Assessing Brain Dynamics for Predicting Postanoxic Coma Recovery: An EEG Based Approach

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Abstract

Postanoxic coma is caused by global anoxia of the brain, most often due to cardiac arrest. Electroencephalography (EEG) has been shown to provide prognostic information, where synchronous EEG activity is linked to cortico-cortical connectivity and arousals are linked to cortico-subcortical connectivity. Previous studies indicated changes in both connectivity dimensions in coma patients. As part of the PhysioNet Challenge 2023, we (ibmtPeakyFinders) investigated a novel approach to predict the recovery from cardiac arrest by evaluating brain dynamics. We used the time delay stability method to assess the coupling behavior between different EEG channels reflecting cortico-cortical connectivity and arousal detection for the assessment of cortico-subcortical connectivity. To monitor the development of brain activity over time, a feature vector was generated from different time steps and extended with patient metadata to predict the recovery outcome of postanoxic coma patients. By reaching a challenge score (CS) of 0.34 our team ranked place 30. Reduction to selected connectivity features increased the CS on a held-out subset of the training set by 52.6 %, but not on the hidden validation set. Our results indicate that selected connectivity features contain information to predict the outcome of recovery from postanoxic coma.

1. Introduction

Cardiac arrest describes the sustained absence of the cardiac contraction, resulting in a severe undersupply of oxygen to the brain and thus to possible ischemic brain injury and coma. Post-cardiac arrest brain injury is the main cause of death after resuscitation [1]. In addition, a considerable number of patients die due to too early withdrawal of life sustaining therapy, which is based on incorrect predictions of poor recovery outcome [2]. One of the key methods for outcome prediction in postanoxic coma is the analysis of the electroencephalogram (EEG) [3]. Besides features of suppression and burst patterns, features of cortico-cortical connectivity have been shown to improve prognostic quality [4]. Furthermore, functional magnetic resonance imaging (fMRI) analyses have shown that cortico-subcortical connectivity is correlated with the state of consciousness [5]. We hypothesize that the occurrence of arousals, which manifest as short episodes of activity in higher EEG frequency bands, indicates the condition of these connections to deeper situated structures in the brain, especially the ascending arousal network. Therefore, as part of the George B. Moody PhysioNet Challenge 2023 [6], our team (ibmtPeakyFinders) investigated the suitability of EEG features to assess the connectivity of surfacing and underlying brain regions for predicting outcome in comatose patients after cardiac arrests.

2. Methods

2.1. Data Preprocessing

We used EEG recordings from the I-CARE database [7]. EEG recordings were low-pass filtered with a cutoff frequency of 30 Hz as visualized in Figure 1. Recording windows with a length of 30 s were analyzed for three kinds of frequently observed artifacts: (1) unphysiological rises in single channel amplitudes (detected by slopes within the recording window that exceeded ten times the signal standard deviation (SD)), (2) value congruent channels for more than 5 s and (3) constant channel values for more than 5 s. Artifact-contaminated recording windows were discarded and all remaining windows with a minimum length of 5 minutes were taken for feature calculation. Features values were averaged and weighted by recording window lengths.

2.2. Spectral Power

For every EEG recording, the mean spectral power density of the delta (0.5 to 4 Hz), theta (4 to 8 Hz), alpha (8 to 12 Hz), and beta (12 to 30 Hz) band as well as the mean spectral power density of slow oscillations in the range of 0 to 1 Hz were extracted by Welch's method [8].

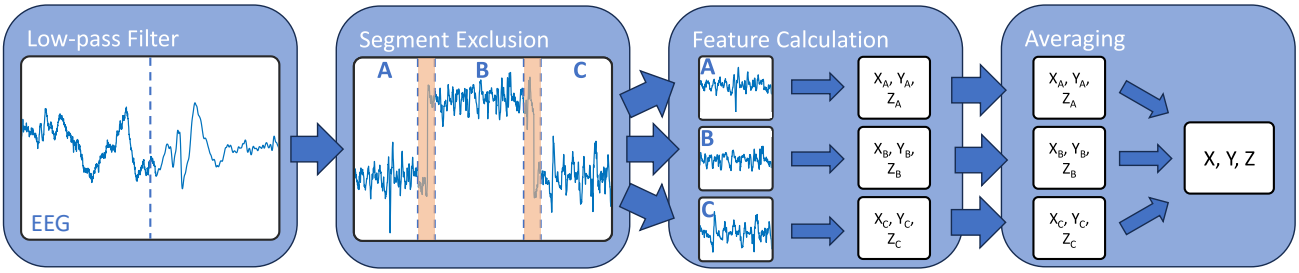

Figure 1. Processing scheme including low-pass filtering of EEG signal, segmentation, feature calculation for each window, and averaging over all windows. Artifact containing windows are highlighted in orange. A, B, C: windows for feature calculation; X, Y, Z: features calculated from EEG signal.

