Human *in vivo* analysis of epileptic interictal patterns generated by periventricular hetereotopic nodules

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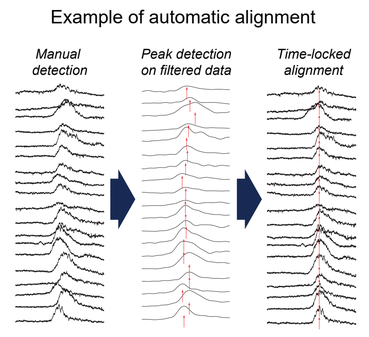
Introduction

1) Periventricular nodular heterotopia (PNH) are nodular masses of gray matter close to the walls of the lateral ventricles.
2) PNH is one of the most common forms of cortical malformation, resulting from abnormal neuronal migration.
3) Pharmaco-resistant epilepsy represents its most common clinical manifestation, affecting the majority of patients.
4) PNH generates continuous epileptic activity, even between seizures, the so-called *interictal* period.
5) How PNH generates interictal epileptic activity remains unclear, and *in vivo* human data remain lacking.

The study's goal is to provide a multi-level characterization of interictal epileptic activity from PNH nodules

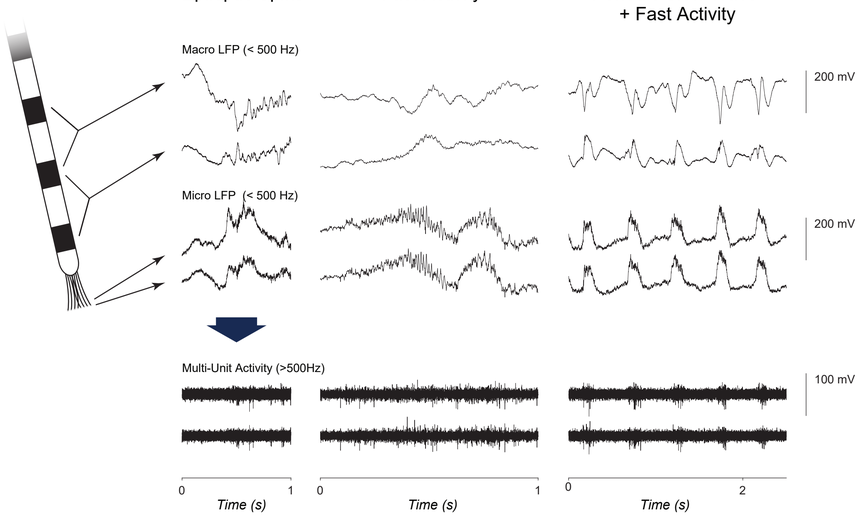
Method

1) Microelectrodes were implanted in three PNH nodules (in two patients) during long-term (3 week) pre-surgical evaluation.
2) Interictal epileptic patterns generated within the nodules were identified, characterized, then manually detected for 24 hrs. (nodule 1) or 6 hrs. (nodule 2 & 3).
3) Patterns were aligned automatically for quantatative ERP and spectral analysis[1].
4) Action-potentials were detected in 6-8 microwires per electrode.
5) Action-potentials were clustered[2] and categorized as putative single- or multi-units, based on morphology and inter-spike-interval.
6) Firing-rates were timelocked to the interictal patterns.
7) Non-parametric cluster analysis[3] were performed to test change in firing rate and spectral power versus baseline.

