ROLE OF ACTIVE ERP PARADIGMS IN AWARENESS DETECTION IN NON RESPONSIVE PATIENTS

Zulay LUGO[1, 2,3], Damien LESENFANTS[1], Rémy LEHEMBRE[1], Steven LAUREYS[1], Quentin NOIRHOMME[1]
[1]Coma Science Group, Cyclotron Research Centre and CHU Neurology Department, University of Liège, Belgium
[2]Department of Psychology I, University of Würzburg, Germany
[3]French Association of Locked-In Syndrome (ALIS), Paris, France

Abstract

The role of active vs. passive ERP paradigms in disorders of consciousness is assessed in this case study of a LIS patient. Results show that despite absent P3 in a passive auditory task, the patient displayed significant differences in the active task. This study shows the importance of using a large battery of tests when assessing DOC patients.

Key words: Event-related potentials, disorders of consciousness, locked-in syndrome

1. Introduction

Detection of consciousness in non-responsive patients with severe brain injury remains a challenging task. Electrophysiological techniques such as electroencephalography (EEG), as well as neuro-imaging techniques such as functional magnetic resonance imaging (fMRI) have been used to assess signs of consciousness in patients emerging from coma (1). Other than allowing the differentiation of Disorders of Consciousness (DOC) as the vegetative state (VS) and the minimal conscious states (MCS), perhaps even more interesting, is the usefulness of these methods to diagnose the presence of consciousness in non-respondent patients due to severe motor and language deficits, who keep intact or almost intact cognitive abilities, such as patients with locked-in syndrome (LIS) (2). Event-related potentials (ERPs) have been widely used both for diagnostic and prognostic purposes in DOC and LIS patients. Usually, a hierarchical approach of assessment is proposed in cases of patients with DOC, ranging from the research of elementary signs of cognitive processing (indicators of certain automatic cognitive process but not of consciousness) to the signs of more complex cognitive processes (for which a volitional capacity, denoting the presence of a higher order cognitive treatment of the information is necessary). However, previous studies have found the presence of an intermediate component although lower order components were absent (3). This suggests that to stop a test in a patient who does not show the most basic indicators of cognitive processing of information may result in the sub-diagnosis of patients with higher cognitive abili**ty** (and a higher degree of consciousness).This situation is illustrated with a case report of a LIS patient, subjected to a hierarchical level assessment of consciousness using auditory ERP paradigms.

2. Experiments

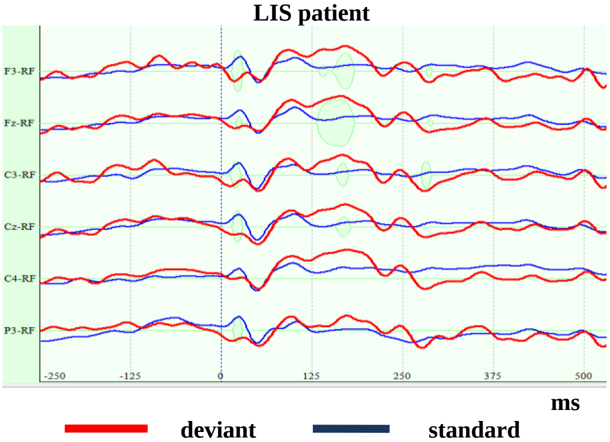
Patient: a 42-years-old woman, university level education, who suffered a brain stem stroke twenty years ago and remained in LIS since then. The patient was evaluated at home following the protocol proposed in the Decoder project. Written informed consent was obtained from the patient. ***Event-related paradigm:*** Six paradigms were tested following a hierarchical battery: an odd ball paradigm to elicit the MMN in which the deviant tone was of shorter (20ms) duration than the standard (50 ms); two semantic-paradigms to elicit the N400 wave: a word-prime paradigm (200 pairs of words with 100 pairs of semantically related words and 100 -e.g. green-red- and 100 pairs containing unrelated words - e.g cold-fish-) and a sentence paradigm in which 200 sentences were presented: 100 sentences with a congruent ending mixed with 100 sentences with a non-congruent ending. Finally, a frequency paradigm consisting of a frequent complex tone (standard: 440+880+1760 Hz) as standard and a rare complex tone (deviant: 247+494+988 Hz) as deviant was used to elicit the P300 wave both in passive (to listen to the tones) and active (instruction to count the deviant tones) condition. ***Event-related potentials' acquisition:*** Stimuli were presented via earphones. The EEG was recorded using a 32-electrode cap (g.tec system, Austria) following the 10-20 system at the positions FP1, Fp2, F7, F3, Fz, F4, F8, FC5, FC1, FC2, FC6, T7, C3, Cz, C4, T8, CP5, CP1, CP2, CP6, P7, P3, Pz, P4, P8, O1, O2. The reference electrode was at the left lobe ear and the ground electrode was placed at the AFz position. Four EOG's were placed (above, below and laterally to one eye). A fiveminute break separated each condition of the event-related paradigm. ***Event-related potentials' analysis:*** EEG recordings were processed and analysed using the NPXlab2012 software ((NPX Lab 2012 rel.: 1.9.8.314). Data were preprocessed with Independent Component Analysis (ICA), independent components corresponding to ocular artifacts were removed. Furthermore, trials showing abnormally high voltages (>70μV in absolute values) were automatically rejected. For each paradigm, trials were averaged within epochs lasting from -250 to 1000 sec, to obtain ERP's. The components (MMN, N400, and P300) of interest for the respective paradigm were analyzed by visual inspection and by running a t-Student test. Differences were considered statistically significant for $p<0.05$, if they appeared simultaneously at a minimum of two electrodes and if they lasted a minimum of 50 consecutive milliseconds.

