Assessing Information Processing in Patients With Long-Term and Severe Disorders of Consciousness

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Abstract. To study the prevalence of the N100, P200, and P300 event related potentials (ERP) in patients with chronic and severe disorders of consciousness, ERPs were recorded in nine healthy participants and 19 long-term vegetative state and minimally conscious state patients during an auditory oddball paradigm in a passive – listen only – and an active – count the odds – condition at two time points. Significant ERPs were detected in all patients. N100 was significantly more frequent than the P300. In contrast to healthy controls, no evidence was found for differential activity between the passive and the active condition in any patient.

Keywords: EEG, t-cwt, wavelet, P300, disorders of consciousness, vegetative state, minimal conscious state, ERP

1. Introduction

The event-related potential (ERP) P300 has been linked to the processing of attention-demanding stimuli, and is thought to indicate the intactness of a wide cortical network ranging from prefrontal to temporal-parietal areas [Polich, 2007].

The vegetative state (VS) is a severe disorder of consciousness (DOC), presumably characterized by a complete loss of conscious experience despite preserved wakefulness. It is sometimes followed by a minimally conscious state (MCS), in which weak and inconsistent signs of awareness can be detected. In a previous study, up to 32% of DOC patients showed a P300 in an auditory oddball paradigm [Kotchoubey et al., 2005].

We hypothesized that healthy subjects would show an increased P300 in the active condition, and we were interested in whether DOC patients would show a similar increase. Such an increase could be an indicator of preserved command following and thus, consciousness and cognition.

2. Material and Methods

Participants 19 patients with disorders of consciousness (sex: 11 male, 8 female; age: $M = 50$, $SD = 14.19$; diagnoses: 5 MCS, 14 VS; years since onset: $M = 6.18$, $SD = 3.17$; aetiology: 10 hypoxia, 3 trauma-related, 3 intra-cerebral haemorrhage, 3 other; hemispheric localization of lesions: 4 left, 2 right, 3 both, 10 none), whose legal representatives gave informed consent, and nine healthy subjects participated in the study. Patients' diagnoses were ascertained using the Coma Recovery Scale (CRS-R) immediately before EEG measurement.

Procedure Subjects listened to an auditory oddball paradigm (60 odd and 420 frequent tones) in a passive ("listen only"), and an active ("count the odd tones") condition. In 17 patients, the experiment was repeated after a minimum interval of 1 week (T2) to compensate for the possibility of fluctuating arousal levels.

EEG recording and analysis EEG and EOG was recorded (512 Hz) from 31 standard 10-20 system electrode

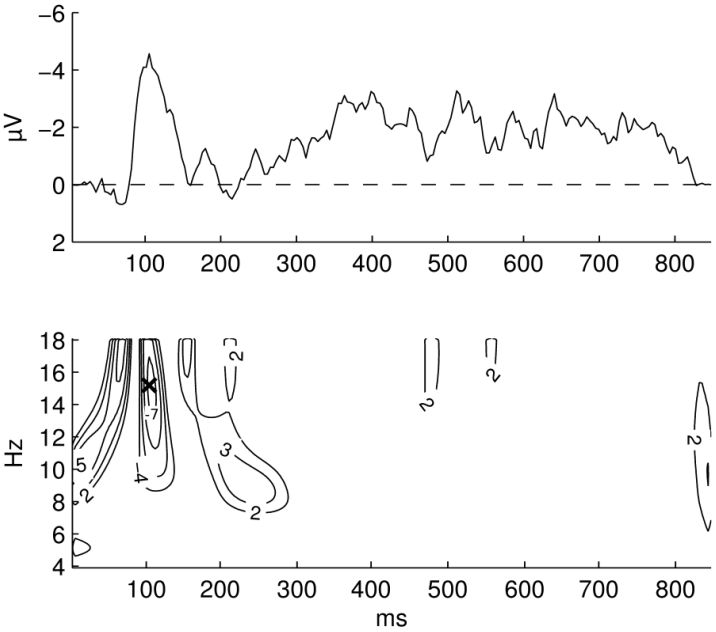

Figure 1. *Top: Average EEG waveform (Fz) of one VS patient showing preserved N100. Bottom: Contour plot of the studentized wavelet coefficients corresponding to the waveform in the top panel in the time-frequency plane. To avoid clutter, contour lines are restricted to the top and bottom ten percent of studentized wavelet coefficients. Bold cross (X) indicates N100.*

locations. Offline, the EEG was bandpass (0.01-70 Hz, 12 dB) and notch filtered, epoched into 850 ms long intervals, and aligned to the 100 ms pre-stimulus baseline. Ocular artefacts were corrected using a regression procedure and trials with absolute voltages in excess of 100 µV excluded. Only datasets with at least 20 trials in each condition (n = 26) were considered for the remaining analyses and re-referenced to linked mastoids.

A variant [Real et al., 2013] of the Studentized Continuous Wavelet Transform (t-CWT) [Bostanov, 2003] was used for ERP detection. The method consists of firstly, calculating the continuous wavelet transform for each trial and channel using a Mexican Hat wavelet [Bostanov et al., 2006]. Secondly, student t-values are calculated from the resulting wavelet coefficients, either across all experimental conditions – if one is interested in detecting activity different from baseline – or between experimental conditions – if the focus is on differences between experimental conditions. Thirdly, local extremes are detected using a 2D peak detection procedure. Fourthly, significance of extremes is ascertained via t-max randomization tests [Blair et al., 1993] with an error level of $\alpha = 0.05$. Fig. 1 shows an example of an average waveform (Fz, 409 trials) from a VS patient and the corresponding time-frequency map of studentized wavelet coefficients. In this representation, the N100 is visible as a high-frequency negative peak.

3. Results

Healthy participants: All healthy subjects showed significant activation in the N100, P200 and P300 ranges in all conditions, with the exception of one subject in which no P200 could be detected in the active condition. Seven of nine healthy subjects showed a significantly larger P300 in the active than in the passive condition.

Patient participants: Reliable ERPs were detected in all 17 patients entering the analysis. A P300 was found in two VS, in one MCS and in one patient who was diagnosed with MCS at T1 but VS at T2. No significant difference between the P300 in the active and passive conditions was found in any patient.

The N100 was found more often than the later P300 in both experimental conditions (binomial tests, all $p < 0.05$) at T1 but not at T2. No difference was found for the P200.

Table 1. *Frequency of ERPs by experimental condition and time points in patients. Number before the slash indicates number of subjects where ERP was found, the number after the slash indicates total number of subjects available for the respective analysis.*

	T1		*T2*	
ERP	*Passive*	*active*	*passive*	*active*
N100	12/13	10/10	5/5	9/10
P200	6/13	6/10	4/5	3/10
P300	2/13	1/10	1/5	3/10

4. Discussion

Our results replicate previous findings of a comparatively higher prevalence of the N100 in comparison to the P300, and an overall rare occurrence of a P300 (4/17 = 24%) in DOC patients [Kotchoubey et al., 2005]. In contrast to healthy subjects, in DOC patients the P300 of the active condition was not enhanced compared to the passive condition, possibly due to lack of language understanding, insufficient attention span, lack of motivation or cognitive abilities, or indeed disrupted conscious awareness.

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