

Unsupervised Detection of Epileptiform Activity for Real-Time Closed-Loop Neurofeedback in Epilepsy

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Introduction

Epilepsy is increasingly recognized as a network-level disorder characterized by dynamic fluctuations in pathological brain activity. Real-time neurofeedback and closed-loop neuromodulation approaches offer the potential to continuously monitor these fluctuations and deliver adaptive interventions.

However, most existing AI systems for epileptiform activity detection rely on supervised learning methods that require large expert-labeled datasets, limiting scalability and clinical deployment.

Beyond the machine-learning challenge itself, developing a practical closed-loop system for epilepsy remains technically demanding. Such systems must continuously acquire and process neural signals, perform causal real-time preprocessing, identify pathological activity with millisecond-scale temporal resolution, estimate evolving brain states, and generate appropriate feedback decisions under strict latency and safety constraints. These requirements create significant challenges for translating computational biomarkers into operational neurofeedback systems.

To address these challenges, we developed an unsupervised machine-learning framework capable of identifying interictal epileptiform discharges (IEDs) directly from intracranial EEG recordings without expert-provided labels and integrated it into a real-time closed-loop neurofeedback platform. The objective of this work was to evaluate the feasibility of combining label-free epileptiform activity detection with continuous neurofeedback delivery in a real-time operational environment.

Methods

Several days of stereo-EEG (SEEG) recordings from patients with drug-resistant epilepsy were analyzed. The processing pipeline consisted of signal preprocessing, artifact reduction, feature extraction based on epileptiform morphology, and unsupervised clustering to identify high-probability IED events.

The detection engine was integrated into EpiXApp, a modular closed-loop neurofeedback platform designed for real-time EEG acquisition, causal signal preprocessing, event detection, pathological burden estimation, adaptive decision-making, and feedback delivery. The platform continuously processes incoming neural activity and transforms detected pathological patterns into feedback signals according to configurable decision rules and safety constraints. Particular emphasis was placed on maintaining real-time operation while preserving clinically relevant temporal resolution required for closed-loop applications.

To validate the detection component, outputs were compared with independent epileptologist annotations using precision, recall, and Cohen's kappa. In parallel, end-to-end latency, stability, and operational performance of the real-time closed-loop workflow were evaluated.

Results

The unsupervised model successfully identified clusters corresponding to clinically meaningful epileptiform activity, including isolated spikes and multi-channel discharges. Comparison with expert annotations demonstrated high agreement, achieving an average precision of 94.5%, recall of 83%, and Cohen's $\kappa = 0.81$ across clinically annotated datasets.

Evaluation on an external publicly available dataset showed greater variability, with recall ranging from 81% to 88% and reaching 100% in two cases; precision ranged from 0.23 to 0.81, and Cohen's κ ranged from 0.34 to 0.80. We attribute this variability partly to differences in annotation methodology: our clinical dataset was labeled using a streamlined one-click user interface dedicated application enabling dense and consistent marking, whereas the public dataset likely relied on conventional manual annotation that may emphasize only the most prominent IEDs.

Integration within the real-time platform demonstrated continuous operation across extended recordings, supporting online event detection and adaptive feedback triggering without requiring manually labeled training data. The system maintained real-time processing performance while enabling dynamic estimation of pathological event burden and closed-loop feedback generation.

Preliminary longitudinal analyses further suggested that the estimated pathological event burden tracked clinically relevant state transitions observed during invasive monitoring. Changes in burden were temporally associated with phases of anti-seizure medication reduction (figure1), peri-ictal periods, and post-ictal recovery states (figure2) routinely encountered during presurgical hospitalization of patients with drug-resistant epilepsy. These observations support the potential utility of the proposed biomarker as a real-time indicator of evolving disease state and motivate further prospective investigation.

Conclusions

These findings demonstrate the feasibility of combining unsupervised epileptiform activity detection with a real-time closed-loop neurofeedback architecture for epilepsy. Unlike conventional supervised approaches, the proposed framework operates without expert-labeled training datasets while maintaining clinically relevant detection performance. Importantly, this work highlights the feasibility of translating computational biomarkers into an operational closed-loop system capable of continuously acquiring, interpreting, and responding to pathological brain activity in real time. This represents an important step toward personalized adaptive neurofeedback and future neuromodulation strategies for epilepsy. Ongoing studies are evaluating the physiological and clinical impact of feedback delivery and investigating how such systems may support individualized interventions based on dynamically evolving brain states.

Figure1: Recording over 8 consecutive days, blue arrows over days 1,2 and 8 indicate medication timing, red stars indicate seizures

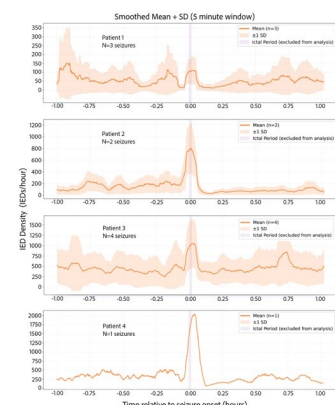


Figure 2: Event-related analysis centered on seizure onset across four sEEG patients