# Original

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# Neuropsychological findings in recent onset schizophrenia and borderline personality disorder: a comparison study

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Introduction. Neurocognitive impairment is considered an essential symptom of schizophrenia, particularly in its early stages. Nonetheless, the neuropsychological features of borderline personality disorder (BPD) could cast doubt on the specificity of neurocognitive dysfunctions. The aim of this study is to determine whether neurocognitive deficits are specific to schizophrenia-spectrum conditions as compared to a similarly severe psychiatric illness like BPD.

Method. A battery of neuropsychological tests was used to assess the abilities for attention, verbal memory and executive functions in a group of 34 borderline personality disorder (BPD) patients, 24 patients with first episode of a schizophrenia-spectrum disorder (FEP) and a group of 19 controls.

**Results.** ANOVA for multiple measures with subsequent post-hoc tests demonstrated significant effect sizes between controls and patients for all cognitive domains. However, the effect sizes of comparisons between both groups of patients were not significant.

**Conclusions.** Results show significant neuropsychological impairment in both disorders when compared with normal controls, but no specific pattern of neurocognitive deficits for schizophrenia-spectrum disorders was found.

Keywords: First Episodes of Psychosis, Borderline Personality Disorder, Neuropsychological Impairment, Neurocognition, Global Functioning

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# Perfil neuropsicológico en primeros episodios de esquizofrenia y trastorno límite de la personalidad: un estudio comparativo

Introducción. El deterioro neurocognitivo es considerado un síntoma esencial de la esquizofrenia, especialmente en sus fases iniciales. Sin embargo, las características neuropsicológicas del trastorno límite de la personalidad (TLP) podrían poner en duda la especificidad de estas disfunciones cognitivas. El objetivo de este estudio es determinar si los déficits cognitivos son específicos del espectro de la esquizofrenia comparado con trastornos igualmente graves como el TLP.

**Metodología.** Se administró una batería de pruebas neuropsicológicas para evaluar atención, memoria verbal y funciones ejecutivas a un grupo de 34 pacientes con TLP, 24 pacientes con primeros episodios psicóticos (PEP) y 19 controles.

**Resultados.** Las pruebas ANOVA realizadas con sus correspondientes pruebas mostraron diferencias significativas entre controles y pacientes en todos los aspectos. Sin embargo, las diferencias entre los dos grupos de pacientes no fueron significativas.

**Conclusiones.** Los resultados muestran un deterioro neuropsicológico significativo en ambos trastornos en comparación con los controles, pero no indican un patrón de déficit neurocognitivo específico para los trastornos del espectro de la esquizofrenia.

Palabras clave: Primeros episodios psicóticos, Trastorno límite de la personalidad, Deterioro neuropsicológico, Neurocognición, Funcionamiento global

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#### INTRODUCTION

The relevance of neurocognitive impairment for the psychopathology of the schizophrenia-spectrum disorders has received considerable attention for research in recent years and it is commonly assumed that cognitive deficits are essential for schizophrenia<sup>1-3</sup>. A considerable number of studies have consistently reported neuropsychological deficits in patients with schizophrenia when compared with healthy subjects, such as global and selective verbal memory, nonverbal memory, bilateral and unilateral motor performance, visual and auditory attention, general intelligence, spatial ability, executive function, language, and interhemispheric tactile-transfer test performance<sup>1-5</sup>, but whether these deficits are primary or secondary to functional deterioration is still unresolved. Nonetheless, more recently accumulated evidence has demonstrated that significant neuropsychological deficits are already present in the prodromal phases of the disease (first episodes of psychosis: FEP)<sup>6,7</sup>.

There is also substantial evidence, derived from recent research reports, of neuropsychological deficits in other psychiatric disorders, suggesting that neurocognitive impairment might not be specific for psychotic disorders. Among these disorders, borderline personality disorder (BPD) has attracted attention as several studies have shown neuropsychological dysfunctions in these patients that could be correlated with the severity of behavioural-impulsive symptoms<sup>8-18</sup>.

