

Towards developing an antiseizure drug efficacy biomarker



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RATIONALE. In clinical practice, the choice of antiseizure drug (ASD) is often not guided by efficacy considerations but rather by ease of use and side effect profile related to the specific patient. This inevitably leads to patients having new seizures during the establishment of treatment and is not only a burden on the quality of life of patients but also holds a significant risk of injury from seizures or even sudden unexpected death. Therefore, a biomarker that allows assessing whether or not a patient will be a responder to a specific ASD, without the need for waiting for the next seizure, would allow to decide more quickly how to continue therapy.

METHODOLOGY. To investigate differences between EEG recordings of patients who respond to an ASD and patients who do not respond several investigations beyond visual analysis can be performed. At Epilog NV different state-of-the-art EEG analysis techniques are available: 1. Spike-Q, 2. Spectral-Q and 3. NET-Q. Each of these techniques results in quantitative features that can be used as input for machine learning algorithm to classify responders from non-responders. In addition to this MRI volumetry and clinical information can also be used and combined with the EEG features in an intelligent way to fine-tune the classifier.

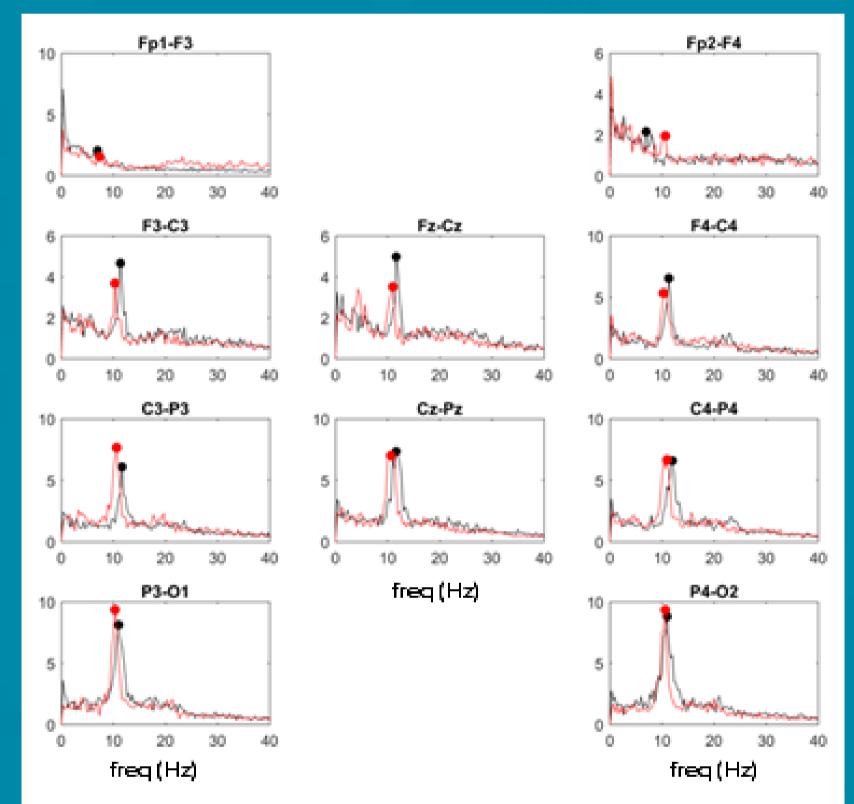
EEG FEATURES

Detected Spike Clusters Spike type: Fp2 #spikes: 41 Spike type: Cx #spikes: 38 Spike type: Cx #spikes: 28 Spike type: Cx #spikes: 28 Spike type: T8 #spikes: 23 Spike type: T8 #spikes: 24

Spike quantification, localization and propagation.

