from healthy controls with moderate to large effect sizes (d = 0.45–0.84). In patients only, HRV decreased overall from unmedicated to medicated state after controlling for age and gender. Furthermore, a multiple linear regression model revealed significant predictors, which accounted for 64.4% of the variance in the variable depressive symptom change (from baseline to endpoint assessment). An increase in REM latency, a decrease in PSQI and relative Very Low Frequency power in REM sleep (REM-VLFrel) predicted the improvement in HAM-D scores. The reduction of REM-VLFrel even showed a positive prediction value of 81.13%.

Implications: While sleep-stage-related HRV is already lower in MDD before AD treatment than in healthy controls, AD treatment has an additional HRV suppressing effect, which is most prominent in VLF-power in REM sleep. Remarkably, this AD effect after one week of treatment is predictive to treatment response at week 4.

Keywords: Depression, biomarker, heart rate variability (HRV), antidepressants.

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FC6

The Value of QEEG Prefrontal Theta Cordance in the Prediction of Response to Various Antidepressants

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Objective: Previous studies have demonstrated the efficacy of reduction of QEEG prefrontal theta cordance (RC) after the first week of treatment in the prediction of antidepressant response. Our study aimed to compare the ability of RC in the prediction of response to various antidepressants.

Methods: 142 inpatients with MDD were treated with various antidepressants for ≥4 weeks. The primary efficacy measure was MADRS score, assessed at baseline, weeks-1, -2, -4, and at the end of study. The EEG was recorded at baseline and after 1 week of treatment. Prefrontal theta cordance [1], was calculated as an average from 3 prefrontal electrodes (Fp1,Fp2,Fz) in theta (4–8 Hz) band.

Results: Logistic regression identified RC as a predictor of response to SSRI, SNRI and NDRI but not for NaSSA. Predictive parameters of RC for response to mentioned antidepressant classes were as follows: For SSRI (N = 58), the AUC of ROC analysis yielded value of 0.77, positive predictive value (PPV) of RC at week 1 was 0.81, negative predictive values (NPV) of RC at week 1 was 0.73 and the accuracy of prediction reached value of 0.78. For SNRI (N = 47), the AUC of ROC analysis yielded value of 0.77, PPV of RC at week 1 was 0.72, NPV of RC at week 1 was 0.84 and the accuracy yielded value of 0.77. For NDRI (N = 22), the AUC of ROC analysis yielded value of 0.87, PPV of RC at week 1 was 0.91, NPV of RC at week 1 was 0.82 and the accuracy yielded value of 0.86. AUC of ROC analysis of RC for response prediction weren't significantly different among antidepressant classes.

Conclusion: Prefrontal QEEG cordance is a promising tool predicting the response to various antidepressants. In this study, the predictive efficacy of 1-week reduction of QEEG prefrontal theta cordance for response to SSRI, SNRI and NDRI was comparable [2]. This work was supported by Ministry of Health of the Czech Republic, grants 15-33250A and 15-29900A and by the Charles University project PROGRES Q35.

Keywords: Antidepressants, treatment response, QEEG cordance, depression.

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FC7

Atomic Decomposition of Human EEG Oscillations in Medical Research and Pharmaceutical Trials

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Frequency spectra and spatial sources of EEG oscillations are highly specific to individuals and may be manifested differently as functions of pharmaceutical treatments or other interventions. However, most analyses of treatment effects on EEG oscillations use an approach based on standard frequency band powers measured at single electrodes. We have developed and applied a method that accurately and efficiently models individual EEG oscillations and tracks their activation over time or treatment conditions.

To obtain robust and repeatable individual measures of EEG suitable for analytical and statistical testing, we developed and refined a novel approach using irregular-resampling auto-spectral analysis (IRASA) to separate fractal and oscillatory components in the EEG power spectrum and three-way parallel factor analysis (PARAFAC) to isolate elemental oscillatory EEG components or ''atoms'' and track their activations; that is, time-scores over time or conditions [1, 2]. We automated the whole process by extracting EEG atoms using a set of PARAFAC model parameters and identifying consistent results by clustering the obtained frequency and spatial loadings of the atoms. We apply standard univariate statistical tests and analysis of (co)variance models to determine statistical significance of changes in atom activations across treatment and experimental conditions.

