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BRIEF COMMUNICATION

Social cognition across bipolar disorder and behavioral-variant frontotemporal dementia: an exploratory study

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Objectives: Bipolar disorder type 1 (BD1) and behavioral-variant frontotemporal dementia (bvFTD) share similar behavioral and cognitive symptoms, rendering the differential diagnosis between them a clinical challenge. We investigated the accuracy of social cognition (SC) measures to differentiate bvFTD from BD.
Methods: We included three groups of participants: early-onset BD1 (in remission, n=20), bvFTD (n=18), and cognitively healthy controls (HC) (n=40), matched for age, schooling, and sex. All participants underwent cognitive assessment, including the Facial Emotion Recognition (FER) and Modified Faux-Pas (mFP) tests, which assess mentalizing.
Results: Compared to HC, BD1 and bvFTD patients underperformed on both SC measures. BD1 and bvFTD did not differ regarding FER or mFP total scores, although patients with bvFTD had significantly higher difficulties than those in the BD1 group to detect social faux-pas ($p < 0.001$, $d = 1.35$).
Conclusion: BD1 and bvFTD share deficits in the core SC functions. These findings should be considered in the development of tasks aiming to improve clinical differentiation between the two disorders.

Keywords: Dementia; cognitive impairment; executive functioning; mania; mood disorder

Introduction

Bipolar disorder (BD) is a chronic, disabling, and complex mental illness associated with poor functionality, including reduced interpersonal functioning.[1] In addition to mood swings, patients with BD might exhibit psychiatric and behavioral symptoms that are also criteria for the diagnosis of behavioral-variant frontotemporal dementia (bvFTD),[2] including impulsivity, disinhibition, and apathy. Besides neuropsychiatric manifestations, BD and bvFTD also share similar cognitive deficits, such as executive dysfunction, which is commonly present in both disorders.[3,4] Social cognition (SC) refers to a set of cognitive functions involved in the processing of social signals and critical for social adaptation and appropriate interpersonal exchanges. Emotion recognition and mentalizing have been described as its core processes. Impairments of SC are frequent in bvFTD,[4] but may be present in BD as well.[1,3]

Distinguishing bvFTD from primary psychiatric disorders (PPD) is a key challenge, particularly in behavioral disorders with onset after age 50 years.[5] For most clinicians, the distinction between FTD and BD can be challenging, and a thorough review of psychopathology is required. BD seems to present more frequently with grandiosity, often accompanied by increased energy and decreased need for sleep, disinhibition, and euphoric features, as well as a history of depression. Conversely, some individuals with FTD may show stereotyped, inadequate sexual behavior, such as public masturbation, as well as repetitive motor behavior and non-sexual stereotypies. bvFTD is the most common cause of early-onset dementia after Alzheimer's disease, and frequently manifests with marked behavioral and personality

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changes, such as disinhibition, loss of empathy, and social misconduct. Patients with bvFTD may also present psychiatric symptoms frequently found in PPD, such as mania, delusions, and hallucinations.[2] These shared features may led to an important delay in the diagnosis of bvFTD, as shown by the fact that at least 50% of patients receive a psychiatric diagnosis prior to correct identification.[6] Almost 25% of patients with bvFTD might receive a lifetime diagnosis of BD.[7] In this context, BD may be the most challenging differential diagnosis to bvFTD.[6]

In the absence of biomarkers, SC tasks might be a useful tool to help to distinguish these conditions.[2] However, there is a critical lack of data to support this recommendation, as head-to-head comparisons between early-onset dementia and late-onset psychiatric conditions are scarce.[5] To date, only one study[5] directly compared SC task performance in patients with BD and bvFTD, demonstrating poorer performance on a mentalizing test in bvFTD. Within this context, we aimed to compare the performance in SC core processes of patients with remitted BD type 1 (BD1) and bvFTD.

Methods

We included 20 patients with remitted, early-onset BD1, 18 patients with bvFTD, and 40 cognitively healthy controls (HC) in the present study. All patients were recruited at the Hospital Universitário, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil. Patients with BD1 were assessed with the Mini-International Neuropsychiatric Interview (MINI), the 17-item Hamilton Depression Rating Scale (HDRS), and the Young Mania Rating Scale (YMRS) to determine the severity of depressive and manic symptoms. Remission was defined by YMRS and HDRS scores < 7 for at least 8 weeks.

