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Letter to the Editor

What are you looking at? Unrippling terminology for high frequency activity

During the last decades, epilepsy researchers have been increasingly interested in brain activity above the traditional 0.3–70 Hz band. Pathological high-frequency oscillations (HFOs; ripples (80–250 Hz) and fast ripples (250–500 Hz)) were first discovered ictally and interictally in epileptic rats and humans implanted with intracranial micro- and macroelectrodes. HFOs turned out to be also visible on scalp electroencephalography (EEG) and magnetoencephalography. Pathological HFOs seem biomarkers of the epileptogenic zone and may thus be of value in epilepsy surgery candidates. Scalp HFOs may help to monitor disease activity and predict therapy response and prognosis. Physiological HFOs also exist and are involved in cognitive processing and used to map brain function. How to reliably distinguish pathological and physiological HFOs remains a problem to be solved. Visual analysis of the high-pass filtered EEG in the time domain and time-frequency analysis (TFA) are mostly used to study high frequencies. Both methods have been compared in the past, and visual analysis may yield more clinically relevant information than TFA (Jacobs et al., 2016).

We note that different high frequencies terms exist, but also that the same term (HFOs) is used for different phenomena in the growing literature on this topic. In this letter, we will propose a distinction between high frequencies subtypes, and give examples of pathological and physiological subtypes in the high-pass filtered time and time-frequency domain.

We propose to use high-frequency activity (HFA) as the umbrella term of all brain activity above 80 Hz. Subsequently, HFA subtypes can be distinguished based on their duration, and on whether and how they show in the time domain and/or the time-frequency domain (Fig. 1).

We define HFOs as discrete EEG or magnetoencephalography events that consist of at least four oscillations that clearly stand out from the background pattern (Fig. 1A and B). This definition prevents marking the typical 'ringing' caused by filtering of sharp events or artifacts as HFOs. An HFO may show as (short-lasting) narrow-band HFA on a time-frequency plot (Fig. 1A and B). Fast ripples may have a too short duration and too low amplitude to show clearly in time-frequency plots.

HFOs have a minimum duration of 50 milliseconds (four oscillations of 80 Hz), but no maximum duration has been defined. Interictal HFOs are typically short (<200 ms), but at seizure onset, pathological HFA can be (semi-)continuous and last longer. We have also seen that channels in the hippocampus and the functionally eloquent cortex, such as the motor and occipital cortex, may show interictal (semi-)continuous waxing-and-waning HFA in the time domain, which can be considered physiological (Melani et al., 2013). Values between 200 and 500 ms have been used in the past to differentiate interictal (semi-)continuous HFA and longer ictal HFOs from the typical short ones (Ochi et al., 2007; Modur et al., 2011; Melani et al., 2013). We propose to use a duration of 200 ms to distinguish the typical short HFOs from longer phenomena, because the typical interictal epileptiform discharge (IED) and HFO do not last longer than 200 ms (Jacobs et al., 2008). We propose to use the term prolonged HFA for oscillating high-frequency (>80 Hz) brain activity visible in the time domain of more than 200 ms (Fig. 1C and D). In the time-frequency domain, prolonged HFA may show as narrow-band HFA of a longer duration.

As mentioned, HFOs often show narrow-band HFA in a time-frequency plot. Brain signals with mixed low and high frequencies - without clear HFOs in the high-pass filtered EEG - may also show HFA in the time-frequency domain, but this will often be broad-band HFA instead of narrow-band HFA. We propose to call high-frequency (>80 Hz) spectral power increases without clear HFOs in the time domain high-frequency augmentation (HF augmentation). HF augmentation can occur both physiologically and pathologically, for example in somatosensory evoked potentials and as delayed responses to cortical single pulse electrical stimulation, respectively (Fig. 1E and F). In these cases, HF augmentation is often averaged over multiple trials to improve the signal-to-noise ratio.

We think distinguishing the HFA subtypes - HFO, prolonged HFA and HF augmentation - is needed, because it benefits correct comparison between studies and thus scientific and clinical applicability. We hope that the proposed terms will enable the use of clear and uniform terminology.