A number of studies have been dedicated to describing the differences between schizophrenia and BPD in social cognition tasks correlated to neurocognitive ability, emotion perception, a history of trauma, and overconfidence in errors<sup>19</sup>; in theory of mind in women<sup>20</sup>; or in psychotic experiences as a reaction to impaired social functioning<sup>21</sup>. Other studies have found similarities and differences in concrete psychotic symptoms for both disorders, such as auditory verbal hallucination<sup>22,23</sup>, splitting<sup>24</sup>, disordered thinking, basic self-disturbance<sup>25</sup> or dissociation<sup>26</sup>, as well as in unspecific symptoms such as violent behaviour<sup>27</sup>. Barnow et al. published a review comparing both disorders regarding these varying features<sup>28</sup>.

However, few studies have compared cognitive performance between schizophrenia and borderline personality disorders, despite the fact that both disorders may share a similar cognitive functioning. Recently<sup>29</sup> suggested that there are similarities related to cognitive deficits between BPD and schizophrenia, and that these are shared with bipolar disorder as well. All three disorders exhibited a common impairment in exerting control over interference arisen from memory but no dysfunction was found for control over perceptual interference. Burgess<sup>30</sup> also found that self-injury was correlated with neurocognitive deficits in both borderline and schizophrenic disorders.

Concretely, no studies have been found comparing neurocognitive deficits between BPD and first episodes of psychosis. Two studies have suggested similarities between both conditions regarding pathologic symptoms<sup>31,32</sup>. We hypothesise that FEP may share several features with BPD regarding cognitive impairment comparing severity of both disorders. Consequently, the aim of this study was to determine whether the pattern of neurocognitive deficits is specific to schizophrenia-spectrum disorders or if it otherwise shares similarities in the early onset as compared to a severe psychiatric illness like BPD, in a head to head comparison between both conditions. To our knowledge this is the first study comparing cognitive functioning between BPD and first episodes of psychosis.

## METHODS

## Sample

A total of 24 patients presenting a first episode of psychosis (FEP) according to the Diagnostic and Statistical Manual for Mental Health (5<sup>th</sup> edition)<sup>33</sup> were included in the study. Diagnoses were the following: schizophrenia (n=10), schizophreniform disorder (n=9) and schizoaffective disorder (n=5). Diagnosis was determined by two expert psychiatrists and confirmed with the Structured Interviews of DSM-IV for axis I and axis II disorders and final diagnosis of disorder type was made only after three months of clinical observation. Patients with acute psychosis or psychotic manic episodes were not included in the study. For comparison, a group of 34 patients with non-psychotic BPD and 19 healthy controls were selected. Selection of patients was made on a consecutive basis along a 12 month period of admission at the Psychosis Unit and the Personality Disorders Unit of a general hospital. At the time of neuropsychological testing all participants were outpatients.

Patients were considered as having a first episode of psychosis if a 15 days period of psychotic symptoms was present for the first time and had not received antipsychotic medications in the past for more than two weeks. Patients with FEP were treated and stabilized for three months before neuropsychological testing was performed. At the time of the study, 12 patients were receiving minimal doses of antipsychotic medication (5 mg haloperidol or equivalent) and 9 patients were not taking any medication (due to subject's own decision). Three patients receiving high to moderate doses of antipsychotic medication at the time of the study were subsequently controlled in the analytical process. All BPD patients were severely symptomatic, with a Clinical Global Impression (CGI)<sup>34</sup> score equal or greater to 5, and highly disabled (Global Assessment of Functioning (GAF)<sup>35</sup>) score below 55. Nine BPD patients were receiving atypical antipsychotic drugs at doses equivalent to 5 mg Haloperidol per day at the time of the study. Six BPD patients were receiving valproic acid at doses between 500 and 1000 mgs per day.

All patients entering the study were free of benzodiacepines for at least two weeks before the tests. Patients with substance use dependence or abuse, a life history of schizophrenia-spectrum disorder, or bipolar or a neuropsychiatric disorder were not admitted in the study. The presence of a current major depressive episode or significant anxiety disorders at the time of the study was also an exclusion criterion due to the risk of interference in the neuropsychological performance. The group of controls included 19 healthy volunteers with no history of major psychiatric disorders (as assessed with structured interviews SCID-I<sup>36</sup> and SCID-II<sup>37</sup> and was recruited among the staff of the health centre, including individuals with educational levels and gender similar to the groups of patients. All subjects of the control group underwent the same clinical and neuropsychological assessment protocol as FEP and BPD groups, with the Spanish versions of the tests and questionnaires.

