The effects of bromazepam over the temporoparietal areas during the performance of a visuomotor task: A qEEG study

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This study investigated the effects of bromazepam on qEEG when 14 healthy subjects were asked to perform a visuomotor task (i.e., motor vehicle driving task). The subjects were exposed to two experimental conditions: the placebo (PL) and 6 mg of bromazepam (Br 6 mg), following a randomized, double-blind design on different days. Specifically, we observe absolute power extracted from qEEG data for theta band. We expected to see a decrease in absolute theta power in the temporal and parietal areas due to the influence of bromazepam for the experimental group when compared with the placebo group. We found a main effect for the condition factor for electrodes T3, T4, P3 and P4. We also observed a main effect for the period factor for electrodes P3 and P4. We observed that the ingestion of 6 mg of bromazepam induces different patterns in theta power at the temporal and parietal sites. We concluded that 6 mg of bromazepam was an important factor in the fluctuation of the activities in the temporal and parietal areas. We then hypothesize about the specific role of this drug during the execution of a visuomotor task and within the sensorimotor integration process.

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stimulus (S2), however, we did not analyze the contingent negative variation (CNV). One of the most influential neurophysiological theories about the S1–S2 paradigm is that it读ies the cortex for processing the next stimulus and response, i.e., S2 stimulus, due to an advisory signal, i.e., S1 stimulus [11]. According to those principles and considering the features of each area, we expected to see the effects of bromazepam in the left and right temporal and parietal cortices. Several studies demonstrated that the temporal areas are involved in the transmission of multimodal sensory information, i.e., neurons in these areas are sensitive to stimuli of different modalities, enabling multisensory interactions [19,9,17]. Moreover, the parietal lobe integrates sensory information from several channels [9,21].

Thus, our objective is to investigate the effects of bromazepam on qEEG when subjects were submitted to a visuomotor task (i.e., motor vehicle driving task). Specifically, we observed absolute power extracted from qEEG data for theta band. The increase of theta power has been related to increases in mental effort during the encoding of sensory information, attention demand, higher task difficulty and increasing cognitive load [18,19,31]. We expected to see a decrease in absolute power for the experimental group when compared with the placebo group in the left and right temporal and parietal areas due to the drug’s influence. Thus, the assessment of qEEG may unveil how the temporal and parietal areas participate in the organization and integration of sensory information, in other words, the performance of cognitive operations and the achievement of motor control during the performance of multiple complex tasks under the effect of bromazepam.

The sample was composed of 14 healthy subjects (nine male and five female; mean age: 32.5, SD: 9.5). The inclusion criteria included the absence of mental or physical impairments and no history of psychoactive or psychotropic substance use (screened by a previous anamnesis and a clinical examination). All subjects were also right handed, according to the Edinburgh inventory [24]. Moreover, they had no less than 6–8 h of sleep prior to the experiment and no previous experience with the task. All subjects signed a consent form and were aware of the experimental protocol. The experiment was approved by the Ethics Committee at the Federal University of Rio de Janeiro according to the principles of Helsinki Declaration [13].

The task was performed in a sound and light-attenuated room, to minimize sensory interference. Each subject was exposed to both the experimental conditions: the placebo (PL) and 6 mg of bromazepam (Br 6 mg), following a randomized, double-blind design. To minimize sensory interference, enabling multisensory interactions [19,9,17]. Moreover, the parietal lobe integrates sensory information from several channels [9,21].

To quantify reference-free data, a visual inspection and independent component analysis (ICA) were applied to remove as many sources of artifacts produced by the task as possible [15]. Data from individual electrodes exhibiting loss of contact with the scalp or high impedances (>10 kΩ) were deleted and data from single-trial epochs exhibiting excessive movement artifacts (>100 μV) were also deleted. ICA was then applied to identify and remove any remaining artifacts after the initial visual inspection. ICA is an information maximization algorithm that is derived from spatial filters through the blind source separation of EEG signals into temporally independent and spatially fixed components. Independent components resembling eye-blink or muscle artifacts were removed and the remaining components were then back-projected onto the scalp electrodes by multiplying the input data by the inverse matrix of the spatial filter coefficients derived from ICA using established procedures. The ICA-filtered data were then re-inspected for residual artifacts using the same rejection criteria described above. Then, 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.). Quantitative EEG parameters were extracted from 2 s periods (the selected epoch started 0.5 ms before and after the appearance of each stimulus, i.e., S1 and S2, respectively), for consecutive (non-overlapping) artifact-free, 2-s EEG epochs (spectral resolution: 0.25 Hz), with rectangular windowing. In this manner, based on artifact-free EEG epochs, the threshold was defined by mean plus three standard deviations. Epochs with a total power higher than this threshold were not integrated into the analysis.

