

Facial emotion recognition in bipolar disorder: a critical review

Reconhecimento de emoções faciais: artigo de revisão

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Abstract

Objective: Literature review of the controlled studies in the last 18 years in emotion recognition deficits in bipolar disorder. **Method:** A bibliographical research of controlled studies with samples larger than 10 participants from 1990 to June 2008 was completed in Medline, Lilacs, PubMed and ISI. Thirty-two papers were evaluated. **Results:** Euthymic bipolar disorder presented impairment in recognizing disgust and fear. Manic BD showed difficult to recognize fearful and sad faces. Pediatric bipolar disorder patients and children at risk presented impairment in their capacity to recognize emotions in adults and children faces. Bipolar disorder patients were more accurate in recognizing facial emotions than schizophrenic patients. **Discussion:** Bipolar disorder patients present impaired recognition of disgust, fear and sadness that can be partially attributed to mood-state. In mania, they have difficult to recognize fear and disgust. Bipolar disorder patients were more accurate in recognizing emotions than depressive and schizophrenic patients. Bipolar disorder children present a tendency to misjudge extreme facial expressions as being moderate or mild in intensity. **Conclusion:** Affective and cognitive deficits in bipolar disorder vary according to the mood states. Follow-up studies re-testing bipolar disorder patients after recovery are needed in order to investigate if these abnormalities reflect a state or trait marker and can be considered an endophenotype. Future studies should aim at standardizing task and designs.

Descriptors: Bipolar disorder; Facial expression; Schizophrenia; Depression; Expressed emotion

Resumo

Objetivo: Revisão da literatura de estudos controlados publicados nos últimos 18 anos sobre déficits no reconhecimento de emoções no transtorno bipolar. **Método:** Foi realizada uma pesquisa bibliográfica no Medline, Lilacs, PubMed e ISI, selecionando-se o período de 1990 a junho de 2008. Foram incluídos apenas estudos controlados, que tivessem uma das amostras com mais de 10 participantes, totalizando 32 artigos. **Resultados:** Bipolares eutímicos apresentaram prejuízo no reconhecimento de nojo e medo. Em mania, mostraram dificuldade para reconhecer medo e tristeza. Transtorno bipolar pediátrico e crianças de risco apresentam dificuldade para reconhecer emoções nos rostos de adultos e de crianças. Bipolares foram mais precisos para reconhecer emoções do que os pacientes esquizofrênicos. **Discussão:** Pacientes com transtorno bipolar apresentam prejuízo no reconhecimento de nojo, medo e tristeza, os quais podem ser apenas em parte atribuídos ao estado de humor. No episódio maniaco, eles têm dificuldade para reconhecer medo e nojo. Entretanto, eles são mais precisos no reconhecimento de emoções do que pacientes deprimidos e esquizofrênicos. Crianças com transtorno bipolar apresentam tendência a julgar expressões faciais extremas como sendo de intensidade leve ou moderada. **Conclusão:** Déficits afetivos e cognitivos em bipolares sofrem variações dependendo do estado de humor. Estudos de seguimento, reavaliando pacientes após a remissão dos sintomas, são necessários para investigar se estas anormalidades refletem um estado ou traço da doença e se podem ser consideradas endofenótipos. Estudos futuros devem padronizar tarefas e metodologia.

Descritores: Transtorno bipolar; Expressão facial, Esquizofrenia; Depressão; Emoções manifestadas

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Submitted: January 6, 2009

Accepted: March 16, 2009

Introduction

The ability to process and identify facial emotions is an essential component of human communication and social interaction. Though social interaction may vary according to cultural norms and customs, cross-cultural studies have repeatedly provided evidence in favor of the universality of facial emotions. Six universal emotions have since been established, including, happiness, sadness, anger, fear, disgust and surprise, each of which corresponds to a specific arrangement of facial muscles and has partially separable neurocircuitry processes.^{1,2}