The age for inclusion in the study for all groups was restricted to a range of 18-35 years in order to avoid biases due to neurocognitive changes in older ages. No significant differences were found among groups for age, gender or education level. Sociodemographic and clinical data are specified in Table 1. The study was approved by the Ethical Committee of the Hospital and was conducted following the ethical principles of the Declaration of Helsinki. All subjects were verbally informed about the objectives of the study and signed written informed consent.

Table 1	Social and clinical data (patients and controls)							
	BPD (X; IQR) n=34	FEP (X; IQR) n=24	Controls (X; IQR) n=19					
Age	28.9 (18-31)	28.5 (19-32)	27.4 (21-35)					
Sex	18 females (52%) 11 males (46%)		10 females (53%)					
Duration of diseas	1.8 years (1–7)	0.17 years (0.05-0.33)						
Years of education	15.2 (13–23)	16.4 (15-21)	17.6 (16–24)					
CGI severity	5.7 (5-7)	5.4 (5–7)	1 (1-1)					
GAF	52 (45–65)	51 (35–60)	87					
Years unemployed	0.9 (0.1-5.2)	0.5 (0–1.5)	0					
Comorbid PD:								
Dependent	14	6	2					
Avoidant	4	5	2					
Obsessive	0	0	1					
Histrionic	9	1	1					
Antisocial	0	0	0					
Narcissistic	8	0	0					
Schyzotypal	0	1	0					

BPD: Borderline Personality Disorder; FEP: Fist Episode of Schizophrenia; X: median; IQR: interquartile range; CGI: Clinical Global Impression; GAF: Global Assessment Functioning; PD: Personality Disorder.

#### Neuropsychological assessment

The neuropsychological protocol included a set of tests rating memory, attention and executive functions through the following: 1) sustained attention (Trail Making Test A<sup>38</sup> and Symbol Digit Modality Test<sup>39</sup>; 2) Memory (Buschke Selective Reminding Test<sup>40</sup>; 3) Verbal fluency (Controlled Oral Word Association Test (FAS)<sup>41</sup> and Semantic category evocation of animals<sup>42</sup>; 4) Cognitive flexibility (Trail Making test-B<sup>38</sup>); 5) Working Memory (Letter Number from Wechsler Scale<sup>43</sup>); 6) Impulse Inhibition (Stroop Test colour-word interference<sup>44</sup>; and 7) Categorization and executive functions (Wisconsin Card Sorting Test, WCST<sup>45</sup>). Regarding WCST, only the variables "number of categories", "number of total trials", and "number of perseverative/non perseverative errors" were analyzed since these are the most commonly used variables in literature. This test was included also to evaluate executive functions such as strategic planning, organized searching or modulating impulsive responding. Neuropsychological tests were administered by an experienced neuropsychologist and the process of administration lasted approximately one hour.

#### **Clinical Assessments**

Besides the diagnosis of mental disorders and personality disorders with SCID-I and SCID-II, psychotic symptoms were rated with the Positive and Negative Syndrome Scale (PANSS)<sup>46</sup> for all participants of the study. Severity of borderline symptoms was rated with the Clinical Global Impression (CGI) and with the Zanarini scale for BPD<sup>34</sup>. Measures of impulsivity were obtained for all subjects with the Barratt Impulsiveness Scale<sup>47</sup>. Psychosocial functioning was rated with the Global Functional scale (GAF) of DSM-IV<sup>35</sup>.

#### **Statistical Analysis**

Analyses were conducted using the SPSS 17.0 version 17.0 (Chicago, IL, USA). Qualitative variables are expressed as frequency distributions and quantitative variables as mean ( $\pm$ SD). Not normally distributed continuous variables are summarized by median and interquartile range (IQR: P25-P75).

Demographics and clinical characteristics were compared between groups by one-way analysis of variance or non-parametric tests as convenient. ANOVA for multiple measures with subsequent post-hoc tests was used to analyse neuropsychological variables, with group (BPD, FEP and controls) as the between-subject factor and scores on the tests as the within-subject factor. Effect size was expressed by using *Cohen's d* in order to quantify the strength of between-groups differences for neuropsychological performance.

# RESULTS

Demographics and clinical variables are summarized in Table 1. Comparisons for qualitative variables were analysed by the chi-square test or the Fisher exact test. For quantitative variables, the Student's t-test or the Bonferroni posthoc Test and the Dunnett post-hoc D3 Test were used.

