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Research paper

Electroencephalography reactivity for prognostication of post-anoxic coma after cardiopulmonary resuscitation: A comparison of quantitative analysis and visual analysis

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HIGHLIGHTS

- Here, we report EEG reactivity assessment through a quantifiable method.
- EEG reactivity through quantitative analysis might predict outcome in adults with post-anoxic coma after cardiopulmonary resuscitation.
- This quantifiable analysis method might increase the objectivity and accuracy of EEG reactivity for prognostication.

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ABSTRACT

Electroencephalogram reactivity (EEG-R) is a positive predictive factor for assessing outcomes in comatose patients. Most studies assess the prognostic value of EEG-R utilizing visual analysis; however, this method is prone to subjectivity. We sought to categorize EEG-R with a quantitative approach. We retrospectively studied consecutive comatose patients who had an EEG-R recording performed 1–3 days after cardiopulmonary resuscitation (CPR) or during normothermia after therapeutic hypothermia. EEG-R was assessed via visual analysis and quantitative analysis separately. Clinical outcomes were followed-up at 3-month and dichotomized as recovery of awareness or no recovery of awareness. A total of 96 patients met the inclusion criteria, and 38 (40%) patients recovered awareness at 3-month followed-up. Of 27 patients with EEG-R measured with visual analysis, 22 patients recovered awareness; and of the 69 patients who did not demonstrated EEG-R, 16 patients recovered awareness. The sensitivity and specificity of visually measured EEG-R were 58% and 91%, respectively. The area under the receiver operating characteristic curve for the quantitative analysis was 0.92 (95% confidence interval, 0.87–0.97), with the best cut-off value of 0.10. EEG-R through quantitative analysis might be a good method in predicting the recovery of awareness in patients with post-anoxic coma after CPR.

1. Introduction

Despite recent progress in critical care, 40–66% of patients do not recover awareness after cardiopulmonary resuscitation (CPR) [1–4]. Therefore, an accurate prediction of outcome is essential for prognostication. Clinical, biochemical and neurophysiological tests show significantly variable accuracy, however [5]. Perhaps the most common measure, absence of brainstem reflexes to stimuli, is often limited by therapeutic hypothermia (TH) or sedative drugs in predicting prognosis of comatose patients. Serum biomarkers, especially neuron specific enolase (NSE), might be uncertain during TH as well [6]. Another metric, absence of N20 responses due to somatosensory evoked potentials (SSEPs) has been shown as a predictive factor with superior specificity but low sensitivity in predicting poor outcomes [7].

Electroencephalogram (EEG) is widely used as a prognostic tool in comatose patients [8,9]. EEG reactivity (EEG-R) to external stimuli has been shown as a positive predictive factor for assessing the outcome of comatose patients, including coma following cardiac arrest [10–13]. The reactivity of the EEG background is regarded as a reproducible change in amplitude or frequency following the application of external stimuli [14].

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Table 1
Summary of patients by outcome at 3-month follow-up.

	Outcome		P
	Awareness (n = 38)	No awareness (n = 58)	
Age (year)	54.21 (18–79)	55.68 (21–80)	>0.05
Sex (n)			
Male/Female	18/20	30/28	>0.05
Glasgow Coma Scale	5 (3–8)	4 (3–8)	>0.05
CPR causes (n)			>0.05
Cardiac causes	16	31	
Pulmonary causes	13	20	
Anesthetic causes	9	7	
Therapeutic hypothermia [a]			0.04
Standard	35	44	
Not Standard	3	14	

[a] Standard, intravascularly or through the body surface, with 34 °C as the target core body temperature for 24 h; not standard, local ice-cap without strict core body temperature restriction.

In current practice, EEG-R is mainly assessed by visual analysis. However, subtle changes in appropriate EEG activity before and after the application of external stimuli might escape visual comparison, or exhibit inter-observer variation and thus decrease overall prognostic value. In addition, accurate visual analysis might be difficult for physicians in who are not trained in EEG assessments. Furthermore, TH and sedative drugs might slow EEG or decrease amplitude [15,16], which may lead to more difficult visual assessment.

The aim of this study was to test the prognostic value of quantitative analysis for the assessment of EEG-R in adults with post-anoxic coma after CPR.

2. Material and methods

2.1. Patients

This retrospective study was performed in a Chinese university hospital with patients selected from March 2006 to March 2015 who met inclusion criteria. Patient inclusion criteria included: age, ranging from 18 to 80 years, incidence of coma after CPR with a Glasgow Coma Scale (GCS) score of ≤8, and an EEG-R assessment 1–3 days after coma or during normothermia after TH to 34 °C for 24 h. Exclusion criteria were as follows: prominent artifacts of EEG data, a life expectancy <3 months, spinal cord injury, and patients lost during follow-up.

