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Quantitative EEG and functional outcome following acute ischemic stroke

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HIGHLIGHTS

- EEG powers in the alpha, beta and delta bands are independent predictors of post-stroke outcome.
- Delta-theta to alpha-beta ratio and alpha relative power are good qEEG stroke outcome predictors.
- Quantitative EEG indices improve the discriminative capacity of outcome models of acute stroke.

ABSTRACT

Objective: To identify the most accurate quantitative electroencephalographic (qEEG) predictor(s) of unfavorable post-ischemic stroke outcome, and its discriminative capacity compared to already known demographic, clinical and imaging prognostic markers.
Methods: Prospective cohort of 151 consecutive anterior circulation ischemic stroke patients followed for 12 months. EEG was recorded within 72 h and at discharge or 7 days post-stroke. QEEG (global band power, symmetry, affected/unaffected hemisphere and time changes) indices were calculated from mean Fast Fourier Transform and analyzed as predictors of unfavorable outcome (mRS $\geq$ 3), at discharge and 12 months poststroke, before and after adjustment for age, admission NIHSS and ASPECTS.
Results: Higher delta, lower alpha and beta relative powers (RP) predicted outcome. Indices with higher discriminative capacity were delta-theta to alpha-beta ratio (DTABR) and alpha RP. Outcome models including either of these and other clinical/imaging stroke outcome predictors were superior to models without qEEG data. In models with qEEG indices, infarct size was not a significant outcome predictor.
Conclusions: DTAABR and alpha RP are the best qEEG indices and superior to ASPECTS in post-stroke outcome prediction. They improve the discriminative capacity of already known clinical and imaging stroke outcome predictors, both at discharge and 12 months after stroke.
Significance: qEEG indices are independent predictors of stroke outcome.

1. Introduction

Stroke is a leading cause of disability and mortality worldwide, and despite advances in disease prevention, acute treatment and rehabilitation, global stroke burden is expected to rise in the future (Feigin et al., 2017). Early post-stroke prognostication is essential both in the short-term (f. ex. in guiding treatment strategies) and

Abbreviations: ADCI, Acute Delta Change Index; ASCI, Acute Symmetry Change Index; ASPECTS, Alberta Stroke Program Early CT score; BSI, Brain Symmetry Index; DTABR, delta-theta to alphabeta ratio; Ln, natural logarithm; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; qEEG, quantitative EEG.

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in the long-term (to aid in rehabilitation management, in order to improve recovery and minimize disability). Predictors of stroke disability and associate death consistently include age and clinical / imaging related stroke severity (Adams et al., 1999; Barber et al., 2000; Frankel et al., 2000; Hankey, 2003; Hankey et al., 2007; Konig et al., 2008; Knoflach et al., 2012; Vogt et al., 2012). However, despite the existence of demographic, clinical and imaging factors that can be associated with functional outcome, early prediction of short and long-term post-stroke outcome is challenging since there is large interindividual variability (Stinear, 2010). Therefore, there is still need to identify reliable, inexpensive biomarkers that can add prognostic information in these patients. Due to accumulating evidence regarding neuro-vascular uncoupling in acute ischemic stroke, neurophysiological biomarkers seem increasingly relevant for predicting outcome (Rossini et al., 2004).

EEG is a non-invasive, inexpensive diagnostic method, with high temporal resolution, contributing to a rapid evaluation of instantaneous brain function. However, its visual interpretation requires technical experience, and may be subject to interrater variability. Hence, quantitative EEG (qEEG) techniques have emerged and have been proven informative in stroke prognostication (Finnigan and van Putten, 2013). These techniques have the advantage of providing objective, rater-independent information, which can be used in a variety of settings, including intensive care units. Previous studies have also shown they can be equal to, or even be more informative, than visual EEG interpretation for detecting cerebral pathology (Sainio et al., 1983; Nuwer et al., 1987; Cillessen et al., 1994; Murri et al., 1998).

In general, EEG parameters such as total power, relative delta and alpha power, ratios between slower and faster frequencies (such as the delta/alpha ratio [DAR] and the [delta + theta/alpha + beta] ratio [DTABR]), and brain symmetry indices (such as the Brain Symmetry Index [BSI] and pair-derived BSI) have been strongly associated with stroke outcome, for up to 12 months (Finnigan and van Putten, 2013). These measures have also been shown, in some studies, to be more reliable in prognostication than standard clinical evaluation (Cuspineda et al., 2003; Finnigan et al., 2007; Diedler et al., 2010; Sheorajpanday et al., 2010, 2011b) or imaging biomarkers (Finnigan et al., 2004; Sheorajpanday et al., 2010, 2011b).

