ORIGINAL RESEARCH

The impact of limbic system morphology on facial emotion recognition in bipolar I disorder and healthy controls

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Introduction: Impairments in facial emotion recognition (FER) have been reported in bipolar disorder (BD) subjects during all mood states. This study aims to investigate the impact of limbic system morphology on FER scores in BD subjects and healthy controls.

Material and methods: Thirty-nine euthymic BD I (type I) subjects and 40 healthy controls were subjected to a battery of FER tests and examined with 3D structural imaging of the amygdala and hippocampus.

Results: The volume of these structures demonstrated a differential pattern of influence on FER scores in BD subjects and controls. In our control sample, larger left and right amygdala demonstrated to be associated to less recognition of sadness faces. In BD group, there was no impact of amygdala volume on FER but we observed a negative impact of the left hippocampus volume in the recognition of happiness while the right hippocampus volume positively impacted on the scores of happiness.

Conclusion: Our results indicate that amygdala and hippocampus volumes have distinct effects on FER in BD subjects compared to controls. Knowledge of the neurobiological basis of the illness may help to provide further insights on the role of treatments and psychosocial interventions for BD. Further studies should explore how these effects of amygdala and hippocampus volumes on FER are associated with social networks and social network functioning.

Keywords: bipolar disorder, social cognition, facial emotion recognition

Introduction

Social cognition refers to the neural processing underlying social interactions, which can be relatively independent from other aspects of cognition and is not assessed by traditional neurocognitive tasks.[1] One of the key aspects of social cognition is the ability to discriminate accurately between different facially expressed emotions. Impairments on facial emotion recognition (FER), as part of social cognition, have been reported in bipolar disorder (BD) patients[2–5] and have been the focus of functional magnetic resonance imaging studies (fMRI) studies that also disclosed differentiated activation of the limbic region.[6–10]

Altered FER responses in BD patients include enhanced recognition for disgust faces,[2] impaired recognition of fear faces,[4,5] as well as a selective effect of mood state[11,12] on surprise recognition. In a recent meta-analysis, Kohler et al concluded that FER impairment in BD patients represents a moderate and stable deficit.[13]

Impairments in FER have been the focus of many fMRI studies of BD, showing altered activation of the ventromedial prefrontal cortex, cingulate, hippocampus, amygdala, and limbic region.[6–10] Recently, it was reported that limbic system volume interferes in the social functioning of humans.[15–18] Bickart and colleagues reported that

a larger amygdala was associated with more complex social networks.[14] A larger amygdala aids in the identification and recognition of socioemotional cues in individuals from the same species,[15] allowing us to develop complex strategies to cooperate and compete.[16]

The amygdala is a key component of a neural system specialized for the rapid and automatic evaluation of stimuli that signal potential threat or danger in the immediate environment.[17] However, other researchers have proposed a more general role of this structure in the processing of signals of distress,[19] including other negative emotions such as sadness, or in the processing of signals that indicate potentially important environmental information that must be disambiguated.[20] In this way, the amygdala would respond to all visual emotional stimuli, regardless of valence, with a stronger activation for faces, thus providing strong support for the relevance detector model, which posits a general role of this structure in the detection of innate, biologically, and socially relevant information.[21] Furthermore, a larger amygdala might enable us to more effectively identify, learn about, and recognize socioemotional cues in conspecifics.[15]

Several magnetic resonance imaging (MRI) studies have demonstrated abnormalities in the structure or function of the amygdala in adults with mood disorders.[22–26] Some studies,[22–24,27] but not all,[25,28,29] have found enlarged amygdala volumes in patients with BD. Other studies,[30] but not all,[31,32] have found reduced amygdala volumes in subjects with major depressive disorder.

This study aims to investigate the association between the volume of the amygdala and hippocampus with FER performance of euthymic BD subjects compared to healthy controls. Given the fact that there is some data indicating morphologic abnormalities in these structures in BD subjects, and associating the activation of these structures with emotional processing, we hypothesize that this morphology differentially impacts FER in BD subjects compared to controls.