Declaration of Competing Interest

None of the authors have conflicts of interest

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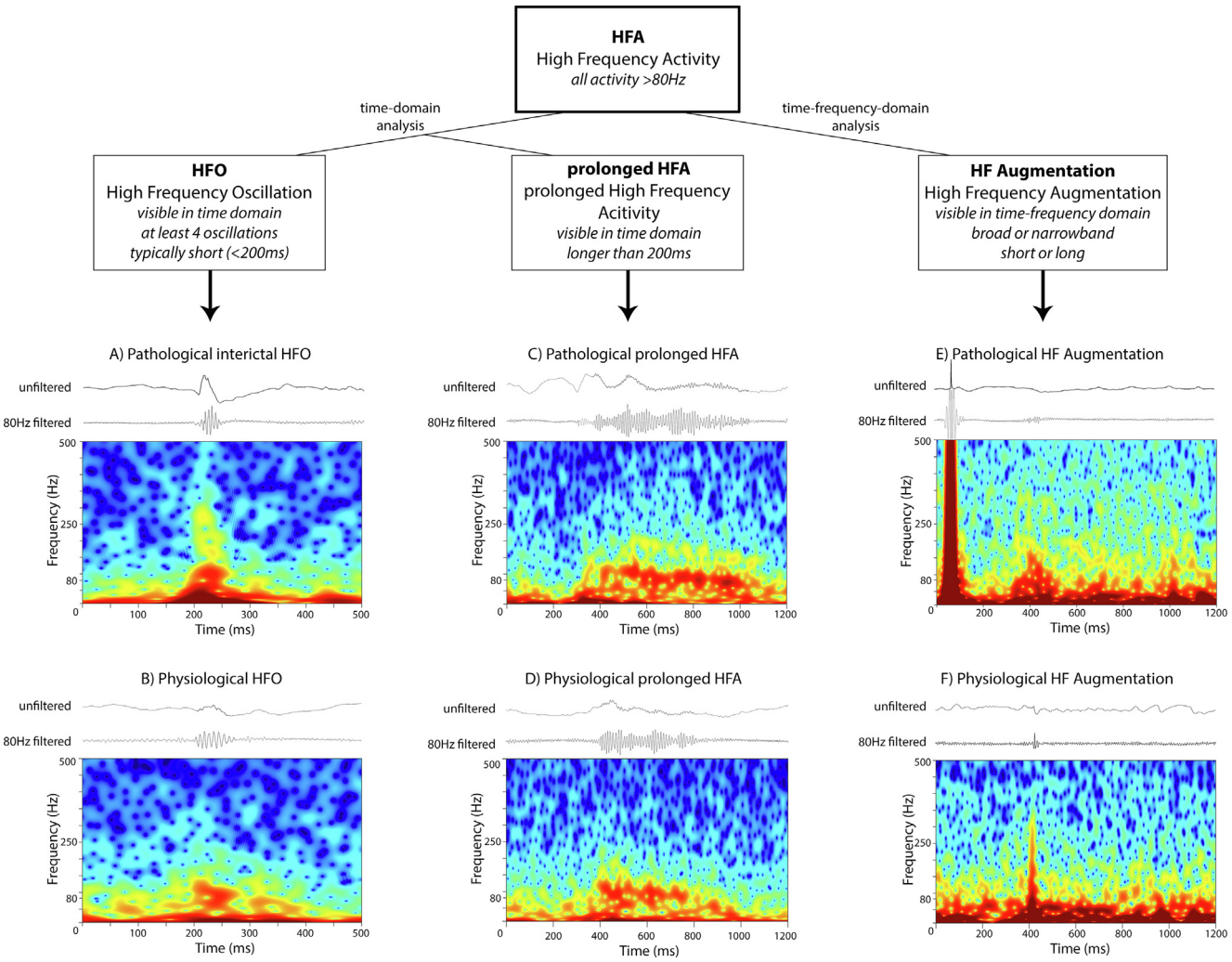

Fig. 1. Overview and examples of our proposed terminology of HFA subtypes. All examples are obtained from intracranial recordings in a 35-year old male with focal structural epilepsy associated with a gliotic lesion in the left parietal lobe with focal motor and sensory seizures, who underwent chronic electrocorticography (ECoG) and subsequently epilepsy surgery. In the subfigures, the raw (0.3–70 Hz) EEG is shown at the top, the filtered (>80 Hz) EEG in the middle, and the corresponding time-frequency plot at the bottom. (A) Pathological HFO during sleep from a channel in the epileptogenic zone. A spike is seen in the raw EEG. The HFO shows in the time-frequency plot as narrow-band HFA or a so-called a high-frequency blob. (B) Physiological HFO from a channel in the primary motor cortex during sleep. The physiological HFO also shows in the time-frequency plot as narrow-band HFA or a high-frequency blob. (C) Pathological prolonged HFA during a cluster of focal motor (tonic) seizures during sleep from the same channel as shown in (A) (epileptogenic zone). Sharp waves and gamma activity are seen in the raw EEG. The prolonged HFA shows in the time-frequency plot as narrow-band HFA of a longer duration (672 ms). (D) Physiological prolonged HFA during sleep from the same channel as shown in (B) (primary motor cortex). The prolonged HFA also shows in the time-frequency plot as longer narrow-band HFA (384 ms). (E) Pathological HF augmentation following cortical single pulse electrical stimulation with delayed responses from a channel over the gliotic lesion. The stimulation artefact is seen in the raw EEG. No clear HFO is seen in the filtered EEG. The time-frequency plot of a single trial shows HF augmentation around 400 ms. For clinical interpretation, time-frequency plots of ten trials could be averaged and analyzed using event-related spectral perturbation, in which (for each frequency) the post-stimulus brain activity is compared to the pre-stimulus baseline (not shown). (F) Physiological HF augmentation during somatosensory evoked potentials from a channel in the primary sensory cortex. The filtered EEG shows high-frequency activity that does not fulfil the criteria for an HFO (less than four oscillations). The time-frequency plot of a single trial shows broad-band HF augmentation around 400 ms. For clinical interpretation, time-frequency plots of all trials could be averaged and analyzed using event-related spectral perturbation (not shown).

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