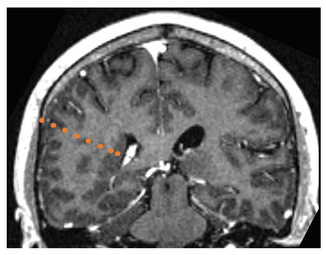


Nodule 1

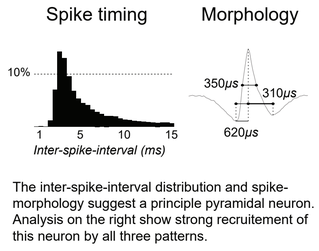
Visual Analysis



Implantation

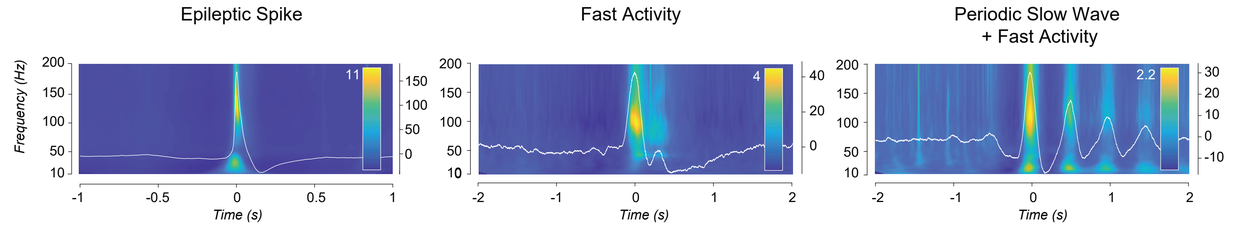


Single Units Clustering

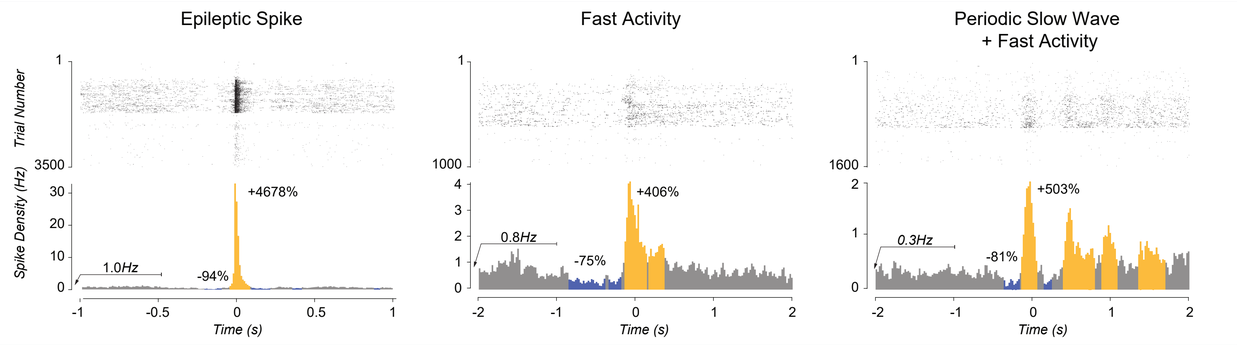


The inter-spike-interval distribution and spike-morphology suggest a principle pyramidal neuron. Analysis on the right show strong recruitement of this neuron by all three patterns.