Material and methods
Subjects

Thirty-nine euthymic subjects with bipolar I disorder were included. Diagnoses were determined by trained psychiatrists based on the Structured Clinical Interview for Axis I Disorders-Patient Edition (SCID-I/P)[33] for the *Diagnostic and Statistical Manual of Mental Disorders* (fourth edition, text revision) (DSM-IV TR).[34] Patients were included if they were not currently in a mood state episode[34] and had been stable for at least 2 months. Subjects with neurological

disorders, previous head trauma, any illness requiring medical intervention, currently abusing any substance, or submitted to electroconvulsive therapy in the preceding 6 months were excluded. The Young Mania Rating Scale (YMRS),[35] and the Hamilton Depression Rating Scale (HDRS-21)[36] were used to evaluate subsyndromal symptoms. In the BD group, 78.6% of the subjects were using lithium, 52.4% were using anticonvulsants, 23.8% were using second-generation antipsychotics, 16.7% were using antidepressants, and 4.8% were using benzodiazepines at the time of neuropsychological evaluation.

Also, forty healthy volunteers aged between 18 and 35 years old were recruited from the University of São Paulo. All controls had no current or past history of psychiatric disorder according to the evaluation conducted by trained psychiatrists using The Mini International Neuropsychiatric Interview (MINI).[37] Similarly, all subjects had no family history (first degree relatives) of mood or psychotic disorders, and in the past 3 months had not used psychotropic medicines, and they did not have a history of substance abuse.

Image acquisition

MRI was carried out using an Intera Achieva 3.0-T system and an eight-channel head coil (Philips, Amsterdam, The Netherlands). Sagittal three-dimensional T1-weighted anatomical images with isotropic 1 mm^3 resolution were obtained with a fast-field echo sequence (TR = 7 ms; TE = 3.2 ms; TI = 900 ms; flip angle = 8°). Three-dimensional T1-weighted MRI images were analyzed with the program Freesurfer version 5.1.0 (Athinoula A. Martinos Center for Biomedical Imaging, Charlestown, MA, USA) to obtain automatic and non-interactive volumes for structures in the right and left hemispheres. Intracranial volume was also measured with the same software for normalization purposes.

Cortical reconstruction and volumetric segmentation was performed with the Freesurfer image analysis suite, which is documented and freely available for download online (http://surfer.nmr.mgh.harvard.edu/). The technical details of these procedures are described in prior publications.[38–47] Briefly, this processing includes removal of non-brain tissue using a hybrid watershed/surface deformation procedure,[48] automated Talairach transformation, segmentation of the subcortical white matter and deep gray matter volumetric structures (including hippocampus, amygdala, caudate, putamen, ventricles),[42,45] intensity normalization,[49] tessellation of the gray matter white matter boundary, automated topology correction,[41,50] and surface deformation following intensity

gradients to optimally place the gray/white and gray/cerebrospinal fluid borders at the location where the greatest shift in intensity defines the transition to the other tissue class.[38–40] Once the cortical models are complete, a number of deformable procedures can be performed for further data processing and analysis including surface inflation,[44] registration to a spherical atlas which utilized individual cortical folding patterns to match cortical geometry across subjects,[51] parcellation of the cerebral cortex into units based on gyral and sulcal structure,[43,52] and creation of a variety of surface-based data including maps of curvature and sulcal depth. This method uses both intensity and continuity information from the entire three-dimensional MRI volume in segmentation and deformation procedures to produce representations of cortical thickness, calculated as the closest distance from the gray/white boundary to the gray/cerebral spinal fluid (CSF) boundary at each vertex on the tessellated surface.[40] The maps are created using spatial intensity gradients across tissue classes and are therefore not simply reliant on absolute signal intensity. The maps produced are not restricted to the voxel resolution of the original data; thus, they are capable of detecting submillimeter differences between groups. Procedures for the measurement of cortical thickness have been validated against histological analysis[53] and manual measurements.[54,55] Freesurfer morphometric procedures have been demonstrated to show good test–retest reliability across scanner manufacturers and across field strengths.[46,56] The numbers used to refer to the amygdala and hippocampus are the result of the correction of the measure in millimeters by the intracranial volume.

FER tests

All subjects included in this study underwent FER tests. FER was tested using the Ekman 60 Faces Test (EK) employing a range of photographs from the Ekman and Friesen series of Pictures of Facial Affect,[57] the most widely used and validated series of photographs in facial expression research. From this series, the faces of ten actors (six female, four male) were chosen, each displaying six basic emotions (happiness, sadness, disgust, fear, surprise, and anger). The EK can be used to assess recognition of facial expression of basic emotions. The maximum test score (indicating best performance) is 60 for all six emotions, with 10 points designated for each basic emotion. The computer software for the test was available on CD-ROM. Patients were allowed unlimited time to respond. Immediately prior to testing, it was verified that patients and healthy controls semantically understood the words happiness, sadness, disgust, fear,

surprise, and anger. Patients and healthy controls were asked to provide an example for each emotion by answering the questions: "Describe a situation when you feel happiness, fear, etc." Any incorrect answer would have led to exclusion from this study, but all participants gave correct answers.

