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The effects of temporal lobe epilepsy on scene encoding

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ABSTRACT

Forty-four patients with temporal lobe epilepsy (TLE) (25 left) and 40 healthy control participants performed a complex visual scene-encoding fMRI task in a 4-T Varian scanner. Healthy controls and left temporal lobe epilepsy (LTLE) patients demonstrated symmetric activation during scene encoding. In contrast, right temporal lobe (RTLE) patients demonstrated left lateralization of scene encoding which differed significantly from healthy controls and LTLE patients (all $p \leq .05$). Lateralization of scene encoding to the right hemisphere among LTLE patients was associated with inferior verbal memory performance as measured by neuropsychological testing (WMS-III Logical Memory Immediate, $p = 0.049$; WMS-III Paired Associates Immediate, $p = 0.036$; WMS-III Paired Associates Delayed, $p = 0.047$). In RTLE patients, left lateralization of scene encoding was associated with lower visuospatial memory performance (BVRT, $p = 0.043$) but improved verbal memory performance (WMS-III Word List, $p = 0.049$). These findings indicate that, despite the negative effects of epilepsy, memory functioning is better supported by the affected hemisphere than the hemisphere contralateral to the seizure focus.

1. Introduction

The hippocampus and the related medial temporal lobe (MTL) structures are essential for encoding episodic memories [1]. Studies in patients with unilateral MTL lesions have demonstrated dissociations between the functions of left hippocampus, mediating verbal memory, and the right hippocampus, facilitating visuospatial memory [2,3], although material-specific memory deficits from right hemispheric lesions tend to be less robust than those from left hemispheric lesions [4]. Temporal lobe epilepsy (TLE), most commonly characterized by seizures originating from the medial temporal structures, is frequently associated with memory impairments [5,6]. In particular, LTLE is typically associated with deficits in verbal memory functioning, whereas seizures originating from the right temporal region may cause visuospatial memory impairments [7]. These memory deficits are, in part, the result of progressive seizure-related damage to MTL structures that are vital for the acquisition, temporary storage, and retrieval of episodic memories [8].

Neural damage associated with chronic epilepsy is known in some individuals to lead to functional reorganization of language and/or memory functions [9,10]. For example, atypical language lateralization is commonly observed in LTLE patients [11] and is most prominent in patients with hippocampal sclerosis [12,13]. A number of small- and medium-scale fMRI studies have investigated functional reorganization of memory in epilepsy patients. Overall, these studies have demonstrated increased lateralization of memory encoding, as assessed through experimental tasks presented in the scanner, to the hemisphere contralateral to the seizure focus [14–18]. In particular, LTLE patients demonstrate increased right lateralization of verbal memory, whereas left lateralization of visuospatial memory has been observed among RTLE patients [19–21]. These findings support the notion that TLE may lead to epilepsy-related reorganization of memory processing. However, the functional importance of this atypical lateralization for memory performance on standardized psychometric measures has received little attention, and the literature has produced mixed findings. In a study by Richardson et al. [20], reorganization of verbal memory to the right hemisphere was associated with superior verbal memory performance in LTLE patients. However, more recently, Powell et al. [19] demonstrated that atypical (i.e., lateralized to the unaffected hemisphere) memory representation was associated with inferior verbal and nonverbal (i.e., figure recall) memory performance. Additionally, Vannest et al. [21] reported that left hemispheric epilepsy patients demonstrated greater right medial temporal activation as well as inferior memory performance when compared to right hemispheric epilepsy patients. The authors concluded that reorganization of memory functioning in left hemispheric epilepsy patients may be associated with impaired verbal memory performance [21].

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Given the incongruous findings to date, the present fMRI study used a large sample of TLE patients and healthy controls in order to further examine whether lateralization of the seizure focus differentially affects lateralization of memory functioning. Additionally, the relationship between lateralization of memory and memory performance on standardized clinical measures was investigated. Healthy controls were used to establish activation patterns elicited by the fMRI scene-encoding task employed in this study, which has previously been known to elicit symmetric medial temporal activation in healthy controls [10,22,23]. This study tested two hypotheses which were formulated based on the existing literature:

Hypothesis 1. Left temporal lobe epilepsy patients will demonstrate increased right lateralization of scene encoding, and RTLE patients will demonstrate increased left lateralization of scene encoding [19–21].

Hypothesis 2. Lateralization of scene encoding to the contralateral (healthy) hemisphere and the degree of lateralization will be negatively correlated with the degree of memory functioning [20,24,25].

Previous studies have demonstrated that memory lateralization, particularly verbal memory lateralization, may depend on lateralization of language functioning [26]. Therefore, additional analyses were completed by investigating the relationship between memory lateralization and language lateralization as determined by the previously published Semantic Decision/Tone Decision (SDTD) fMRI task [27]. This and similarly designed semantic decision fMRI tasks are known to elicit lateralizing activation patterns for semantic language functions [28,29], correlate with language intracarotid amobarbital procedure (IAP) results [30], and predict postoperative naming abilities [31].

