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Frontal EEG delta/alpha ratio and screening for post-stroke cognitive deficits: The power of four electrodes

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ABSTRACT

This study analysed correlations between post-stroke, quantitative electroencephalographic (QEEG) indices, and cognition-specific, functional outcome measures. Results were compared between QEEG indices calculated from the standard 19 versus 4 frontal (or 4 posterior) electrodes to assess the feasibility and efficacy of employing a reduced electrode montage. Resting-state EEG was recorded at the bedside within 62–101 h after onset of symptoms of middle cerebral artery, ischaemic stroke (confirmed radiologically). Relative power for delta, theta, alpha and beta, delta/alpha ratio (DAR) and pairwise-derived brain symmetry index (pdBSI) were averaged; over all electrodes (global), over F3, F4, F7, F8 (frontal) and P3, P4, T5, T6 (posterior). The functional independence measure and functional assessment measure (FIM–FAM) was administered at mean 105 days post-stroke. Total (30 items) and cognition-specific (5 items) FIM–FAM scores were correlated with QEEG indices using Spearman's coefficient, with a Bonferroni correction. Twenty-five patients were recruited, 4 died within 3 months and 1 was lost to follow-up. Hence 20 cases (10 female; 9 left hemisphere; mean age 68 years, range 38–84) were analysed. Two QEEG indices demonstrated highly-significant correlations with cognitive outcomes: frontal DAR ($\rho = -0.664$, $p \leq 0.001$) and global, relative alpha power ($\rho = 0.67$, $p \leq 0.001$). After correction there were no other significant correlations. Alpha activity – particularly frontally – may index post-stroke attentional capacity, which appears to be a key determinant of functional and cognitive outcomes. Likewise frontal delta pathophysiology influences such outcomes. Pending further studies, DAR from 4 frontal electrodes may inform early screening for post-MCA stroke cognitive deficits, and thereby, clinical decisions.

1. Introduction

Cognitive impairment and vascular dementia are common sequelae of stroke. Prevalence and incidence statistics vary between studies but even conservative estimates suggest that more than 20% of patients exhibit substantial cognitive impairments within 3 months of stroke (Douiri et al., 2013). The costs of stroke care in patients with cognitive impairments are three times higher than those without (Claesson et al., 2005). In addition post-stroke cognitive impairment is a risk factor for depression (Nys et al., 2006) and poor functional recovery (Pahlman et al., 2012). The Clinical Guidelines for Stroke Management of the National Stroke Foundation of Australia recommend that all stroke patients be screened for cognitive deficits and referred for appropriate therapy (National Stroke Foundation, 2010).

Brief cognitive screening tools such as the MoCA (Montreal Cognitive Assessment) (Freitas et al., 2012) and MMSE (Mini Mental State Examination) (Folstein et al., 1975) administered pre-discharge have been shown to be somewhat informative for predicting cognitive impairment at three to six months post-stroke (Dong et al., 2012). However the latter study only employed a dichotomous outcome variable: no-mild impairment or moderate to severe impairment. Others report that brief screening tests (such as MoCA or MMSE) alone can have limited efficacy for predicting cognitive impairment in stroke patients (Srikanth et al., 2006). In addition, completion of these requires alertness, unimpaired language function, usage of the dominant hand and arm, and functional eyesight and hearing; yet one or more of these are often compromised in stroke patients. Potential subjectivity or inter-assessor reliability issues also should be considered. Hence there remains a need for a more reliable, objective and robust methodology for early screening of post-stroke cognitive impairment. Additionally an ideal method would be available for use on all stroke patients without being limited by functionality as brief cognitive assessments are. This could help realise more

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informed and effective clinical management decisions regarding, for example, the required level of care, rehabilitation strategies, or patients' capacity to return to work.

In the current study we investigated the potential of quantitative electroencephalography (QEEG) in this setting. QEEG produces objective indices of brain dysfunction which have proven useful in various clinical applications. The clinical value of QEEG in assessment of ischaemic stroke was first reported some decades ago (Pfurtscheller et al., 1984). Further a recent review focusing on studies over the past decade highlights that two classes of global QEEG indices can uniquely inform clinical stroke management including prognostication of neurological and general functional outcomes (Finnigan and van Putten, 2013). These are: (1) frequency-specific power measures, particularly of slow relative to faster band-power, such as the delta/alpha ratio (DAR), or; (2) measures of interhemispheric power (a)symmetry, such as the pairwise derived brain symmetry index (pdBSI). In addition numerous outcomes indicate that QEEG indices are sensitive to cognitive function (e.g. Klimesch, 2012; Mitchell et al., 2008; Finnigan and Robertson, 2011) and to (future) mild cognitive impairment or dementia, not necessarily resulting from cerebral ischaemia (Jackson and Snyder, 2008; Cummins et al., 2008). Hence QEEG may well prove valuable for screening of post-stroke cognitive deficits, yet such studies have not been reported to date.

