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Research report

Frontal cortex absolute beta power measurement in Panic Disorder with Agoraphobia patients

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ABSTRACT

Panic disorder patients are hypervigilant to danger cues and highly sensitive to unpredictable aversive events, what leads to anticipatory anxiety, that is one key component of the disorder maintenance. Prefrontal cortex seems to be involved in these processes and beta band activity may be related to the involvement of top-down processing, whose function is supposed to be disrupted in pathological anxiety. The objective of this study was to measure frontal absolute beta-power (ABP) with qEEG in panic disorder and agoraphobia (PDA) patients compared to healthy controls. *Methods*: qEEG data were acquired while participants (24 PDA patients and 21 controls) watched a computer simulation (CS), consisting of moments classified as "high anxiety" (HAM) and "low anxiety" (LAM). qEEG data were also acquired during two rest conditions, before and after the computer simulation display. The statistical analysis was performed by means of a repeated measure analysis of variance (two-way ANOVA) and ABP was the dependent variable of interest. The main hypothesis was that a higher ABP in PDA patients would be found related to controls. Moreover, in HAM the ABP would be different than in LAM. *Results*: the main finding was an interaction between the moment and group for the electrodes F7, F8, Fp1 and Fp2. We observed a higher ABP in PDA patients when compared to controls while watching the CS. The higher beta-power in the frontal cortex for the PDA group may reflect a state of high excitability, together with anticipatory anxiety and maintenance of hypervigilant cognitive state. *Conclusions*: our results suggest a possible deficiency in top-down processing reflected by a higher ABP in the PDA group while watching the CS and they highlight the recruitment of prefrontal regions during the exposure to anxiogenic stimuli. *Limitations*: the small sample, the wide age range of participants and the use of psychotropic medications by most of the PDA patients.

1. Introduction

Panic disorder (PD) is a multidimensional anxiety disorder that involves the activation of a complex brain circuitry (Dresler et al., 2013) and is characterized by abrupt and intense physiological sensations, accompanied by fear of its consequences (APA, 2000).

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It is associated with impaired quality of life, and is also related to psychiatric comorbidities (Goodwin and Gotlib, 2004). Agoraphobia is one of those, and is related to increased morbidity of PD (Kessler et al., 2006). Panic Disorder with Agoraphobia (PDA) patients tend to be hypersensitive even for lower anxiety stimulus, exhibiting hyperarousal responses, as they are hypervigilant to danger cues (Beck et al., 1992). Because PD patients experience unexpected panic attacks, they tend to be concerned about having more panic attacks, being highly sensitive to unpredictable aversive events what, over time, may lead to anticipatory anxiety, which contributes to the maintenance of the disorder (Grillon et al., 2008).

The current neuroanatomical models of PD suggest that the neuropathological process underlying panic symptoms may be heterogeneous; involving limbic, cortical and subcortical regions. Electroencephalogram (EEG) can collect neuroelectric data from cortical structures and it is also able to reflect the activation of subcortical structures on the cerebral cortex in real time. In PD, quantitative EEG (qEEG) power indices may be more reflective of brainstem modulation of cortical excitation (Malmivuo and Plonsey, 1995; Knott et al., 1996; Niedermeyer and da Silva, 2005). The most commonly electrophysiological changes observed in PD patients, either in studies with quantitative EEG (Hanaoka, 2005; Locatelli et al., 1993) as well as in conventional EEG examinations (Bystritsky et al., 1999; Dantendorfer, 1996), are attributed to frontal and temporal cortex activation.

Despite the few studies, the alpha band decreased activity and the beta band increased activity have been a pattern for PD patients (Wiedemann et al., 1998; Gordeev, 2008; Wise et al., 2011). The alpha band (8–13 Hz) reflects top-down, inhibitory control processes. Thereby, an absolute alpha-power decrease in the frontal cortex in PD may reflect a dysfunction in thalamic–cortical circuits, that is associated with incapacity to inhibit irrelevant information, role played especially by the prefrontal cortex (PFC) (Klimesch et al., 2007; de Carvalho et al., 2013). The beta-band (13–30 Hz) activity seems to be related to the maintenance of the current cognitive state. Thereafter, it is hypothesized that excessive enhancement of beta-band activity may result in an abnormal persistence of the current state and a deterioration of flexible behavioral and cognitive control (Engel and Fries, 2010).

