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Determinants of autobiographical memory in patients with unilateral temporal lobe epilepsy or excisions☆

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ABSTRACT

Patients with unilateral temporal lobe epilepsy from hippocampal origin and patients with unilateral surgical excision of an epileptic focus located in the medial temporal lobe were compared to healthy controls on a version of the Autobiographical Interview (AI) adapted to assess memory for event-specific and generic personal episodes. For both types of episodes, patients with unilateral (left and right) temporal lobe epilepsy or excision (TLE) reported fewer *internal details*, which are bits of information pertaining to the recollected episode. The source of this deficit was mainly the paucity of perceptual information about the personal episodes, but temporal and spatial information was also deficient. Information about the episode's story elements was preserved in both AM conditions. Participants were also tested on a script generation task to assess retrieval of semantic information. Patients with TLE excision, but not pre-surgical patients, reported significantly fewer actions per script in comparison to controls, suggesting that the temporal neocortex is more involved than mesial temporal structures in recall of this type of information. Together, these results indicate that the hippocampus is essential to the recollection of sensory perceptual aspects of past experiences. Detailed story elements and gist information, as collected during the AI and the script generation task, respectively, are more resilient to hippocampal damage. The similarity of the impairment between the event-specific and the generic memory conditions also suggests that temporal specificity is not a key determinant of hippocampal engagement in autobiographical retrieval.

Autobiographical memory (AM) represents knowledge about facts and events that concern an individual. Theorists have classified AM according to dimensions such as *temporal specificity*, which refers to how precisely a memory is bound in time (e.g. a single afternoon versus a life-period or a relative's name), and *recollective or re-experiential qualities*, which allow one to re-experience an event in a vivid, richly-detailed manner (Brewer, 1986, 1996; Conway, 1996; Conway & Pleydell-Pearce, 2000). In his seminal work on recollection, Tulving (1985) emphasized that retrieval of experiential detail was a critical feature separating recollective experience from familiarity. Although temporal context could certainly be postulated as a core attribute of recollected events, there is nothing in Tulving's original formulation that specifies that recollection must refer to a single instance versus a 'blended' experience; that is, whether Proust's madeleine evokes a particular prior experience or a conjunction of similar experiences (see also Neisser, 1981). In either case, according to Tulving, the re-experiencing is akin to mental time travel. Here, we examine Tulving's key construct of retrieval of episodic detail in the context of normal and disordered autobiographical memory.

A considerable amount of evidence indicates that the hippocampus plays a central role in AM, but the nature of its role is debated. Multiple Trace Theory (MTT) was formulated to explain variability in retrograde amnesia for different types of memories seen in association with hippocampal damage (Nadel & Moscovitch, 1997). This theory stipulates that the hippocampus is involved in the encoding and subsequent retrieval of memory for personal episodes, or event-specific AM. MTT suggests that when event-specific AM is encoded in a defined spatial and temporal context, it forms a hippocampal trace. The hippocampus supports the recollection of event-specific AM by reactivating the trace and retrieving the memory along with detailed contextual information. MTT also stipulates that forms of declarative memories that are not temporally specific and lack contextual information, also known as semantic memories, can be supported by other neural structures, and thus retrieved without a functioning hippocampus (Moscovitch et al., 2005; Nadel

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& Moscovitch, 1997). Examples of semantic memories include facts about one-self (e.g. I grew up in Rimouski) and general knowledge (e.g. Luanda is in Angola).

In support of MTT, there are many studies demonstrating that patients with damage to the medial temporal area, which includes the hippocampus and related structures, show a deficit in memory for personal episodes but relatively preserved memory for autobiographical facts and other semantic information (Addis, Moscovitch, & McAndrews, 2007; Cipolotti et al., 2001; Gilboa et al., 2005; Graham & Hodges, 1997; Rosenbaum, McKinnon, Levine, & Moscovitch, 2004; Rosenbaum et al., 2005, 2008; Steinvorth, Levine, & Corkin, 2005; Vargha-Khadem et al., 1997; Viskontas, McAndrews, & Moscovitch, 2000; Voltzenlogel et al., 2006). Evidence from functional neuroimaging also indicates that the hippocampus is consistently activated during event-specific AM retrieval (Addis, McIntosh, Moscovitch, Crawley, & McAndrews, 2004; Addis, Moscovitch, Crawley, & McAndrews, 2004; Denkova, Botzung, Scheiber, & Manning, 2006; Gilboa, Winocur, Grady, Hevenor, & Moscovitch, 2004; Maguire & Mummery, 1999; Maguire, Henson, Mummery, & Frith, 2001; Maguire & Frith, 2003; Piolino et al., 2004; Ryan et al., 2001; Steinvorth, Corkin, & Halgren 2006; Vandekerckhove, Markowitsh, Mertens, & Woermann, 2005; also see Maguire, 2001; Svoboda, McKinnon, & Levine, 2006 for reviews).

MTT predicts that the detailed recollection of event-specific AM depends on the hippocampus whereas semantic memories, whether public or personal, can be mediated by extra-hippocampal structures. However, MTT's predictions are less firm when it comes to AM for events experienced repeatedly, or generic AM. Generic AM is a form of AM that shares some but not all characteristics of event-specific AM. Although generic AM lacks the temporal specificity of event-related AM, relevant contextual information can be recovered and, consequently, this form of memories can be vividly recollected (Brewer, 1986, 1996, but see Conway, 2001). For example, the memory of a weekly meeting can contain details about the people usually present, the perceptual qualities of the meeting room, or the order in which things would usually take place over the course of the event. MTT suggests that the repeated encoding of an event could lead to the formation of multiple traces that may render the memory for this event more resilient to hippocampal damage. However, empirical evidence is needed to establish whether generic AM is supported by the hippocampus to the same extent as event-specific AM, or whether AM becomes hippocampally independent if experienced repeatedly.