Statistical analysis

The subjects were classified into two groups (BD and control). Chi-square test was used for comparison of categorical data (gender), and Student's *t*-test for continuous data (age, education, amygdala, and hippocampus volume). We used a multivariate analysis of covariance (MANOVA) model in which EK scores were entered as dependent variables, while group, age, gender, right amygdala volume, left amygdala volume, right hippocampus volume, and left hippocampus volume were entered as covariates. All results were corrected for multiple comparison error (Bonferroni $P > 0.008$).

Ethics

The research ethics board of the Hospital das Clínicas of the University of São Paulo approved the study. Written informed consent was obtained from all participants.

Results

Sociodemographic data of both groups are presented in Table 1. The BD group had a higher mean age than the control group. Mean YMRS and HDRS scores of the BD group were 2.3 (±1.8) and 4.1 (±2), respectively. FER scores were lower in the BD group than the control group in all FER tests (Table 1). The amygdala and hippocampus volumes did not differ between the BD and control groups (Table 1).

The analysis of the whole sample (BD and control groups) revealed that the left hippocampus volume was positively associated with greater recognition of fear faces (Table 2).

In the control group, we found an association between the recognition of fear faces and age (B = −0.42, df = 1, $P = 0.004$). Moreover, the recognition of sad faces was negatively influenced by the volume of the left amygdala (B = −4058, df = 1, $P = 0.004$) (Table 3).

In the BD group, the recognition of happy faces was associated negatively with the volume of the left hippocampus (B = −1040, df = 1, $P = 0.003$) and positively with the volume of the right hippocampus (B = 955, df = 1, $P = 0.001$) (Table 3).

Discussion

This study aimed to investigate the impact of limbic system morphology on FER scores in BD subjects and

Table I Comparison of sociodemographic and clinical characteristics between control group and bipolar disorder group

	Controls (n = 40)	Bipolar (n = 39)	t-test
	Mean ± standard deviation	Mean ± standard deviation	
Gender (female/male)	20/20	24/15	0.21*
Age	25.9 ± 5.8	32.9 ± 10.9	0.01
Education	14.1 ± 2.8	12.6 ± 3.1	0.1
YMRS		2.3 ± 1.8	
HDRS		4.1 ± 2.0	
Amygdala volume	0.0045 ± 0.001	0.0047 ± 0.001	0.64
Hippocampus volume	0.0071 ± 0.001	0.0063 ± 0.001	0.08
Anger	8.11 ± 1.91	16.41 ± 5.17	<0.0001
Disgust	7.54 ± 1.63	17.62 ± 4.02	<0.0001
Fear	5.19 ± 2.95	16.24 ± 4.42	<0.0001
Happy	9.78 ± 0.48	19.59 ± 1.19	<0.0001
Sad	7.11 ± 2.42	19.27 ± 1.17	<0.0001
Surprise	9.89 ± 7.60	18.57 ± 1.76	<0.0001

Note: *Chi-squared. Significance level: $P < 0.05$.
Abbreviations: HDRS, Hamilton Depression Rating Scale; YMRS, Young Mania Rating Scale.

healthy controls and our results indicate that amygdala and hippocampus volumes have effects on FER in BD subjects and healthy controls, but amygdala and hippocampus volumes appear to have distinct effects on FER in BD subjects compared to controls.

In our control sample, larger right amygdala volume was associated with less recognition of fear faces. Nonetheless, our data are consistent with previous fear recognition experiments that both directly and indirectly demonstrate differences between the left and right amygdala.[58,59] Gläscher and Adolphs[59] proposed a comprehensive explanatory model for emotional information processing in which the left and the right amygdala have different functions during emotion processing; namely, when an emotionally arousing stimulus occurs, it will first automatically activate the right amygdala, which mediates a relatively global emotional reaction. Subsequently, the left amygdala is involved in a more specific, sustained emotional reaction that decodes variations in arousal magnitude. Curiously, in our BD subjects, there was no impact of amygdala volume on FER, but we observed an impact of the left and right hippocampus volume in the recognition of happiness. This data indicates a differential effect of the volume of limbic structures on FER in BD subjects and controls and reinforces the theory of laterality of limbic structures.[60,61]

