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Time-Varying Functional Connectivity for Understanding the Neural Basis of Behavioral Microsleeps

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Abstract— **Episodes of complete failure to respond during attentive tasks — lapses of responsiveness ('lapses') — accompanied by behavioral signs of sleep such as slow-eye-closure are known as behavioral microsleeps (BMs). The occurrence of BMs can have serious/fatal consequences, particularly in the transport sectors, and therefore further investigations on neurophysiological correlates of BMs are highly desirable. In this paper we propose a combination of High Resolution EEG techniques and an advanced method for time-varying functional connectivity estimation for reconstructing the temporal evolution of causal relations between cortical regions of BMs occurring during a visuomotor tracking task. The preliminary results highlight connectivity patterns involving parietal and fronto-parietal areas both preceding and following the onset of a BM.**

I. Introduction

During attention-demanding tasks, subjects can frequently fail responses to certain stimuli. Three different types of failures can occur: response error (incorrect response), slowed response (increased reaction time), and absence of any response. Episodes of complete failure to respond — lapses of responsiveness ('lapses') — accompanied by behavioral signs of sleep such as slow-eye-closure are known as behavioral microsleeps (BMs) [1]. The occurrence of such BMs in professionals, such as truck drivers, locomotive drivers, pilots, air traffic controllers, health professionals, and process control workers can have serious/fatal consequences [1, 2]. For this reason, the prediction of BMs, and subsequent wake-up warnings, has become an important objective towards helping minimize such accidents.

In order to predict the occurrence of these events, an investigation into neurophysiological correlates of BMs is necessary. Several studies, based on the analysis of behavioral, fMRI, and EEG data, were conducted to understand the neuronal processes underlying BMs. Multiple behavioral cues including eye-closure, head-nodding, facial video, and responsiveness have been used to identify BMs. For example, changes in the duration of eye-closure are correlated with the error rate during tracking tasks [3]. fMRI studies have revealed a substantial decrease in bilateral thalamic activity associated with loss of arousal [4], transition to sleep [5], and slowed reactions after sleep deprivation [6]. Decreases in activity in the posterior cingulate gyrus and medial frontal cortex, and increased activity in occipitoparietal and frontal areas, associated with loss of vigilance [7], have confirmed the role of wake-sleep neural mechanisms in BMs [8].

EEG studies [1] have shown increased spectral power in the delta, theta, and alpha bands, and decreased spectral activity in the beta, gamma, and higher bands, during drowsiness. However, few correlations between the occurrence of lapses and the changes in power spectrum were found [1].

Among all the techniques used for the neurophysiological characterization of BMs, EEG is the most promising, due to its high temporal resolution and its portability which may allow early detection – and even prediction – of BMs in more real-world environments.

In this paper, we have investigated the possibility of better defining the neural processes underlying BMs by applying a powerful body of techniques to EEG data recorded during the occurrence of multiple BMs in a visuomotor tracking task. A combination of high-resolution EEG techniques [9] and advanced methods for time-varying functional connectivity estimation [10, 11] allowed us to improve the low spatial resolution of EEG, by reconstructing the cortical sources of EEG activity, and to describe the temporal evolution of causal relations between such cortical regions during and immediately before BMs.

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II. METHODS

A. Partial Directed Coherence

The PDC [12] is a full multivariate spectral measure, used to determine the directed influences between any given pair of signals in a multivariate data set. This estimator has been demonstrated to be a frequency-domain version of the concept of Granger causality.

In this paper, an adaptive formulation of PDC, based on an adaptive MVAR (AMVAR) model was used [10]. The time dependent parameters matrices were estimated by means of the Recursive Least Square algorithm with a forgetting factor.

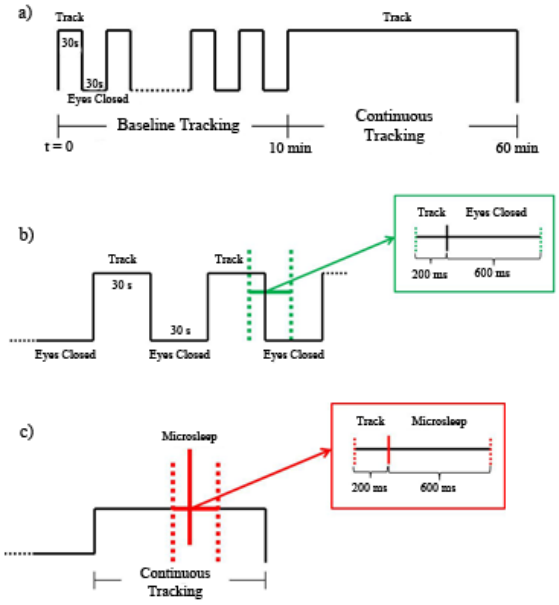

Figure 1. The experiment timeline consisted of 10 min of baseline, in which tracking task and eye-closed condition were alternated (30 s each) and in 50 min of continuous tracking task (panel 'a'). The interval (-200; 600) ms across the eye-closed/microsleep onset was selected for the segmentation of data acquired during baseline (panel 'b') and continuous tracking task (panel 'c').