Patients with bvFTD fulfilled consensual diagnostic criteria for probable bvFTD,[8] i.e., had a consistent history of personality and behavioral changes associated with functional decline and evidence of focal atrophy or hypoperfusion in frontotemporal regions on brain magnetic resonance imaging (MRI) or on single-photon emission computed tomography (SPECT), respectively. Previous diagnosis of BD or schizophrenia was an exclusion criterion for this group. HC were recruited from the local population and had no history of psychiatric or neurologic disorders. They had no cognitive complaints on interview and had normal scores on the Mini-Mental State Examination (MMSE).

All participants underwent a cognitive evaluation that included the MMSE, the Frontal Assessment Battery (FAB), and the Figure Memory Test (FMT) of the Brief Cognitive Screening Battery (BCSB).

SC was assessed with the mini-Social Cognition and Emotional Assessment (Mini-SEA), composed of a Facial Emotion Recognition (FER) task and the Modified Faux-Pas (mFP) test, both assessing mentalizing. For the mFP, in addition to the total score, subscores (detection, attribution, identification, knowledge, intentionality, and empathy) were also considered. Moreover, two components of the test were distinguished: the correct recognition of social norms violation (the sum of scores for questions 1, 2, and 3); and mentalizing ability (the sum of scores for questions 4, 5, and 6). The total Mini-SEA score is the sum of the FER and mFP scores, with higher scores indicating better performance.

Statistical analyses

Statistical analyses were conducted using SPSS 22.0. The Shapiro-Wilk test refuted the assumption of normality. Thus, nonparametric Kruskal-Wallis and Mann-Whitney tests and Cohen's *d* measure of effect size were used for group comparisons. We adopted Bonferroni's correction for multiple comparisons; the level of significance (α) was set at 0.025. The accuracy of SC measures was investigated with receiver operating characteristics (ROC) curve analyses.

Ethics statement

The local ethics committee approved the study. All participants or their legal representatives provided written informed consent.

Results

Table 1 presents demographic, clinical, and neuropsychological data. Participants did not differ regarding age, sex, or schooling. Compared to HC, patients with bvFTD and BD1 performed poorly on all cognitive measures. Patients with remitted BD1 and bvFTD had similar performance on all SC scores, except detection of faux-pas (i.e., ability to identify whether or not there is a faux-pas), with bvFTD performing worse than BD1 ($p < 0.001$, $d = 1.29$) (Figure 1). Results were similar when controlling for executive performance (FAB).

The area under the curve (AUC) values (BD vs. bvFTD) for mFP, FER, and Mini-SEA total scores were 0.61 (sensitivity = 0.78, specificity = 0.28), 0.29 (sensitivity = 0.67, specificity = 0.12), and 0.63 (sensitivity = 0.78, specificity = 0.34), respectively. For the detection of faux-pas, the AUC value was 0.80 (sensitivity = 0.72, specificity = 0.78).

Discussion

This is the first study to compare the performance of patients with remitted BD1 and patients with bvFTD on SC core processes (FER and mentalizing). These clinical groups did not differ in any cognitive and SC measures, except for the detection of faux-pas.

BD1 and bvFTD patients had lower scores than HC on MMSE, FAB, and episodic memory scores, but did not differ between each other. Executive and episodic memory impairment are commonly observed in bvFTD[4] and might be present in BD.[3] Our findings highlight that

