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Personality traits in juvenile myoclonic epilepsy: Evidence of cortical abnormalities from a surface morphometry study

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ABSTRACT

Cluster B personality disorders (PD), characterized as emotional instability, immaturity, lack of discipline, and rapid mood changes, have been observed among patients with juvenile myoclonic epilepsy (JME) and have been associated with a worse seizure outcome. Proper understanding of the neurobiology of PD associated with JME could contribute to understanding the basis for earlier and more effective interventions. In the present study, volumetric and geometric features of cortical structure were assessed through an automated cortical surface reconstruction method aiming to verify possible structural cortical alterations among patients with JME. Twenty-two patients with JME with cluster B PD, 44 patients with JME without psychiatric disorders, and 23 healthy controls were submitted to a psychiatric evaluation through SCID I and SCID II and to an MRI scan. Significant cortical alterations in mesiofrontal and frontobasal regions, as well as in other limbic and paralimbic regions, were observed mainly in patients with JME with PD. The present study adds evidence to the hypothesis of frontal and limbic involvement in the pathophysiology of cluster B PD in JME, regions linked to mood and affective regulation, as well as to impulsivity and social behavior. Moreover, a multidimensional pattern of frontal, limbic, and paralimbic changes was observed through a method of structural analysis which offers different and simultaneous geometric features, allowing the elaboration of important pathophysiologic insights about cluster B PD in JME.

1. Introduction

Juvenile myoclonic epilepsy (JME) is a well-defined type of idiopathic generalized epilepsy (IGE) that affects 5–11% of patients with epilepsy, characterized by myoclonic jerks, generalized tonic-clonic seizures (GTCS), and typical findings of generalized 4- to 6-Hz spike-and-wave or polyspike-and-wave discharges in the electroencephalogram (EEG) [1,2]. Studies involving patients with JME have highlighted difficulties in their treatment, which have been attributed to some specific psychological and personality traits described as emotional instability and immaturity, lack of discipline, hedonism, frequent and rapid mood changes, and indifference towards their disease [3–9]. These observations have been confirmed by studies utilizing current psychiatric criteria, in which these behavioral characteristics were classified as cluster B personality disorders (PD) (histrionic, narcissistic, antisocial, and borderline) [10–16]. Since such behavioral abnormalities have been described as associated with a worse seizure outcome and more psychosocial dysfunctions, there has been an increased interest to characterize the neurobiological underpinnings of such manifestations in the last decades [15–19].

Although qualitative magnetic resonance imaging (MRI) assessment in JME is generally negative [20], several quantitative neuroimaging studies have revealed multiple subtle structural and metabolic brain abnormalities. Bilateral thalamic volume loss and increased mesial frontal and frontobasal gray matter concentration (GMC) and gray matter volume (GMV), as well as altered thalamic and prefrontal metabolic functions, have been observed [17,21–28]. Taken together, these findings suggest alterations in cortical architecture, such as malformations of cortical development (MCD), as a possible neurobiological basis underpinning this epilepsy syndrome [20–23,29,30]. Moreover, recent voxel-based and spectroscopy studies have reported that structural and metabolic brain abnormalities are more pronounced among patients with JME with cluster B PD when compared with patients with JME without psychiatric disorders [15,16].

Despite the presence of thalamic and frontal lobe structural and functional abnormalities in patients with JME, other brain regions

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should also be investigated and considered [29–31]. Structural abnormalities have been found in the hippocampus, cerebellum, and insular, occipital, and posterior cingulate cortices, suggesting that brain dysfunction in JME extends beyond the thalamofrontal circuitry [17,23,29,30]. Furthermore, most of the altered regions reported in these previous studies are associated with a variety of emotional and behavioral processes and, therefore, can be dysfunctional in patients with JME with cluster B PD [15,16].

To date, most structural neuroimaging studies in BPD performed have utilized techniques based on voxel-based morphometry (VBM), which is a mixture of geometric parameters including thickness, surface area, and folding. As a consequence, VBM-based findings cannot be attributed to a single biologically meaningful process [32–35]. In the literature, there are tools that allow estimation of cortical thickness based on T1-weighted images and represent a viable methodological alternative to volumetric measurements for assessment of subtle cortical changes in the human brain. Freesurfer is a popular software package that measures cortical thickness and cortical and subcortical volumes. The routines implemented in Freesurfer provide a technique that uses MRI intensity contrasts to obtain accurate volumetric and geometric parameters that have been used to investigate several psychiatric and neurological disorders [36–39]. In addition, accurate methods for measuring the thickness of cerebral cortex could provide powerful tools to support the diagnoses of a variety of brain disorders [32,36–39].

In this study, a multidimensional approach based on Freesurfer image analysis suite was performed aiming to investigate, in a more detailed way, structural cortical abnormalities in patients with JME with cluster B PD. We aimed to demonstrate that the neuroanatomical patterns discriminating individuals with JME with cluster B PD from controls are complex and involve multiple cortical features. In addition, we hypothesized that differences of geometric, volumetric, and cortical thickness parameters in limbic and paralimbic structures would be associated with the disorder.

