Epilepsy Research (2009) **87**, 18—24

journal homepage: www.elsevier.com/locate/epilepsyres

Intracranial EEG power and metabolism in human epilepsy

J.W. Pan[a,b,*], **H.P. Zaveri**[b], **D.D. Spencer**[a], **H.P. Hetherington**[a,c], **S.S. Spencer**[b]

[a] *Department of Neurosurgery, Yale University School of Medicine, New Haven, CT 06520, USA*
[b] *Department of Neurology, Yale University School of Medicine, New Haven, CT 06520, USA*
[c] *Department of Radiology, Yale University School of Medicine, New Haven, CT 06520, USA*

Received 17 December 2008; received in revised form 24 March 2009; accepted 15 July 2009
Available online 20 August 2009

KEYWORDS
Intracranial EEG;
Gamma power;
N-acetyl aspartate;
Human

Summary EEG power and high frequency activity in the seizure onset zone has been increasingly considered for its relationship with seizures in animal and human studies of epilepsy. We examine the relationship between quantitative EEG measures and metabolic imaging in epilepsy patients undergoing intracranial EEG (icEEG) analysis for seizure localization. Patients with mesial temporal lobe epilepsy (MTLE) and neocortical epilepsy (NE) were studied. Metabolic imaging was performed with MR spectroscopic imaging using N-acetyl aspartate (NAA) and creatine (Cr). All data were acquired from the mesial temporal lobe such that a direct comparison of the same anatomical regions between the two groups could be performed. While no difference was seen in the total power recorded from the mesial temporal lobe, the MTLE group had significantly greater power in the high frequency bands. There was a significant positive exponential relationship between total icEEG power with NAA/Cr in MTLE, $R = +0.84$ and $p < 0.001$, which was not seen in NE. There was also a significant negative relationship between fractional gamma power with NAA/Cr in MTLE, $R = -0.66$ and $p < 0.02$, also not seen in NE. These data argue that within the seizure onset zone, the tight correlation between total power and NAA/Cr suggests that total electrical output is powered by available mitochondrial function. These data are also consistent with the hypothesis that high frequency activity is an abnormal manifestation of tissue injury.

Introduction

Over the past decade, much work in quantitative intracranial EEG has focused on developing and understanding measures for seizure localization and prediction (Mormann et al., 2007; Iasemidis et al., 2005). More recently there has been greater interest on high frequency activity, for its

* Corresponding author at: Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06520-8082, USA.
Tel.: +1 203 785 4802; fax: +1 203 785 6702.
E-mail address: jullie.pan@yale.edu (J.W. Pan).

0920-1211/$ — see front matter © 2009 Elsevier B.V. All rights reserved.
doi:10.1016/j.eplepsyres.2009.07.006

possible specificity to the seizure onset zone (Urrestarazu et al., 2007; Bragin et al., 2002), and manifestation of synaptic re-organization in the seizure onset region (Staba et al., 2007; Worrell et al., 2008). However, there is relatively less known in terms of the basic quantitative intracranial EEG measures and their relationships to parameters of tissue injury in different patient groups. Zaveri et al. (2001) studied a group of 14 medial temporal lobe epilepsy (MTLE) patients with and without sclerosis to evaluate their neuropathology with respect to quantitative EEG. They reported that the intracranial EEG (icEEG) measures of total and delta power were significantly lower in those with sclerosis in comparison with MTLE patients without sclerosis. While this latter observation may seem counter-intuitive, it suggested that tissue loss intrinsically decreases total EEG power. Interictal discharges have been related to a range of measures, including SPECT and metabolic MR imaging (Guillon et al., 1998; Guye et al., 2002), which as a clinical measure of brain irritability has been suggestive. More recently, Bartolomei et al. (2008) studied $n = 17$ MTLE patients with icEEG, finding that a time dependent ratio of high to low band power (denoted by ''epileptogenicity index'') was greater in the seizure onset zone and also in MR negative patients.

