Predicting Comatose Patient's Outcome Using Brain Functional Connectivity with a Random Forest Model

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Abstract

As part of the 'Predicting Neurological Recovery from Coma After Cardiac Arrest: The George B. Moody PhysioNet Challenge 2023', our team DEIB_POLIMI explored the predictive power of graph topological features extracted from brain connectivity networks, computed using electroencephalogram (EEG) recordings. We investigated the performance of two different phase synchronization measures on the delta band to compute channel-wise EEG connectivity, the weighted phase lagging index and the corrected imaginary phase locking value (ciPLV). Using ciPLV, we computed patients' functional brain networks and characterized their topology by extracting centrality, efficiency, and clusterization graph measures, resulting in 60 features. These features were then concatenated with the mean synchronization of each channel, and patients' clinical information, for a total of 85 features. Using a random forest model we achieved an official Challenge Score of 0.431 (ranked 23rd out of 36 teams) on the hidden test set.

1. Introduction

The George B. Moody PhysioNet Challenge 2023 [1, 2] proposed the participants to develop an automated open-source algorithm that used longitudinal electroencephalogram (EEG), electrocardiogram (ECG) and other signals' recordings to predict patients' outcomes after cardiac arrest. A detailed description of the dataset provided by the challenge can be found in [3].

Recent research highlights the promising brain functional connectivity (FC) assessment using neuroimaging and EEG for improving prognosis prediction in comatose cardiac arrest survivors. FC explores the statistical dependency among neural signals coming from different brain areas [4]. For instance, Stefan et al. [5] explored EEG-based measures to gauge consciousness and forecast outcomes in patients with severe disorders of consciousness, including unresponsive wakefulness syndrome and minimally conscious states. Connectivity metrics showed promising results in differentiating consciousness levels and prognostication. Also, Kustermann et al. [6] reported that topological features of FC, extracted from EEG recording during the first day of coma, sucessfully discriminated long-term outcomes. Furthermore, studies of FC using fMRI data have also supported the prognosis ability of these metrics. Sair et al. [7] demonstrated that early MRI-based assessment of brain FC, particularly within the default mode network, could strongly correlate with positive recovery outcomes in anoxic-ischemic encephalopathy post-cardiac arrest patients. In summary, several studies in the literature point to FC measures and topological features as potential neural correlates of comatose outcomes.

Based on these findings, we aimed to explore EEG-based FC methods for the extraction of relevant connectivity features coupled with machine learning for predicting comatose outcomes at 12, 24, 48 and 72 hours from the time of return of spontaneous circulation (ROSC).

2. Methods

In this section we present our analysis pipeline, consisting in EEG signal preprocessing and feature extraction. The selected features and patients' data (sex, age and targeted temperature management) were fed into both random forest (RF) classifier and regressor to predict the neurological outcome (good or poor) and the cerebral performance category (CPC), respectively. Figure 1 illustrates the developed pipeline.

2.1. EEG Signal Preprocessing

Preprocessing of EEG signals was developed to clean the signals from high-frequency noise and utility frequency interferences. A global quality index (GQI) score was developed to identify the best 5-minutes segment of the last available hour of recording preceding the 72^{nd} hour since ROSC.