2.3. Arousal Detection

We used two approaches for arousal detection. For approach 1, the continuous wavelet transform (CWT) of EEG channel F3 was calculated. Subsequent, a scalogram was derived from the absolute CWT coefficients. The mean value of the scalogram in the range of 16 to 21 Hz was taken with the expectation that higher values would show higher arousal activity [9]. Approach 2 is intended to capture short episodes of activity in higher frequency bands. For this purpose, the spectral power within the 8 to 30 Hz band was calculated for recording windows of 3 s and set in relation to the spectral power of the previous 10 s. These ratios were accumulated and their distribution was described by a histogram with ten bins [10].

2.4. Time Delay Stability

To quantify the cortico-cortical connections, we chose a correlation-based approach that evaluates the changes in the time lag between two time series: The TDS method introduced by Bashan *et al.* [11] detects coordinated bursting activities in different cortical regions by examining the occurrence of prominent events in multiple EEG channels with a stable time delay. The delay was calculated for a sliding window of 5 s with 50 % overlap via cross-correlation. If the time delay of five consecutive windows did not change for more than one second, the connection was labeled stable for this point in time. The ratio of stable points to the total number of points in a recording (TDS values) was given in %TDS. For every channel combination, TDS values were accumulated in the TDS matrix. To assess the general connectivity, we calculated the mean and SD of the TDS matrix.

2.5. Model Design and Training

In addition to features describing spectral power, arousals, and time delay stability (TDS) extracted from the EEG, patient metadata were used within our approach. To incorporate the temporal development of brain dynamics, we evaluated the first and last available 3 hours of recording. The prognostic value of the features was determined by training random forest classifiers with different feature group combinations as input. The target variable was the recovery outcome (0: good outcome, 1: poor outcome). To achieve lower complexity in one model, we selected four features to represent the feature groups. For this case we chose the TDS standard deviation, the mean slow oscillation spectral energy density, spectrogram energy in the 16 to 21 Hz range, and a bin of an arousal feature histogram. Predictive power of single features was assessed by means of statistical testing on the group differences of good and poor outcomes (Student's-*t*-test for continuous variables, chi-squared test for discrete variables). For local model evaluation, 500 patients (82.4 %) were assigned to the local training dataset in five equally-sized, patient-exclusive folds for cross-validation, and the remaining 107 patients (17.6 %) were assigned as held-out subset of the training set. Besides the challenge score (CS), the receiver operating characteristic area under the curve (ROC-AUC) was calculated to estimate the general model performance. Local training model performance was calculated by averaging ROC-AUC or CS over the five cross-validation models.

3. Results

Table 1 contains the performance metrics ROC-AUC and CS for the training (cross-validation fold average) and the held-out subset of the training set. Differences in model performance became more apparent in CS (SD: 0.18) than in ROC-AUC (SD: 0.09). However, the correlation between these metrics was strong (Pearson's $r = 0.70$, $p = 0.011$). The best performance across all local data sets was achieved by the model trained on patient metadata and selected features (held-out subset set: ROC-AUC: 0.79, CS: 0.58). In comparison, the model solely trained on metadata achieved ROC-AUC score of

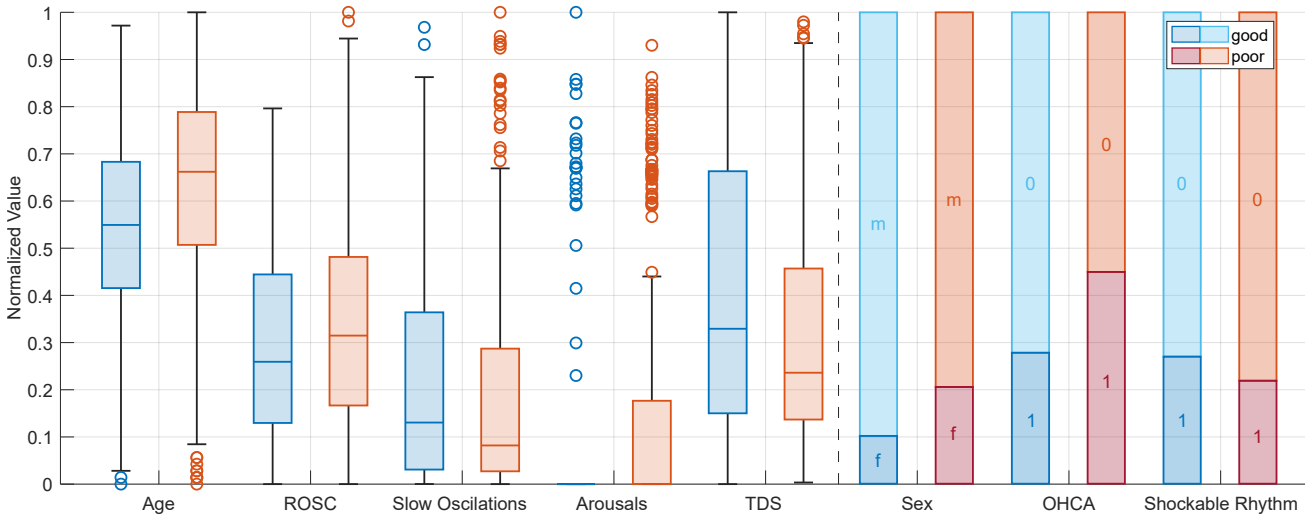

Figure 2. Group differences between good and poor outcomes of all evaluated features normalized to their minimum and maximum values. Features with a continuous distribution are shown as boxplots on the left, and features with discrete distribution are shown as stacked bar graphs on the right. Sex is separated into female (f) and male (m). Out of hospital cardiac arrest (OHCA) and shockable rhythm are separated into true (1) and false (0).