2.2. EEG data

For all enrolled patients, EEG was recorded bedside using disposable disc electrodes. Recordings included standard arrangements of 16 electrodes placed according to the international 10–20 system using a portable 32-channel digital EEG system (DAVINCI-SAM, Micromed, Mogliano Veneto, Italy). The 16 electrodes were Fp1, Fp2, F3, F4, F7, F8, C3, C4, T3, T4, T5, T6, P3, P4, O1 and O2. Fz was used as ground. Cz, A1, and A2 were used as references. EEG-R was tested bilateral on sections of the EEG recordings using painful stimulation (nail bed pressure).

The standard definition of EEG-R through visual analysis was a clear change in the frequency or amplitude of activity compared with pre-stimulus activity. EEG-R was assessed offline by two certified neurophysiologists (certified by Brain Injury Evaluation Quality Control Centre of China) separately who were blinded to the clinical outcomes and, they could change the filters, signal gain, and montages. The outcome of EEG-R was dichotomized as reactive or non-reactive.

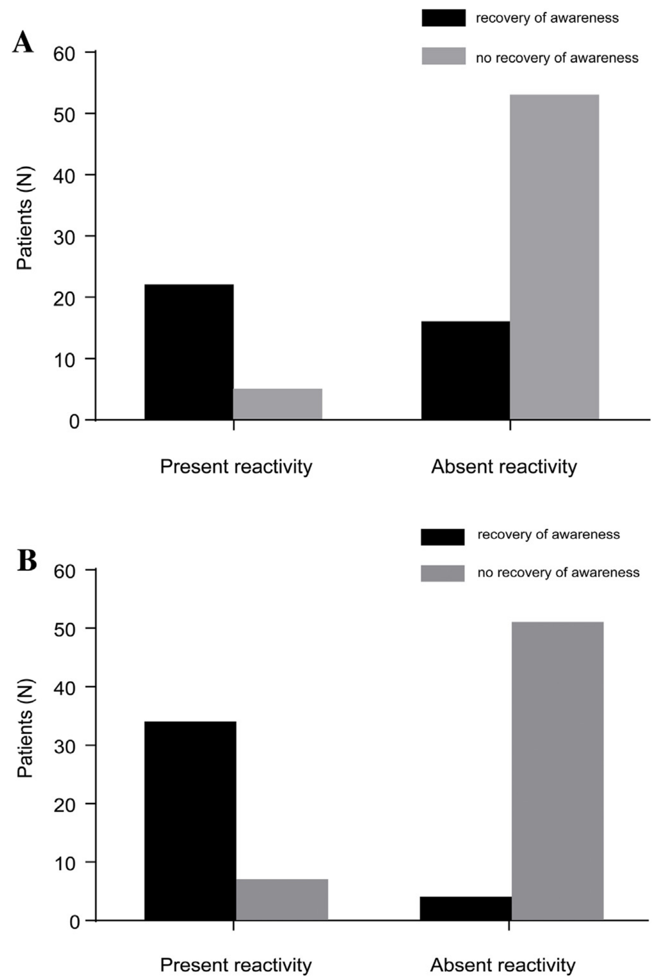

Fig. 1. Summary of EEG-R outcomes at 3-month follow-up. (a) In visually-read EEGs, 22 of 27 patients with EEG-R recovered awareness and 16 of 69 patients without EEG-R recovered awareness. (b) In the quantitative analysis EEGs, 34 of 41 patients with EEG-R recovered awareness, and 4 of 55 patients with no EEG-R recovered awareness when using the best cut-off value.

Quantitative analysis was performed by EEG signal analysis experts who were blinded to the clinical outcomes and visual analysis outcomes. The EEGLAB was used to perform a time-frequency analysis of the average reference montage. EEG-R was calculated by evaluating the spectral power before and after the administration of nail bed pressure. For the quantitative analysis, 60 s of EEG activities were extracted. The pre-stimulation epoch, duration of the baseline, was defined as 30 s. The post-stimulation epoch was the subsequent 30 s after the onset of painful stimulation. The reactivity was calculated as: reactivity $= |P_{after} - P_{before}|/P_{before}$, where P_{after} was the mean power in a 0.5–20 Hz frequency bands of post-stimulation epoch and P_{before} was the mean power in that bands of pre-stimulation epoch. The reactivity was measured as a normalized value between zero and one. Smaller changes will indicate lower reactivity. In case of obvious differences between the repeated tests, the average ratios were chosen for the final analysis because we performed tests on each lateral region at least twice. The best cut-off value of reactivity was determined with the follow-up outcomes as a golden standard. Through quantitative analysis, the reactivity was classified as present when the value ≥ cut-off pint, and absent if the value <cut-off point.