In this report we develop further the notion of the role of different EEG power bands and how they may be influenced by tissue injury and metabolic dysfunction. We do this by examining $n = 26$ epilepsy patients undergoing intracranial EEG study for seizure localization. All data were acquired from the medial temporal lobe as it is a common site of study and seizure onset. 14 of these patients were ultimately determined to suffer from neocortical epilepsy with or without dual pathology, and 12 from medial temporal lobe epilepsy. As these patients were studied in the context of an ongoing program of metabolic imaging, 22 of these patients also had MR spectroscopic (MRS) studies of NAA/Cr available as a measure of tissue function and injury (Vermathen et al., 2002; Pan and Takahashi, 2005). NAA synthesis is localized to neuronal mitochondria and known to correlate with ATP synthesis rates as shown in in vitro models of mitochondrial function (Bates et al., 1996; Heales et al., 1995). Such in vivo metabolic measurements have previously been correlated with a variety of cognitive performance scales, most pertinently being linked with memory (Chao et al., 2005; Pan et al., 2001). Comparison of these data from the 2 patient groups provides a consistent evaluation of how the medial temporal lobe behaves electrically and metabolically when it is or is not the site of seizure onset. We determined the interictal power values (total power and power in delta, theta, alpha, beta and gamma frequency bands) and Teager energy, a high frequency weighted evaluation of signal energy (Kaiser, 1990).

Methods

Patients

Patients (age 18—55) from the Yale University Epilepsy Surgery Program undergoing intracranial EEG (icEEG) monitoring for surgical evaluation were invited to participate in the MR imaging protocols as approved by the Yale Human Investigations Committee (HIC). Only patients with medial temporal lobe contacts (strips and/or depths, Ad-Tech Medical, Racine, WI) were included in this analysis. There was a total of 26 patients, $n = 12$ medial temporal lobe epilepsy (MTLE) patients and $n = 14$ neocortical epilepsy with or without dual pathology patients (Table 1). MTLE patients were defined by location of electrical seizure onset. Patients with dual pathology ($n = 4$) were classified with the neocortical group and were defined based on clinical, surgical and histologic criteria: $n = 3$ patients #19, #20 and #21 who had a neocortical resection in addition to the standard medial temporal lobe resection; $n = 1$ patient #16 who underwent medial temporal lobe resection with no effect on seizure frequency and showed heterotopic neurons in their pathology. 23 of the 26 patients ($n = 12$ MTLE, $n = 11$ neocortical epilepsy) had completed temporal lobe metabolic imaging studies. Of the 12 MTLE patients, 7 had MRI-detected hippocampal atrophy and 5 were MRI negative. Of the 14 neocortical epilepsy patients, all 4 classified as dual pathology had MRS data; 10 were without dual pathology of which 6 had MRS data. Because all data were acquired from the medial temporal lobe, we also denote the MTLE group as ''within-seizure-zone'' group; the neocortical group as ''outside-seizure-zone'' group.

icEEG data acquisition

The intracranial electrodes in this study were placed under stereotactic guidance and included a combination of strip and depth electrodes. The subdural strip electrodes are 4 mm diameter platinum disks (2.3 mm exposed surface diameter) with an inter-contact (center-to-center) distance of 10 mm. The depth electrodes are 2.3 mm length platinum contacts with an inter-contact (center-to-center) distance of 10 mm. Patients are monitored continuously using a commercial EEG acquisition and storage system (Bio-logic Systems Corp., Mundelein, IL). Up to 128 channels of EEG are recorded with 256 Hz sampling and stored in digital form along with a time synchronized video signal of the patient. Offline analysis is performed with custom software written in a mixture of high level languages and MATLAB (The Math Works Inc., Natick, MA). Intracranial EEG epochs, 1 h in duration, at least 6 h removed from a seizure, are selected for analysis. The epoch is selected from either day 2 or day 3 of the monitoring (that is, 3 or 4 days after surgery to place intracranial electrodes). The measurements are made during wakefulness, typically either between 9 and 10 AM or between 4 and 5 PM. The icEEG is examined for artifacts which are marked at a 1-s resolution. Power and Teager energy of artifact free icEEG segments is obtained for each electrode contact studied and averaged over the epoch. Delta power was assigned 0—4 Hz, theta 4—8 Hz, alpha 8—13 Hz, beta 13—24 Hz, and gamma 24—50 Hz bands. The total power is calculated as the signal power between 0.1 and 50 Hz, and power in the frequency bands is calculated after Fourier transform of the data and as the average of the power within the frequency bands defined above. As a result, direct summation of the frequency band powers does not match the total power; however after scaling of the bands to the number of frequencies in each band they do. Because typically one to three contacts were available in the medial temporal lobe for each patient, data from all such contacts were averaged for each subject prior to further analysis. Given the variety of final locations of contacts, we did not further subdivide our patient group based on location of EEG contacts. The majority of contacts studied were located in the pes and body of the hippocampus. We did consider evaluating spike activity with the power measures. However, the objective detection of spike activity is technically problematic given the variability in the electrode spatial coverage, in contrast to the relative consistency of the quantitative power measures and was not a main goal of this investigation.