Clinical Neurophysiology 122 (2011) 2157–2168

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Determination of awareness in patients with severe brain injury using EEG power spectral analysis

Andrew M. Goldfine [a,b,*], Jonathan D. Victor [a], Mary M. Conte [a], Jonathan C. Bardin [a], Nicholas D. Schiff [a]

[a] Department of Neurology and Neuroscience, LC-803, Weill Cornell Medical College, 1300 York Ave., New York, NY 10065, USA
[b] Burke Medical Research Institute, 785 Mamaroneck Ave., White Plains, NY 10605, USA

ARTICLE INFO

Article history:
Accepted 16 March 2011
Available online 21 April 2011

Keywords:
Consciousness
EEG spectral analysis
Motor imagery
Traumatic brain injury
Locked-in-state
Minimally conscious state

HIGHLIGHTS

- Motor and spatial imagery change EEG power spectra over a wide range of channels and frequencies.
- Patterns of spectral change vary between healthy subjects performing the same task.
- Brain injured subjects can demonstrate command following through changes in EEG power spectra.

ABSTRACT

Objective: To determine whether EEG spectral analysis could be used to demonstrate awareness in patients with severe brain injury.
Methods: We recorded EEG from healthy controls and three patients with severe brain injury, ranging from minimally conscious state (MCS) to locked-in-state (LIS), while they were asked to imagine motor and spatial navigation tasks. We assessed EEG spectral differences from 4 to 24 Hz with univariate comparisons (individual frequencies) and multivariate comparisons (patterns across the frequency range).
Results: In controls, EEG spectral power differed at multiple frequency bands and channels during performance of both tasks compared to a resting baseline. As patterns of signal change were inconsistent between controls, we defined a positive response in patient subjects as consistent spectral changes across task performances. One patient in MCS and one in LIS showed evidence of motor imagery task performance, though with patterns of spectral change different from the controls.
Conclusions: EEG power spectral analysis demonstrates evidence for performance of mental imagery tasks in healthy controls and patients with severe brain injury.
Significance: EEG power spectral analysis can be used as a flexible bedside tool to demonstrate awareness in brain-injured patients who are otherwise unable to communicate.

1. Introduction

Recent studies using functional MRI (fMRI) and event-related potentials (ERP) demonstrate that some severely brain-injured patients retain a range of cognitive capacities despite minimal or no behavioral evidence of awareness (Kotchoubey et al., 2005; Owen et al., 2006; Perrin et al., 2006; Schnakers et al., 2008; Monti et al., 2010; Bardin et al., 2011). Importantly, Monti et al. (2010) used fMRI detection of motor and spatial navigation imagery to establish communication with a patient who had no overt behavioral ability to communicate.

These results, while compelling, raise an important ethical obligation to seek out patients who may retain significant cognitive abilities not evidenced by behavioral testing as in principle such patients may have a desire and capacity to participate in their own decision-making (Fins and Schiff, 2010). Currently available methods are limited in the types of patients they can assess and in the paradigms available for determination of awareness. For example, fMRI cannot be used in patients who are unable to be transported to the scanner, have implanted ferromagnetic material or make frequent head movements. The need to bring patients to the scanner also makes repeated assessments difficult, and can overlook evidence of awareness in patients whose arousal levels fluctuate through the day (Bardin et al., 2011). ERPs, meanwhile, require exact and consistent timing of subject performance. This limits the range of applicable behavioral paradigms and risks false

Abbreviations: FDR, false discovery rate; FLD, Fisher linear discriminant; HC, healthy control; HLM, Hjorth Laplacian montage; PS, patient subject; TGT, Chronux two group test; TBI, traumatic brain injury.

* Corresponding author at: Burke Medical Research Institute, 785 Mamaroneck Ave., White Plains, NY 10605, USA. Tel.: +1 914 269 8454; fax: +1 866 212 1404.
E-mail address: andygoldfine@gmail.com (A.M. Goldfine).

1388-2457/$36.00 © 2011 International Federation of Clinical Neurophysiology. Published by Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.clinph.2011.03.022

negative results in patients with delayed or variable response times.

An alternative is a quantitative approach to EEG using power spectral analysis. Unlike fMRI, EEG can be recorded at the bedside, allowing for multiple testing sessions across different states of arousal. EEG measurements can be carried out in patients with ferromagnetic implants, and the EEG signal can be parsed with a precise temporal resolution, allowing for removal of transient movement artifacts. Unlike ERP-based analysis methods, power spectral analysis of EEG allows for detection of responses that are delayed or not tightly synchronized to a stimulus. Finally, EEG power spectral analysis has already been used as a communication tool in patients with stroke and motor neuron disease (Bai et al., 2008) and therefore can in principle serve both as a diagnostic method and basis for development of a communication device.