MANOVA with post-hoc comparative tests demonstrated that neuropsychological performance was significantly different in patients with respect to controls for all cognitive functions tested, as is shown in Table 2. Healthy subjects performed better than both FEP and BPD groups, as demonstrated by statistically significant effect sizes (p<0.05). However, no significant effect sizes for any tests were found between both groups of patients. Apparently, FEP and BPD patients showed a similar generalized pattern of neuropsychological dysfunction that affected impulse inhibition, verbal fluency, categorization, working memory rate of information processing, cognitive flexibility and complex executive functioning (Table 2).

#### CONCLUSIONS

The main objective of this study was to test whether neurocognitive deficits in first episode psychosis were unique and different from those of severe borderline personality disorder. Both disorders are characterized by severe emotional and behavioral disturbances causing intense functional impairment. The role of cognitive deficits in schizophrenia is currently considered as essential for the expression of clinical manifestations of the disease. A review of neurocognitive impairment in schizophrenia<sup>2</sup> found significant impairment of neuropsychological performance of schizophrenic patients in more than 200 studies investigating verbal and nonverbal memory, motor performance, attention, intelligence, spatial ability, executive functions, language, and others.

Regarding borderline personality disorder, cognitive and neuropsychological deficits have only received some attention in the last decade, when it became evident that a majority of patients with BPD remained functionally impaired even after emotional and impulsive symptoms had remitted for many years<sup>48</sup>. In recent years several articles have reported neuropsychological performance deficits in BPD patients and a meta-analysis by Ruocco<sup>8</sup> showed that impairment of attention, cognitive flexibility, speeded processing, learning, memory, planning and visuospatial abilities are commonly reported in these patients. Nevertheless,

#### Table 2

Results of neuropsychological testing. Score differences between groups.

Neuropsychological tests	BPD	FFP	CONTROL		Cohen's d size effect		
	Mean** (SD)	Mean (SD)	Mean (SD)	FEP-BPD	BPD-control	FEP-Control	
FAS A. (a)	11.8 (4.6)	10 (3.8)	15.5 (3.4)	0.43	0.92*	1.52*	
FAS F. (a)	11 (4.8)	10.6 (4)	14.4 (4.1)	0.090	0.76*	0.95*	
FAS S. (a)	12.3 (4.8)	10.4 (3.6)	15.7 (3.4)	0.45	0.82*	1.51*	
FAS TOTAL. (a)	35.1 (13.1)	31 (9.2)	45.6 (10.2)	0.36	0.90*	1.50*	
ANIMALS. (a)	16 (5.8)	15.6 (4)	23.3 (4.9)	0.08	1.36*	2.15*	
COWAT (NOE). (a)	10.4 (4.3)	9.6 (3.4)	15.8 (5.4)	0.20	1.11*	1.40*	
Stroop Test. (a)	37 (13.6)	34.3 (11.2)	54.8 (8.9)	0.21	1.58*	2.05*	
Symbol Digit Modality Test. (a)	38.1 (12.1)	43.7 (10.2)	54.8 (8.1)	0.50	1.65*	1.21*	
Letter Number. (a)	8.9 (3)	9.2 (4.1)	12.8 (1.9)	0.08	0.79*	1.20*	
WCST - % conceptual level response. (b. d)	81.9 (17.6)	84.1 (16)	94.9 (11.2)	0.13	0.90*	0.79	
WCST - Total errors. (b. c)	81.4 (17.7)	83.6 (15.9)	96.8 (12.1)	0.13	1.03*	0.94*	
WCST - % errors. (b. c)	82 (16.4)	84.3 (14.8)	95.1 (11)	0.14	0.95	0.83	
	mean (IQR)	mean (IQR)	mean (IQR)		Signification leve	l p	
Interference NOE. (c)	0 (0-1)	1 (0-2)	0 (0-0)	0.163	0.054	0.002*	
Trail Making Test A. (c)	35 (30-56.2)	35 (28.2-43)	25 (20-28)	0.376	0*	0*	
Trail Making Test B. (c)	95 (65.5-145)	84 (62.5-136.2)	45 (37-60)	0.438	0*	0*	
Errors_TMT_B. (c)	0 (0-1)	0 (0-1)	0 (0-0)	0.743	0.006*	0.006*	
Errors_Stroop. (c)	0 (0-1)	1 (0-3)	0 (0-1)	0.146	0.097	0.004*	
WCST - % Perseverative Errors. (c)	80 (60.2-95)	77 (67.5-102.7)	93 (81.5-101)	0.587	0.013*	0.079	
Trials to complete 1st category. (c)	12 (11-26.7)	15.5 (11-23.7)	11 (11-11.7)	0.688	0.035	0.006*	
Failure to maintain set. (c)	0.5 (0-1)	0.5 (0-1.7)	0 (0-0)	0.810	0.047	0.044	
Categories completed. c)	6 (2-6)	5.5 (3.2-6)	6 (6-6)	0.585	0.022	0.040	