2. Methods

2.1. Participants

2.1.1. Temporal lobe epilepsy patients

Forty-four (32% female) TLE patients aged 19 to 66 (mean age = 39) were included in this study. Participants had a mean age at epilepsy onset of 21 years and a mean duration of epilepsy of 17 years, both of which are typical for patients undergoing evaluation for epilepsy surgery [32–34]. Participants were recruited prospectively as part of an ongoing study focusing on language and memory assessments in patients with pharmacoresistant focal-onset epilepsy [21,22,35,36]. An additional 24 patients were recruited into the parent study but were excluded from our analyses: 11 due to seizures of extratemporal origin and 13 because they were administered a different version of the scene-encoding fMRI task [22]. Twenty-five patients were determined to have LTLE and 19 RTLE (see Table 1 for demographic information). Data from the first 14 patients (LTLE = 8; RTLE = 6) were included in our previous publication [21]. Diagnoses of all patients were based on seizure semiology, neuroimaging results, and neurologists' impressions from prolonged video-EEG recordings. Final decisions regarding epilepsy type were made by at least two epileptologists. All participants underwent fMRI within 1–3 months of their video-EEG monitoring and neuropsychological testing.

2.1.2. Healthy controls

In order to establish activation patterns in healthy controls using this fMRI scene-encoding paradigm, 40 healthy control participants (39% female) aged 19 to 59 (mean age = 33) with no history of neurological disorders or memory complaints were recruited (10 of these participants were included in our previous study [21]). This study was approved by the Institutional Review Board at the University of Cincinnati, and all participants provided written informed consent prior to enrollment.

Table 1
Demographic data for healthy controls and left and right TLE patients.

	Healthy controls	LTLE	RTLE
N	40	25	19
Age (M (SD))	33.32 (12.37)	35.88 (10.23)	42.26 (12.34)*
Sex (% female)	42%	40%	21%
Education (M (SD) years)	15.77 (2.74)	14.08 (2.78)	13.47 (2.22)
Dominant handedness			
Right	31	22	17
Left	4	2	2
Both	5	1	0
Age at onset (M (SD))		17.70 (13.91)	25.47 (16.82)
Seizure duration (M (SD) years)		18.16 (13.37)	16.42 (12.20)
Memory lateralization with IAP			
Left		11	10
Right		8	2
Symmetric		1	1
Total		20	13
Language lateralization with IAP			
Left		17	12
Right		4	1
Total		21	13

Note. *$p<0.05$ when compared to healthy controls.

2.2. Procedure

2.2.1. Neuropsychological testing

As in our previous studies, all epilepsy patients underwent an extensive neuropsychological assessment as part of their presurgical clinical evaluation [5,21,37,38]. In this study, measures of verbal memory included the Logical Memory, Paired Associates Learning, and Word List Learning subtests of the Wechsler Memory Scale—III (WMS-III; [39]). The WMS-III Auditory Memory subtest is designed to measure immediate and delayed recall of verbal information presented in an auditory modality. The WMS-III Logical Memory subtest requires patients to recall verbal information read to them in the context of a story. On the Paired Associates subtest, participants are required to learn word pairs across multiple trials. For the Word List subtest, patients are required to learn and recall a list of words presented to them auditorily. Each of these subtests involves an immediate as well as a delayed recall component. The Benton Visual Retention Test (BVRT, [40]) and Warrington's Recognition Memory for Faces (RMF, [41]) test were both included as assessments of nonverbal memory functioning. The RMF is a facial recognition task in which participants view photos of 50 unfamiliar men, and memory for these faces is tested immediately with a forced-choice (2 choices) recognition test. The BVRT requires participants to view and immediately draw complex visual forms. All statistical analyses were performed on standard scores corrected for age (and for some tests, gender and education) based on published normative data. Neuropsychological data were not gathered from healthy controls.

2.2.2. Functional MRI activation tasks

2.2.2.1. Scene-encoding task. A "box-car" design functional MRI scene-encoding task was employed for the purposes of this study [10,21,23]. As previously, participants were presented with stimuli that represented a balanced mixture of indoor (50%) and outdoor (50%) scenes that included both images of inanimate objects as well as pictures of people and faces. Attention to the task was monitored by asking participants to indicate whether the scene was indoor or outdoor on a button box held in the right hand; participants were instructed to memorize all scenes for later memory testing. In the control condition, participants viewed pairs of scrambled images and were asked to indicate with the use of the button box whether both images in each pair were the same or different (50% were the same). Use of the control condition allowed for subtraction of visuo-perceptual,