Time-locked spectral analysis

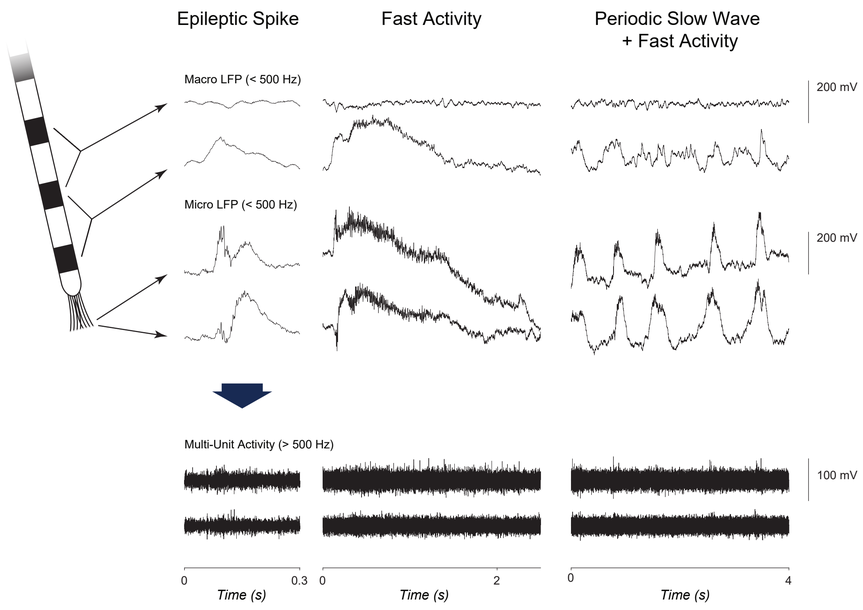


Time-locked spike analysis

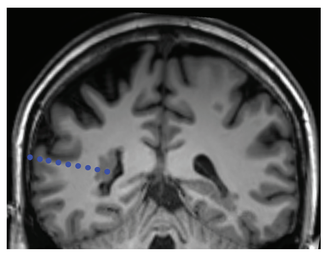


Nodule 2

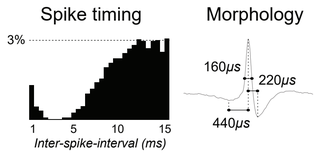
Visual Analysis



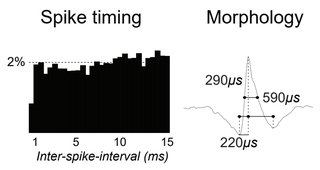
Implantation



Single Units Clustering

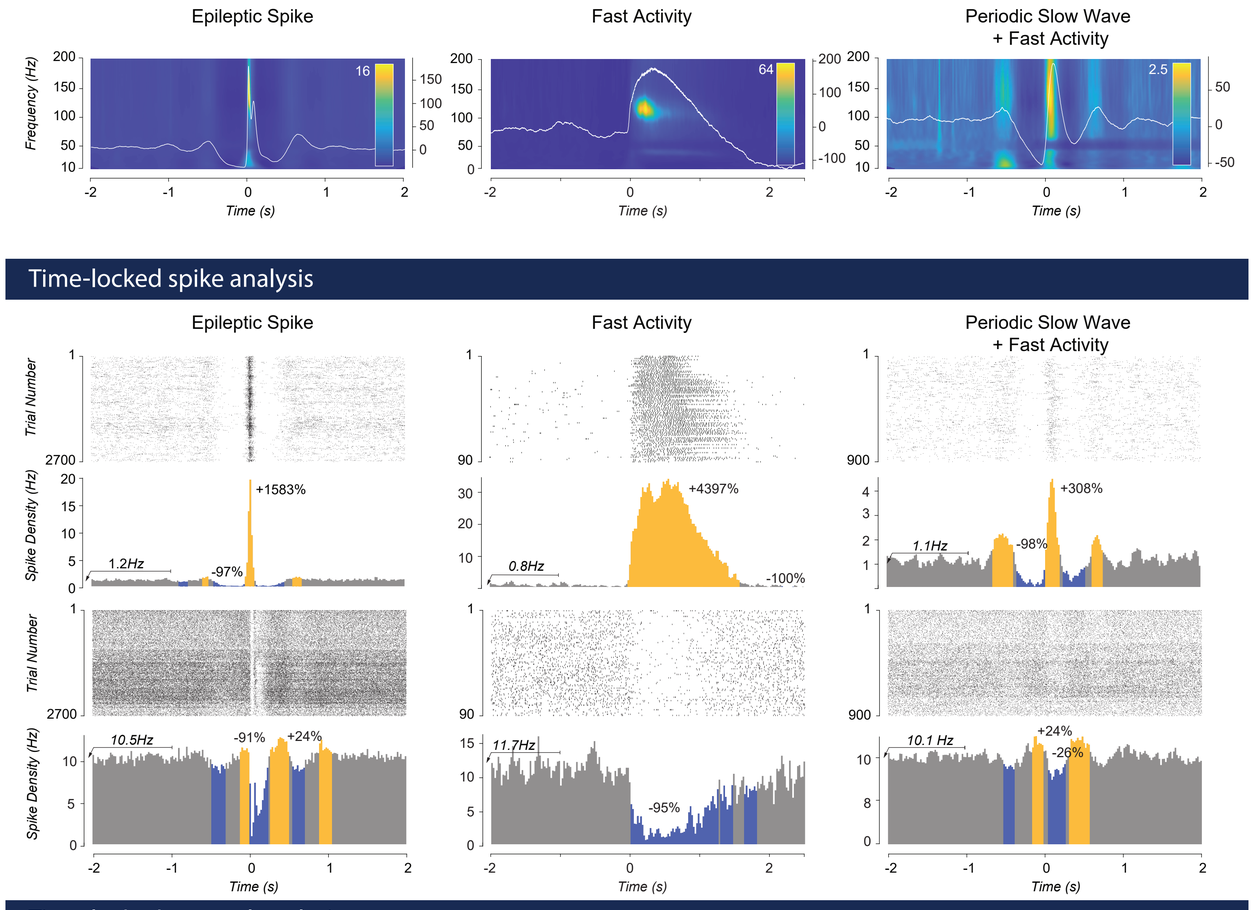


The inter-spike-interval distribution and spike-morphology suggest an interneuron. Analysis on the right show strong recruitement of this neuron by all three patterns.



