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An investigation of implicit memory through left temporal lobectomy for epilepsy

Joseph I. Tracy [a,b,*], Karol Osipowicz [a], Samuel Godofsky [a], Atif Shah [a], Waseem Khan [a], Ashwini Sharan [c], Michael R. Sperling [a]

[a] Department of Neurology, Thomas Jefferson University, Jefferson Medical College, United States
[b] Department of Radiology, Thomas Jefferson University, Jefferson Medical College, United States
[c] Department of Neurosurgery, Thomas Jefferson University, Jefferson Medical College, United States

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ABSTRACT

Temporal lobe epilepsy patients have demonstrated a relative preservation in the integrity of implicit memory procedures. We examined performance in a verbal implicit and explicit memory task in left anterior temporal lobectomy patients (LATL) and healthy normal controls (NCs) while undergoing fMRI. We hypothesized that despite the relative integrity of implicit memory in both the LATL patients and normal controls, the two groups would show distinct functional neuroanatomic profiles during implicit memory. LATLs and NCs performed Jacoby's Process Dissociation Process (PDP) procedure during fMRI, requiring completion of word stems based on the previously studied words or new/unseen words. Measures of automaticity and recollection provided uncontaminated indices of implicit and explicit memory, respectively. The behavioral data showed that in the face of temporal lobe pathology implicit memory can be carried out, suggesting implicit verbal memory retrieval is non-mesial temporal in nature. Compared to NCs, the LATL patients showed reliable activation, not deactivation, during implicit (automatic) responding. The regions mediating this response were cortical (left medial frontal and precuneus) and striatal. The active regions in LATL patients have the capacity to implement associative, conditioned responses that might otherwise be carried out by a healthy temporal lobe, suggesting this represented a compensatory activity. Because the precuneus has also been implicated in explicit memory, the data suggests this structure may have a highly flexible functionality, capable of supporting implementation of either explicit memory, or automatic processes such as implicit memory retrieval. Our data suggest that a healthy mesial/anterior temporal lobe may be needed for generating the posterior deactivation perceptual priming response seen in normals.

1. Introduction

Dominant, typically left, temporal lobe epilepsy (LTLE) provides a unique model for investigations of implicit and explicit memory. LTLE patients who have undergone left anterior temporal lobectomy (LATL) demonstrate deficits in explicit verbal memory procedures, while implicit memory remains relatively intact (Zaidel, Oxbury, & Oxbury, 1994; Zaidel, Esiri, & Beardsworth, 1998; Del Vecchio, Liporace, Nei, Sperling, & Tracy, 2004). Explicit memory is characterized as a conceptually-drive, conscious recollection of previously stored information, regulated by an intentional "top-down" network (Ciaramelli, Grady, & Moscovitch, 2008; Soto, Humphreys, & Rotshtein, 2007). Implicit memory is considered to reflect either data-driven or conceptually-driven processing systems, unintentional and automatic in their implementation, best measured by indirect tests of memory such as word-stem completion, word-fragment completion, word-association generation, category-exemplar generation tasks, or repetition priming (Graf, Squire, & Mandler, 1984). The anatomic structures subserving explicit memory are well-established, involving a hippocampal dependent system (Degonda et al., 2005; Eichenbaum & Lipton, 2008; Squire & Zola-Morgan, 1991), with other structures such as posterior parietal cortex (Wagner, Shannon, Kahn, & Buckner, 2005) and anterior prefrontal cortex (Rugg & Curran, 2007) crucially involved. While much work has been done to help define the functional neuroanatomy of implicit memory, there continues to be debate about whether it is truly a hippocampal-independent system.

Patients with hippocampal damage and anterograde amnesia seem able to show the benefits of repetition or perceptual priming, suggesting that these cognitive systems utilize a perceptual or "bottom up" network that is hippocampal independent (Cabeza & Nyberg, 2000; Schacter & Buckner, 1998). Amnesic patients also demonstrate intact conceptual priming, suggesting this priming

* Corresponding author at: Cognitive Neuroscience and Brain Imaging Laboratory, Neuropsychology Service, Department of Neurology, Thomas Jefferson University, Jefferson Medical College, 900 Walnut Street, Suite 206, Philadelphia, PA 19107, United States. Fax: +1 215 503 2481.

E-mail address: joseph.i.tracy@jefferson.edu (J.I. Tracy).

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system is hippocampal independent (Billingsley, McAndrews, & Smith, 2002). However, there is counter evidence implicating temporal lobe structures in implicit memory. For instance Zaidel et al. correlated neuronal density in hippocampal subfields and found associations between CA1 integrity and implicit memory performance (word-stem completion) in left, but not right, temporal lobectomy patients (Billingsley et al., 2002; Schendan, Searl, Melrose, & Stern, 2003; Weber, Kügler, & Elger, 2007; Zaidel et al., 1998). Also, some studies in motor skill learning have suggested the hippocampus is involved in implicit memory when evaluated through tasks such as motor sequence learning (Schendan et al., 2003). Other studies have found implicit memory paradigms can activate the medial temporal lobe structures in healthy controls in a fashion that suggests lateralized material specific effects are present (Weber et al., 2007). One way of reconciling these examples of hippocampal involvement in implicit memory is to emphasize the relational nature of the task, with the implementation of implicit encoding and retrieval occurring through neural-response learning rather than a neural tuning mechanism (Schacter, Dobbins, & Schnyer, 2004). From this perspective, implicit memory can be seen as stemming from the mesial temporal lobe's expertise in associative memory (see Cohen et al., 1999).