3. Results

There was no evidence of the presence of the MMN, N400 and P3 (passive) in this patient, neither with the visual inspection nor with the statistical analyses of the waveforms. Figure 1 illustrates the lack of a significant P3 passive component at the 300ms in the patient in comparison to a healthy control. For the P3 active paradigm, a significant positive deviation was observed in several electrodes (Fig.2).

Fig 1: P3 passive. The green spot shows the electrodes and latency with a significant t-test. Notice the absence of clearly discernible P3 component in the patient at 300 ms when compared with a control subject

LIS patient



Healthy control

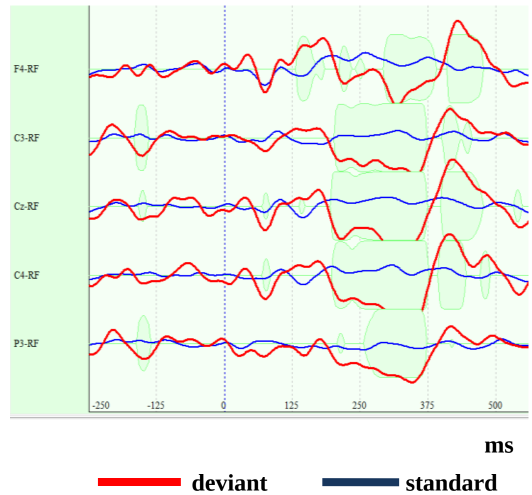
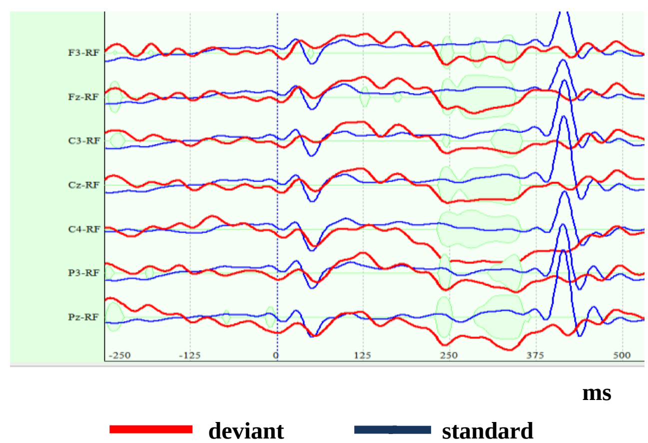


Fig 2: P3 active LIS patient. Notice the positive t-test (green spot) between approximately 250 and 375 ms in several electrodes lasting more than 50 consecutive milliseconds.



4. Discussion

The present case seems to confirm previous observations about, not only the presence of a larger P3 component in the active condition than in the passive one in LIS patients (2), but also to confirm the possibility of finding an evoked response to an active paradigm when the equivalent passive paradigm failed to trigger a significant response. This has important implications for the diagnosis of altered states of consciousness. It suggests that the hierarchical scheme is not completely valid or recommended, because it would be possible to find higher-level components within the cognitive processing hierarchy in these patients in the absence of lower level processing.

In Patients with DOC, the lack of some ERP components may be associated to the fluctuation of vigilance (4), which may include the extension and location of the lesions. In the LIS patients, although in most cases the primary lesion is of vascular etiology and located in the anterior portion of the protuberance (with predominant involvement of motor pathways), several other etiologies of this condition have been described, involving other sub-cortical and even cortical structures which might affect the ERPs (5) .

In conclusion, with this case study we want to highlight the importance of running a complete test for all non-responsive patients, even in the absence of lower-level components, to minimize the risk of missing a sign of consciousness.

5. References

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