We analyzed the anterior-temporal (T3 and T4) and the parietal (P3 and P4) areas. The first one plays an important role in supplying multimodal sensory information for the performance of voluntary movements and sensorimotor integration [12]. The parietal areas are functionally related to the integration of sensory information from different modalities [21], manipulation of objects, attention and visuospatial processing [2,6]. The theta band (4.5–8 Hz), was chosen due to its association with cognitive functions such as stimuli encoding [3], attention mechanisms [29] and information transmission [19].

The qEEG absolute power values were log10-transformed by SPSS software (version 16.0) to approximate a normal distribution. A two-way ANOVA was used to analyze between the conditions (i.e., PL × Br 6 mg), and between the periods (i.e., pre-S1, post-S1, pre-S2, post-S2) for each electrode (i.e., T3, T4, P3, P4). A Scheffé test was applied to analyze significant differences between the periods (p < 0.05).
The two-way ANOVA with repeated measures indicated a main effect for the condition factor at T3 ($p = 0.003; F = 7.070$; Fig. 1A), T4 ($p = 0.006; F = 5.921$; Fig. 1B), P3 ($p = 0.001; F = 55.793$; Fig. 1C) and P4 ($p = 0.001; F = 13.764$; Fig. 1D) electrodes. The analysis of the T3 and T4 electrodes demonstrated a lower power value for Br 6 mg when compared to PL. The analysis of the P3 and P4 electrodes showed a lower power for Br 6 mg when compared to PL.

The two-way ANOVA also revealed a main effect for the period factor for electrodes P3 (Fig. 2A) and P4 (Fig. 2B). Further post hoc analyses revealed a significant difference among periods for both electrodes. The analysis of the electrode P3 demonstrated a lower power value in pre-S1 when compared to post-S1 ($p = 0.007$) and post-S2 ($p = 0.007$). Post-S1 demonstrated a higher value when compared to pre-S2 ($p = 0.012$). And the power value in pre-S2 was lower than post-S2 ($p = 0.012$). The analysis of the electrode P4 showed a lower power value in pre-S1 when compared to post-S1 ($p = 0.007$) and post-S2 ($p = 0.035$). Post-S1 demonstrated a higher value when compared to pre-S2 ($p = 0.005$). And the power value in pre-S2 was lower than post-S2 ($p = 0.024$).

This study aimed to verify the effects of bromazepam on qEEG absolute theta power when subjects were submitted to a visuo-motor task (i.e., motor vehicle driving task). Our task involved unpredictable situations where a car must be controlled on a virtual track with different types of curves at different velocities. In this manner, the assessment of qEEG may unveil how the cerebral cortex participates in the organization and integration of sensory information, thus the performance of cognitive operations and the achievement of motor control during the performance of multiple complex tasks under the effects of bromazepam.

We observed a decrease in theta power for the Br 6 mg group when compared with the PL group for the T3, T4, P3 and P4 electrodes. It is well-documented that the temporal areas are influenced by the somatosensory cortex, which plays an important role in supplying multimodal sensory information to sensorimotor integration processes (supplying the right hemisphere) and voluntary movements (i.e., supplying the left hemisphere) [12,28]. The reduction in theta power for Br 6 mg appears to be strongly associated with the encoding of sensory integration, such as stimulus detection and attention (i.e., stimuli appearance – S1–S2) based on its temporal relation to the onset of targets and its spatial distribution over the left temporal areas (i.e., T3 electrode). Moreover, the temporal region is involved with the formation of new memories, and in this case, those of a spatial nature (i.e., T4 electrode). The subjects were submitted to a task that involved unpredictable situations demanding attention in order to control a car on a virtual track that presents various forms and types of curves at different speeds, thus creating an increasing cognitive load (i.e., spatial and temporal perception) [17]. We observed a reduction of activity over temporal area in the presence of bromazepam when compared to placebo. This finding is interpreted as an interference of bromazepam in the multimodal transmission demanded by the task, producing changes in the communication of different sensory modalities.

