Mechanisms of Physiological and Pathological HFOs

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The progress in experimental techniques and analytical methods has led to the discovery of High-Frequency Oscillations (> 80 Hz) in the brain. Although HFOs have been widely observed and described in physiological and pathological conditions, the underlying neuronal processes are still not well understood. Physiological HFOs in the ripple band (100 – 200 Hz) have been observed in the hippocampal-entorhinal networks of rodents, monkeys and humans during quiet wakefulness and slow-wave sleep [1,2]. They usually co-occur with large-amplitude sharp waves that originate from the synchronized firing of CA3 cells and spread along the CA1–subicular–entorhinal axis [3]. Evidence of cellular mechanisms suggests that ripples are generated by the increased firing of pyramidal cells tightly regulated by interneuron perisomatic inhibition [4]. On the other hand, pathological HFOs mostly in the fast-ripple (> 200 Hz) bands are considered biomarkers of epileptogenic tissue. They have been found in patients with mesial temporal lobe epilepsy as well as in animal models of epilepsy [5,6]. They have been observed before the seizure or co-occurring with interictal and preictal epileptic discharges (IID and PID respectively). Cellular evidence suggests that they are generated by synchronous failure of perisomatic inhibition, generating a massive pyramidal cell burst firing [7,8]. However, insights of cellular mechanisms of HFOs are still controversial. In order to explore these mechanisms, we performed in vitro recordings of human epileptic subiculum [9]. We observed pathological oscillations in the ripple band (150 – 250 Hz) associated with IIDs and PIDs, similar to physiological ripples in normal mammals. Furthermore, we observed two different cellular mechanisms for these pathological oscillations in the ripple band. Some thoughts about the pathological nature of ripple oscillations will be discussed, as well as the importance of considering cellular mechanisms, spatial distribution, and co-ocurrence of other events to classify physiological and pathological HFOs.

References

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