hour
O More than one hour
O Don't know

4. When did this feeling of *'déjà vu'* occur last in the context of a seizure?

O More than 6 months ago
O 2 to 6 months ago
O Within the last month
O Within the last week
O Within the last 3 days
O Don't know

Appendix B

Questionnaire for Déjà vu Experiences in Epilepsy

Questionnaire for Déjà vu Experiences in Epilepsy

Participant Number: .....

Date: .....

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INTRODUCTION

This questionnaire is about the 'déjà vu' experience. 'Déjà vu' refers to the feeling of having experienced some event, thought, or sensation before while at the same time realizing that this cannot be true. It may feel as though you have seen or experienced something before but to the best of your knowledge you are actually experiencing that situation or sensation for the first time.

The following questions refer only to the feelings of 'déjà vu' that occur in the context of your epileptic seizures. Specifically, these questions refer to the 'déjà vu' experiences that precede your seizures.

Please take your time to read each question carefully. If you have any questions or concerns you are welcome to ask.

1. In the moments preceding a seizure do you ever have the feeling that you have experienced the present situation before when in fact you are experiencing it for the first time?

O Never
O Yes, infrequently
O Yes, often
O Yes, always
O Don't know

2. While you have this feeling of *'déjà vu' preceding a seizure*, is it the case that you cannot remember exactly <u>where and when</u> you experienced this strangely familiar situation before?

O Yes
O No, I vaguely remember
O No, I can remember exactly
O Don't know

3. Is this feeling of *'déjà vu' preceding a seizure* usually related to some specific part of the present situation, or to the situation as a whole?

O Total
O Some part of it
O It depends
O Don't know

If you answered 'some part of it' or 'it depends' please explain:

4. Does this feeling of *'déjà vu'* that precedes a seizure usually pertain to an exact (in all respects) repetition of the past or to approximately the same thing?

O Exactly the same
O Approximately the same
O Vaguely the same
O Not the same
O Don't know

5. While having this feeling of *'déjà vu'* preceding a seizure, do you ever have the feeling that you can predict what is going to happen next?

O Never
O Yes, infrequently
O Yes, often
O Yes, always
O Don't know

6. While having this feeling of *'déjà vu'* preceding a seizure, does it ever feel as if everything around you was not real, as if it was not really happening?

O Never
O Yes, infrequently
O Yes, often
O Yes, always
O Don't know

7. How long does this feeling of *'déjà vu'* preceding a seizure usually last?

O One second or less
O A few seconds
O One minute or several minutes
O Up to one hour
O More than one hour
O Don't know

8. When did this feeling of *'déjà vu'* occur last in the context of a seizure?

O More than 6 months ago
O 2 to 6 months ago
O Within the last month
O Within the last week
O Within the last 3 days
O Don't know

NOTE

You can give the same answer to more than one item for the following questions.

9. A person can have a feeling of *'déjà vu'* in relation to several different contexts. It can pertain to a specific place, a situation, an activity, meeting someone, a conversation, a thought, etc.

Preceding your seizure, does your feeling of *'déjà vu'* ever pertain to one or more of the following specific contexts?

		Never	Very Infrequently	Sometimes	Often	Always
a.	A certain **place**	O	O	O	O	O
b.	A certain **situation**	O	O	O	O	O
c.	A certain **activity**	O	O	O	O	O
d.	**Meeting** someone	O	O	O	O	O
e.	**Telling** someone about something	O	O	O	O	O
f.	**Listening** to a conversation or music	O	O	O	O	O
g.	Having a certain **thought**	O	O	O	O	O
h.	**Reading** something	O	O	O	O	O

Please provide any additional information that speaks to these options:

10. Is there something common to the state you are in when your déjà vu' experiences occur in the context of a seizure?

	Never	Very Infrequently	Sometimes	Often	Always
a. I am mentally fatigued	O	O	O	O	O
b. I feel gloomy or depressed	O	O	O	O	O
c. I feel nervous or under stress	O	O	O	O	O
d. I am physically fatigued	O	O	O	O	O
e. I am cheerful and happy	O	O	O	O	O
f. I feel confused or absent-minded	O	O	O	O	O
g. I feel relaxed	O	O	O	O	O
h. I feel angry	O	O	O	O	O
i. I feel frightened	O	O	O	O	O
j. I feel drowsy	O	O	O	O	O
k. I am physically ill	O	O	O	O	O

Please provide any additional information that speaks to these options:

11. In general, how does the feeling of *'déjà vu'* in the context of a seizure affect you? Note that the question specifically addresses the *'déjà vu'* experience not the subsequent seizure itself?

	Never	Very Infrequently	Sometimes	Often	Always
a. It leaves me indifferent	O	O	O	O	O
b. It frightens me	O	O	O	O	O
c. It is reassuring	O	O	O	O	O
d. It is nice and pleasant	O	O	O	O	O
e. It is uncomfortable or oppressive	O	O	O	O	O
f. It is surprising or amazing	O	O	O	O	O
g. It interrupts whatever I am doing	O	O	O	O	O

Please provide any additional information that speaks to these options:

12. Does this feeling of *'déjà vu'* preceding a seizure involve experiences from the following senses?

		Never	Very Infrequently	Sometimes	Often	Always
a.	Vision	O	O	O	O	O
b.	Audition	O	O	O	O	O
c.	Smell	O	O	O	O	O
d.	Taste	O	O	O	O	O
e.	Touch	O	O	O	O	O

NOTE

The following three questions pertain to 'déjà vu' experiences that are <u>not</u> accompanied by seizures.

13. Do you ever experience the feeling of *'déjà vu'* in situations that are <u>not</u> accompanied by seizures?

O Never
O Yes, a few times a year
O Yes, about once a month
O Yes, about once a week
O Yes, more than once a week
O Don't Know

14. How similar are the feelings of *'déjà vu'* in situations <u>without</u> seizures to those that precede a seizure?

O Exactly the same
O Somewhat similar
O Not very similar
O Completely different
O Don't Know

If the experience is not the exact same please explain how it differs:

15. Since the time you started having seizures has the frequency of 'déjà vu' experiences that <u>are</u> <u>not</u> accompanied by seizures changed.

O It has increased
O It has decreased
O It has stayed the same
O I don't know

NOTE

The following two questions pertain to experiences that are slightly different than, but related to, the feelings of déjà vu that precede your seizures.

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16. In the moments preceding a seizure do you ever have the feeling that you have never experienced the present sensation or situation before, when in fact you know that you have experienced it before?

For example: You see some place or someone you know very well, but you feel as if you have never seen this place or person before.

O Never
O Yes, infrequently
O Yes, often
O Yes, always
O Don't know

17. In the moments preceding a seizure do you ever have the feeling that while something is happening to you it is not happening to yourself, but to someone else?

O Never
O Yes, infrequently
O Yes, often
O Yes, always
O Don't know