However, direct comparison of these measures and indices for predicting stroke outcome has yielded conflicting results (Finnigan and van Putten, 2013). Moreover, few previous studies attempted to control for independent known outcome factors, such as age at stroke onset, clinical severity at admission or infarct size.

Therefore, the principal objectives of this study were: (1) to identify the most accurate qEEG measure(s) associated with outcome at discharge and 12 months after stroke, (2) to compare the discriminative capacity of outcome models based exclusively in already known demographic, clinical and imaging prognostic markers and including one qEEG variable, and (3) to compare qEEG and visual EEG analysis in stroke outcome prediction, in a large, well defined cohort of acute anterior circulation ischemic stroke patients.

2. Methods

2.1. Study design

Study design has been previously described (Bentes et al., 2017b). We performed a prospective longitudinal study of consecutive anterior circulation ischemic stroke patients admitted to the Stroke Unit of the Neurology Department of a University Hospital, over a period of 24 months (from October 2011 to October 2013) and followed for 12 months. The Ethics Committee "Comissão de Ética para a Saúde" of our hospital approved the study. All subjects or their next of kin gave written informed consent for participation. All included patients had to be previously independent (modified Rankin Scale [mRS] ≤ 1), have a National Institutes of Health Stroke Scale score (NIHSS) ≥ 4 (Goldstein et al., 1989) upon admission to the emergency department, have an acute ischemic brain lesion (CT scan or MRI) in the internal carotid artery territory and no previous history of epileptic seizures nor traumatic head injury requiring hospital admission.

2.2. Clinical assessment

All patients received standardized clinical and diagnostic assessment, during admission and after discharge. An investigator blinded to the neurophysiological evaluation conducted a phone interview at six months and a clinical appointment 12 months after stroke to access the occurrence of epileptic seizures and functional outcome. Clinical stroke severity was assessed by NIHSS at admission. The functional outcome at discharge and at 12 months was assessed by the mRS scale (Banks and Marotta, 2007).

2.3. Neuroimaging interpretation

A senior neuroradiologist, (C.M. or C.C.) blinded for clinical and electroencephalographic findings analyzed the neuroimaging studies. Doubts were decided by consensus. In patients with middle cerebral artery stroke, infarct size was quantified by the Alberta Stroke Program Early Computed Tomography Score (ASPECTS) (Barber et al., 2000) in an acute brain CT (computed tomography) scan performed in the first 24 h after stroke.

2.4. Neurophysiological evaluation

Patients underwent a neurophysiological evaluation protocol that included a 64-channel video-EEG with a maximum duration of 60 min in the first 72 h after stroke (first EEG). A similar EEG was also collected at discharge or on the 7th day post-stroke (second EEG). The neurophysiological protocol was previously described (Bentes et al., 2017a). The record included an eyes-closed, wake resting condition and eyes-open, hyperventilation and photic stimulation activation maneuvers. Raw EEG review was performed by a certified clinical neurophysiologist (CB) using international criteria and terminology (Noachtar et al., 1999; Beniczky et al., 2013; Hirsch et al., 2013), blinded for clinical and imaging findings. All doubts were decided by consensus with another clinical neurophysiologist (ARP).

2.4.1. EEG acquisition

The EEG was recorded in a Nihon-Kohden device with a sample frequency of 1000 Hz. Consecutive samples of EEG, acquired in similar technical conditions (eyes closed, resting condition outside hyperventilation, photic stimulation or sleep) and with the best possible technical quality, were selected forming an EEG segment of 1–10 min.

2.4.2. EEG processing

EEG segments (high cutoff filter 70 Hz; low cutoff filter 0.5 Hz; notch filter 50 Hz, average montage) were exported for FTT analysis in BESA software (BESA Research 6.0, June 2013, BESA GmbH, Graefelting, Germany). In BESA, visual and automatic rejection of artifacts was done. When present, blinking artifacts were also removed by principal component analysis. The EEG was then segmented into 2.05s mini-epochs and FFT analysis was performed for each of these segments. Mean Fast Fourier Transform (FFT) of all the 2.05 s mini-epochs of the selected EEG segment was computed