The aim of this study is to observe absolute beta-power in the scalp frontal region as a whole (F3, F7, Fz, F4, F8, Fp1, and Fp2 electrodes) in PDA patients compared to healthy controls while watching an anxiogenic computer simulation (Freire et al., 2010) comprised of high anxiety moments (HAM) and low anxiety moments (LAM). We were expecting a higher absolute beta-power in PDA patients on all electrodes when compared to healthy controls, due to a possible deterioration of flexible behavioral and cognitive control that exists in anxiety. Moreover, we formulated the hypothesis that, in high anxiogenic moments, absolute beta power might be different than in low anxiety moments. Both moments are characterized by potentially fearful stimuli for the PDA patients, but the low anxiety situations refer to the situations where the difficulty of exposure to anxiogenic events tends to be smaller (although it still exists), that is, they refer to those moments when the patient will be about to leave the situations of greater discomfort and, for this reason, might experience less anxiety.

2. Methods

2.1. Participants

We selected a convenience sample of 24 PDA patients (8 male and 16 female; ages varying between 25 and 61 years old, mean: 38.75, SD: ± 10.09), who were in psychopharmacological treatment at the Laboratory of Panic and Respiration at the Institute of Psychiatry, and were evaluated in the Department of Applied Psychology at the Institute of Psychology before treatment; both institutes are located at the Federal University of Rio de Janeiro (UFRJ). The subjects' recruitment was done through posters with information about the research that were pasted on the walls of the outpatient sector of the Institutes of Psychiatry and Psychology at UFRJ. All patients that met the study inclusion criteria were invited to participate. The patients were interviewed with the
M.I.N.I. 5.0 (Sheehan et al., 1998; Amorim, 2000) and fulfilled DSM-IV [1] criteria for PDA. Another inclusion criterion was the occurrence of at least two panic attacks in a 30-day period before the visit. Patients with comorbid dysthymia ($n=1$), generalized anxiety disorder ($n=2$), social phobia ($n=1$) or depression ($n=3$) were included only when PDA was judged to be the primary diagnosis (Table 1). Some of them began the treatment unmedicated ($n=7$), while others were already taking antidepressants ($n=3$), benzodiazepines ($n=5$) or both antidepressants and benzodiazepines ($n=9$) (Table 2). The patients performed three self-evaluation questionnaires to measure the severity of anxiety, depression and PDA symptoms: Beck Anxiety Inventory (BAI) (Beck et al., 1988) (mean score: 22.68 and SD: ± 14.17; which means moderate anxiety); Beck Depression Inventory (BDI) (Beck et al., 1961) (mean score: 16.37 and SD: ± 10.99; which means mild depression) and Panic and Agoraphobia Scale (PAS) (Bandelow, 1995) (mean score: 23.82 and SD: ± 9.96; which means moderate PDA symptoms).

There was also a control group with 21 healthy participants (4 male and 17 female; ages from 23 to 61 years old, mean: 40.52, SD: ± 12.47), who were screened with the M.I.N.I. 5.0 (Sheehan et al., 1998; Amorim, 2000) and did not fulfill criteria for any psychiatric disorder. Subjects with other psychiatric disorders, neurological, cardiologic or respiratory diseases were not included in this study, neither in the patient nor in the control group. Patient and control group did not differ from each other in age ($p=0.848$). Our local Ethics Committee (Comitê de Ética em Pesquisa do Instituto de Psiquiatria da Universidade Federal do Rio de Janeiro-CEP-IPUB/UFRJ) approved the protocol, which complied with the principles of the Declaration of Helsinki. After the experiment was fully explained, the subjects signed a voluntary written consent.

Table 1
PDA patients' comorbidities.

Disorder	*n*	%
Dysthymia	1	4.17
Generalized anxiety disorder	2	8.33
Social phobia	1	4.17
Major depression	3	12.50
None	17	70.83
Total	**24**	**100**

Table 2
PDA patients on medication.

Medication	*n*	%
Antidepressants	3	12.50
Benzodiazepines	5	20.83
Antidepressants and benzodiazepines	9	37.50
Unmedicated	7	29.17
Total	**24**	**100**