For each EEG signal, a notch filter centered at the utility

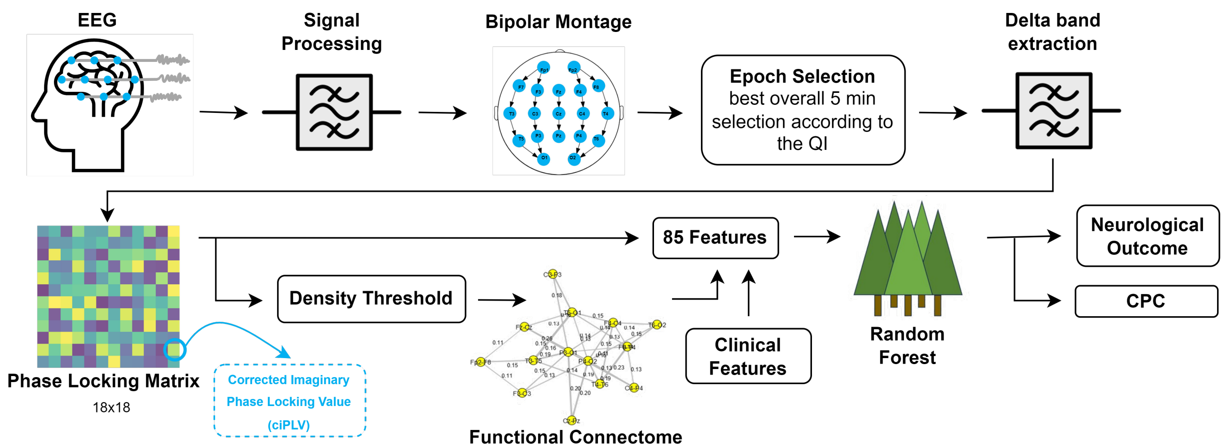

Figure 1. Overview of the developed pipeline consisting of signal preprocessing, epoch selection, FC computation based on ciPLV, extraction of networks' topological features and model training.

frequency was first applied, followed by a pass-band filter with lower and upper cut-off frequencies of 0.1 and 40 Hz, respectively. The signal was then resampled at 125 Hz (2 $\times$ high cutoff frequency to comply with Nyquist–Shannon sampling theorem, + 45 Hz of margin) since anything above 40 Hz was assumed as not relevant. Resampling was performed by considering, for each new sample, the value of the nearest original time point to every new sample's time point, which ensured simplicity and very high conversion speed. This operation allowed to reduce memory consumption of 75% without degrading the signal quality. EEG signals were converted to the standard 18-channels longitudinal bipolar montage for all patients.

A GQI was computed for each channel and was based on three different quality indices. The *outlier peak quality index* (QI_1) was used to find high-voltage peaks due to artifacts:

$$QI_1(t) = max\left(0, |signal(t)| - 60\ \mu V\right), \quad (1)$$

where the threshold of 60 μV was empirically chosen as the optimal threshold. The binary *flat signal quality index* (QI_2) detected physiologically impossible flat signals:

$$QI_2(t) = 0\ if\ signal(t) \neq signal(t-1)\ else\ 1. \quad (2)$$

The *standard deviation quality index* (QI_3) detected uncommon standard deviation in a moving window: for each sample at time t, the standard deviation $std(t)$ of the two seconds of signal centered at t was computed. Then,

$$QI_3(t) = 0\ if\ std(t) \leq 12\ \mu V,\ else\ 1, \quad (3)$$

where the threshold of 12 μV was empirically chosen as the optimal threshold. The GQI (Figure 2) was then defined as:

$$GQI(t) = QI_1(t) + 100QI_2(t) + 100QI_3(t). \quad (4)$$

To find the best five minutes of recording for each channel the signal was split in adjacent 5 minutes windows, each overlapping half of the previous one. For each window, also the 30 s before and after the window were temporarily considered to provide a certain margin from any eventual close-by disturbances. The mean GQI over the extended window was then computed. Figure 2 shows, for a single channel, the mean quality index over the moving 5-minutes window. The cleanest 5 minutes were then chosen as the ones associated with the lowest mean GQI score among all channels. Recordings lasting overall less than five minutes were not considered.

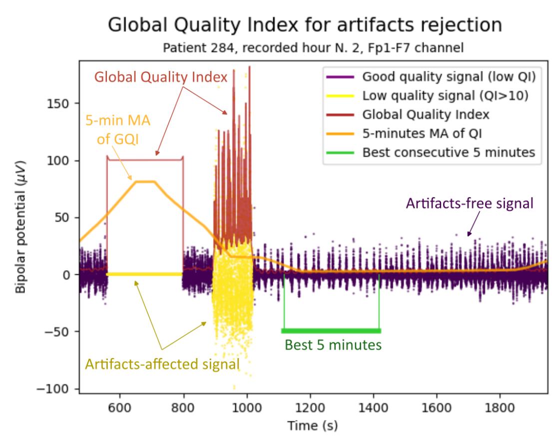

Figure 2. Preprocessed EEG signal plot of patient 284 (2^{nd} hour of recording) showing the best 5-minute recording selection based on the moving average (MA) GQI score algorithm.

2.2. EEG features: Graph-based theory measures

After preprocessing the signal and identifying the best 5 consecutive minutes from the last available hour of EEG recordings, a graph was built to characterize patients' brain FC, and to extract features from it.

Calculating EEG functional connectivity: Two non-linear phase synchronization (PS) metrics, weighted phase lagging index (wPLI) [8] and corrected imaginary phase locking value (ciPLV) [9], were defined and compared to express the connectivity between the 18 bipolar channels. The wPLI assesses the equiprobability of phase leads and lags between two signals. The ciPLV estimates the distribution of phase differences, under the assumption that two signals' phases will evolve together if there is an underlying connectivity between brain regions, thus the smaller the spread the higher its strength. Both indexes have emerged as robust measures against common source effects, which would lead to the appearance of spurious couplings between signals simply due to current volume conductions through the tissues of the head [4].