Previous studies about the effect of limbic structures' volume on FER are very sparse, but there are some studies about the effect of limbic structures' volume on other measures of social cognition that corroborate with our data.[44–49,54–56,62] In this way, recognition of emotional versus neutral scenes[44–48] and emotional versus neutral context is associated with activity in a number of regions, including the amygdala, temporal pole, occipital cortex and hippocampus, orbitofrontal and inferior frontal regions, and parietal cortex. Increased amygdala activation has also been reported during retrieval of visual details for emotional versus neutral items.[49] Moreover, limbic structures', volume is associated with social play in primates[62] and the magnitude of emotion associated with autobiographical memories also influences activity in the amygdala, frontal cortex,[54,55] and hippocampus[56] when these memories are retrieved.

Although there are no data about the effect of the volume of limbic structures on FER in BD subjects, our results are in line with the literature about other neuropsychiatric disorders and the effect of the volume of the amygdala on social cognition.[63,65] Moreover, there are some studies about emotional memory deficits and amygdala volume in depression,[63] schizophrenia,[64] and Alzheimer's disease.[65] Mori et al studied Alzheimer's disease patients and reported that amygdala size correlated with emotional memory.[65] Exner et al studied schizophrenia and reported that emotional memory and learning correlated with amygdala size.[64] Weniger et al reported in a sample of depressed subjects that larger amygdala volume predicted impaired emotional memory.[63] In a different perspective, Bickart et al reported that a larger amygdala was associated with larger and more complex social networks, which could be associated with better social network functioning.[14] In the same way, Ille et al tested patients with Huntington's disease and healthy controls and showed that patients with Huntington's disease have normal affective experience, but impaired recognition of negative emotions (disgust, anger, sadness).[66] The patients with Huntington's disease perceived the emotions as less intense and made more classification errors than the controls. These deficits were

Table 2 Multivariate analysis of covariance in the whole sample (BD and controls) using FER tests as dependent variables and age, group, gender, left and right hippocampus volume, and left and right amygdala volume as covariates

Dependent variable	B	P-value	df	F	Partial eta squared	Observed power
Anger						
Age	−0.1	0.198	1	1.690	2.7%	24.9%
Group	−7.9	<0.001	1	46.600	42.9%	100.0%
Gender	0.5	0.655	1	0.201	0.3%	7.3%
Left hippocampus	2271.6	0.263	1	1.276	2.0%	19.9%
Left amygdala	81.8	0.984	1	<0.001	0.0%	5.0%
Right hippocampus	−1445.5	0.471	1	0.526	0.8%	11.0%
Right amygdala	−990.9	0.779	1	0.080	0.1%	5.9%
Disgust						
Age	0.0	0.860	1		0.1%	5.3%
Group	−10.6	<0.001	1	0.031	70.0%	100.0%
Gender	1.6	0.049	1	144.880	6.1%	50.7%
Left hippocampus	−2110.0	0.173	1	4.030	3.0%	27.3%
Left amygdala	160.4	0.958	1	1.897	0.0%	5.0%
Right hippocampus	115.4	0.940	1	0.006	0.0%	5.1%
Right amygdala	819.8	0.760	1	0.094	0.2%	6.1%
Fear						
Age	−0.1	0.058	1	3.730	5.7%	47.7%
Group	−10.1	<0.001	1	103.440	62.5%	100.0%
Gender	−0.7	0.457	1	0.560	0.9%	11.4%
Left hippocampus	5235.3	0.004	1	9.028	12.7%	84.1%
Left amygdala	399.2	0.907	1	0.014	0.0%	5.2%
Right hippocampus	−3300.3	0.060	1	3.657	5.6%	46.9%
Right amygdala	−1740.5	0.569	1	0.328	0.5%	8.7%
Happy						
Age	0.0	0.659	1	0.197	0.3%	7.2%
Group	−9.7	<0.001	1	1397.800	95.8%	100.0%
Gender	0.4	0.106	1	2.690	4.2%	36.5%
Left hippocampus	196.4	0.668	1	0.186	0.3%	7.1%
Left amygdala	−770.4	0.391	1	0.746	1.2%	13.6%
Right hippocampus	423.7	0.351	1	0.883	1.4%	15.2%
Right amygdala	78.5	0.922	1	0.001	0.0%	5.1%
Sad						
Age	−0.1	0.001	1	11.740	15.9%	92.1%
Group	−11.3	<0.001	1	517.600	89.3%	100.0%
Gender	−0.1	0.877	1	0.024	0.0%	5.3%
Left hippocampus	329.6	0.705	1	0.144	0.2%	6.6%
Left amygdala	−1556.0	0.364	1	0.837	1.3%	14.7%
Right hippocampus	64.2	0.941	1	0.006	0.0%	5.1%
Right amygdala	112.3	0.941	1	0.005	0.0%	5.1%
Surprise						
Age	−0.1	0.100	1	2.790	4.3%	37.7%
Group	−7.3	<0.001	1	21.160	25.4%	99.5%
Gender	1.3	0.372	1	0.809	1.3%	14.4%
Left hippocampus	−1414.9	0.612	1	0.260	0.4%	7.9%
Left amygdala	−7053.8	0.200	1	1.680	2.6%	24.8%
Right hippocampus	2109.7	0.446	1	0.588	0.9%	11.7%
Right amygdala	2676.4	0.583	1	0.305	0.5%	8.5%