With this motivation, we investigated whether spatially- and spectrally-localized changes in EEG power spectra can identify behaviorally covert responses to commands in healthy subjects and patients with severe brain injury.

2. Methods

2.1. Subjects

Five healthy control (HC) volunteers with no history of neurological disease (three males; mean age 34 years, range 25–52 years) participated in the study. The three patient subjects (PSs) chosen for this study were drawn from a convenience sample enrolled in a multi-modal imaging and behavioral study of the natural history of recovery from severe brain injury. Clinical profiles of the PSs are in Table 1, Fig. 1 and Supplementary Appendix A. The five HCs and three PSs in this study demonstrated the capacity to generate mental imagery on the same tasks used here, via independent fMRI studies (Bardin et al., 2011). Studies described herein were approved by the Weill Cornell Medical College Institutional Review Board. HCs gave their written consent. Consent was obtained for PSs from their legally authorized representatives.

2.2. Experimental paradigm

HCs and PSs were asked to perform multiple trials of one or two imagery tasks while the EEG was recorded (Fig. 2). Each trial consisted of a pair of pre-recorded commands in a male voice, delivered 15 s apart to the subjects via noise-cancelling headphones (JVC, Wayne, NJ). Commands lasted approximately 2 s, providing subjects with 13 s to perform the mental imagery task. A sequence of eight contiguous trials of the same start – stop command pair constituted a run; so a run lasted approximately 4 min.

In the motor imagery task, subjects alternately heard the commands "imagine yourself swimming," and "stop imagining swimming". Prior to each run we instructed subjects to imagine themselves swimming from the time they heard the command, until they heard the command to stop. In the spatial navigation task, subjects alternately heard the commands "imagine walking through the rooms of your house" and "stop imagining walking through your house". Prior to each run we instructed subjects that

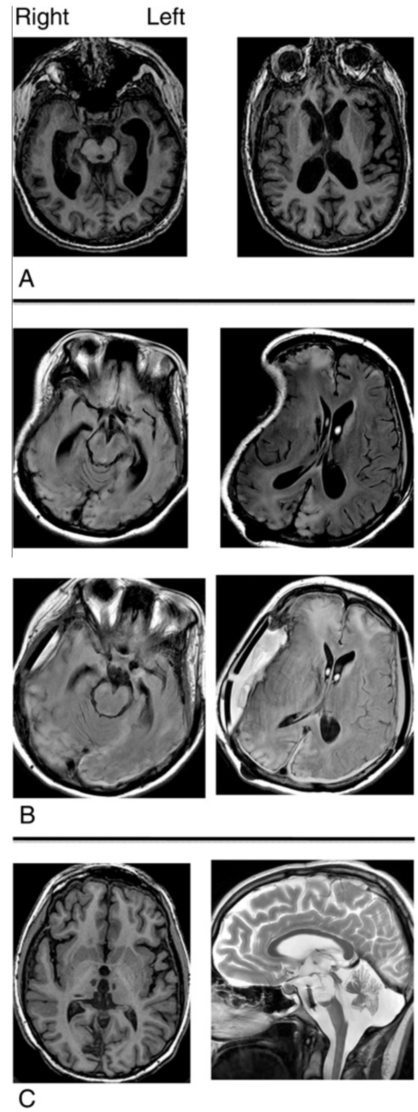

Fig. 1. Brain MRIs showing major features of structural damage in the three patient subjects (PSs). (A) PS 1: T1-weighted MRI shows diffuse atrophy. (B) PS 2: T2 FLAIR MRI shows focal injuries to frontal and occipital lobes and distortion from craniectomy on right (visit 1, top), and right occipital and bifrontal injuries, and fluid collection under cranioplasty site on right (visit 2, bottom). C. PS 3: T1-weighted axial image shows bithalamic and right medial temporo-occipital lobe strokes with minimal cerebral atrophy; T2-weighted sagittal image shows loss of majority of midline pons and midbrain.

Table 1
Summary of Patient Subjects' clinical status and experiments performed.

Patient subject		Age	Time since injury (months)	Mechanism of injury	Diagnosis	Timing of studies
1		25	25	Trauma	LIS	2 Runs in 2 h
2	Visit 1	19	6	Trauma	MCS	3 Runs in 30 min
	Visit 2	19	10		Emerged from MCS	Day 1: runs 1–4 over 2 h Day 2: runs 5 and 6 over 1 h
3	Visit 1	24	31	Stroke	MCS	4 Runs over 2 h
	Visit 2	25	43		MCS	Day 1: Run 1 in afternoon Day 2: Run 2 in morning, Run 3 in afternoon

Abbreviations: LIS – locked-in-state; MCS – minimally conscious state.