For the parietal cortex we found the same result seen in the temporal cortex. However, the changes produced by the bromazepam over the cortex parietal suggest an interference in the integration of sensory information, particularly those associated with the identification of spatial features due to the characteristics of the task. In the right parietal areas, we observed a decrease in absolute theta
subjects have to pay attention on the curves, and to respond as quickly as possible, when the action command appears. To execute this task, an improvement of spatial attention is necessary. It requires integration and coordination between the sensorial information and motor control over the joystick. Six milligrams (6 mg) of bromazepam impaired the early stages of sensorimotor integration, hindering the detection of stimulus and attention. This result demonstrates a decrease in attention for the detection of stimuli S1 and S2, resulting in an increased difficulty in performing the task and a delayed onset of motor action. We conclude that bromazepam affects the processing of information. It probably suggests that the drug interferes in the transmission of different multimodal sensitive information in the temporal areas and then in the integration of these information in the parietal areas, thereby slowing all the mechanisms for the execution of motor task.

We found a main effect for the factor period at electrodes P3 and P4. We observed a lower absolute theta power in pre-S1 when compared to post-S1 and -S2. We also verified a higher value in post-S1 when compared to pre-S2 and a lower value in pre-S2 when compared to post-S2. The S1 stimulus is a warning to the next stimuli and the S2 stimulus is imperative, in other words, the subject must perform a motor task when S2 appears (for more detailed information see Ref. [11]). Our results are explained by to the characteristics of each stimulus (S1 and S2). We will focus on the differences between pre-S1 and post-S1, and the pre-S2 and post-S2. Although, we observed a difference between post-S1 and pre-S2, our discussion is concerned with the main stimuli.

Our findings demonstrated a decrease in absolute theta power before the stimuli when compared with the post-stimuli, for both warning and imperative. The increase in post-stimulus may be associated with a decoding of information. Thus, the warning and imperative stimuli are processed similarly to the parietal cortex. However, the explanation of the stimulus processing becomes differentiated due to the features of each stimulus. The function of the S1 stimulus is to warn that something will happen (i.e., the appearance of imperative stimulus). As a result of the S1 presentation, we observed a period of alertness, expectation and highest attention. The alertness is related to the expectation of the appearance of the next stimulus (i.e., S2). Our result demonstrates a peak of absolute theta power 0.5 s after the warning stimulus and we interpreted it as an increase in spatial functions with the approximation of the imperative stimulus. Previous studies demonstrated that an increase in theta power is associated with mental effort during the encoding of information and increasing cognitive load [18,19,31]. When we observe a highest absolute theta power over the parietal cortex after the warning stimulus, we interpret it as an increase in attention in order to recognize the appearance of the S2 stimulus.

Observing the pre- and post-S2 periods, we found a decrease of absolute theta power 0.5 s after the warning stimulus and we interpreted an increase in spatial functions with the approximation of the imperative stimulus. Previous studies demonstrated that an increase in theta power is associated with mental effort during the encoding of information and increasing cognitive load [18,19,31]. When we observe a highest absolute theta power over the parietal cortex after the warning stimulus, we interpret it as an increase in attention in order to recognize the appearance of the S2 stimulus.

Fig. 2. (A) Main effect for factor period observed in the electrode P3 by mean and SD. *Significant difference (Scheffé test; p < 0.007). **Significant difference (Scheffé test; p < 0.012). (B) Main effect for factor period observed in electrode P4 by mean and SD. *Significant difference (Scheffé test; p < 0.007). **Significant difference (Scheffé test; p < 0.035). ***Significant difference (Scheffé test; p < 0.005). ****Significant difference (Scheffé test; p = 0.024).
tor integration, i.e., identification of stimulus, therefore retard the identification of S1 and S2 stimulus.

References