2. Methods

2.1. Participants

All patients included in this study were followed in the outpatient clinic of a tertiary center (Department of Neurology of the Universidade Federal de São Paulo, São Paulo, Brazil) from July 2005 to July 2011. After the Ethical Committee approval, advantages and risks for participation were explained and informed consent was obtained. The inclusion criteria for the patient groups were the presence of electroclinical diagnosis of JME based on ILAE classification [2] and having been treated in our unit for at least six months. Patients with JME had typical EEG showing generalized 3- to 6-Hz spike-and-wave or polyspike-and-wave activity maximum in frontocentral regions. We excluded patients with other clinical and/or neurological illnesses besides epilepsy.

2.2. Psychiatric evaluation

A clinical and sociodemographic questionnaire including age, gender, schooling, psychiatric family antecedents, previous psychiatric treatment and hospitalizations, and drug treatment was applied before imaging acquisition. The psychiatric evaluation was performed through two structured questionnaires — Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, axis I and axis II (SCID I and SCID II, respectively) [40,41].

Table 2
Clinical data of patients with juvenile myoclonic epilepsy with and without cluster B personality disorders.

Clinical data	JME without PD	JME with PD	p value
Number of patients	44	22	
Duration of disease (mean ± SD)	13.1 ± 9.2	14.6 ± 8.5	0.68
Age at epilepsy onset (mean ± SD)	12.2 ± 4.7	13.2 ± 3.5	0.83
Adequate treatment (%)	38 (86.3)	17 (77.2)	0.76
Photosensitivity (%)	14 (31.8)	8 (36.3)	0.67
Inadequate control of myoclonia (%)	4 (9.0)	10 (45.4)	0.005*
Inadequate control of absences (%)	3 (6.8)	6 (27.2)	0.03*
Inadequate control of GTCS (%)	6 (13.6)	4 (18.1)	0.30
Patients with GTCS + absence + myoclonia (%)	2 (4.6)	7 (31.8)	0.02*
Patients taking VPA (%)	44 (100)	21 (95.4)	0.96
Patients taking TPM (%)	12 (54.5)	14 (63.6)	0.74
Patients taking LTG (%)	10 (22.7)	6 (27.2)	0.85
Patients taking CLN (%)	25 (56.8)	14 (63.6)	0.75
Patients taking one medication	8 (18.1)	0 (0)	0.001*
Patients taking two medications	31 (70.5)	11 (50.0)	0.23
Patients taking three medications	5 (11.4)	11 (50.0)	0.02*

JME: juvenile myoclonic epilepsy; PD: personality disorder; GTCS: generalized tonic-clonic seizures. CLN: clonazepam; TPM: topirmate; LTG: lamotrigine; VPA: valproate.
* $p<0.05$.

2.3. Procedures

The MRI findings of 22 patients with JME who fulfilled diagnostic criteria of cluster B PD only (histrionic, borderline, and passive–aggressive) were compared with that of 44 patients with JME without any psychiatric diagnosis. The control group consisted of 23 age- and gender-matched healthy volunteers who were also evaluated by the same psychiatrist (GMAF). None of them presented any seizures or alcohol consumption within 72 h prior to the psychiatric evaluation.

2.4. MRI data acquisition

The MRI examination of the brain was performed in all subjects using a 1.5T MAGNETOM Sonata (Maestro Class — Siemens AG, Medical Solutions, Erlangen, Germany) using an eight-channel head coil. To minimize variation, the subjects were positioned by the same investigator using the orbitomeatal line as a landmark. Two conventional sequences were performed in order to exclude structural lesions: a) axial T2-weighted FLAIR (fluid-attenuated inversion recovery) in a plane parallel to the anterior commissure–posterior commissure (AC–PC) line [TR (repetition time) = 8500 ms, TE (echo time) = 107 ms, IT (inversion time) = 2500 ms, slice thickness = 5.0 mm, slice interval = 1.5 mm, FOV (field of view) = 240 mm, matrix size = 256 × 256, NEX = 1] and b) sagittal T1-gradient echo volumetric acquisition for multiplanar reconstruction (TR = 2000 ms, TE = 3.42 ms, flip angle = 15°, FOV = 245 mm, 1.0-mm slice thickness with no gaps,

Table 1
Demographic data of both groups with juvenile myoclonic epilepsy and a healthy control group.

Demographic data	JME without PD	JME with PD	HC	p value
Number of participants	44	22	23	
Age (mean ± SD)	27.5 ± 8.5	28.1 ± 7.9	30.1 ± 8.2	0.71
Gender (females)	24 (54.5%)	14 (63.6%)	14 (60.8%)	0.76
Number of right-handed (%)	37 (84.1%)	18 (81.8%)	20 (86.9%)	0.62
Years of schooling	8.4 ± 2.5	7.7 ± 3.1	9.1 ± 2.8	0.26

HC: healthy controls; JME: juvenile myoclonic epilepsy; PD: personality disorder.