The FC matrices [size:18x18] of both synchronization metrics were computed using the *spectral_connectivity_time* function available in the *MNE-Connectivity* python package [10]. We chose the Morlet mode for the time-frequency decomposition method using a temporal window with a fixed length. The signal was decomposed into the delta frequency band using a Chebyshev filter. The delta frequency band (0.1 to 3.5 HZ) has been long associated to states of diminished consciousness, and therefore we considered it the most relevant frequency band to study comatose states. A promising indicator of this emerged with the findings of [11] which successfully distinguished different consciousness states using functional connectivity in the delta-theta band. The first 18 features were computed directly by averaging the FC matrix by channel. Additionally, the weighted adjacency matrix was thresholded using a density-based global thresholding by preserving 20% of the strongest connections. In this way, we removed possible noisy links while emphasizing key topological patterns in the network.

Extracting graph-theory features: Once the adjacency matrices were preprocessed, the weighted graph was obtained using *igraph* python library [12]. We then proceeded to compute topological features of interest. To assess the efficiency with which patients' brain networks integrate information between regions, the average path length and the global efficiency for the largest fully connected subgraph were considered, which assessed how easy it is to find the shortest path via a random walk [13]. Following, some measures of centrality such as maximum degree value were considered to assess the number of links corresponding to the most influential node in the network, as well as the hub score for each channel and nodes' betweenness, which estimate how much a node falls between many shortest paths of neighborhood nodes. To evaluate networks' clusterization, the clustering coefficient [14] and modularity [15] were computed. The first estimates the probability that two nodes, each directly connected to a third node will also be directly linked to each other, representative of functional specialization, while the latter evaluates, after a partition of the network, the quality of the clustering. Finally, the average connectivity for each channel was considered [16]. This resulted in a vector of 78 EEG features consisting of the average ciPLV for each channel and 60 graph-based measures, both global and channel-wise.

2.3. Random Forest Classifier and Regression Training

The dataset was split based on the hospitals data sources. Patients from hospitals A and B were included in the training set (n=381), and patients from hospitals D, E and F in the held-out training subset (n=226). Missing values were imputed using a k-NN imputer (k=5). Two RF models were trained, one classifier and one regressor with the following hyperparameters: 200 estimators and maximum of 25 leaf nodes in each tree and a random state of 42. These hyparameters were choose a-priori.

3. Results

In Table 1 we present the performance of the presented models evaluated on the held-out subset of the training set. All the illustrated scores refer to the 72h prediction task. The ciPLV achieved higher performance on all metrics except for the challenge score, for which wPLI attained equal results.

Metrics	*wPLI*	*ciPLV*
Challenge Score	0.420	0.420
AUC-ROC	0.702	0.747
AUC-PR	0.832	0.873
Accuracy	0.677	0.721
F1-score	0.611	0.655
CPC MSE	2.895	2.706
CPC MAE	1.546	1.495

Table 1. Phase Synchronization Measures Comparison.

In Table 2 we report the results regarding the official challenge score (true positive rate at a false positive rate of 0.05) at 72h, for our best model entry which used ciPLV as a functional connectivity proxy.

Training	Validation	Test	Ranking
0.707	0.373	0.431	23/36

Table 2. Official Challenge Score.

4. Discussion and Conclusions

In this study, we present a model geared towards the prediction of comatose patients' outcome after cardiac arrest. The approach employed graph theory to measure brain connectivity. Two methods for computing the FC matrix were compared, and it was found that using ciPLV achieved better results. The model displayed moderate accuracy in forecasting patient outcomes.

Although topological characterization of brain networks have demonstrated potential as neural correlates of consciousness states, the brain network computation involves subjective metric choices, since there is no standardized pipeline or ground truth. Moreover, depicting networks' topology might not be sufficient to distinguish comatose outcomes as the complete dynamics of brain recovery can hardly be captured within a specific timeframe.

In conclusion, it was demonstrated that a basic machine learning model employing brain network properties calculated from 5 minutes of brain delta activity can achieve a certain degree of generalization. To enhance our outcomes, forthcoming research could investigate using the brain connectivity graph as input for a Graph Neural Network (GNN) and contemplate integrating spatial and temporal characteristics not considered in our prevailing model.

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