We simulated effects of dose-related EEG changes by including a range of amplitude effects and signal-to-noise ratios, serving to define the sensitivity and specificity of the approach in com-

parison to the standard EEG testing based on wider spectral band ranges and separate spatial locations. In one application, using EEG data obtained during the longitudinal motor neurorehabilitation treatment of stroke patients, i) we successfully identify dominant oscillatory patterns associated with the induced motor-related EEG changes, ii) tracked their changes during the treatment period, and iii) demonstrated consistent long-term effects. In another application set, we modelled and tracked the changes in atomic EEG activations as functions of drugs under development for treatment of CNS disorders. In a prior Phase 1B clinical trial of a small molecule being developed for treatment of major depressive disorder, we used PARAFAC atoms to track changes in oscillatory sources in the alpha band and demonstrated significant differences between placebo and actively dosed healthy volunteers. Currently we are using PARAFAC to track EEG changes over time after dosing with other molecules being developed to treat central nervous system disorders. We plan a wide range of future applications to drugs being tested for CNS disorders, which will allow us to verify and validate the atomic EEG decomposition method in comparison to classic EEG band-power analyses.

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FC8

Automatic Human Sleep Stage Scoring Using Deep Neural Networks

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Introduction: The analysis of polysomnography (PSG) is a crucial part of sleep research and medicine. The current standard requires visual scoring of sleep stages by an expert. Visual sleep scoring is very time consuming and subjective. Artificial neural networks (ANNs) are a state-of-the-art tool for data classification. One of the best ANNs are Deep Neuronal Networks (DNNs). They perform better than other machine learning (ML) methods for different problems and datatypes. Especially for pattern recognition in images and time-series. Convolutional Neural Networks (CNNs) are the best for images processing and Recurrent Neural Networks (RNNs), particularly the Long-Short Term Memory (LSTM) networks are good for time-series processing.

Methods: Data were collected in two laboratories: 1) 18 healthy young males (3 nights each); 2) patients suffering from narcolepsy (n = 23) or hypersomnia (n = 5). Sleep at night and a Multiple Sleep Latency Test (MSLT). We implemented networks using CNN and LSTM modules. The networks worked with raw data. We trained these networks using a part of the data (healthy subjects only; mixed data) and validated their performance using remaining.

Results: All our methods trained on healthy participants performed well on the data of healthy subjects for all sleep stages (Cohen's Kappa 0.80–0.90) except stage 1 (kappa ~0.4) and slightly worse on patients (0.6–0.8). LSTM networks were better for stage 1 than other methods. Deep learning methods performed better than classical ML methods on the patient data.

Conclusions: We showed that performance of DNNs on sleep scoring task is very close to human expert in both healthy subjects and patients. The scoring of stage 1 was also similar to experts. Taking the temporal structure of sleep into account was important for good performance. DNNs generalized better than other methods.

Keywords: Machine learning, EEG, sleep scoring.

EEG-Biomarkers

FC9

A Comparison of EEG Connectivity Outcome Measures for Alzheimer's Disease in a Double-Blinded Randomized Clinical Trial of PQ912

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Background: In treatment trials in Alzheimer's Disease (AD), an improvement of functional connectivity (FC) could provide biological support for the efficacy of the drug. In the phase-2a SAPHIR-trial in early AD with glutaminylcyclase inhibitor PQ912, electroencephalography (EEG) analysis showed a significant improvement of global relative theta power (4–8Hz) in the intervention group compared to placebo. However, FC, measured by global phase lag index (PLI), did not improve. We hypothesized PLI may not be sensitive enough for the detection of small effects due to its correction for volume conduction. Therefore, we anal-