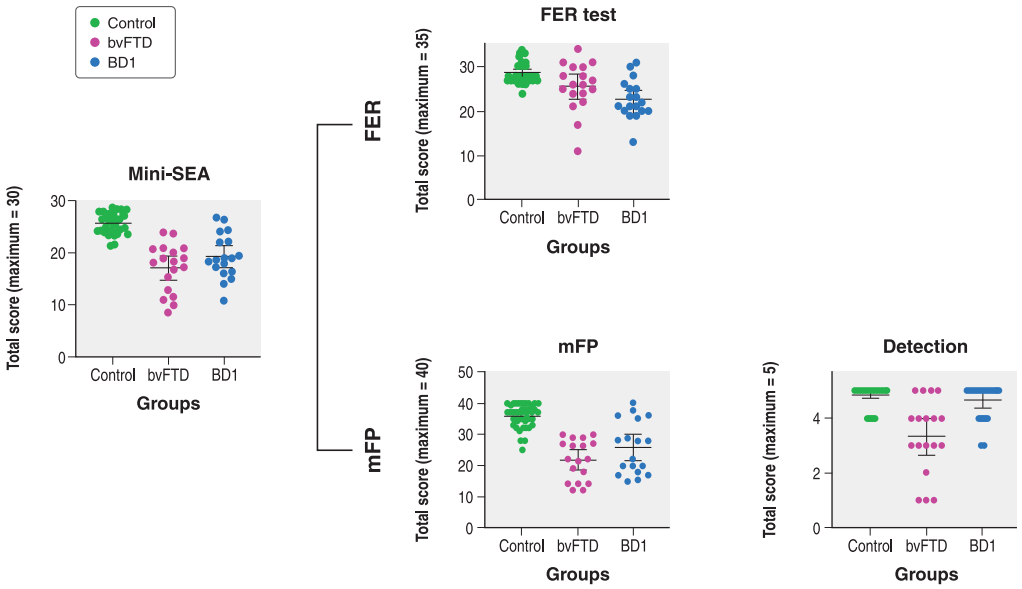

Figure 1 Social cognition tests. Individual and group performance of controls and patients with behavioral-variant frontotemporal dementia (bvFTD) and remitted bipolar disorder type 1 (BD1) on the short-form Social Cognition and Emotional Assessment (Mini-SEA), which is composed of a Facial Emotion Recognition (FER) task and the Modified Faux-Pas (mFP) test.

standard cognitive measures do not contribute to the diagnostic differentiation between bvFTD and BD.

Clinical follow-up is typically envisaged as useful to distinguish the two conditions in the challenging context of global cognitive deterioration, as longitudinal studies demonstrated that cognitive performance remained stable in BD over a 6-year period.[9,10] A recent systematic review suggested that BD is associated with a threefold risk of dementia, although the authors noted high heterogeneity of the included studies and low certainty of evidence.[11] Interestingly, some case reports have suggested an association between bvFTD and BD.[12] This highlights the need to find specific cognitive markers that can distinguish both disorders reliably.[2]

As expected, BD and bvFTD had lower performance than HC in emotion recognition and mentalizing, two core dimensions of SC; this is consistent with previous studies.[1,3,4] A single study[5] reported that patients with bvFTD had lower scores than BD (types I and II) on the Reading the Mind in the Eyes (RMET) task. However, there is controversy regarding the necessary involvement of mentalizing abilities (vs. emotion recognition) in this task's performance. In our study, aiming to assess the core components of SC, we employed the mFP, which does involve both mentalizing and social context decoding abilities, alongside the FER. Our methodology also relied on strict correction (Bonferroni) for multiple comparisons, thus increasing the reliability of our findings. Our results suggest that the decreased ability to detect faux-pas could be considered as a specific marker of bvFTD – which is in line with previous studies.[13,14] Interestingly, while patients with BD are able to detect faux-pas, they were unable to explain the faux-pas correctly, similarly to patients with bvFTD. Future studies should explore the qualitative differences in the responses given as potential indicators of diagnosis.

Patients with BD and bvFTD did not differ on the FER. Previous data show that patients with bvFTD[4] and BD[15] show impaired emotion recognition, although, to the best of our knowledge, this is the first study to directly compare BD and bvFTD regarding this ability. A previous study demonstrated that FER might differentiate bvFTD and depressive disorders,[16] but more studies are warranted to investigate the utility of such tests to differentiate bvFTD from PPD.

We acknowledge that sample sizes, as well as narrowing the assessment of executive functions to the FAB, are limitations of this study. Therefore, we cannot rule out that a more accurate distinction between BD and bvFTD could be provided by an extended cognitive and SC assessment. The effect of medications on cognitive performance was not considered here, which might also be an issue given the use of antipsychotics and mood stabilizers in both disorders, although this is a common limitation in the field.

In the absence of biomarkers, the distinction between bvFTD and BD remains a challenge. Altogether, our results should be considered in the development of tasks aiming to improve the clinical differentiation between bvFTD and BD. While the use of SC tests has been recently recommended in consensus guidelines in this context,[2] our study emphasizes the importance of multidimensionality in this assessment. Beyond the need to assess several functions rather than a single one, our

Table 1 Demographical and neuropsychological data (mean ± SD) for the study population