a. Bonferroni post-hoc Test

b. Dunnett post-hoc D3 Test

c. Bonferroni's adjustment. significative p if<0.016

\* Level of significance: p<0.05 (p<0.016 according to Bonferroni's adjustment)

\*\* Raw scores for all tests except for WCST where scores are presented as standard scores.

BPD: Borderline Personality Disorder; FEP: First Episodes of Psychosis; SD: Standard Deviation; WCST: Wisconsin Card Sorting Test; ICR: Interquartile range; TMT: Trail Making Test

most clinicians assume that cognitive disturbance in schizophrenia is more severe and generalized than it is in other major psychiatric syndromes such as bipolar disorder or borderline personality disorder. Our hypothesis was therefore based on the clinical evidence that schizophrenia and BPD have greater neuropsychological impairment than healthy subjects and in the commonly accepted clinical evidence that neurocognitive deficits are more extensive and intense in schizophrenia than in BPD. However, our study found that the group of patients with borderline personality disorder presented a profile of neuropsychological dysfunction similar to the group of patients with first episode of a schizophrenia-spectrum disorder. Both groups of patients performed poorly in all tests applied, with significant effect sizes favoring healthy controls in all tests. However, a difference statistically significant between both disorders could not be found, with effect sizes between the groups lower that 0.5 for all tests.

Therefore our study cannot support the idea of greater neuropsychological impairment in patients with a schizophrenia-spectrum disorder than in other severe psychiatric disorders as BPD, at least in the particular neurocognitive domains we measured. Furthermore, we could not demonstrate the hypothesis that BPD patients suffer greater impairment than FEP in tests exploring impulsivity and behavioural inhibition<sup>9</sup>, such as the Stroop test<sup>49</sup> since both groups presented similar scores for these measures.

Our findings are in agreement with numerous studies reporting significant deficits of verbal capacities and executive functions in early stages of schizophrenia<sup>50,51</sup>. However, the natural relationship of neurocognitive deficits with the clinical manifestations and with the outcome of schizophrenia is still controversial and needs further longitudinal research approaches. Some authors have proposed that neuropsychological deficits predict a worse outcome for FEP in the long term<sup>52-54</sup>, although this could not be confirmed in other studies<sup>7,55</sup>. Neuropsychological impairment has been reported in association with more intense negative symptoms7,55 and with poor functional outcome in patients with schizophrenia<sup>53,56</sup>. In addition, impaired neuropsychological performance has also been correlated with lower premorbid functioning and more frequent relapses in BPD<sup>8,14,57,58</sup>. In both conditions, FEP and BPD, the possibility that neuropsychological impairment could follow the deteriorating progress of the disease cannot be discarded yet54,59.

Contrary to our findings, several studies comparing neuropsychological performance in patients with first episodes of schizophrenia, bipolar disorder or other psychotic disorders<sup>56,60</sup> found significant differences between groups, with schizophrenic patients showing more severe deficits than the rest of groups. However, there are also some studies reporting similar neuropsychological impairment in schizophrenia and bipolar disorder, which is more in accordance with the findings of our study<sup>61</sup>, and our results agree with those of a recent study by Lozano et al<sup>29</sup> showing similar cognitive functioning in BPD, schizophrenia and bipolar disorder. Regarding BPD, there are no previous studies comparing neurocognitive functioning with schizophrenia but a number of them have reported neuropsychological impairment in BPD patients compared with healthy subjects, including impairment of memory, language and spatial processing<sup>14,62</sup>, executive functioning<sup>57</sup>, visual spatial ability, information processing and non-verbal memory<sup>58</sup>. Our results support the idea that neuropsychological impairment in highly dysfunctional BPD patients is generalized to most cognitive functions and is at least equally prevalent as in patients with early psychosis.