Abbreviations: BD, bipolar disorder; FER, facial emotion recognition.

correlated with regional atrophy in emotion-relevant areas (insula, orbitofrontal cortex) and in memory-relevant areas (dorsolateral prefrontal cortex, hippocampus).[66]

In a general way, we can say that previous studies reported a positive correlation between amygdala volume and social function in controls, schizophrenia, Huntington's disease, and Alzheimer's disease, but in our data the recognition of sad faces was negatively influenced by the size of the left amygdala.[14,64–66] On the other hand, a previous study reported that in depression there is a negative correlation with amygdala

Table 3 Multivariate analysis of covariance using FER tests as dependent variables and age, gender, left and right hippocampus volume, and left and right amygdala volume as covariates in BD and control groups

Group	B	*P*-value	df	F	Partial eta squared	Observed power
Controls						
Anger						
Age	−0.277	0.184	1	1.850	5.8%	26.1%
Gender	1.032	0.569	1	0.331	1.1%	8.6%
Left hippocampus	4285.791	0.231	1	1.496	4.7%	22.0%
Left amygdala	4665.356	0.514	1	0.437	1.4%	9.8%
Right hippocampus	−5270.068	0.203	1	1.694	5.3%	24.3%
Right amygdala	−4270.061	0.562	1	0.344	1.1%	8.8%
Disgust						
Age	0.088	0.580	1	0.313	1.0%	8.4%
Gender	2.264	0.113	1	2.662	8.1%	35.2%
Left hippocampus	−2035.753	0.458	1	0.564	1.8%	11.2%
Left amygdala	−622.528	0.910	1	0.013	0.0%	5.1%
Right hippocampus	−491.830	0.876	1	0.025	0.1%	5.3%
Right amygdala	−144.169	0.980	1	0.001	0.0%	5.0%
Fear						
Age	−0.422	0.004	1	9.620	24.3%	85.1%
Gender	−0.380	0.753	1	0.101	0.3%	6.1%
Left hippocampus	5680.847	0.021	1	5.903	16.4%	65.2%
Left amygdala	−2878.838	0.546	1	0.374	1.2%	9.1%
Right hippocampus	−2527.843	0.357	1	0.876	2.8%	14.8%
Right amygdala	−1576.541	0.748	1	0.105	0.3%	6.1%
Happy						
Age	−0.069	0.143	1	2.265	7.0%	30.8%
Gender	0.745	0.076	1	3.380	10.1%	42.9%
Left hippocampus	729.342	0.364	1	0.846	2.8%	14.5%
Left amygdala	−835.202	0.604	1	0.247	0.9%	8.0%
Right hippocampus	−14.531	0.987	1	0.000	0.0%	5.0%
Right amygdala	109.456	0.947	1	0.004	0.0%	5.0%
Sad						
Age	−0.079	0.041	1	4.547	13.2%	54.1%
Gender	0.072	0.826	1	0.049	0.2%	5.5%
Left hippocampus	451.529	0.484	1	0.502	1.6%	10.5%
Left amygdala	−4058.325	0.004	1	9.994	25.0%	86.4%
Right hippocampus	−69.231	0.926	1	0.009	0.0%	5.1%
Right amygdala	722.041	0.590	1	0.267	1.0%	8.3%
Surprise						
Age	−0.050	0.430	1	0.639	2.1%	12.1%
Gender	0.161	0.772	1	0.086	0.3%	5.9%
Left hippocampus	889.503	0.415	1	0.683	2.2%	12.6%
Left amygdala	−5025.014	0.027	1	5.374	15.2%	61.2%
Right hippocampus	1445.502	0.254	1	1.352	4.3%	20.3%
Right amygdala	−896.214	0.691	1	0.161	0.5%	6.7%
BD						
Anger						
Age	−0.055	0.121	1	2.568	9.0%	33.9%
Gender	0.488	0.554	1	0.359	1.4%	8.9%
Left hippocampus	−1653.754	0.320	1	1.028	3.8%	16.4%
Left amygdala	−883.674	0.763	1	0.093	0.4%	6.0%
Right hippocampus	1470.811	0.267	1	1.286	4.7%	19.4%
Right amygdala	955.508	0.678	1	0.176	0.7%	6.9%