	bvFTD (n=18)	BD1 (n=20)	HC (n=40)	Kruskal-Wallis test (all groups)	bvFTD vs. BD1 (Mann-Whitney test)	bvFTD vs. HC (Mann-Whitney test)	BD1 vs. HC (Mann-Whitney test)
Sex	9F/9M	12F/8M	27F/13M	NA	p = 0.51 χ^2	p = 0.07 χ^2	p = 0.02 χ^2
Disease duration (years)	3.6 (± 2.1)	32.1 (± 13.1)	NA	NA	p < 0.0001; *d* = 3.04	NA	NA
Age (years)	65.0±8.8	57.4±11.4	61.2±9.9	p = 0.12	p = 0.04; *d* = 0.76	p = 0.21; *d* = 0.42	p = 0.23; *d* = 0.35
Educational level (years)	12.7±3.2	12.0±2.7	12.5±2.9	p = 0.91	p = 0.88; *d* = 0.21	p = 0.93; *d* = 0.03	p = 0.63; *d* = 0.02
MMSE (out of 30)	26.1±1.9	27.1±1.7	28.9±1.2	p < 0.001	p = 0.65; *d* = 0.55	p = 0.38; *d* = 1.84	p = 0.0001; *d* = 1.26
FAB (out of 18)	11.7±3.6	13.7±3.7	16.3±1.6	p < 0.001	p = 0.07; *d* = 2.65	p < 0.0001; *d* = 1.59	p < 0.0001; *d* = 1.15
FMT (5-minute recall)	6.7±2.4	7.5±2.3	9.2±1.4	p < 0.001	p = 0.35; *d* = 0.47	p < 0.0001; *d* = 1.31	p < 0.002; *d* = 0.92
FER (out of 35)	20.6±6.3	22.6±4.4	28.7±2.4	p < 0.001	p = 0.03; *d* = 0.59	p = 0.01; *d* = 0.76	p < 0.0001; *d* = 1.73
Theory of mind: FPRT							
Total score (out of 40)	20.4±7.4	25.7±8.4	35.9±3.8	p < 0.001	p = 0.20; *d* = 0.53	p < 0.0001; *d* = 2.65	p < 0.0001; *d* = 1.55
Detection of faux-pas (out of 5)	3.3±1.3	4.7±0.6	4.9±0.4	p < 0.001	p < 0.001; *d* = 1.29	p < 0.0001; *d* = 1.54	p = 0.23; *d* = 0.39
Detection of absence of faux-pas (out of 5)	4.0±1.0	3.4±1.4	4.8±0.6	p < 0.001	p = 0.27; *d* = 0.50	p < 0.0001; *d* = 0.95	p < 0.0001; *d* = 1.27
Attribution (out of 10)	2.9±1.4	3.3±1.4	4.8±1.0	p < 0.001	p = 0.44; *d* = 0.27	p = 0.38; *d* = 1.59	p < 0.001; *d* = 1.25
Identification (out of 10)	2.1±2.0	2.4±1.6	4.3±0.9	p < 0.001	p = 0.42; *d* = 0.21	p < 0.0001; *d* = 1.51	p < 0.0001; *d* = 1.41
Knowledge (out of 10)	0.9±1.0	1.8±1.5	3.8±1.0	p < 0.001	p < 0.12; *d* = 0.55	p < 0.0001; *d* = 2.37	p < 0.0001; *d* = 1.50
Intentionality (out of 10)	2.6±1.4	2.4±1.5	4.0±0.9	p < 0.001	p < 0.42; *d* = 0.27	p < 0.001; *d* = 1.04	p < 0.0001; *d* = 1.29
Empathy (out of 10)	2.6±1.2	3.3±1.5	4.6±0.7	p < 0.001	p < 0.25; *d* = 0.44	p < 0.0001; *d* = 1.82	p < 0.001; *d* = 1.13
Recognition of social norms violation (out of 20)	12.0±4.6	13.8±4.3	18.7±1.9	p < 0.001	p < 0.27; *d* = 0.38	p < 0.38; *d* = 1.89	p < 0.0001; *d* = 1.48
Mentalizing (out of 20)	6.5±3.5	7.4±4.2	12.4±2.1	p < 0.001	p < 0.65; *d* = 0.23	p < 0.38; *d* = 2.02	p < 0.0001; *d* = 1.47
Mini-SEA total score (out of 30)	17.1±4.8	19.3±4.3	25.7±1.9	p < 0.001	p < 0.28; *d* = 0.50	p < 0.0001; *d* = 2.44	p < 0.0001; *d* = 1.92

χ^2 = chi-square test; BD1 = bipolar disorder type 1; bvFT*d* = behavioral variant frontotemporal dementia; *d* = Cohen's *d*; F = female; FAB = Frontal Assessment Battery; FER = Facial Emotion Recognition Test; FMT = Figure Memory Test; FPRT = Faux-Pas Recognition Test; HC = healthy controls; M = male; Mini-SEA = Social Cognition and Emotional Assessment; MMSE = Mini-Mental State Examination; NA = not applicable.

findings also underline the utility of a more qualitative approach in the assessment of SC, as differences were found in a single dimension of the mFP, but not in the total score.

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Disclosure

The authors report no conflicts of interest.

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