

Ripples recorded from mesial temporal epileptogenic brain are phase amplitude coupled to inter-ictal discharges and theta oscillations.

Weiss SA¹, Orosz I², Moy S¹, Wei LQ¹, Van 't Klooster MA⁴, Bragin A¹, Fried I³, Engel J Jr.^{1*}, Staba R^{1*}

¹Dept. of Neurology, David Geffen School of Medicine at UCLA, Los Angeles, California, U.S.A.

²Dept. of Radiology, David Geffen School of Medicine at UCLA, Los Angeles, California, U.S.A.

³Dept. of Neurosurgery, David Geffen School of Medicine at UCLA, Los Angeles, California, U.S.A.

⁴Brain Center Rudolf Magnus, Dept. of Neurology & Neurosurgery, University Medical Center Utrecht, Utrecht, The Netherlands

* denotes co-senior authorship

Rational: We hypothesized that pathological phase amplitude coupling of ripple oscillations may occur exclusively in mesial temporal epileptogenic regions.

Methods: We used an automated HFO detector to characterize coupling of the phase of the EEG (4-30Hz) with the amplitude of ripples (80-150Hz) in a cohort of 10 patients with mesial temporal lobe epilepsy (MTLE). Recordings were obtained during sleep (including SWS). We detected a total of 23,793 ripples from 545 contacts.

Results: In clinical macroelectrode recordings discrete ripple events were transformed to phasors on the basis of phase relationships with the EEG. Macroelectrode recordings from all 10 patients with MTLE exhibited statistically significant ($p < 0.05$) phase locking of ripple phasors in a subset of the electrodes. Two types of phase locking were evident, type 1: in which the ripples were phase amplitude coupled to inter-ictal discharges, and type 2: in which the ripples were coupled with predominantly theta oscillations. Both types were seen in hippocampus, amygdala, and entorhinal cortex. The probability that an electrode was in the seizure onset zone correlated with the rank order of the Rayleigh Z-statistic of the ripple phasors (a measure of phase locking strength). The precision of phase locked ripple phasors for the seizure onset zone (81%, $z = 1.87$) exceeded that of ripples across a broad range of thresholds (77.5%, $z = 2.07$).

Significance: These preliminary results show that in patients with MTLE the phase of inter-ictal discharges and theta oscillations modulates the amplitude of ripples in the seizure onset zone. Across different brain regions the strength of this phase amplitude coupling often correlates with epileptogenicity.