0.73 (-6 %) and CS of 0.50 (-8 %) on the held-out subset. Results for the hidden validation dataset were obtained for the model trained on metadata, mean spectral power density features and TDS features (CS $= 0.54$), and the model with metadata and selected features (CS $= 0.51$). The second model was also used for scoring on the hidden test dataset (CS $= 0.34$).

Figure 2 illustrates group differences for good and poor outcomes of selected features. The mean spectral power density of slow oscillations, for example, was significantly lower for the poor outcome group in the first three hours of recording (mean $\pm$ SD: 0.001259 $\pm$ 0.001857 $\mu V^2 \cdot Hz^{-1}$ vs. 0.000727 $\pm$ 0.001414 $\mu V^2 \cdot Hz^{-1}$, -42 %, $p < 0.001$) and in the last three hours (0.001229 $\pm$ 0.002185 $\mu V^2 \cdot Hz^{-1}$ for good outcomes and 0.000859 $\pm$ 0.001445 $\mu V^2 \cdot Hz^{-1}$, -31 %, $p < 0.05$) for poor outcomes. Also, the mean of the SD of TDS was significantly reduced for the poor outcome group in the first three hours of recording (15.64 $\pm$ 10.95 %TDS vs. 12.79 $\pm$ 9.98 %TDS, -18 %, $p = 0 < 0.01$). Arousal features showed no statistically significant group differences. Visual differences occur due to the distribution of outliers.

Table 1. Performance metrics for local evaluation of models with different features. ROC-AUC: receiver operating characteristic-area under the curve. CS: challenge score. Meta: patient metadata. TDS: time delay stability. SP: spectral power.

	ROC-AUC		CS	
Features Included	Train	Held-out	Train	Held-out
Meta*	0.72	0.73	0.14	0.50
Arousals*	0.59	0.61	0.06	0.17
TDS*	0.59	0.55	0.10	0.21
SP*	0.57	0.61	0.04	0.05
Meta + TDS + SP†	0.72	0.79	0.14	0.38
Meta + Sel. Features§	0.74	0.79	0.17	0.58

*No CS for the hidden datasets; †CS for the hidden validation dataset: 0.54; §CS for the hidden validation and test dataset: 0.51 and 0.34.

4. Discussion and Conclusion

By Student's-*t*-test we found significant differences in the mean spectral power density of slow oscillations between groups with good and poor outcomes in both, the first and last three hours of recording, indicating differences in the status of the thalamo-cortical network [12]. Significant differences by Student's-*t*-test in the SD of the TDS values suggest that patients with good outcomes have more variety in cortico-cortical network connectivity. In the case of the arousal feature of 3 s to previous 10 s window spectral energy ratios, we expected outcome group specific distributions. We hypothesized the good outcome group to have a two-peak distribution, where the first peak originates from non-arousal states (no large differences in EEG activity) and the second peak originates from arousals (short-term increase of EEG activity). In contrast, we an-

ticipated patients with poor outcomes to exhibit a single peak distribution due to the lack of arousal. Both expectations could not be confirmed as the group differences between histogram distributions were statistically not significant. There was also no significantly different activity in the 16 to 21 Hz range of the scalogram. However, it should be noted that these features originate from research on arousals during sleep. The relation to disorders of consciousness like coma is not well understood and features of sleep medicine might not be optimal for coma analysis [13].

The CS on the held-out subset of the training set was aignificantly larger compared to the cross-validation CS. That indicates that the held-out subset contained a subgroup of patients that was better separable by the selected features. Among the models with features from single feature groups, the model trained on metadata showed the best performance for the local cross-validation folds and the held-out set. Models trained on combinations of whole feature groups were not able to exceed the CS of the metadata model. However, the model trained on metadata and selected features representing the feature groups outperformed the metadata model in the cross-validation and on the held-out set. Two conclusions can be drawn from this: (1) The features apart from metadata contain additional information for the outcome of recovery. This is in line with the significant group differences we found. (2) Models were unable to utilize this additional information if the whole feature groups were included, which may be attributed to the additional dimensions which result in an increase in complexity regarding the outcome separation.

The large variance in CS between cross-validation, held-out set, and hidden validation and test set indicates limited representative capabilities of the features for the whole dataset. This becomes even more apparent as the two models with a CS on the hidden validation set perform inversely on the held-out set. Accordingly, the subsets lack representativeness for the whole patient cohort but represent different subgroups. The proposed measurement of sleep arousal to assess the state of the ascending arousal network and to predict coma outcome showed no significant results in the hidden validation set. Nevertheless, features for state assessment of thalamo-cortical and cortico-cortical connections have potential for separating the groups of good and poor coma outcomes.

Future investigations would benefit from a more sophisticated detection of artifacts to improve arousal detection. Furthermore, the influence of the recording window length for feature calculation should be investigated.

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