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fMRI correlates of behavioural microsleeps during a continuous visuomotor task

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Abstract—**Behavioural microsleeps (BMs) are brief episodes of absent responsiveness accompanied by slow-eye-closure. They frequently occur as a consequence of sleep-deprivation, an extended monotonous task, and are modulated by the circadian rhythm and sleep homeostatic pressure. In this paper, a multimodal method to investigate the neural correlates of BMs using simultaneous recording of fMRI, eye-video, VEOG, and continuous visuomotor response is presented. The data were collected from 20 healthy volunteers while they performed a continuous visuomotor tracking task inside an MRI scanner for 50 min. The BMs were identified post-hoc by expert visual rating of eye-video and visuomotor response using a set of pre-defined criteria. fMRI analysis of BMs revealed changes in haemodynamic activity in several cortical and sub-cortical regions associated with visuomotor control and arousal.**

I. Introduction

Transient failure to respond can occur frequently during any attention-demanding task. Some of these failures manifest as response error (incorrect response) and slowed response (increased reaction time), while others are more serious, such as complete failure to respond. Episodes of complete failure to respond — lapses of responsiveness ('lapses') — accompanied by behavioural signs of sleep such as slow-eye-closure are known as behavioural microsleeps (BMs) [1]. The occurrence of BMs in occupations in which public safety depends on extended unimpaired performance, such as truck drivers, locomotive drivers, pilots, air traffic controllers, health professionals, and process control workers can be of particular concern [1, 2].

BMs occur due to an increased drive to sleep as a consequence of boredom during monotonous tasks and sleep-deprivation, and is modulated by the circadian rhythm and sleep homeostatic pressure. Short episodes (3—15 s) of theta and decreased alpha activity in the EEG are often used as indicators of microsleeps [3]. However, EEG activity provides minimal information on the behavioural state of an individual, which is crucial for task performance. In fact, unlike BMs in which individuals completely fail to respond, during EEG-defined microsleeps individuals often continue to respond, albeit poorly [3]. Therefore, multiple behavioural cues including eye-closure, head-nodding, facial video, and responsiveness have been used to identify episodes of BMs.

Peiris et al. [1] detected BMs using facial video and visuomotor responsiveness and found a high rate of BMs during an extended visuomotor task, even in well-rested individuals. This finding generally follows observations from earlier studies that changes in the duration of eye-closure are correlated with tracking error [4] and with time-on-task [5].

The neural mechanisms underlying BMs remain poorly understood. However, some understanding can be gained from recent fMRI studies of responses during short-term attention tasks. Slowed responses in the rested-awake state stem primarily from transient disruption of the fronto-parietal attentional network, occipital visual-processing areas, and inability of the frontal-midline default-mode network to re-engage to the task at hand [6, 7]. In contrast, slowed responses in the state of lowered arousal, such as due to sleep-deprivation, involve additional disruptions in thalamo-cortical arousal networks and visual-processing areas [8]. Similarly, observations from fMRI studies of wake-sleep transition suggest important roles for the posterior cingulate cortex, thalamus, and prefrontal cortices, which show decreased activity in initial sleep-stages compared to wakefulness [9]. While these studies provide important indicators of brain networks likely involved in BMs, the exact spatial and temporal nature of BOLD activity underlying BMs can only be determined through their precise identification from multiple behavioural cues.

In this study, we have used simultaneous fMRI, eye-video, vertical-electrooculogram (VEOG), and continuous visuomotor recording to investigate the brain mechanisms underlying BMs. We predicted that at least some subjects would have frequent BMs during extended performance on a visuomotor task during post-lunch-dip hours inside the MRI scanner. We hypothesized that by analyzing fMRI during BMs, widespread BOLD changes in sensory-motor, attention, and arousal-related cortical and sub-cortical structures would be revealed.

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II. METHODOLOGY

A. Participants

Twenty right-handed volunteers (10 males and 10 female, aged 20 to 45 years, mean age 29.8 years) with no history of neurological, psychiatric, or sleep disorder participated in the study.

Subjects were asked not to consume any stimulants or depressants, such as alcohol, coffee, and nicotine, during the 4 hours prior to the session. Experimental sessions were conducted between 1:00 pm and 4:00 pm. Subjects were required to keep a detailed diary of their sleep habits and to wear an Actiwatch (Mini Mitter Inc., Bend OR, USA) to measure their sleep-wake activity during the 6 days and 5 nights prior to the scan session. The diary and Actiwatch data were used to verify that the subjects had regular sleep habits in the week prior to the session. A set of questionnaires was used to assess the subjects' general health, sleep quality, morningness-eveningness, and daytime sleepiness.

B. Simultaneous fMRI, VEOG, eye-video recording

A system was set up to simultaneously record fMRI, eye-video, VEOG, and continuous visuomotor response. A schematic of the connection between the different modules in the system is shown in Fig. 1. This allowed proper synchronization of the multimodal data.

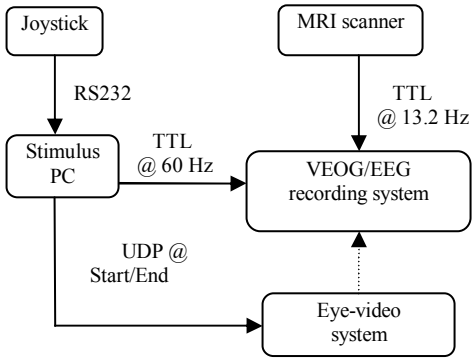

Fig.1. Schematic diagram of the simultaneous recording system.

A Signa HDx 3.0T MRI Scanner (GE Medical Systems, Waukesha, WI) was used to acquire structural and functional MRI data. Structural images of the whole brain were acquired using T1-weighted anatomical scans (repetition time (TR): 6.5 ms; echo time (TE): 2.8 ms; inversion time (TI): 400 ms; field of view (FOV): 225 × 250 mm; matrix: 512 × 512; slice thickness: 1 mm). Functional images were acquired using echo-planar imaging (TR: 2.5 s; TE: 35 ms; FOV: 220 × 220 mm; slice thickness: 4.5 mm; number of slices: 33). A fieldmap (echo spacing: 700 μs; TR: 580 ms; TE: 6.0 ms and 8.2 ms) was acquired for each subject to enable correction of EPI distortion due to magnetic field inhomogeneity. Participants were provided with ear plugs to reduce the high-volume acoustic noise from the scanner. Additional pads were placed on both sides of the head to minimize head motion.

Continuous VEOG was acquired by placing bipolar Ag-AgCl sintered electrodes above and below the left eye and transmitting the signal via carbon fibres (MagLink) using Synamps2 amplifiers and Scan 4.4 software (Compumedics Neuroscan, Charlotte, NC, USA). The reference electrode was placed between Cz and Pz and the ground electrode was placed close to Fz. Data was acquired at 10 kHz, after a low-pass filtering with a cutoff at 2 kHz. EEG (64 channel), bipolar chest ECG, and a pulse oximeter signal were also recorded but are not discussed further in this paper. Synchronization triggers from the MRI scanner and the task computer were recorded continuously by the Synamps2 system. The eye-video was synchronized with VEOG signal by asking subjects to briefly open and close their eyes five times at the start and end of the session.

Eye-video was captured using a Visible Eye™ system incorporating a fibre-optic camera in the scanner (Avotec Inc., Stuart FL, and USA). The video was recorded on a PC at 25 fps using custom software.

C. Experimental protocol

Between 1:00 pm and 4:00 pm subjects undertook a 50-min (2 runs of 25 min each) visuomotor tracking task session in which they had to manipulate an MRI-compatible joystick to pursue a target moving continuously with a random 2-D pattern on a computer screen [10]. The horizontal and vertical components of the target were produced by summing 7 sinusoids with frequencies evenly spaced from 0.033 to 0.231 Hz. This produced a 2-D periodic target trajectory (T = 30 s) with a velocity range of 63—285 pixels/s. The target (yellow disc, d = 23 pixels) and the joystick response (red disc, d = 20 pixels), generated by custom-designed software, were presented via MRI-compatible goggles (Avotec, Stuart, FL, USA) with a resolution of 1024 x 768 pixels and a field of view of 30° x 23°. The background was a uniform gray.

D. Data Analysis

VEOG artifact removal: The gradient artifact in VEOG data was removed using the artifact reduction module in Scan 4.4 software.

Tracking error: Tracking error signal was generated by calculating the euclidean distance between the centres of the target and response discs.

Event marking: A custom-built SyncPlayer™ program was used to simultaneously replay synchronized eye-video, VEOG, and tracking target (x and y), response (x and y), velocity, and error signals. An expert rater visually inspected the data, second-by-second, to identify events of interest using pre-defined criteria as follows:

Type 0 — Episodes of markedly increased tracking error, but response speed > 0, for greater than 500 ms accompanied by droopy eyes (full or partial slow-eye-closure).

Type 1 — Episodes of approximately flat or incoherent response for greater than 500 ms, accompanied by droopy eyes (full or partial slow-eye-closure). Episodes shorter than 15 s are considered to be BMs and longer than 15 s are considered to be sleep.

Type 2 — Forced eye-closure and odd events.

Type 3 — Episodes of flat or incoherent response without droopy eyes.

Preprocessing of fMRI data: The fMRI data were preprocessed using several modules available in the FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl) software. The preprocessing steps included slice time correction, motion correction using MCFLIRT, distortion correction using PRELUDE and FUGUE, spatial smoothing using a Gaussian kernel with a full-width-half-maximum of 7 mm, and high-pass temporal filtering. For group level analysis, fMRI data were registered to the standard MNI space using FLIRT.

General linear model analysis: To identify significant BOLD activity associated with BMs, fMRI data were analyzed using FEAT (FMRIB expert analysis tool). For this analysis, BMs shorter than 5 s were modeled as events with an impulse function at their onset convolved with a double-gamma haemodynamic response function. Other events, including longer BMs, sleep, type 0, type 2, and type 3, were modeled as variable epochs. Scan nulling regressors were used for any large motion events (> 3 mm in any direction). fMRI data was linearly modeled on a voxel-by-voxel basis using FILM (FMRIB's improved linear model) with autocorrelation correction. The general linear model based analysis generated statistical parametric maps for each subject and condition. Average group statistical maps were generated using mixed-effect model analysis. A cluster-based correction of the z-statistic images was performed and thresholded at z scores > 4.5 and $p < 0.01$.

III. Results

A. Behavioural results

The rate of BMs was highly variable across subjects (mean ± SE: 85.27±14.7 BMs/h; range: 0─188 BMs). Out of 20 subjects, only 14 had a sufficient number of BMs in at least one run to be included in the fMRI analysis (Fig. 2). For most subjects, the majority of BMs were < 5 s duration.

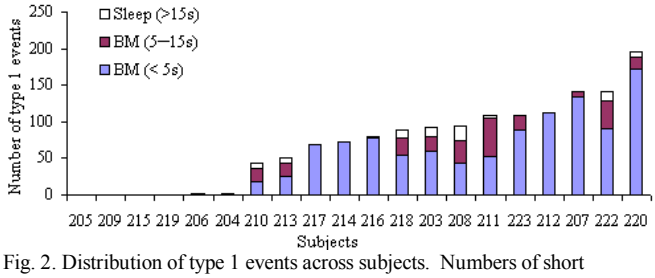

Fig. 2. Distribution of type 1 events across subjects. Numbers of short BMs, long BMs, and sleep episodes are plotted for each subject. Only BM < 5 s were used in fMRI analysis.

The behavioural response during BMs was a flat response with markedly lowered response speed and increased response error (Fig. 3).

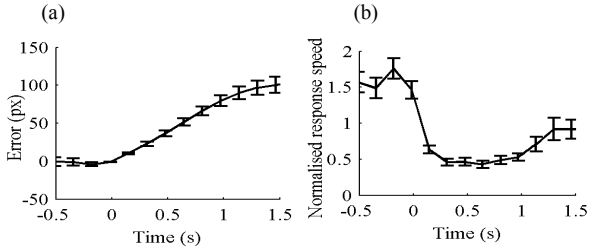

Fig. 3. Mean ± SEM of (a) response error and (b) normalized response speed. Normalised response speed was calculated by dividing response speed by target speed. BM onset is at 0 s.

B. BOLD activity during behavioural microsleeps

The group statistical map of activations and deactivations during BMs is shown in Fig. 4.

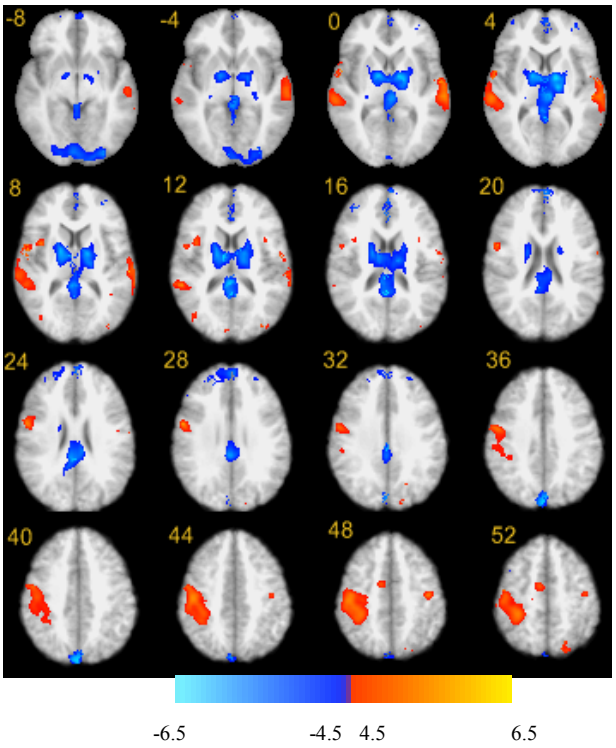

Fig. 4. The spatial pattern of group level BOLD activation (red) and deactivation (blue) during short BMs (< 5 s). Images have been registered into the standard MNI space and are shown in radiological convention.

During BMs, increased BOLD activity was observed in the bilateral precentral gyrus, bilateral superior parietal cortex, bilateral parahippocampal gyrus, and bilateral middle temporal gyrus. Decreased BOLD activity (relative to baseline tracking) was observed in a large cluster encompassing the bilateral thalamus and basal ganglia structures, and in the posterior cingulate cortex, primary visual cortex, and parts of the medial frontal cortex. The BOLD signal changes in the bilateral thalamus and bilateral precentral gyrus are shown in the Fig. 5.

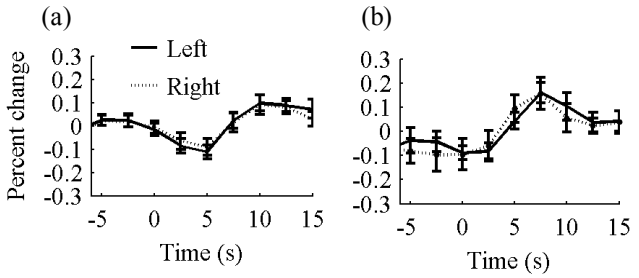

Fig. 5. Percentage BOLD signal change surrounding BM (onset at 0 s) in the (a) bilateral thalamus and (b) bilateral precentral gyrus. Vertical bars represent SEM.

IV. Discussion

In this study, we identified BMs during an extended visuomotor task using multiple behavioural measures including tracking response, eye-video, and VEOG. Most subjects had frequent BMs during an extended visuomotor task inside an MRI scanner.

Univariate analysis of fMRI data revealed several cortical and sub-cortical structures with significant BOLD signal changes during BMs. The bilateral thalamus, which showed decreased activity, is involved in the maintenance of arousal [11] with decreased activity associated with transition into sleep [9], time-on-task [12], and slowed reactions after sleep deprivation [8]. Similarly, the posterior cingulate gyrus and medial frontal cortex are part of the default mode network which shows decreased activity during transition into sleep [9], confirming the role of wake-sleep neural mechanisms in BMs.

We also observed increased activity in sensory-motor areas during BMs. This is surprising given that sensory-motor function is disrupted during BMs. We suggest that this activity is related to the brain's cortical compensatory mechanism during BMs. An increase in activity in occipito-parietal and frontal areas during decreased vigilance has been reported previously in the literature [13]. This notwithstanding, some of the increased activity could be related to attentional recovery [6], as most of the behavioural BMs were of short duration (< 2s) and the sampling rate of the BOLD signal was longer. Some of the increased activity, particularly in the visual areas, could also be related to eye-closure during BMs [14].

The EEG data collected in this study will be used in future work to increase the temporal resolution of brain activities through joint fMRI-EEG analyses. This will allow better exploration of the spatiotemporal dynamics of BMs and of other lapses and poor-performance events during tracking.

It is hoped that an improved understanding of the brain activities and mechanisms underlying BMs may prove of value in helping detect and even predict BMs from a combination of physiological and behavioural cues. This, in turn, may lead to the development of devices for preventing serious, often-fatal, consequences of lapses, especially in the transport sector.

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