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Effect of sampling rate and filter settings on High Frequency Oscillation detections

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HIGHLIGHTS

- Sampling rate and anti-aliasing filters (AAF) affect High Frequency Oscillation (HFO) detection.
- Sampling rate ⩾2 kHz and AAF ⩾500 Hz should be used to analyze HFOs; lower settings are still useful.
- Calculating peak HFO frequency is unreliable and highly dependent upon the sampling rate.

ABSTRACT

Objective: High Frequency Oscillations (HFOs) are being studied as a biomarker of epilepsy, yet it is unknown how various acquisition parameters at different centers affect detection and analysis of HFOs. This paper specifically quantifies effects of sampling rate (FS) and anti-aliasing filter (AAF) positions on automated HFO detection.
Methods: HFOs were detected on intracranial EEG recordings (17 patients) with 5 kHz FS. HFO detection was repeated on downsampled and/or filtered copies of the EEG data, mimicking sampling rates and low-pass filter settings of various acquisition equipment. For each setting, we compared the HFO detection sensitivity, HFO features, and ability to identify the ictal onset zone.
Results: The relative sensitivity remained above 80% for either FS ⩾2 kHz or AAF ⩾500 Hz. HFO feature distributions were consistent (AUROC < 0.7) down to 1 kHz FS or 200 Hz AAF. HFO rate successfully identified ictal onset zone over most settings. HFO peak frequency was highly variable under most parameters (Spearman correlation < 0.5).
Conclusions: We recommend at least FS ⩾2 kHz and AAF ⩾500 Hz to detect HFOs. Additionally, HFO peak frequency is not robust at any setting: the same HFO event can be variably classified either as a ripple (<200 Hz) or fast ripple (>250 Hz) under different acquisition settings.
Significance: These results inform clinical centers on requirements to analyze HFO rates and features.

1. Introduction

High Frequency Oscillations (HFOs) are short, rare events with high power in approximately 80–500 Hz and have been suggested as a biomarker of epilepsy (Bragin et al., 2002; Engel et al., 2009; Wu et al., 2010; Blanco et al., 2011; Park et al., 2012; Haegelen et al., 2013; Kerber et al., 2014). Research often focuses on HFOs as a biomarker of ictal onset tissue (Cho et al., 2014; Dumpelmann et al., 2014; Malinowska et al., 2014; Okanishi et al., 2014; Gliske et al., 2016). HFOs have also been considered as a biomarker of a pre-ictal state (Pearce et al., 2013; Malinowska et al., 2014). Most prior HFO studies require offline processing of high temporal resolution EEG. This processing is either done manually (Urrestarazu et al., 2007) or using automated algorithms (Blanco et al., 2011; Pearce et al., 2013; Gliske et al., 2016). However, as HFOs have gained considerable favor as a potential clinical biomarker (Jacobs et al., 2012), the need to implement them in the clinical realm is becoming more pressing. Regardless of the mechanism by which HFOs become available to more clinicians, it is imperative to account for the inevitable differ-

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ences that exist between different acquisition systems. The most obvious example is that many HFO studies utilized high temporal resolution acquisition systems sampling up to 30,000 Hz, yet now many EEG companies are offering sampling rates of 1000–16,000 Hz within the clinical hardware—will these newer clinical systems successfully record HFOs? The objective of this paper is to analyze this question by quantifying how sampling rate and anti-aliasing filter (AAF) parameters affect HFO detection and analysis. We then propose guidelines that will assure acquisition equipment has sufficient accuracy to allow comparison with past HFO research.

In order to compare the effect of various sampling rates on the same data set, we analyze "gold standard" 5 kHz intracranial EEG data, then perform similar analyses on the same data after downsampling and/or low-pass filtering to simulate different acquisition parameters. In this manner, we can directly compare each HFO detection in the original 5 kHz data sample with the HFO detections at the other sampling rates and AAF settings. This analysis allows direct comparison of the number of HFOs detected in each paradigm, using each channel as its own internal gold standard. It also provides insight into how acquisition settings affect HFO correlation with patient outcomes and the measured signal properties of the HFOs. This paper utilizes data from 17 patients from two centers, representing 1.5 million interictal HFOs at 5 kHz and over 68 days of interictal recording time.

