Pathological High-Frequency Oscillations

Pathological High-Frequency Oscillations (HFOs) are abnormal patterns of electrical activity in the brain that occur at higher frequencies than the normal brain waves. These abnormal oscillations are often associated with neurological disorders, particularly epilepsy. Here's a breakdown:

Normal Brain Activity: Imagine your brain as a bustling city with different neighborhoods (regions) where friends (neurons) communicate by sending signals. These signals usually have a regular and rhythmic pattern.

Abnormal Electrical Activity: In some cases, especially in individuals with epilepsy, certain areas of the brain may experience abnormal bursts of electrical activity. Pathological HFOs are like rapid and irregular “chatter” among neurons in these specific brain regions.

Frequency: Pathological HFOs occur at higher frequencies than the typical brain waves. The normal brain waves have specific frequency ranges, but pathological HFOs often fall into ranges such as ripples (80-200 Hz) and fast ripples (200-600 Hz).

Association with Epilepsy: Researchers and clinicians closely study pathological HFOs because they are often found in or near the regions of the brain where seizures originate. Detecting these abnormal oscillations can help identify the specific area, known as the “seizure onset zone,” where seizures may begin.

Diagnostic and Research Significance: Monitoring and analyzing HFOs can be valuable for diagnosing epilepsy and understanding the underlying mechanisms of seizures. Researchers aim to unravel why these abnormal oscillations occur, how they spread in the brain, and how they might be targeted for therapeutic interventions.

In simpler terms, pathological HFOs are like unusual bursts of activity in certain parts of the brain, and scientists study them to learn more about epilepsy and how to develop treatments that can help people experiencing seizures.

To confirm and investigate why pathological HFOs (pHFOs), including ripples [80-200 Hz] and fast ripples [200-600 Hz], are generated during the UP-DOWN transition of the slow wave and if information transmission mediated by ripple temporal coupling is disrupted in the seizure onset zone (SOZ).

Weiss et al. isolated 217 total units from 175.95 iEEG contact hours of synchronized macro- and microelectrode recordings from 6 patients. Sleep slow oscillation (0.1-2 Hz) epochs were identified in the iEEG recording. iEEG HFOs that occurred superimposed on the slow wave were transformed to phasors and adjusted by the phase of maximum firing in nearby units (i.e., maximum UP). We tested whether, in the SOZ, HFOs and associated action potentials (AP) occur more often at the UP-DOWN transition. We also examined ripple temporal correlations using cross-correlograms.

At the group level in the SOZ, HFO and HFO-associated AP probability was highest during the UP-DOWN transition of slow wave excitability ($p \ll 0.001$). In the non-SOZ, HFO and HFO-associated AP was highest during the DOWN-UP transition ($p \ll 0.001$). At the unit level in the SOZ, 15.6% and 20% of units exhibited more robust firing during ripples (Cohen's $d=0.11$-0.83) and fast ripples ($d=0.36$-0.90)

at the UP-DOWN transition (p<0.05 f.d.r corrected), respectively. By comparison, also in the SOZ, 6.6% (d=0.14-0.30) and 8.5% (d=0.33-0.41) of units had significantly less firing during ripples and fast ripples at the UP-DOWN transition, respectively. Additional data shows ripple and fast ripple temporal correlations, involving global slow waves, between the hippocampus, entorhinal cortex, and parahippocampal gyrus were reduced by >50% in the SOZ compared to the non-SOZ (N=3).

The UP-DOWN transition of slow wave excitability facilitates the activation of pathological neurons to generate pHFOs. Ripple temporal correlations across brain regions may be important in memory consolidation and are disrupted in the SOZ, perhaps by pHFO generation [1)].

1)
Weiss SA, Fried I, Engel J Jr, Bragin A, Wang S, Sperling MR, Wong RKS, Nir Y, Staba RJ. Pathological neurons generate ripples at the UP-DOWN transition disrupting information transfer. Epilepsia. 2023 Dec 2. doi: 10.1111/epi.17845. Epub ahead of print. PMID: 38041560.