Characterizing the recurrence of high-connectivity iEEG network states before epileptic seizures

Reliable pre-seizure biomarkers could significantly improve neuromodulation therapies for drug-resistant patients. Recent research using stereo-electroencephalography (sEEG) has revealed transient changes in network dynamics preceding seizures. In particular, our previous work showed that these alterations are driven by recurrent, short-lasting (0.6 s) high-connectivity network configurations, termed high-connectivity states (HCSs). Here, we aim to replicate and further characterize HCS as a biomarker in a multicentric patient cohort, assess its robustness across recording modalities and montages, explore its relationship with interpretable physiological variables, and examine its network-level association with seizure-onset zone (SOZ) dynamics.

We analyzed long-term intracranial EEG recordings from 12 patients with sEEG and electrocorticography. In two patients with extensive clinical information, we examined the interplay between HCS and SOZ dynamics. We also developed a low-dimensional stochastic network model to investigate mechanistic rationales of HCS emergence. Additionally, we compared HCS dynamics with gamma-band activity and heart rate, and tested robustness across different montage configurations.

In most patients, HCS probability reliably increased hours before seizure onset. In the two deeply characterized patients, this increase was specifically linked to an increased network centrality within the SOZ. The network model revealed that changes in HCS probability stem primarily from topological reconfigurations rather than changes in mean connectivity, underscoring the importance of dynamic interactions between epileptogenic and non-epileptogenic regions. In sum, these results support HCS probability as a promising biomarker for early seizure prediction and offer mechanistic insights into pre-seizure brain network dynamics.