Previous attempts at comparing the neural correlates of event-specific and generic AM have been sparse. Levine et al. (2004) designed a paradigm for a prospective memory study that exposed participants to their own tape-recorded narratives of event-specific and generic autobiographical episodes. Although no hippocampal activity was observed in either condition, several regions including the bilateral parahippocampal cortex distinguished between these two types of AM. Addis and colleagues (Addis et al., 2004a,b) also compared the neural correlates of event-specific versus generic AMs using functional MRI. They showed that the hippocampus was equally activated by the two conditions, suggesting it was insensitive to the difference in temporal specificity between event-specific and generic AM (Addis et al., 2004a). Instead, hippocampal activity was positively correlated with other characteristics that reflected contextual information, such as self-rated perceptual details (vividness), emotionality, and personal significance.

For this study, we adopted a lesion approach to compare the role played by the hippocampus in event-specific AM and generic AM. We compared both types of AM in patients with unilateral medial temporal lobe epilepsy and patients who had undergone unilateral surgical excision of an epileptic focus within the temporal lobe (including the hippocampus). A significant number of patients with unilateral temporal lobe epilepsy typically suffer from seizure-induced medial temporal sclerosis (MTS), which results in observable hippocampal atrophy in the epileptogenic hemisphere. Patients were compared to neurologically intact matched controls. Our goal was to extend MTT, by establishing whether it is temporal specificity or the amount of contextual information that makes AM hippocampally dependant. Our goal was also to address one of the key questions about hippocampal function: is it implicated only in memory acquired over unique episodes or does it also support the remembrance of contextual details acquired over multiple episodes?

Patients and controls were tested on a version of the Autobiographical Interview (AI) (Levine, Svoboda, Hay, Winocur, & Moscovitch, 2002) adapted to assess both generic and event-specific AM. The original version of the AI, which was designed to assess memory for single personal episodes, was used in the event-specific AM condition. Importantly, patients with medial temporal lobe damage which includes the hippocampus have been shown to be impaired on this task (Addis et al., 2007a; McKinnon et al., 2008; Rosenbaum et al., 2004, 2008; Steinvorth et al., 2005). Also, previous evidence from this clinical population has shown that patients with temporal lobe excision and patients with MTS and epilepsy awaiting the same surgery show an equivalent event-specific AM impairment (Viskontas et al., 2000), giving us confidence that both types of patients could be merged into a single clinical group. In the generic AM condition, a modified version of the interview was used to assess memory for personal events that were repeated at least 10 times. We also used a script generation task adapted from Godbout and Doyon (1995) as a control task. We elected to use the script task to control for the contribution of semantic memory, narrative skills and verbal fluency of performance on our adapted version of the AI.

1. Methods

1.1. Participants

All participants gave their informed consent in accordance with a protocol approved by the research ethics board of the University Health Network. Fourteen patients with left temporal lobe epilepsy or temporal lobe excision (LTLE) (10 pre-surgery, 3 male), and 11 patients with right temporal lobe epilepsy or temporal lobe excision (RTLE) (6 pre-surgery, 5 male) were recruited through the Epilepsy Program of Toronto Western Hospital. All patients were diagnosed with epilepsy from unilateral hippocampal origin, except for one pre-surgical RTLE patient in whom an independent left temporal focus was also observed. This participant's performance was indistinguishable from other TLE patients on the AI and the script generation task, so we elected to include him. The temporal lobe excision consisted in the removal of the amygdala, of 2–4 cm from the hippocampus and parahippocampal gyrus and of 4–6 cm along the lateral convexity of the middle, inferior and fusiform gyri of the temporal lobe.

Information was obtained from the patients' medical chart following their consent. All of the patients who had undergone surgery were seizure-free post-operatively, except for one RTLE patient whose ablated epileptogenic cyst had re-grown since his surgery. Three LTLE patients (2 pre-surgery and 1 post-surgery) had a small lesion in their occipital cortex. Other patients showed no damage to portions of the brain other than the medial temporal area that was unrelated to either seizure activity or to a temporal lobe excision. Five out of nine pre-surgery LTLE patients and three out of six pre-surgery RTLE patients were diagnosed with medial temporal sclerosis by a radiologist according to clinical criteria (atrophy on T1-weighted MRI scans and gliosis on T2-weighted MRI scans).

In order to characterize hippocampal atrophy in our pre-surgery patients as a function of their epileptogenic hemisphere, we took a linear measurement of hippocampal width (Gao et al., 2003) on pre-surgery patients' MRI scans (except for one RTLE case for whom scans were unavailable), which we compared to measurements obtained from a group of healthy controls (the healthy control measurements have been reported previously by Addis et al., 2007a). The control group was composed of 14 right-handed adults (six male) who ranged in age between 24 and 56 years old ($M = 34.14$, S.D. = 10.76). Their age did not differ significantly from RTLE and LTLE patients groups (Mann–Whitney U-test: $U = 33.50$, $p = .482$, and $U = 32.50$, $p = .054$, respectively). Images were either acquired with a 3 or a 1.5 T GE MR system using a three-dimensional T1 weighted sequence (FOV = 200–256; 60–148 axial slices, 1–2.6 mm thick).

For each hemisphere, we used ANALYZE AVW Software (Biomedical Imaging Resource, Mayo Foundation, Rochester, MN) to reconstruct a slice four slices above