The processing of facial emotions, which ranges from the interpretation of the stimulus to the preparation of an appropriate behavioral response, is supported by specific neural systems, that include ventromedial prefrontal areas, orbito-frontal areas, cortical areas of the fusiform gyrus, inferior temporal gyrus and occipital gyrus and, sub-cortical structures, such as the amygdala, ventral striatum, hippocampal formation, and dorsomedial nucleus of the thalamus.^{3,4} Specifically, the amygdala seems to play a crucial role as it is involved with the recognition of emotions from facial expressions, especially certain negatively valenced emotions such as fear.⁵ Supporting this hypothesis, functional studies in healthy individuals show that facial emotional processing is associated with activation of the amygdala.^{6,7}

Bipolar disorder (BD) has consistently been coupled to cognitive impairments that hinder the cognitive and social functioning of BD patients.^{8,9} However, for years, these cognitive deficits were believed to disappear during euthymic states of the disorder. Growing bodies of evidence suggest that even when stable, BD patients suffer from trait-associated cognitive impairment.^{10,11}

Recent studies have reported impairments on tests of face and facial emotion perception in BD but this body of literature is still somewhat limited. For example, it has not yet been determined whether these deficits are specific for facial affect and, whether they transcend all mood episodes of the disorder or are state dependent.

The objective of this study was to critically review the deficits of facial emotion perception and recognition detected in BD patients as well as subjects at risk for developing BD in order to investigate whether the detected deficits can serve as an endophenotype for the disorder.

Method

The research consisted of a literature review focused on controlled studies that described the characteristics of the processing of facial emotions in subjects with bipolar disorder, selecting the period from 1990 to 2008. A systematic search was conducted through Medline, using the following key words: "*bipolar disorder and face recognition*", "*emotion recognition and bipolar disorder*", "*bipolar disorder and facial affect*".

Inclusion criteria: studies published in English with a minimum sample size of ten (per group), examining facial emotion processing in bipolar disorder adults, children, including children at risk for bipolar disorder (n = 32).

Exclusion criteria: studies that analyzed only the group of bipolar patients without a control group (n = 3).

The studies were organized by the comparison between BD and the following samples: schizophrenia (n = 6), major depressive disorder (MDD) (n = 2), and healthy controls (n = 6). We also included neuroimaging studies (n = 7) and studies with pediatric BD samples (n = 11). Twenty-nine studies had a healthy control group that was compared to the clinical samples.

Results

Studies included in this review are displayed in Table 1.

1. BD vs schizophrenia

Impaired emotion recognition had been more frequently documented in schizophrenic patients than in bipolar patients. The studies regarding the recognition of faces expressing emotions have given support to the hypothesis of a probable dysfunction of the right hemisphere (hypofunctioning) in patients with schizophrenia and those with mood disorders, especially major depressive disorder (MDD). The perception of emotional faces is accomplished primarily by the right brain hemisphere, which is also responsible for processing spatial information.¹² In bipolar disorder, the findings are not clear yet.

David and Cutting evaluated the role of right hemisphere activation in positive and negative affect in schizophrenic, manic and depressive patients in comparison with a healthy control group using a happy-sad chimeric face test to examine.¹³ This test can elicit a left-sided perceptual bias in right-handed healthy subjects. Healthy controls and manic patients had significant left bias, while depressive patients had a weaker bias and schizophrenic patients showed no significant bias. Possible explanations are right hemisphere hyperfunction in mania, moderate relative hypofunction in depression, and severe relative hypofunction in schizophrenia. The marked difference between mania and schizophrenia supports distinct pathophysiologies underlying these two conditions.

In 1996, Bellack et al. noticed that schizophrenic and BD patients made more errors than control subjects on Face Recognition and Speech-Sounds Perception tests.¹⁴ Performance was not correlated to symptom measures of the Brief Psychiatric Rating Scale (BPRS) or associated with the use of medication. It was suggested that while patients with schizophrenia and BD may suffer difficulties in accurately processing cues in their direct environment, these are not specific for the perception of emotional expressions.