As discussed in a recent review (Finnigan and van Putten, 2013), access to EEG hardware and expertise can be a potential challenge and relatedly, so can the total time required for EEG set-up and recording. Adoption of a "lower-density" EEG electrode montage could help overcome such issues and indeed DAR measures averaged from just four frontal electrodes (F3, F7, F4, F8) were significantly correlated with neurological outcomes in a small sample of anterior circulation stroke patients (Finnigan and van Putten, 2013). This is an interesting finding, as a four-electrode EEG montage is substantially more feasible to acquire than one comprising nineteen (or more) electrodes. In addition frontal lobe function is particularly critical to numerous aspects of cognitive function, such as attention (Stuss and Knight, 2002), and frontal QEEG band-power has been found to correlate with measures of cognitive function in healthy older adults (Finnigan and Robertson, 2011). Given these various findings we analysed correlations between frontal (as well as global and posterior) QEEG indices, with cognitive (and general functional) outcome measures. On the basis of the information reviewed above, including the sensitivity of delta to post-stroke pathophysiology and of alpha to cognitive function, we hypothesised that QEEG indices sensitive to delta and/or alpha power would correlate with post-stroke outcome measures. Furthermore given the previously-reported links between frontal delta or DAR and outcomes (after middle cerebral artery stroke), as well as between alpha activity with frontal lobe function and cognition, we hypothesised that this correlation would hold in the case of frontal delta and/or alpha power.

2. Methods

2.1. Patients

Approval to carry out the study was obtained from the local University and Hospital Human Research Ethics Committees. Written informed consent from each patient or substitute decision maker was obtained. Patients with acute neurologic symptoms consistent with anterior circulation stroke were initially considered. Patients under 18 years old, pregnant or with previous craniotomy were excluded from the study. All patients underwent acute, non-contrast computed tomography (NCCT) scanning and the majority of cases also had CT perfusion (CTP) and angiogram (CTA). Ischaemic stroke and arterial territory affected by the same was confirmed via acute CT and, in six cases, also follow-up magnetic resonance imaging (MRI) including diffusion-weighted imaging (DWI). Only patients with middle cerebral artery (MCA) ischaemic stroke thus confirmed were included. Time of stroke onset was defined at the time that the patient was last seen without stroke symptoms.

2.2. EEG data acquisition and initial assessment

EEG was recorded continuously at the bedside in the acute stroke unit at approximately 72 h post stroke symptom onset. In (five) "wake-up" stroke cases, time of stroke onset was defined as the mid-point between time to bed (without symptoms) and time of wake-up (with symptoms). A NicOne Brain Monitor system (Natus Medical Inc.) was used with a sampling rate of 500 Hz. Nineteen Ag/Ag–Cl electrodes (Nicolet) were applied according to the International 10–20 system. In addition a reference electrode was positioned midway between Fz and Cz, and a ground electrode positioned on collar bone. Electrode impedances were predominantly 5–10 kΩ or less. EEG was recorded for approximately 20 min total in resting, awake state with eyes closed. Alertness or sleepiness was assessed throughout each recording, primarily via periodic behavioural assessments. Within 30 min of the EEG recording the National Institute of Health Stroke Scale (NIHSS) was administered.

2.3. EEG data analysis

EEG signal processing and analyses were performed offline using methods that we have previously reported (Finnigan and Robertson, 2011; Finnigan et al., 2007; Sheikh et al., 2013). These were computed using EEGLAB, Edit 4.5 (Compumedics-Neuroscan) and in-house software, respectively. EEG data were filtered (lowpass; 35 Hz, 12 dB/octave) and re-referenced to the common average reference. Each continuous data file was segmented into contiguous epochs each of 4096 ms duration (2048 data points), epochs were baseline-corrected and epochs in which EEG amplitude exceeded ± 100 μV were automatically rejected. Following this, the data were examined visually and, when appropriate, any remaining epochs containing clear, lower-amplitude artefacts (such as arising from blinks or patient movement) were rejected and excluded from further analyses.

From the first remaining 45 epochs (184 s) of artefact-free EEG data per participant a Fast Fourier Transform (FFT) was applied. This process resulted in a power value for each 0.488 Hz iteration, at each electrode. From the resulting power spectra, absolute power was summed across the delta (0.98–3.91 Hz), theta (4.39–7.32 Hz), alpha (7.81–12.21 Hz), and beta (12.70–29.79 Hz) bands (inclusive). These are minor variations from clinical values; 1–4 Hz, 4–7.5 Hz, 7.5–12.5 Hz and 12.5–30 Hz, respectively. Relative power values for each resulting frequency band were computed as the ratio of summed absolute band-power to total summed power across the 0.98–29.79 Hz range. DAR was computed as the ratio of absolute power for the respective frequency bands of interest. These indices were all initially computed separately for each electrode, then were averaged over all nineteen scalp electrodes to create "global" QEEG indices as is standard current practice. Specific frontal QEEG indices were computed by averaging the respective measures from the four lateral frontal electrodes (F3, F4, F7, F8). These electrode locations were chosen given that the frontal lobes are critical to various cognitive processes and also because, in MCA and anterior circulation strokes at least, scalp delta power is typically highest at these (and adjacent) electrodes (Finnigan and van Putten, 2013). In addition Szelies et al (2002) report that delta and alpha power measures derived particularly from these (and adjacent) electrodes differed significantly between samples of stroke patients whom subsequently had favourable versus unfavourable outcomes (Szelies et al., 2002). The fronto-polar electrodes (FP1, FP2) are not included in our frontal analyses because the above does not hold in the case of these, and we aimed to constrain this analysis to a few electrodes, plus they generally are relatively more susceptible to artefacts (including those caused by eye movements or blinks), as discussed elsewhere (Finnigan and van Putten, 2013). QEEG indices averaged across the four corresponding lateral posterior electrodes (P3, P4, T5, T6) were also analysed, for comparison with results from frontal indices.

van Putten and Tavy, (2004) were the first to investigate the brain symmetry index (BSI) in stroke studies and found it to correlate with concomitant NIHSS in acute ischaemic stroke. Another study reported it