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High-frequency oscillations are under your control. Don't chase all of them

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Investigators dedicated to epilepsy surgery have made respectable efforts to find a biomarker allowing accurate localization of the regions responsible for epileptic seizures. The candidate biomarkers include interictal high-frequency oscillations (HFOs) on electrocorticography (ECoG), and its clinical significance in epilepsy surgery has been gradually clarified during the past decade (Gloss et al., 2014; Höller et al., 2015). A number of previous studies replicated the observations of interictal HFOs frequently generated by the seizure onset zone (Jacobs et al., 2009; Akiyama et al., 2011). A substantial proportion of studies inferred that $HFOs_{>250\ Hz}$ (also known as fast ripples) may be more useful than $HFOs_{80–250\ Hz}$ (ripples) in localization of the epileptogenic zone, since fast ripples, compared to ripples, were generated by more restricted regions often including the seizure onset zone (Ogren et al., 2009). Nonetheless, refined usage of fast ripples was suggested in epilepsy presurgical evaluation, partly because fast ripples, based on visual assessment, rarely take place during interictal state, particularly in patients with neocortical epilepsy (Wang et al., 2013). Furthermore, fast ripples may be spontaneously generated by eloquent areas (Nagasawa et al., 2012; Nonoda et al., 2016).

In this issue of *Clinical Neurophysiology*, van 't Klooster et al. demonstrated the feasibility of stimulation-evoked HFOs in prediction of the seizure onset zone and eloquent cortex (van 't Klooster et al., 2017). A total of 10 single-pulse electrical stimuli were delivered to each pair of subdural electrodes implanted on the affected hemisphere. Occurrence of delayed HFOs (i.e.: those occurring at >100 ms after stimulus)was treated as a measure reflecting increased epileptogenicity. The team found that single-pulse stimulation evoked delayed fast ripples consistently across patients with and without spontaneous fast ripples, and that delayed fast ripples predicted the seizure onset zone with accuracy equivalent to that of spontaneous fast ripples. The current study, together with previous work (Valentín et al., 2005; Alarcón et al., 2012; Nayak et al., 2014), provided evidence that single-pulse stimulation paradigms can quantify the diverse profiles of HFOs in a rapid and controlled manner and can play a role in directing the surgical decision.

A unique aspect of the current study is that the team analyzed HFO measures within the eloquent areas defined by conventional 50-Hz stimulation mapping (Nonoda et al., 2016).

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They found that both spontaneous and stimulation-evoked fast ripples involved portions of the eloquent areas, and that none of the analyzed pro-files satisfactorily distinguished epileptogenic from physiologic HFOs. This observation supports the notion that the resection margin should not be determined solely based on the spatial extent of interictal fast ripples (Asano et al., 2013). The authors also emphasized that one should utilize HFO biomarkers with care by taking into account the clinical context of each patient (van ’t Klooster et al., 2015). Don’t try to remove HFO regions blindly.

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