Neurovascular Coupling in Patients with Acute Ischemic Stroke

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Background. The study of the mechanistic behavior of the ischemic brain is of paramount importance to neurocritical care as it sheds light on the mechanisms underlying ischemic insults and helps in therapeutic guidance. The impact of ischemic attacks on the neurophysiological dynamics regulating neuronal activity and cerebral blood flow – known as neurovascular coupling (NVC) – remains poorly understood. It is hypothesized that neurovascular coupling may be altered following ischemic stroke attacks. We here investigate the alteration of NVC in patients with acute ischemic stroke who underwent endovascular recanalization. We analyzed bedside noninvasive continuous co-recordings of scalp electroencephalography (EEG) and cerebral blood flow velocity (CBFV) acquired within 24 hours of recanalization intervention.

Methods. Synchronized recordings of 8-electrode surface EEG and bilateral transcranial doppler acquired within 24h of mechanical thrombectomy in 14 patients with acute occlusion of middle cerebral or intracarotid arteries were analyzed. EEG data was band-pass filtered. A total of 18 EEG recordings were analyzed in bipolar montage. 10 of 18 recordings (10 of 14 patients) were available in referential montage. Artifacts were removed manually and using blind source separation algorithms. CBFV was low-pass filtered to remove high frequency noise. Directed transfer function (DTF) and partial directed coherence (PDC) were estimated between EEG and CBFV channels in 5-minute sliding window using time-varying multivariate autoregressive model (MVAR) retaining only statistically significant values at 99% confidence interval. Time-frequency profiles of DTF and PDC in both connectivity directions (EEG □CBFV and CBFV□EEG) were then compared and analyzed for predictability of neurological outcome at discharge (assessed using modified Rankin scale, mRS). A k-nearest neighbors (k-NN) algorithm was trained to predict a binary outcome at discharge (unfavorable; mRS $\leq$ 3, Favorable; mRs > 3) using temporal profiles of DTF and PDC. DTF and PDC profile values were class-balanced and split 70/30 % between training and testing sets respectively. In-sample 10-fold cross validation was carried out to learn k-NN optimal decision boundaries.

Results. Strong connectivity was observable bilaterally in a subset of connections in the FV □ EEG direction but not in the EEG □ FV direction, indicating a neuronal drive of CBF dynamics in some but not all connections/areas. EEG unipolar channels showing maximum connectivity were mostly contralateral to occlusion side (10 of 18 recordings/9 of 10 patients). Areas of maximum connectivity between EEG channels and bilateral CBFV channels were generally concordant (fig. 1). 11 of 14 patients had favorable outcome at discharge. Clinical outcome at discharge was predictable above chance (Area under the receiver operating characteristic curve (AUC) = 0.81, accuracy = 0.75, precision = 0.83).

Conclusion. Noninvasive recordings of brain vascular and electrical activity may prove useful in acute neurocritical care. Measures of neurovascular coupling derived from bedside recordings of EEG and CBFV may be predictors of short-term clinical outcome in patients with acute ischemic stroke. Maximum connectivity observed in brain areas contralateral to occlusion side may reflect a compensatory neurovascular mechanism in the healthy hemisphere. These results are preliminary and need validation on large datasets with recordings form healthy controls.

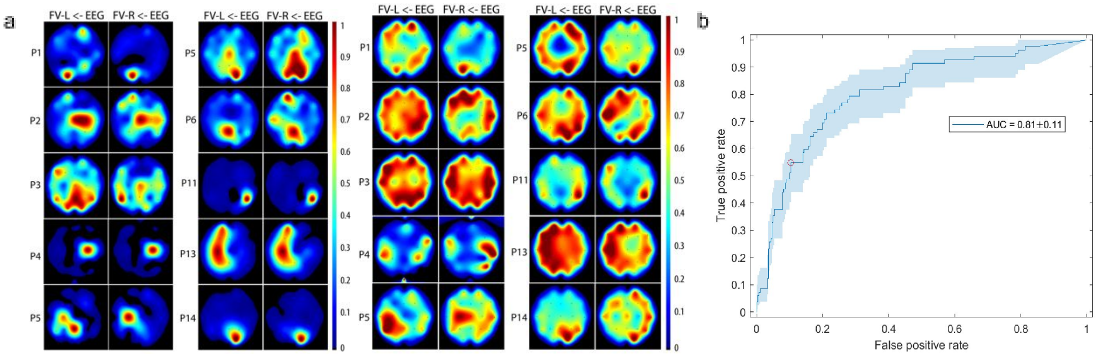

Fig. 1: a- Topographic PDC (left) and DTF (right) connectivity in 10 of 14 patients. b- ROC curve of outcome prediction.