

Alterations in the autobiographical retrieval network associated with left mesial temporal dysfunction

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The hippocampus is a key structure in the network supporting retrieval of autobiographical memory (AM), as has been shown in functional neuroimaging (1,2) and lesion (3,4) studies. We have previously reported reduced activation during autobiographical retrieval in the left hippocampus and other components of this network in patients with left temporal-lobe epilepsy (LTLE) (5). Here, we used structural equation modeling (SEM) to explore the integrity of network connections in LTLE patients.

Participants included 11 patients with LTLE (based on EEG criteria) and 14 age-matched controls. An event-related design was used, in which participants retrieved specific AMs (20 episodes to individualized cues) and semantic information (20 items each for size discrimination and sentence completion). Selection of regions for the structural model was based on previous connectivity analyses (1) with the addition of several right hemisphere regions found to be activated in our AM versus semantic contrasts (2,5). There were 11 regions and 18 connections included following preliminary analyses to identify a stable omnibus model (stability indices < 1).

For each group, percent signal change (AM vs. semantic) was extracted for each region and pairwise correlations were calculated. SEM was used to estimate the strength and direction of effective connections between regions, and whether these differed across groups. This analysis revealed a significant chi-square difference between the null and alternate models [$\chi^2_{\text{diff}}(18)=59.17$, $p<.0001$], indicating that the connectivity of the AM network differed between groups.

Fig 1 illustrates common connections as well as those that differed significantly ($p<0.01$) between the groups. A network of regional interactions common to both groups was found to involve all right hemisphere intrinsic and cross-hemisphere connections as well as several connections involving the left temporal regions. The principal differences associated with LTLE were a diminished set of excitatory influences into and from the left hippocampus and parahippocampal gyrus and a concomitant increase in the excitatory connection from left retrosplenial to medial prefrontal cortex. Of note, some influences involving these left medial temporal regions were constant across groups (see Fig 1) indicating that regional dysfunction and diminished activation does not invariably alter all connections in a task-relevant network. Interestingly, there was no increase in connectivity within right hemisphere regions observed in patients with unilateral left temporal-lobe dysfunction, suggesting that there were no compensatory interactions supporting AM retrieval. The enhancement of other limbic influences on prefrontal cortex may explain how AM retrieval is supported, albeit in a reduced behavioral capacity, in individuals with dysfunction in the "hub" of the network.