B. The Recursive Least Square

The Recursive Least Square algorithm, extended to the multi-trial case, is an approach introduced in [10] for the estimation of time varying MVAR parameters. The algorithm is based on the minimization of the squared prediction error

$$E_n = \sum_{i=1}^{n} (1-c)^{n-i} \left\| Z_i \right\|^2 \quad , \; 0 \le c < 1 \qquad (1)$$

where n is the current sample, c is an adaptation constant and

$$Z_n = Y_n - W_n \hat{\Lambda}_{n-1}^T \quad , \quad W_n = (Y_{n-1}, \ldots, Y_{n-p}) \qquad (2)$$

where $\hat{\Lambda}_n$ is the adaptive estimation of Λ_n and p is the MVAR optimal order.

Details on the solution of the algorithm are in [10]. In the present study, c was set to 0.02, in order to have a higher adaptation speed without losing the estimation accuracy, as suggested in [11].

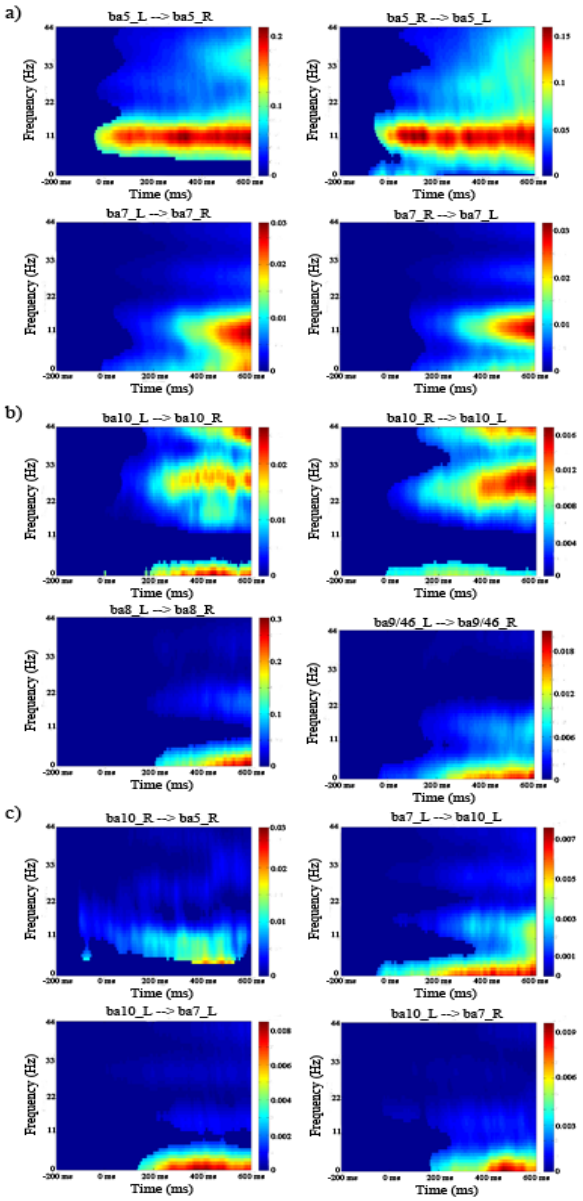

Figure 2. Time-frequency distribution of the time-varying PDC functions for some significant functional connections belonging to the network elicited during the occurrence of BMs. a) connections between parietal regions (ba5L → ba5R, ba5R → ba5L, ba7L → ba7R); b) connections between frontal regions (ba10L → ba10R, ba10R → ba10L, ba8L → ba8R, ba9/46L → ba9/46R); c) connections between frontal and parietal areas (ba10R → ba5R, ba7L → ba10L, ba10L → ba7L, ba10L → ba7R). Only the results with a significance level of 5% with respect to the baseline, corrected with False Discovery Rate criterion for multiple comparisons, are presented.