The relationship of neurocognitive deficits with specific brain dysfunctions has been investigated previously. Impairment of executive functions has been attributed to abnormal functioning of the dorso-lateral prefrontal cortex in psychiatric patients<sup>63</sup> and in patients with schizophrenia this abnormal functioning could be correlated with neuropsychological deficits, especially in executive functions and working memory<sup>62</sup>. Regarding BPD some evidence suggests that neuropsychological deficits may be essential for the development of the disorder<sup>16,64</sup> and possibly associated with microstructural white matter damage at prefrontal brain areas<sup>65</sup>.

The idea that all severe mental disorders including schizophrenia, manic-depressive psychosis and severe personality disorders share some biological dyathesis was extended among psychiatrists during the past century and fostered the concept of "unique psychosis". Some authors defined borderline disorders as a syndromal condition grounded in the phenomenological border of schizophrenia, and characterized by severe identity disturbance, peculiar cognitions and marked lack of affective and behavioural regulation<sup>66</sup>. According to this concept, generalized neuropsychological impairment affecting mechanisms that are crucial for external and internal information processing could explain the intense psychosocial disability present not only in schizophrenic patients but also in patients with psychotic bipolar disorder or severe personality disorders<sup>67</sup>. Consequently, neuropsychological deficits become a principal target for therapeutic intervention such as cognitive remediation treatments in all three disorders.

Our conclusions are limited by the heterogeneous clinical nature of both BPD and first episode psychoses samples. For research purposes, it would be more adequate to select BPD patients according to the presence of key symptoms and domains (i.e. suicide attempts, affective instability, and impulsive aggression) and controlling for the presence of diagnostic criteria for other comorbid personality disorders. Particularly, neuropsychological deficits have been consistently replicated in patients with schizotypal personality disorder<sup>56</sup> which obligates to control research samples of BPD for the schizotypal dimension. In order to avoid this interference, our study excluded patients with comorbid schizotypal personality disorders, although some could present limited traits of the disorder. Concerning FEP, we tried to make the diagnostic samples more specific by excluding patients with brief or acute psychoses from the study, since many patients with these conditions receive comorbid diagnosis of borderline personality disorder. For that reason, we restricted the inclusion criteria in order to obtain a sample of patients phenomenologically close to schizophrenia and diagnosed as schizophreniform, schizophrenia or schizoaffective disorder at the time of the study.

The findings of our study cannot be generalized to all BPD patients since our patients were severely affected by the disorder and therefore do not represent the average population of BPD. Indeed, all patients included in the study scored at least 5 ("severely ill") in the CGI scale and were treated at a day hospital for marked functional impairment. We sought to select BPD patients with a level of functional impairment similar to what is expected in a sample of patients with a schizophrenia-spectrum disorder, following the hypothesis that neuropsychological impairment is directly correlated with functional disability<sup>55</sup>.

Other limitations we aimed to solve included the lack of control for external variables with possible effects on neurocognitive functioning along the course of the disease, including drug misuse or previous prescribed medications. Substance dependence disorder was an exclusion criteria as well as abuse on the days previous to the neuropsychological testing. To reduce the possible effects of medication, we administered the neuropsychological testing at a period of clinical stabilization, which allowed us to use minimal doses of medication without sedating effects on the patients. However, more studies with larger samples are still necessary to address the effects of previous medications and drug intakes, such as cannabis and alcohol, on neuropsychological performance of both first episode psychoses and borderline personality disorder.

In summary, our study selected two samples of patients with first episode of a schizophrenia-spectrum disorder or with borderline personality disorder and compared them for performance in a neuropsychological assessment battery of most neurocognitive domains. At conclusion, both samples of patients appeared significantly impaired for neurocognitive function in comparison with a sample of healthy controls, but presented no significant differences between them neither in type nor in severity of neuropsychological impairment. This suggests that neuropsychological deficits might possibly represent a common and nonspecific pathological diathesis, which may lead to clinical, behavioural and emotional dysregulation in severe mental conditions.

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#### CONFLICT OF INTERESTS

The Authors have declared that there are no conflicts of interest in relation to the subject of this study.

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