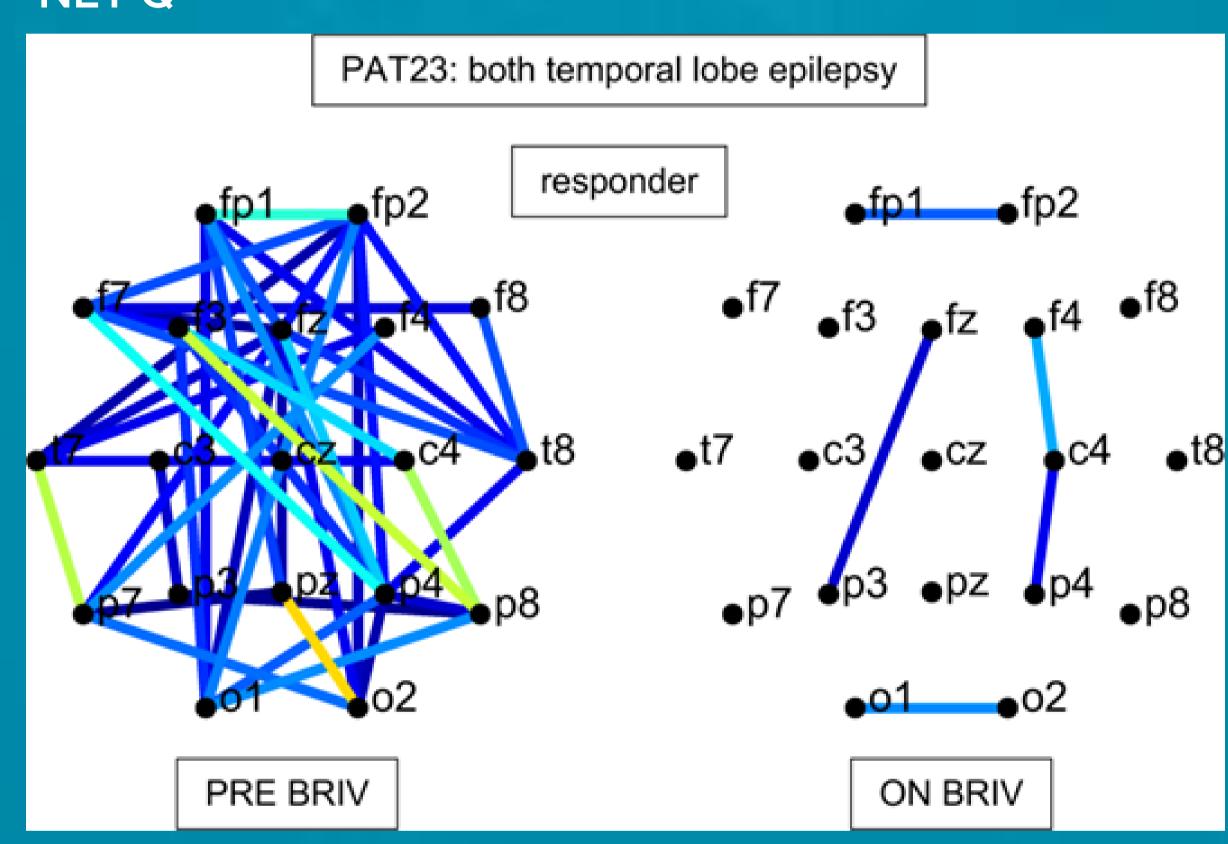
In the EEG spikes are detected and clustered according to their topography. The occurrence of spikes before and during ASD treatment can be investigated.