C. Application to BMs

Experimental Design. Five right-handed healthy male volunteers, aged 26-38 years (mean = 29.5) with no history of neurological, psychiatric, or sleep disorder, participated in the study. They were equipped with an Actiwatch (Mini

Mitter Inc., Bend OR, USA) to verify that the subjects had regular sleep habits in the week prior to the session. Subjects were provided with lunch approximately 15 min before the session. The experiment consisted of a tracking task in which subjects had to maneuver a finger-based joystick in order to follow the movements of a 2-D target on the screen. The experimental paradigm was designed to obtain baseline tracking versus eyes-closed data for 10 min, immediately followed by 50 min of continuous tracking, as shown in Fig.1a. The first 10 min of baseline comprised 30-s epochs of tracking followed by 30-s epochs of eyes-closed rest. This was then immediately followed by 50-min continuous tracking task. EEG data were recorded from 64-channel scalp locations using the QuickCap (Compumedics, Neuroscan, Charlotte, NC, USA). Simultaneously an eye-video recording was performed for the offline extraction of behavioral data.

Signal Processing. EEG data were band-pass filtered (1-45 Hz + Notch 50 Hz) and ocular artifacts were removed by means of Independent Component Analysis. The occurrence of BMs was determined by flat-spots in tracking performance concomitant with eye-based evidence of drowsiness and prolonged full or substantial eye-lid closure, sometimes accompanied by head-nodding and terminated by waking head jerks. The data were segmented according to the behavioral data, as showed in Fig. 1, and residual artifacts were rejected. By means of a realistic head model available from the Montreal Neurologic Institute and the weighted minimum norm solution for the associated linear inverse problem [9] the waveforms for 12 cortical regions of interest (Brodmann Areas (ba): 19L/R, 7L/R, 5L/R, 8L/R, 9/46L/R, 10L/R) were reconstructed. The reconstructed cortical waveforms were subjected to time-varying functional connectivity estimation via the RLS algorithm. Then, to highlight only the information flows at the basis of microsleeps and not due to the transition between the execution of tracking task and the condition of eyes closed without any lapses of consciousness, a statistical comparison between microsleep and baseline conditions was performed. In particular, the PDC values were considered significantly different from the baseline only if they were above a threshold extracted by applying the percentile on the baseline condition for a significance level of 5% corrected with False Discovery Rate criterion for multiple comparisons.

III. Results

Time-frequency distributions of the time-varying PDC function for some significant functional connections belonging to the network elicited during the occurrence of BMs for a representative subject are shown in Fig. 2. The most significant links involved frontal (Fig. 2a), parietal (Fig. 2b) and fronto-parietal areas (Fig. 2c), mainly in the theta and alpha bands after the onset of BMs. Connections preceding the BMs occurrence can be seen between ba5L and ba5R (right-hand in Fig. 2a) and between ba10R and ba5R (left-hand Fig. 2c) in the theta band. The significant time-varying connectivity patterns were then averaged in theta band, defined according to the Individual Alpha Frequency (IAF) [13] and in four time intervals defined according to the microsleep onset. The results are shown in

