HIPPOCAMPAL EEG SIGNAL COMPLEXITY CORRELATES WITH NAA/CR

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Introduction: While it is clear that MR imaging of epilepsy has revolutionized the management and diagnosis of epilepsy, the abnormal EEG remains the primary electrophysiologic manifestation of seizures and is the defining clinical feature of the epileptic focus. The intracranial EEG (icEEG) obtained in patients undergoing invasive monitoring is a relatively artifact-free measure of neural activity involving the epileptic region. If the neural activity of the seizure focus depends on mitochondrial and metabolic function, we might anticipate a relationship between imaging based measures with EEG-based parameters, such as measures of power or signal complexity, i.e., approximate entropy, or ApEn (1,2). It has been suggested that in the seizure focus there is greater electrical volatility compared with normal tissue, which would suggest increased approximate entropy (ApEn, a measure used to quantify signal complexity) in these areas. In this study we examined the relationship between spectroscopic measures of neuronal mitochondrial function, NAA/Cr with intracranial measurements of ApEn in n=9 hippocampal epilepsy patients who underwent intracranial EEG monitoring.

Methods: Pre-operative 1H spectroscopic imaging studies of the bilateral hippocampi were all acquired at 4T using a modified LASER sequence and volume TEM head coil. Shimming was performed using an internally written field mapping procedure as previously described (3). The SI was acquired with 24x24 encoding (1 average, 19.2cm^2 FOV), 10mm thick slice with nominal voxel size of 0.64cc. A semi-automated single voxel reconstruction was used to optimize consistency of voxel selection between patients (3).

Patients/EEG: All patients were undergoing surgical evaluation for seizure localization with intracranial electrode monitoring. Chronically placed depth electrodes were stereotactically implanted using MRI guidance and a computerized planning system. To ascertain final electrode locations, contacts were marked on postoperative CT scans and coregistered to post-, pre-operative MRI scans. Digital intracranial EEG data were acquired using a commercial EEG system (Biologic Systems Corp.) with up to 1024Hz sampling and 100dB CMRR amplification. ApEn measures the (logarithmic) likelihood that runs of patterns that are close (within a specified value r) for m observations remain close (within the same tolerance width r) on next incremental comparisons (4). Two input parameters, m=2 and r=20% of the SD of an individual's variability, are specified to compute the ApEn and is thus model invariant. ApEn estimates of icEEG 1sec segments were averaged over a period of 1hr taken during wakefulness and before medication withdrawal to provide optimal comparison to imaging data.

Results: Typical spectra from the hippocampus from an epilepsy patient is shown Figure 1A. Studying 9 hippocampal epilepsy patients (two patients with bilateral probes), we identified a negative correlation between the ApEn of background hippocampal icEEGs and NAA/Cr (Figure 1B), R=-0.86, p<0.001. This relationship would be consistent with the view that worsening mitochondrial function as reflected by decreased NAA/Cr characterizes those regions with increasing ApEn and greater seizure likelihood.

Discussion: The ApEn measurement, as a parameter of electrical volatility has been increasingly pertinent in the evaluation of epilepsy as an in vivo electrophysiologic evaluation of cerebral activity. The present data further argue that the ApEn of hippocampal icEEG, determined at a time distinct from seizure onset, intrinsically demonstrates a signal complexity that correlates with neuronal mitochondrial function of the region. This suggests that mitochondrial function is a key factor governing the consistent and normal flow of neurotransmission (lower ApEn in healthier tissue), and that in epilepsy increasing mitochondrial injury progressively results in a higher likelihood for neurotransmission volatility.

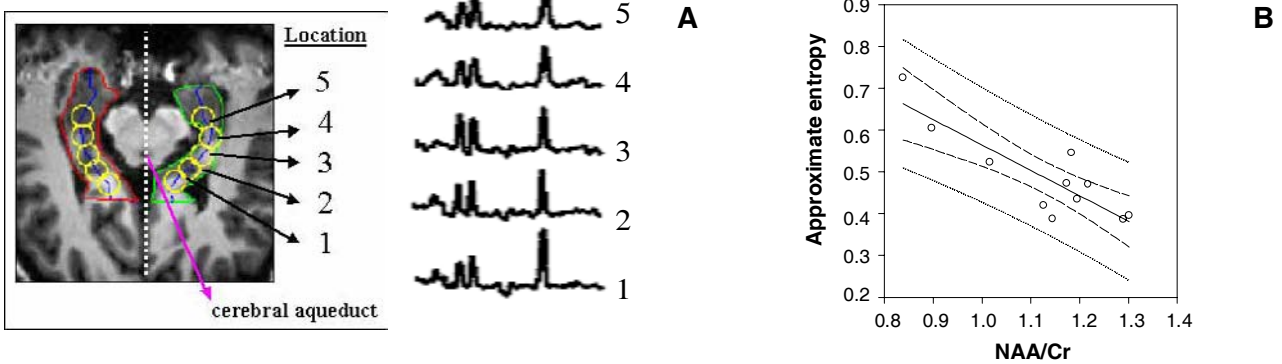

Figure (A). Hippocampal loci and spectra; (B) Correlation between NAA/Cr with ApEn

References. 1. Lehnertz and Elger, EEG and Clin Neurophys 1995; 2. Pijn et al Brain Topogr 1997; 3 Chu et al 2004 ISMRM Kyoto Japan; 4 Pincus SM. PNAS USA 1991;88:2297-2301