fMRI and MRS Correlates of Memory Function in Temporal Lobe Epilepsy Patients

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Introduction

Temporal lobe epilepsy (TLE) is commonly associated with memory impairment. Consequently, surgical intervention for pharmaceutically resistant TLE patients often requires pre-surgical evaluation of memory function to assess the potential for neurological deficits following cortex resection. The Wada test (intracarotid amobarbital procedure) has been the primary neuropsychological tool for lateralizing memory function for over 50 years, despite its invasiveness and possibility for inaccurate lateralization. Over the last decade, fMRI has been used to non-invasively investigate the role of the hippocampus and related medial temporal lobe structures in memory encoding, temporary storage, and retrieval. In particular, experimental paradigms employing visual encoding tasks to explore the encoding and storage of novel information have demonstrated consistent bilateral activation within the hippocampi and parahippocampal gyri of both control subjects and epilepsy patients[1,2], suggesting that asymmetries in the activation produced from this paradigm could lateralize memory impairment. Additionally, ^{1}H MRS is capable of non-invasively detecting N-acetylaspartate (NAA), which is a marker for neuronal integrity that has been shown to be decreased in the epileptogenic hippocampi of TLE patients. Since neuronal dysfunction in the hippocampi could result in memory impairment, hippocampal NAA levels may provide an additional indicator of memory performance. *The purpose of this study was to elucidate the possible correlations between hippocampal BOLD activation asymmetries, hippocampal NAA levels, and neuropsychological evaluation of memory function.*

Methods

fMRI and ^{1}H MRS data were collected from 5 strongly lateralized refractory TLE patients (3 females, 2 males, aged 43 ± 16 years) on a 4.0 T Varian ^{UNITY}*INOVA* whole-body scanner equipped with Siemens Sonata gradients and a transmit/receive quadrature hybrid birdcage RF coil. A block paradigm consisting of visually presented novel and repeated scenes was used to investigate the laterality of memory encoding function. Functional (BOLD-sensitive) images were continuously collected from 21- 3.5 mm thick contiguous oblique planes (oriented parallel to the long axes of the hippocampi) using a segmented (4-shot) gradient echo sequence with spiral readout gradients (64 x 64 matrix size, FOV = 22.4 cm, TE = 15 ms, TI = 1.2 s, volume acquisition time = 3 s, tip-angle = 60°). The BOLD activation maps (generated with voxel-by-voxel general linear model regression analyses) were anatomically registered using high-resolution images acquired with the same oblique FOV using a 3D spiral gradient echo sequence (256 x 256 x 96 matrix size, 1.75 mm slice thickness, TI = 1.3 s, TE = 3 ms, TR = 50 ms, tip-angle = 20°). Short TE water suppressed LASER[3] localized spectra (TR = 3200 ms, TE = 46 ms, 128 averages) were obtained from 2.78 ± 0.51 cm^3 voxels in both the left and right hippocampus for each subject, and the data were rigorously quantified using previously published[4] methods. fMRI (hippocampal laterality indices) and MRS (NAA levels) data were correlated with neuropsychological scores of verbal and visual memory encoding (including elements of the California Verbal Learning Test – 2nd Edition, Wechsler Memory Scale – 3rd Edition, Rey-Osterrieth Complex Figure Test, and the Brief Visuospatial Memory Test – Revised) routinely collected during clinical patient evaluation (scores standardized with age- and gender-specific normative data).

Results

Significant BOLD activation was shown bilaterally (Fig. 1) in the hippocampi of 4 TLE patients ($p < 0.005$, uncorrected), with laterality indices correctly lateralizing the seizure focus in 3 patients. Group comparisons of patient NAA levels in the hippocampus ipsilateral to the seizure focus versus the contralateral hippocampus showed no significant difference (Fig. 2). Neuropsychological testing revealed visual and verbal memory encoding deficits in 2 patients, and mild visual memory encoding impairment in another patient. Correlations between the fMRI, MRS, and neuropsychological measures did not reach statistical significance from the present data.

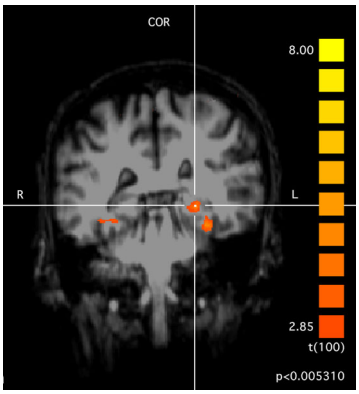
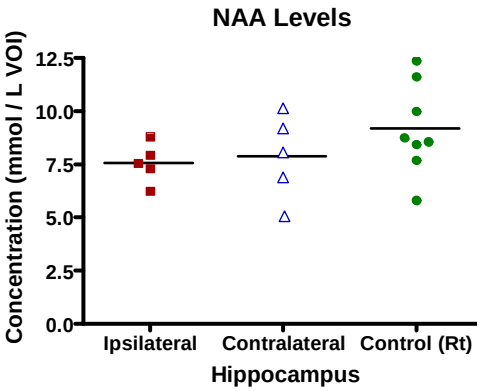


Fig. 1. *(left)* Coronal BOLD activation map produced from visual memory encoding paradigm in a TLE patient with right lateralized seizure focus. Cross hairs indicate significant voxel cluster in the left hippocampus.

Fig. 2. *(left)* Absolute NAA concentrations (referenced to tissue water) in the hippocampi ipsilateral and contralateral to the seizure focus in 5 strongly lateralized TLE patients, and in previously reported control (right) hippocampi[4].



Conclusions

Preliminary results suggest that asymmetry in visual memory encoding measured by fMRI may correctly lateralize seizure foci in TLE patients. However, significant correlations between BOLD activation, NAA levels and neuropsychological scores were not observed, likely due to the small sample size. By investigating these potential correlations, new non-invasive and quantitative methods for evaluating memory function to aid in surgical planning for TLE patients may be realized.

References

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