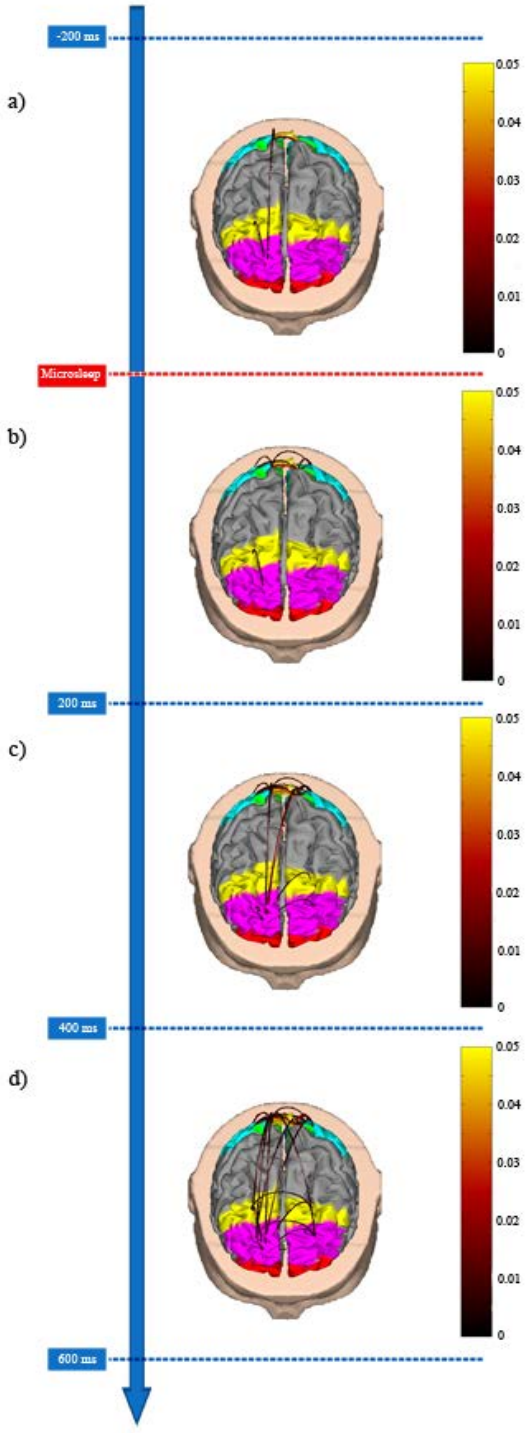

Figure 3. Functional connectivity patterns in a representative subject before and during BMs. Each network is related to a specific time interval defined according to the microsleep onset: (-200 ; 0) ms (panel a), (0 ; 200) ms (panel b), (200 ; 400) ms (panel c), (400 ; 600) ms (panel d). Connectivity patterns are represented on a realistic cortical model seen from above with the nose pointing the bottom part of the page. The colors and size of the arrows code the strengths of the connections. The cortical regions of interest are highlighted with different colors.

Fig. 3 for the same representative subject. In the figure, each network is related to a specific time interval defined according to the microsleep onset: (200 ; 0) ms (Fig. 3a), (0 ; 200) ms (Fig. 3b), (200 ; 400) ms (Fig. 3c), (400 ; 600) ms (Fig. 3d). Connectivity patterns are represented on a realistic cortical model. The colors and size of the arrows code for the strengths of the connections. The cortical regions of interest are highlighted with different colors. In the period preceding the microsleep onset, connections between ba5R and ba5L in both directions and a link from ba10R to ba5R were seen. Such connections persisted and were reinforced in the patterns related to BM occurrence. In the 200-400 ms after the microsleep onset (Fig. 3c), connections were seen between the left and right frontal region and a fronto-parietal network, directed from right frontal areas to both parietal regions. In the 400-600 ms after the microsleep onset (Fig. 3d), the fronto-temporal network involved both hemispheres.

Similar connectivity patterns were seen in the second of the two subjects analyzed.

IV. Discussion

We have reported preliminary results of an advanced analysis of the time and frequency distribution of multivariate cortical networks obtained from non-invasive high density EEG recordings during the spontaneous occurrence of lapses of responsiveness. Multivariate approaches, like the one here applied, have been demonstrated to significantly increase the accuracy of the connectivity patterns obtained, with respect to classical bivariate approaches, especially in terms of avoiding false positives [14]. The time-varying approach adopted here allowed a major requirement for stationarity of the data to be overcome, thus opening the way for the study of cortical connectivity during transient events, such as microsleeps, to be explored.

Previous studies [1] have shown that lapses in this task are associated with increased power and positive correlations in the delta, theta, and alpha bands and decreased power in the beta, gamma, and higher bands, even if the correlations between EEG band power and definite BMs are low. Other studies showed a correlation between theta activity and fluctuations in a simulated driving task and in a pursuit tracking task [15, 16]. In the present study, the focus shifted from the analysis of the changes in the EEG spectral power to the analysis of the changes in the functional connections between cortical areas. The results of the statistical comparison between the time interval around the microsleeps onset and an appropriate baseline showed the existence of a clear connectivity pattern arising at the BM onset in the theta, alpha, beta and gamma bands and, in some cases, shortly before, in the theta frequency band. Very similar results were obtained across subjects, in the small sample analyzed. If confirmed on a larger sample of subjects sample, these results may open the way to a new understanding of the neural phenomena underlying microsleeps.

V. Conclusion

This study provides an important insight into the time-varying functional connectivity correlates of phasic BMs during an extended tracking task. It is hoped that an improved understanding of the brain activities underlying these behaviors will prove of value in the detection and, ultimately, prediction of such behaviors from a combination of physiological and behavioral cues.

This is of importance in the development of devices for preventing serious, and often fatal, consequences of drowsiness and microsleeps.

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