



## Letter to the Editor

### EEG reactivity predicts recovery of consciousness in patients with acute brain injury and signs of intracranial hypertension



To date, there are models that predict prognosis in patients with acute brain injury based on admission characteristics (Hemphill et al., 2009; Lingsma et al., 2010; Jaja et al., 2018). It would be important to have indicators also during the patients' course that can add prognostic information after the initial treatment. In patients with postanoxic encephalopathy, electroencephalography (EEG) reactivity during the first 3 days predicts outcome and seems to be the best predictor of good versus bad outcome when compared to other predictors (Rossetti et al., 2017). We tested the hypothesis that appearance of EEG reactivity predicts consciousness recovery in comatose patients with acute brain injury and signs of intracranial hypertension at admission; we compared their performance with that of known outcome predictors.

This study was done in the Neurosurgical Intensive Care Unit (ICU) of the Ospedale Papa Giovanni XXIII, Italy and was approved by our institution. Patients (who regained consciousness), or the next of kin, gave informed consent to use data for research. Inclusion criteria were: comatose patients after traumatic brain injury (TBI) or intracerebral/subarachnoid hemorrhage with at least 2 of the following: pupillary abnormalities; compressed/absent basal cisterns; midline shift >5 mm; lesion volume >30 ml, or obstructive hydrocephalus. Exclusion criteria: previous neurodegenerative disease that would not allow an accurate evaluation of consciousness and recovery of consciousness during the first day after admission in the ICU and before the first EEG. The EEG was recorded according to the 10–20 International System, and reactivity was defined as reproducible change in either amplitude or frequency after an auditory, visual and noxious stimulus (Rossetti et al., 2017). Stimulus-induced rhythmic discharges and muscle

artifacts were excluded. The main outcome was evaluated at ICU discharge and was dichotomized as favorable (consciousness recovery—patients able to obey simple commands) and unfavorable (death or “unresponsive wakefulness syndrome”). EEG reactivity was then compared with known outcome-predictors such as age, admission Glasgow Coma Scale (GCS), pupillary reactivity, basal cistern status and midline shift.

Continuous variables were presented as average and standard deviation and comparisons were performed using unpaired t-tests. Scores are presented as medians and comparisons were done using the Mann-Whitney U test. For categorical variables a Fisher exact test was performed.

Fifty patients were studied, mean age was  $54 \pm 17$  years. Forty-eight % of patients were admitted after TBI, the remaining after intracerebral/subarachnoid hemorrhage. All patients had clinico-radiological signs of intracranial hypertension on admission. Median total GCS was 4 (interquartile range, IQR 3–7). We observed 32 patients with reactive versus 17 with non-reactive EEG (one patient could not be evaluated). Traumatic brain injury and intracerebral/subarachnoid hemorrhage were evenly distributed in the 2 groups. The groups with reactive vs. non-reactive EEG were similar at admission: age was  $54 \pm 17$  vs.  $55 \pm 18.5$  years ( $p = 0.8$ ); admission median GCS was 5 vs. 4, with a median motor score of 2.5 and 2 respectively ( $p = 0.4$  and  $0.2$ ). Pupillary abnormalities were present in 57% of patients, 66% of patients had compressed/absent basal cisterns and 68% had midline shift >5 mm. However also the percentage of cases with pupillary abnormalities, compressed/absent basal cisterns and significant midline shift were not different in the 2 groups.

Twenty-five patients (50%) recovered consciousness, 16 (32%) died, and 9 (18%) were in the state of “unresponsive wakefulness” at ICU discharge. Univariate analysis showed that pupillary abnormalities and compressed/absent basal cisterns in the CT-scan were associated with reduced probability of consciousness recovery; in contrast higher total and motor GCS score, EEG reactivity and

**Table 1**

Univariate and multivariate analysis of outcome predictors and EEG-pattern associated with outcome.

Predictors	Univariate OR (95%-CI)	p	Multivariate OR (95%-CI)	p
Age	1.03 (0.99–1.07)	0.08	-	-
GCS (total score)	0.79 (0.64–0.99)	<b>0.04</b>	0.77 (0.25–2.31)	0.64
GCS (motor score)	0.62 (0.41–0.95)	<b>0.03</b>	1.0 (0.19–5.33)	0.99
Pupils (nonreactive)	7.61 (1.44–40.33)	<b>0.02</b>	1.24 (0.09–16.76)	0.87
Basal cistern (compressed/absent)	4 (1.13–14.17)	<b>0.03</b>	11.66 (1.04–130.65)	<b>0.05</b>
Shift (>5 mm)	3.38 (0.95–12.01)	0.06	-	-
EEG (reactive)	0.02 (0.0–0.19)	<b>0.001</b>	0.02 (0.0–0.31)	<b>0.006</b>
EEG (continuous)	0.04 (0.0–0.34)	<b>0.03</b>	0.19 (0.0–9.78)	0.41

GCS: admission Glasgow Coma Scale, total score and motor component used as continuous variables. OR and 95%-CI: odds ratio and 95% confidence interval.

continuity were associated with consciousness recovery (see Table 1). Multivariate analysis showed that compressed/absent basal cisterns remained marginally significantly associated with poor outcome, but EEG reactivity was the strongest predictor of consciousness recovery, with a positive predictive value (PPV) of 95.8% (95% CI 79.8–99.3) and an accuracy of 81%.

In conclusion EEG reactivity was associated with consciousness recovery in comatose patients presenting with acute brain injury and intracranial hypertension.

#### Declaration of Competing Interest

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