

TITLE: Measuring drug effects on brain dynamics through electroencephalography

AUTHORS:

Aarti Sathyanrayana
Rima El Atrache
Michele Jackson
Kenneth Mandl
Tobias Loddenkemper
William J. Bosl

RATIONALE:

Use of antiseizure medication (ASM) is currently guided by clinical markers including seizure frequency, semiology, etiology, and other diagnostic evaluations. A neuro-physiological biomarker for the effect of ASM on epileptic seizure activity may be useful for clinical decision making. As an early step in this direction, we evaluate changes in brain dynamics of patients on versus off ASM.

METHODS:

We used electroencephalograms (EEGs) recorded on the 10-20 system from patients admitted to the long term epilepsy monitoring unit at Boston Children's Hospital. Patients may routinely undergo discontinuation and re-initiation of ASM in this setting. ASM dosage and timing were used to determine medication on and off periods. The ASM-on period begins on the first day of EEG recording while the patient continues on his/her regular ASM dosage. The off period is defined by the lowest amount of medication during the hospital stay.

EEG signal features, including sample entropy, Recurrence Quantitative Analysis (RQA), Lyapunov exponents, and other dynamical measures, are computed on multiple scales or frequency bands from a 30 second EEG interval of 22 pre-surgical epileptic inpatients (7 females; median age ~9 years). The effect on brain dynamics is computed as the change in area under the curve of a multiscale curve for each signal dynamic averaged across all electrodes. We consider localization of interictal epileptiform discharges on surface EEG as the irritative zone/network.

RESULTS:

Our results show a difference between the dynamics of the irritative zone of the brain for ASM-on periods versus off. Figures 1 and 2 illustrate the change in determinism for the 4 paradigms: ASM-off and non-irritative, ASM-off and irritative, ASM-on and non-irritative, ASM-on and irritative. The change in dynamics of the irritative region from off to on ASM, was at least 95% greater than the change in corresponding dynamics on the non-irritative region, for sample entropy, laminarity, determinism, and the Lyapunov exponents. Also, for the irritative region, the dynamical state of ASM-on periods converges 34% closer to the state of the non-irritative region, as compared to the state when off ASMs.

CONCLUSIONS:

Multiscale nonlinear analysis on EEG signals holds promise for underpinning digital biomarkers to potentially 1) quantitatively measure changes in brain electrodynamics, 2) evaluate ASM efficacy by

measuring the medication effect on the irritative region(s) as it converges to the non-irritative region(s), and 3) identify the irritative region(s) of the brain by observing the difference in the size of effect influenced by medication.

FUNDING: AS was supported by T32HD040128 from the NICHD/NIH. TL, RE and MJ were supported by the Epilepsy Research Fund.

