Electrophysiological Analysis Comparing Epileptogenic Human Cortex and Hyperexcited Rat Cortex

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Abstract

Introduction: Epilepsy is characterized by highly synchronized paroxysmal bursts of activity within aberrant networks of cortical neurons. A central task in epilepsy research is to elucidate the network-level mechanisms responsible for neuronal hyperexcitability. To address this issue, many investigators have examined electrical activity in slices of rat cortex bathed in culture medium containing high potassium, low magnesium, Bicuculline, and/or Picrotoxin to increase neuronal activity and/or reduce inhibition. However, the following question remains unanswered: how similar is the activity in excited slices of rat cortex to that in epileptogenic human cortex?

Methods: To answer this question, we compared excited slices of rat cortex (n = 10) to a slice of human parietal cortex (n = 1) obtained from the peritumoral epileptogenic zone in a pediatric patient with medically intractable seizures. For each slice, we recorded local field potential activity with a 60-channel microelectrode array for over 1 hr.

Results: Both human and rat cortex slices produced local field potential signals in the form of interictal spikes on almost all electrodes. However, unlike rat cortex, human cortex was spontaneously active in normal cerebrospinal fluid. Moreover, the activity from the human slice showed a high degree of synchrony across electrodes, which was not present in rat cortex.

Conclusions: Although these results are preliminary, they suggest that hyperexcited slices of rat cortex may fail to capture some important features of network activity found in epileptogenic human cortex. Further studies are currently underway to evaluate this hypothesis more completely.

Introduction

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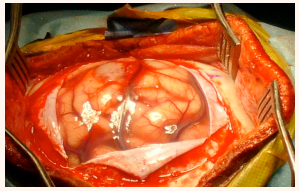
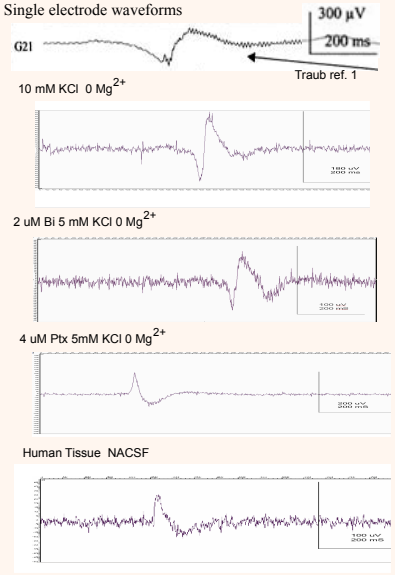
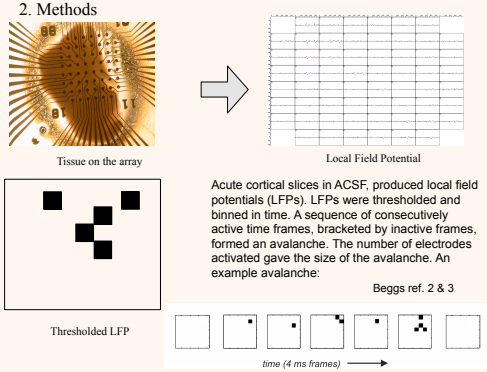


Fig. 1: Exposed cortical surface from 15 yo boy with medically refractory Seizures undergoing surgery for resection of seizure focus

1. Single electrode waveforms



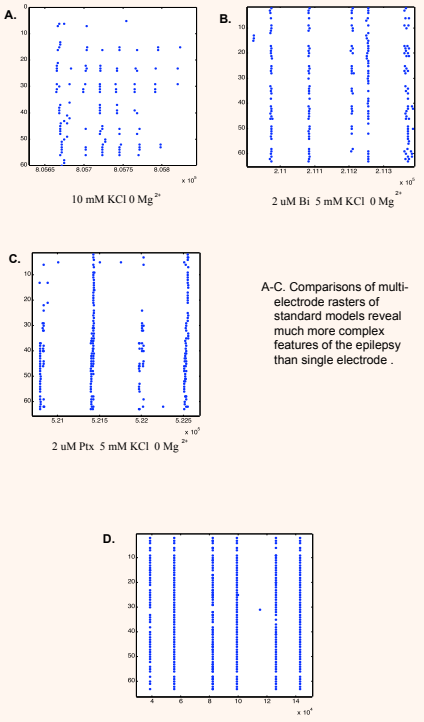
2. Methods



Acute cortical slices in ACSF, produced local field potentials (LFPs). LFPs were thresholded and binned in time. A sequence of consecutively active time frames, bracketed by inactive frames, formed an avalanche. The number of electrodes activated gave the size of the avalanche. An example avalanche:

Beggs ref. 2 & 3

3. Raster plots reveal degree of synchrony in a large network

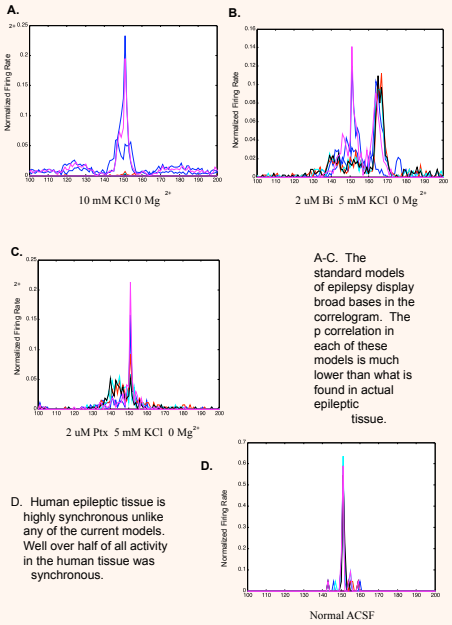


A-C. Comparisons of multi-electrode rasters of standard models reveal much more complex features of the epilepsy than single electrode .

D. The Raster plot of the human epileptic tissue is more synchronous than the other data from hyperexcited rat tissue

*It is also important to note that the human epileptic tissue was bathed in normal ACSF.

4. Correlograms of firing



A-C. The standard models of epilepsy display broad bases in the correlogram. The p correlation in each of these models is much lower than what is found in actual epileptic tissue.

D. Human epileptic tissue is highly synchronous unlike any of the current models. Well over half of all activity in the human tissue was synchronous.

Conclusion: Models of epilepsy based on altered cerebrospinal fluid, and altered levels of GABA transmission fail to capture some important features of human epileptogenic tissue

References:

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2. Beggs JM and Plenz D (2003). Neuronal avalanches in neocortical circuits. J Neurosci, Dec 3;23(35):11167-77.
3. Beggs JM and Plenz D (2004). Neuronal avalanches are diverse and precise activity patterns that are stable for many hours in cortical slice cultures. J Neurosci, Jun 2;24(22):5216-29.

Support: