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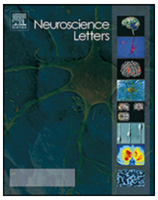

Hemispheric differences over frontal theta-band power discriminate between stimulus- versus memory-driven saccadic eye movement

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ABSTRACT

Although several electrophysiological studies have demonstrated the role of theta band during the execution of different visuospatial attention tasks, this study is the first to directly investigate the role of theta power during the planning, execution and cognitive control of saccadic eye movements (SEMs). The current study aims at addressing this issue by investigating absolute theta power over the frontal cortex during the execution of random and fixed SEMs. Twelve healthy volunteers, performed two tasks involving different conditions in the planning, execution and cognitive control of SEMs while their brain activity pattern was recorded using quantitative electroencephalography. We found an interaction between SEM condition and electrode (F3, F4, Fz), and a main effect of time point and electrode. Our key finding revealed that the stimulus presentation induces different patterns over frontal theta power increase between the left and right hemisphere. We conclude that right and left frontal regions are an important factor to discriminate between memory- versus stimulus-driven SEMs, and speculate on their different contributions to visuospatial attention.

Saccadic eye movements (SEMs) are directly related to attention processes by integrating visual information with specific oculomotor movements, which can therefore be considered the first stage of sensorimotor integration and information processing [18,30]. Sensorimotor integration is a complex process that allows for the generation of an internal plan, beginning with the input of sensory stimuli, in order to perform a motor task [31]. The planning of SEM is comprised of a motor and a cognitive component [2,8,17] with the motor component mainly regulating the generation and oculomotor control of the saccades, and the cognitive component being involved in the selection of relevant stimulus features or the modulation of voluntary SEM [8,17]. Because of the crucial contribution of SEM to visual attention processes, SEM is often used as a behavioral parameter to measure and quantify the attention process during the selection of relevant stimuli [5,17,19].

Functional brain imaging studies have consistently revealed similar frontal brain regions (e.g., frontal-eye-fields) as being activated during the execution of tasks requiring SEM in which subjects were required to direct their attention to particular

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stimuli or spatial locations [1,5,21,23]. These frontal brain regions which underlie the preparation and execution of SEM and at the same time represent core regions of the visual attention network in the brain critically include the frontal-eye-fields (FEF) of both hemispheres [19,24,27]. This relationship between selective visual attention and SEM is particularly strong during tasks in which a target-stimulus has to be spatially located [9,10,16].

Several electrophysiological studies indicate that increase in the theta band (4.5–7 Hz) represent the neural correlate for the integration of sensory information with a respective motor response and the generation of voluntary behavior [3,4,6,14]. Caplan et al. [4] demonstrated that theta oscillations underlie the coordination of sensory and motor brain activity. Other human studies have also shown an association between theta band activity and the execution of different spatial attention and spatial navigation tasks [4,7,28]. However, although the role of theta band activity for spatial attention and sensorimotor integration tasks has been demonstrated, no study hitherto has directly investigated the specific role of theta band power activity during the planning, execution and cognitive control of SEM.

The current study aims to directly address this issue by investigating absolute theta power over the frontal cortex during the execution of two different SEM paradigms. The “fixed” SEM paradigm requires subjects to perform repetitive, i.e., fixed SEMs to the same peripheral spatial location, while in the “random” SEM paradigm, subjects are asked to perform SEM driven by a pure random series of presented target-stimuli. Using these paradigms, we first wanted to investigate whether theta power increase over the frontal cortex plays a role for the planning, execution and cognitive control of SEM per se, and secondly, we aimed to reveal whether the role and/or lateralization of these theta increases may discriminate between fixed and random SEM.

Twelve healthy volunteers (3 males; mean age: 26.25 (SD 4.13)) were recruited for this study. All participants had normal or corrected-to normal vision and no sensory, motor, cognitive or attentional deficits that would affect saccadic eye movement. Inclusion criteria were: absence of mental or physical impairments and no history of psychoactive or psychotropic substance use (screened by a previous anamnesis and a clinical examination) and right handed [32]. Subjects signed a consent form which thoroughly described the experimental procedure. The experiment was approved by the Ethics Committee of the Psychiatric Institute of Federal University of Rio de Janeiro (IPUB/UFRJ) (number FR-233406).

Subjects were seated on a comfortable chair in a darkened and sound-protected room in order to minimize sensory interference. At the participants’ eye level, a bar composed of 30 light emitting diodes (LEDs) was positioned with 15 of these LEDs located on the left side of fixation, and 15 on the right side. The bar had a length of 120 cm. The distance between participants’ eyes and the LED bar was standardized to 100 cm. Computer software controlled the LED bar and determined the presentation of the stimulus. Participants were asked to keep their eyes fixed on the center of the bar, and to shift their eyes when they perceived one of the diodes lighting up. Participants were instructed to follow the LEDs with their eyes in such way that their heads remained static.

The SEM paradigm consisted of two different conditions: a fixed pattern and a random pattern. In the fixed pattern, the target-stimulus (target LED) always appeared at a pre-defined position, i.e. LED 12, of either the left or right side (alternating between left and right). This condition is characterized by the predictability of the appearance of the stimulus at a pre-defined spatial location in the periphery of the visual field, and was thus considered to be memory-driven. In contrast, the random pattern presented a fully randomized series of target LEDs at completely unpredictable spatial positions across the central and both peripheral visual fields (the light could appear at any of the 30 LEDs). This experimental condition was considered purely stimulus-driven. In both conditions, each LEDs remained lit for 250 ms, with a inter-LED-time of 2 s. Each participant underwent 12 consecutive blocks, 6 blocks fixed SEM and 6 blocks random SEM, with 20 trials per block. The probability of a light to appear on the left or right side was counterbalanced within and across blocks, so were both SEM conditions.

The International 10/20 EEG electrode system [13] was used with a 20-channel EEG system (Braintech-3000, EMSAMedical Instruments, Brazil). The 20 electrodes were arranged on a nylon cap (ElectroCap Inc., Fairfax, VA, USA) yielding monopolar derivations using the earlobes reference. Impedance of EEG and EOG electrodes was kept between 5 and 10 kΩ. The data recorded had a total amplitude of less than 70 μV. The EEG signal was amplified with a gain of 22,000, analogically filtered between .01 Hz (high-pass) and 80 Hz (low-pass), and sampled at 200 Hz. The software *Data Acquisition* (Delphi 5.0) at the Brain Mapping and Sensory Motor Integration Lab, was employed with the following digital filter: notch (60 Hz).

Four additional electrodes of 9 mm in diameter mounted in a bipolar form were used to measure the electrooculogram (EOG). Electrodes were arranged horizontally from the outer canthi of both eyes to determine the horizontal EOG (hEOG) and vertically above both eyes to determine the vertical EOG (vEOG).

We applied a visual inspection and independent component analysis (ICA) to remove possible sources of artifacts produced by the task (i.e., blink, muscles and saccade-related artifacts). The data were collected using the bi-auricular reference and they were transformed (re-referenced) using the average reference after we conducted the artifact elimination using ICA. We removed those trials that clearly showed a blink and a saccade-related artifacts “influence” by visual inspection and we removed the components that showed blink and saccade-related artifacts “contamination”’ using independent component analysis (ICA). A classic estimator was applied for the power spectral density (PSD), or directly from the square modulus of the FT (Fourier transform), which was performed by MATLAB 5.3 (Matworks, Inc.). The number of samples was 800 (4 s × 200 Hz) with rectangular windowing. We extracted Quantitative EEG parameters within a time window between 500 ms before the stimulus presentation and 500 ms after the target stimulus (LEDs) (the selected epoch started 500 ms before and ended 500 ms after the trigger, i.e., moment 1 and moment 2, respectively). Thereafter, all raw EEG trials were visually controlled and trials contaminated with ocular or muscle artifacts were discarded. The Fourier transform resolution was 1/4 s to .25 Hz (FFT). To examine a stationary process, the “run-test” and “reverse-arrangement test” were applied. Specially, the stationary process was accepted for each 4 s (epoch’s duration in this period). In this manner, based on artifact-free EEG epochs, the threshold was defined by the mean plus three standard deviations with epochs showing a total power higher than this threshold not being included into the analysis.

Absolute theta power (4.5–7 Hz) was the dependent variable of interest. The statistical analyses of the absolute theta power was performed using a three-way repeated measures ANOVA with the factors SEM condition (2 levels: fixed versus random SEM), electrode (3 levels: F3, F4 and FZ), and time point (2 levels: pre- versus post-stimulus epoch) as the three within-subject factors.

The three-way repeated measures ANOVA revealed a main effect for the factor “electrode” ($F = 362.431$, $p < .001$) with the Fz electrode showing the strongest absolute theta power increase, followed by F4 and F3 (Fig. 1). We also revealed a main effect of the factor “time point” ($F = 340.244$, $p < .001$) with the epoch 500 ms post target-stimulus showing stronger theta power increase as compared to the epoch 500 ms before the target-stimulus (Fig. 2). Most importantly, we also found a significant interaction between