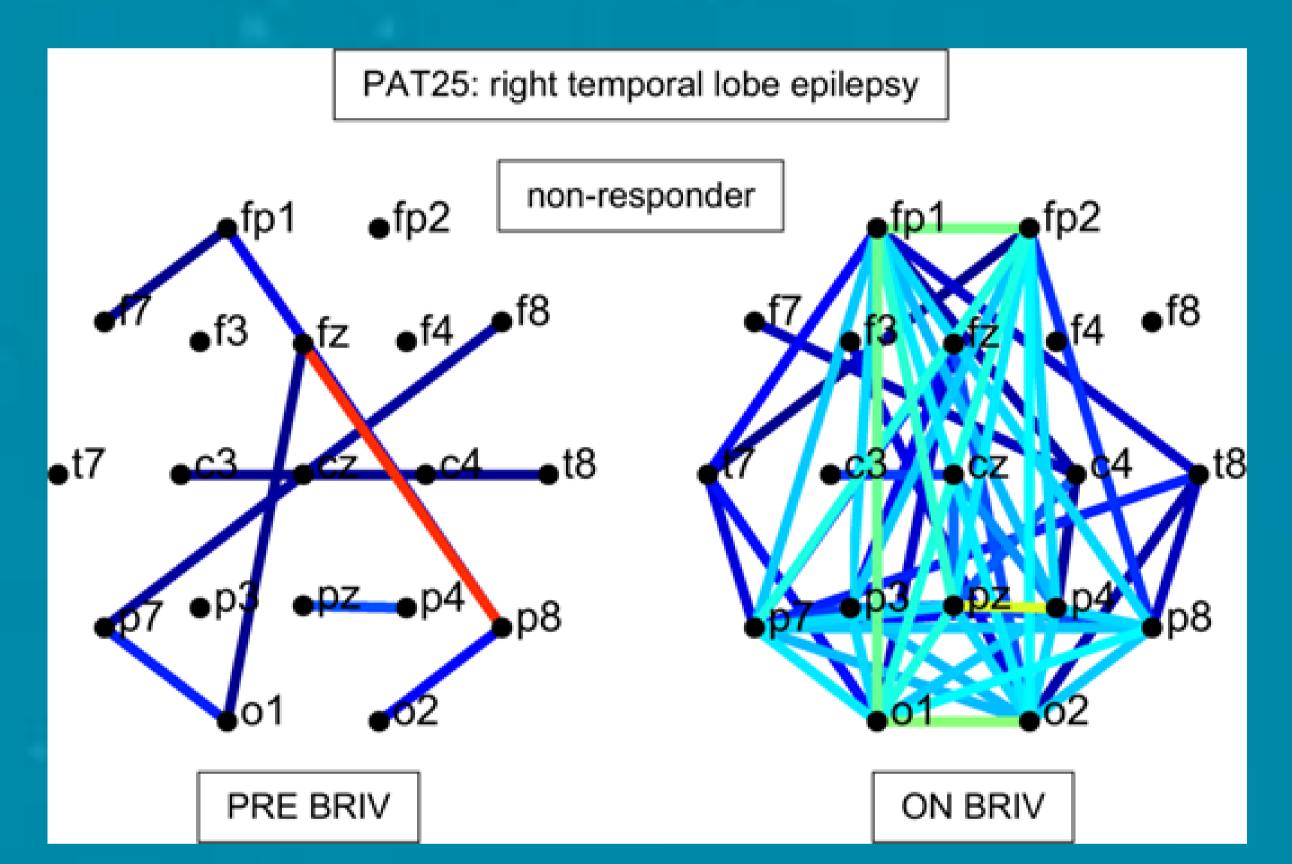
SPECTRAL-Q



Trending, time-frequency analysis
The spectral power, the peak
frequency and power at the peak
frequency are studied before and
during ASD treatment.

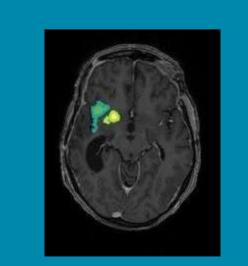
NET-Q

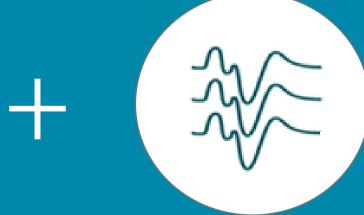




<u>Functional brain connectivity analysis</u> investigates how brain regions communicate by looking at causal dependencies between the EEG signals. Hereby corrections for volume conduction effects are necessary. The figure shows prelimenary results of a responder and non-responder of the ASD Brivaracetam.. A decreasing network connectivity was seen in the responder when comparing ON with PRE, while an increase in connections was seen in the non-responder. Because of the limited number of patients, extra studies are necessary to validate these findings.

INTELLIGENT FEATURE COMBINATION





From MRI volumetry the regions that are most different from a healthy control population are found. The EEG features linked to these regions can be used as input for the classification.

CLASSIFICATION



Machine learning will be used to integrate the EEG, MRI and clinical features. A classifier will be build that can discriminate responders from non-responders of the ASD treatment.

CONCLUSION. Qualitative changes in Spike-Q, Spectral-Q, NET-Q and MRI volumetry were observed between responders and non-responders. Combining EEG with MRI and clinical features in an intelligent way might improve the performance of the ASD efficacy biomarker. This will pave the path towards developing a biomarker for ASD efficacy.