(*Continued*)

Table 3 (*Continued*)

Group	B	*P*-value	df	F	Partial eta squared	Observed power
Disgust						
Age	−0.032	0.307	1	1.087	4.0%	17.1%
Gender	0.349	0.632	1	0.235	0.9%	7.5%
Left hippocampus	−1677.897	0.255	1	1.354	4.9%	20.2%
Left amygdala	1504.018	0.562	1	0.346	1.3%	8.7%
Right hippocampus	769.917	0.508	1	0.451	1.7%	9.9%
Right amygdala	−131.096	0.949	1	0.004	0.0%	5.0%
Fear						
Age	−0.075	0.168	1	2.014	7.2%	27.7%
Gender	−0.232	0.856	1	0.034	0.1%	5.4%
Left hippocampus	594.801	0.816	1	0.050	0.2%	5.6%
Left amygdala	6191.529	0.179	1	1.905	6.8%	26.5%
Right hippocampus	−2708.134	0.190	1	1.815	6.5%	25.4%
Right amygdala	−1814.826	0.612	1	0.264	1.0%	7.9%
Happy						
Age	0.000	0.958	1	0.003	0.0%	5.0%
Gender	0.131	0.423	1	0.662	2.5%	12.3%
Left hippocampus	−1040.691	0.003	1	10.380	28.5%	87.3%
Left amygdala	177.139	0.760	1	0.960	0.4%	6.0%
Right hippocampus	955.078	0.001	1	13.831	34.7%	94.7%
Right amygdala	59.104	0.897	1	0.017	0.1%	5.2%
Sad						
Age	−0.106	0.015	1	6.718	20.5%	70.4%
Gender	−0.444	0.653	1	0.207	0.8%	7.2%
Left hippocampus	−465.317	0.814	1	0.057	0.2%	5.6%
Left amygdala	1590.344	0.650	1	0.211	0.8%	7.3%
Right hippocampus	563.077	0.720	1	0.131	0.5%	6.4%
Right amygdala	−1309.718	0.635	1	0.231	0.9%	7.5%
Surprise						
Age	−0.167	0.244	1	1.423	5.2%	20.9%
Gender	3.304	0.331	1	0.982	3.6%	15.9%
Left hippocampus	−5550.344	0.414	1	0.689	2.6%	12.6%
Left amygdala	−6867.535	0.568	1	0.335	1.3%	8.6%
Right hippocampus	2889.621	0.591	1	0.296	1.1%	8.2%
Right amygdala	5672.409	0.549	1	0.369	1.4%	9.0%

Abbreviations: BD, bipolar disorder; FER, facial emotion recognition.

volume and emotional memory; in the same way, our data reported negative impact of the left hippocampus volume and positive impact of the right hippocampus volume in the recognition of happiness.[63]

One limitation of our study is related to the fact that the sizes of the left and right amygdala and the left and right hippocampus are highly correlated, which makes separating their unique influence on each emotional recognition test highly difficult.

Conclusion

To sum up, we reported evidence that amygdala and hippocampus volumes have effects on FER in BD subjects and healthy controls, but amygdala and hippocampus volumes appear to have distinct effects on FER in BD subjects compared to controls. Further studies should explore how these effects of amygdala and hippocampus volumes on FER are associated with social networks and social network functioning. Understanding how the neurobiology of patients with BD affects behavior may help to provide further insights on the role of the treatment and psychosocial interventions of BD.

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