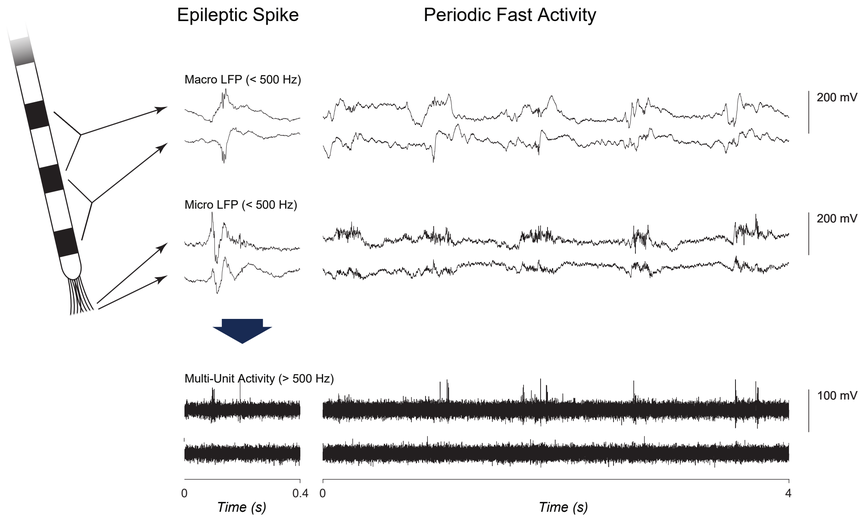
The inter-spike-interval distribution and spike-morphology suggests multiunit activity. Analysis on the right show strong suppression of this neuronin phase with all three patterns.

Time-locked spectral analysis

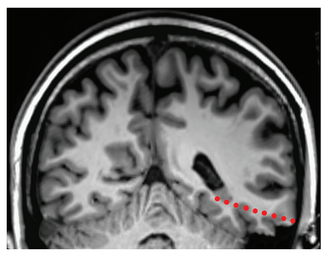


Nodule 3

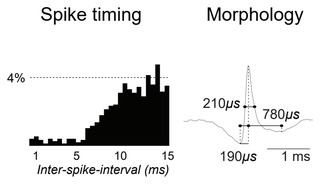
Visual Analysis



Implantation

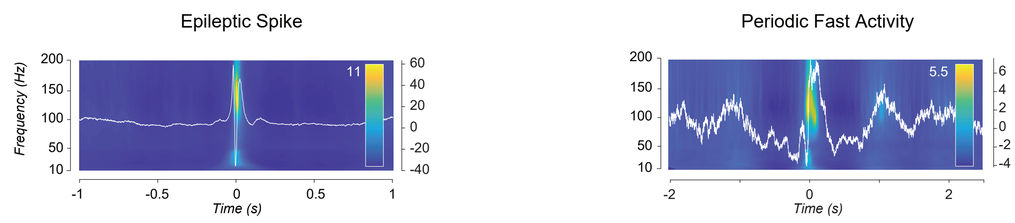


Single Units Clustering



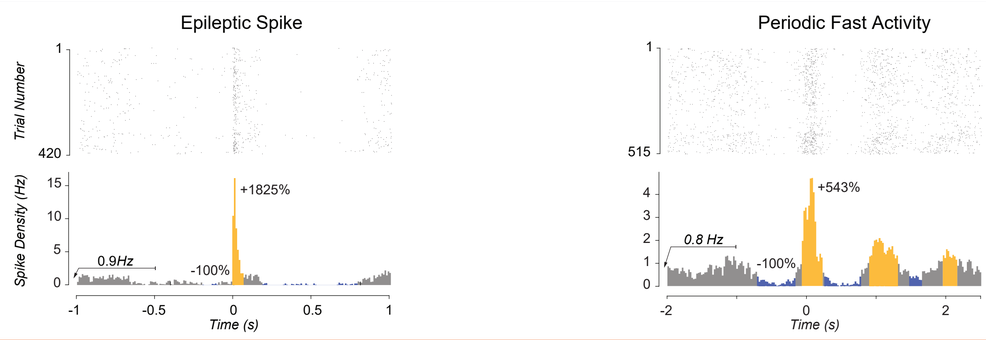
The inter-spike-interval distribution and spike-morphology suggest an interneuron. Analysis on the right show strong recruitement of this neuron by both patterns.

Time-locked spectral analysis



Nodule 3 shows a variation of the two patterns found in Nodule 1 & 2, namely periodicity of fast activity, but without clear slow deflections.

Time-locked spike analysis



Discussion

1) This study presents the first *in vivo* multi-level description of local PNH networks in humans and their organization into multiple pathological electrophysiological patterns.
2) Three different interictal LFP patterns were identified, showing striking similarities across the two patients, with both patients showing all three patterns.
3) The same neurons were recruited by - or causally involved in - the generation of different epileptic patterns.
4) Both putative principal neurons and interneurons were involved in all three patterns, suggesting the involvement of different cellular types in the epileptogenic networks. In fact, both increases and decreases in firingrate were found.

References

1) Oostenveld, R., Fries, P., Maris, E., & Schoffelen, J.-M. (2011). FieldTrip: Open Source Software for Advanced Analysis of MEG, EEG, and Invasive Electrophysiological Data. *Computational Intelligence and Neuroscience.*
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3) Maris, E. (2012). Statistical testing in electrophysiological studies. *Psychophysiology*