Metabolic connectivity in controls and epilepsy patients

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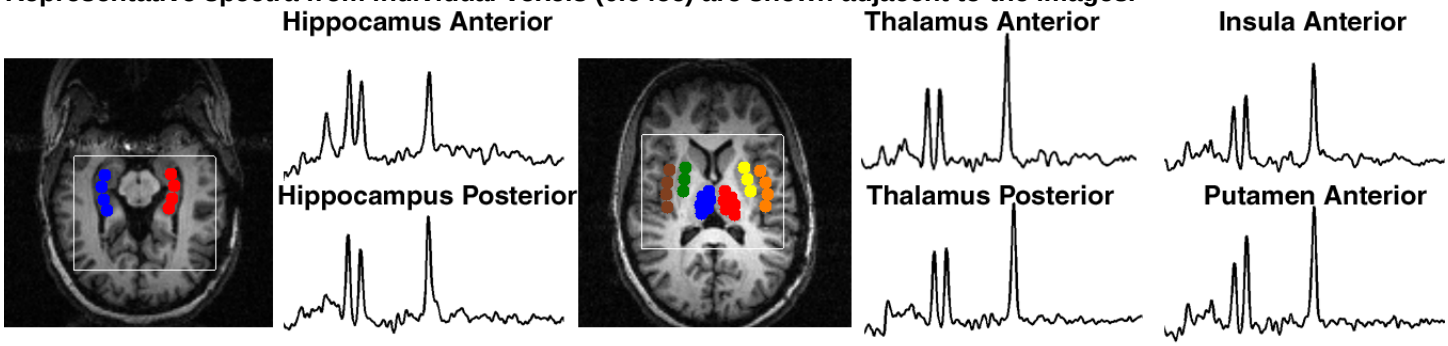
Introduction: Recently we demonstrated that in patients with mesial temporal lobe epilepsy (mTLE) there exists a metabolic network of decreased NAA subcortical structures including the anterior thalamus, putamen and insula which are correlated with the extent of NAA decrease in the ipsilateral and contralateral hippocampi. In mTLE this network reflects known neuronal pathways linking key brain structures involved in seizure generation and propagation. Specifically, the degree of injury (reduction in NAA) in the subcortical loci was significantly correlated with the degree of reduction of NAA in the hippocampi. The extent to which this network is also present in patients with neocortical epilepsy, primarily involving the temporal neocortex (as opposed to the hippocampus) is not known. The goal of this study was to evaluate the pattern and extent to which the correlated reductions in NAA from these multiple locations (hippocampus and subcortical loci) define a unique network of impairment which can resolve mTLE from NE.

Methods: Spectroscopic imaging studies were acquired from controls (n=20), MTLE patients (n=27) and non-MTLE patients (including neocortical, tumor and AVM etiologies, n=18). The MTLE patient group was verified with ILAE class I or II outcome 2 years following surgery. All data were acquired at 4T using a Varian INOVA console and a quadrature head coil. The hippocampal and subcortical data were collected using a modified LASER sequence (10mm thickness, 80x100mm in-plane FOV selection) in combination with two dimensions of phase encoding (24x24, FOV=192x192mm, 19.2 min). Voxels from the hippocampus (4), anterior thalamus (3), posterior thalamus (3), insula (4) and putamen (3) were selected and averaged from the ipsilateral and contralateral lobes, producing 10 values per volunteer (Figure 1). These multivariate data (NAA/Cr values from 10loci per volunteer) were analyzed using a Principle Component Analysis (PCA) to determine the orthogonal factors of covarying loci. Using the coefficients of the PCA analysis for the mTLE patients, the Hotellings distance (the multivariate equivalent of the t-statistic measuring the extent to which an individual's network varies from the group mean of the mTLE patients) was calculated. For comparison purposes a PCA analysis was also carried out using the control group and these factors were then used to calculate a Hotellings statistic using the control subject's network.

Figure 1 : Scout images showing the loci analyzed for the hippocampus, thalamus, insula and putamen. Representative spectra from individual voxels (0.64cc) are shown adjacent to the images.



Results: In controls, the PCA demonstrated covarying loci from the bilateral thalami, R hippocampus and bilateral insula/operculum. The MTLE patients demonstrated a more extensive network, involving all loci including the bilateral thalami, hippocampi, basal ganglia and insula. When using the PCA factors determined from the control group to calculate the Hotelling's distance (control group, 9.5±3.3), the values from the mTLE and NE groups were significantly larger and more variable (64.7±49.4 and 59.7±33.3 respectively), indicating significant differences between the networks. In comparison, when the mTLE PCA factors were used to calculate a Hotellings distance for the NE group, again, a significant difference was found, with the mTLE Hotellings statistic being 9.6±3.7, and 30.4±22.6 in the mTLE and NE groups respectively. This implies that the network seen in NE is different from that of MTLE.

Conclusions: There are significant differences in NAA levels throughout the network of hippocampal and subcortical structures in controls and patients with mTLE and NE. These relationships reflect a pattern of function and/or injury which may be able to help distinguish between different epilepsy types. In the epilepsy patients, this may reflect either how damage is propagated along known neuronal pathways, or alternately, reflect a network which facilitates the generation and propagation of seizures.