Neuroimaging studies to date suggest that implicit memory is distinct from explicit memory (Donaldson, Petersen, & Buckner, 2001), with implicit memory characterized by reduced neural activity of key cortical regions (Buckner, Koutstaal, Schacter, & Rosen, 2000; Schacter & Buckner, 1998; Schott et al., 2005), such as left frontal gyrus, left inferior prefrontal cortex, inferior temporal regions (Buckner et al., 2000; Wagner, Koutstaal, Maril, Schacter, & Buckner, 2000), occipital, and occipitotemporal cortex (Badgaiyan, Schacter, & Alpert, 1999; Buckner et al., 1995; Reber, Gitelman, Parrish, & Mesulam, 2003; Squire et al., 1992). These decreases emerge from experimental paradigms that gauge a subject's response to recently observed stimuli, an effect called "repetition suppression" (Henson, 2003; Schacter, Wig, & Stevens, 2007). Subsequent work by Dobbins and colleagues provide a response learning explanation of these repetition-related neural reductions (Dobbins, Schnyer, Verfaellie, & Schacter, 2004). With regard to perceptual priming, the involved areas will depend on the nature of the stimulus with occipital cortex mediating visual stimuli and superior temporal regions mediating auditory stimuli (Blaxton, 1999; Gabrieli, 1998; Schacter & Badgaiyan, 2001; Schacter & Buckner, 1998; Schacter et al., 2007; Squire, 1995).

In contrast, in conceptual priming, a performance benefit arises strictly from the semantic aspects of a stimulus, and is associated with neural activity reductions in the inferior/superior temporal, and left prefrontal regions (Demb et al., 1995; Raichle et al., 1994; Verfaellie & Keane, 1997). Based on a study by Blaxton and colleagues, the distinction between data-driven perceptual memory and conceptually-driven memory may be particularly important in the context of epilepsy as they found that left temporal lobe epilepsy patients failed to show a breakdown in data-driven memory, but produced abnormal performance on conceptually-driven memory tasks (Blaxton, 1992).

To date, the major neuroanatomical studies of implicit memory in epilepsy have been hampered by problems such as the influence of implicit on explicit memory and vice versa (Billingsley et al., 2002; Blaxton, 1992; Zaidel et al., 1994). For instance, the Blaxton study (Blaxton, 1992) counterbalanced the order of the implicit and explicit tasks, making it possible for implicit memory processes to be contaminated by explicit memory under certain experimental conditions.

In our previous behavioral study we utilized a Process Dissociation Procedure (PDP), based on the work of Jacoby (1991) to separate and quantify implicit (also referred to as automatic) and explicit (also referred to as intentional) forms of memory (Jacoby, 1991). We demonstrated that LATL patients performed worse than normal controls (NCs) on a measure of explicit memory, but performed similarly on an implicit memory measure. The data demonstrated the integrity of implicit memory in LATL patients and implied a potential dissociation in the functional neuroanatomy of these two forms of verbal memory in LATL patients (Del Vecchio et al., 2004).

The goal of the present study was to determine the functional neuroanatomy associated with implicit memory processing in LATL, as a means of clarifying the role of medial temporal memory structures. The PDP was utilized in a single task, containing both direct and indirect tests of memory in order to quantify both explicit and implicit word retrieval (Cermak, Verfaellie, Sweeney, & Jacoby, 1992; Jacoby, 1991; Verfaellie & Treadwell, 1993). Regardless of whether one counterbalances, or conducts implicit or explicit memory tasks first, none have the advantage of the Jacoby approach, which combines the measures in one task, overcoming the problem of task equivalence (e.g., differing task demands, differing task difficulty,) and task order. Such task differences pose rival hypotheses for the study data and results, rival factors that are not at work in the Jacoby method. Lastly, the approach also provides a way of quantifying automatic and intentional forms of memory by putting them in opposition to each other to verify which is stronger in a given individual during a given task.

We predicted that LTL patients would show impaired explicit verbal memory retrieval scores, while leaving implicit memory retrieval relatively intact because of the latter's potential implementation by extra-temporal lobe structures. We hypothesized that despite the relative integrity of implicit memory in both the LATL patients and normal controls, the two groups would show distinct functional neuroanatomic profiles during implicit memory. We expected our LATL patients would show a set of brain deactivations consistent with an impairment in the temporal-lobe based conceptual priming system, and a relative preservation of a posterior perceptual priming system, which would operate on the visual dimensions and word form recognition properties of the task. In contrast, we expected our NCs to engage both conceptual and perceptual processing systems given the integrity of the frontal/temporal circuits and occipital regions that implement these systems.

2. Material and methods

2.1. Participants

Table 1 displays the sample demographic characteristics and memory performance scores. A total of 16 NCs and 12 LATL patients were recruited for the study. All four left-handed LATL patients demonstrated left hemisphere dominance through the intracarotid-amobarbital exam conducted at the Thomas Jefferson University Comprehensive Epilepsy Center (Tracy et al., 2009). The LATL patients completed the pre-surgical algorithm of the TJU Comprehensive Epilepsy Center, received a left anterior temporal lobectomy, and were at least 6 months post-surgery but less than 3 years post-surgery when completing the current study. Details of the Thomas Jefferson Comprehensive Epilepsy Center algorithm are described in Sperling et al. (1992). The anterior temporal lobectomy (ATL) procedure involves an "en bloc" resection. Details of the Thomas Jefferson Comprehensive Epilepsy Center algorithm are described in Sperling et al. (1992). The anterior temporal lobectomy (ATL) procedure involves an "en bloc" resection. The typical anterior temporal lobectomy procedure involves resection of 4–5 cm of tissue back from the temporal pole. It is important to note that all the patients displayed strong evidence that their pathology was unilateral and limited to the temporal lobe,