2. Methods

2.1. Patient population

EEG data from patients who underwent intracranial EEG monitoring were selected from the IEEG Portal (Wagenaar et al., 2015) and from the University of Michigan. All patients had intracranial subdural or depth electrodes manufactured by either PMT (Chanhassen, MN) or Ad-Tech (Racine, WI), with standard electrode size and spacing. From the IEEG Portal, all patient data available in May 2014 were searched for the following inclusion criteria: sampling rate of at least 5000 Hz, a recording time of over two hours including at least one hour of interictal data, data recorded with traditional, clinical intracranial electrodes, and metadata regarding the resected volume (RV) or clinically determined epileptogenic zone. Patients that had both macro- and microelectrode recordings were included, but the microelectrode data were not analyzed herein. This yielded nine patients, which had all been recorded at the Mayo Clinic using a Neurolynx (Bozeman, MT) acquisition system with sampling rate of 32 kHz and 9 kHz cutoff frequency AAF (Worrell et al., 2008), then later downsampled to 5 kHz when stored to the Portal. Of these nine patients, eight have been analyzed in previous publications (Blanco et al., 2010, 2011; Pearce et al., 2013; Gliske et al., 2016). Additionally, data from eight patients at the University of Michigan were recorded at 30 kHz (Blackrock, Salt Lake City, AAF 10 kHz) and down-sampled to 5 kHz, resulting in a total patient population of 17. Four of the eight Michigan patients were previously analyzed (Gliske et al., 2016), but with a 3 kHz rather than 5 kHz sampling rate. The downsampling procedure, used for all patients' data, included a lowpass filter at 2 kHz. Of the 17 patients, nine were known to have undergone resection with ILAE Class I surgery outcome. One of these patients had the entire region resected (MC-12), and thus eight Class I patients are usable for assessing the correlation between HFOs and RV. These eight patients are hereafter labeled the "good surgery outcome patients". For three of the Michigan patients (UM-05, UM-07, UM-08), one 24-h block of interictal data was also analyzed at 30 kHz, 15 kHz, and 10 kHz sampling rates, to verify that the chosen 5 kHz "gold standard" sampling rate is sufficiently high.

All patients were adults with refractory epilepsy who underwent long-term monitoring in preparation for resective surgery. All data were acquired with approval of local IRB and all patients consented to share their deidentified data. Further details about the patient population and attribution for studies on the IEEG portal are provided in Table 1.

For each patient, the RV was determined based on official clinical reports, written by the treating physicians/surgeons. Patients UM-02 and UM-03 had multiple subpial transections in addition to resection, as the clinical ictal onset zone was found to extend to eloquent areas. For the purposes of this paper and identifying the ictal onset zone, these regions are considered part of the RV as they represent surgically modified regions. We also note that, while HFOs are used in a pseudo-prospective fashion to identify the ictal onset zone prior to resection, the verification is performed after surgical resection, in which case it is actually the theoretical "epileptogenic zone" that has been removed, which may be larger than the clinical onset zone (Luders et al., 2006). However, for the remainder of this paper only the term "ictal onset zone" will be used for simplicity.

2.2. HFO detections

To investigate the effect of sampling rate on HFO detections, the 5 kHz data were down-sampled to either 500 Hz, 1 kHz, 2 kHz, 2.5 kHz, or 4 kHz. We chose these values to span the common range of acquisition equipment that might be considered for HFO detections. For sampling rates that are downsampled by an integer factor, the Matlab (Mathworks, Natick, MA) function downsample was used, which applies a Chebyshev lowpass filter at 0.4 times the desired frequency as an AAF and then resamples the data at a given integer factor. For the other two sampling rates (2 kHz and 4 kHz), a custom function was designed using identical filters but including linear interpolation in the resampling step. The qHFO detection method (Gliske et al., 2016) was applied to the 5 kHz data to establish a gold standard for HFOs, artifacts, and data quality. This method was previously manually validated by expert reviewers, using patients from both centers that were included among the patient cohort of this study (Gliske et al., 2016). The qHFO method utilizes a common average reference, calculates baseline HFO detections with a sensitive HFO detector (in this case, the Staba HFO detector (Staba et al., 2002)) then excludes those detections that are coincident with automatically-detected artifacts and low-quality data. Note, the Staba detector identifies HFOs by using a bandpass filter in 80–500 Hz, and identifies times where the rectified signal is over five standard deviations from baseline, rejecting detections with less than 6 peaks. For sampling rates other than 5 kHz, the HFO detection step was performed independently on the data from each sampling rate, but the same set of artifact and data-quality detections from the 5 kHz data are used, rather than recomputing all of these detections at the lower sampling rate. The rationale is that the focus of this work is the effect of sampling rate upon just the HFO detections, and we desired to remove the confounding factor of the sampling rate's effect upon the data quality assessment. Note, the Staba HFO detector utilizes a bandpass filter with an upper threshold of 500 Hz. In cases where 500 Hz was above the Nyquist frequency, 0.4 times the sampling rate was used as the upper edge for the band pass filter to compute Staba detections. To investigate the effect of the AAF, Staba HFO detections were again computed using the 5 kHz data, but in this case an additional lowpass filter was applied before using the Staba HFO detector. A 10th order, bidirectional Butterworth filter was used to apply AAFs at nine positions spanning 100 Hz to 1 kHz. Note that these calculations used the original 5 kHz data without any of the above downsampling. The type and order of filter is representative of filters commonly used in commercial acquisition