Addington and Addington compared 40 stable schizophrenic patients, 40 euthymic BD patients and 40 control subjects on the Continuous Performance Test (CPT), Forced-Choice Span of Apprehension Test (SPAN), a Facial Affect Recognition Test, a Facial Affect Discrimination Test, a Face Recognition Test, and the Rey Memory Test.¹⁵ Schizophrenic patients were tested at two illness stages: 1) at acute relapse and, 2) 3 months later during partial remission. No differences were found in schizophrenic patients in stages 1 and 2 on tests of face recognition and attention. In stage 1, negative symptoms correlated to accuracy scores on the facial discrimination task; and in stage 2 they correlated to both facial affect, face recognition and attention tasks. In comparison to control subjects, schizophrenic patients made significantly more mistakes on facial affect tasks, the face recognition test, the SPAN, CPT and the Rey. BD patients differed from controls only in the facial discrimination task and the Rey recall. Scores on attentional tasks were correlated to facial affect scores only for the schizophrenic group.

In 1999, Lior applied a chimeric face test to 15 schizophrenic patients with positive symptoms, 20 schizophrenic patients with negative symptoms, 10 manic BD patients, 10 depressed BD patients and 37 control subjects.¹⁶ All patients were taking antipsychotic medications. The task was composed of 4 schematic drawings of chimeric faces (one hemi-face happy or sad), which were mirror-imaged, and two composite faces. Subjects were asked to answer two questions for each stimulus: 1) what does the person feel, and 2) how intensely is the emotion being expressed.

Table 1 - Results from the studies included in this review

| Authors and year | Subjects | Neuropsychological tests | Results |
|--|---|--|---|
| David and Cutting (1990) ³ | 25 MDD inpatients; 15 with mania or hypomania; 20 SCH; 60 HC | The Happy-Sad Chimeric Faces Test | Depression and mania: associated with ↓ and ↑ biases respectively, while SCH showed no bias. |
| Rubinow and Post (1992) ¹⁹ | 7 BD type I; 5 BD type II; 5 MDD; 31 HC | Non-Verbal Photograph Matching Test; Sentence-Matching Test | Patients impaired on face but not on sentence task Patients: more mistakes for sad and interest faces, and near significantly more mistakes for happy faces. For sentence task: fewer matches on surprise sentences. |
| Bellack et al (1996) ¹⁴ | 25 SCH; 10 schizoaffective patients; 11 BD; 19 HC | Videotaped Affect Perception Test; Facial Emotion Identification Test (Kerr and Neale, 1993); Facial Emotion Discrimination Test; Benton Face Recognition Test; Speech Sounds Perception Test (Halstead, 1947) | Patients: worse judgment about sad scenes with audio compared, and happy scenes without audio. Facial emotion tasks: no differences between groups Controls: better on Benton and Speech test. |
| Addington and Addington (1998) ¹⁵ | 40 SCH; 40 stable BD; 40 HC | Continuous Performance Test; Forced-Choice Span of Apprehension Task; Facial Affect Recognition; Facial Recognition; Rey Osterrieth Memory for Design | SCH: worse on facial recognition and facial affect recognition than the other groups. SCH: correlations between attention tasks and facial tasks. |
| Lior (1999) ¹⁶ | 15 positive SCH; 20 negative SCH; 10 manic BD; 10 MDD | Chimeric Facial Emotion Task | Negative SCH: judged positive expressions in the left hemifaces as depicting negative emotions, and negative expressions as depicting positive emotions Controls and depressed BD: normal judgement of chimeric faces. Positive SCH and manic BD: judges all chimeric faces as positive. Patients performances were interpreted in terms of differential dysfunctions in posterior areas of the right cerebral hemisphere which might be associated with bilateral effects of dysfunctions in anterior cerebral areas. |
| Yurgelun-Todd et al. (2000) ²⁷ | 14 BD; 10 HC | fMRI scanning during a Facial Affect Recognition Task (using fearful and happy faces) | BD: ↓ dorsolateral PFC activation, and ↑ amygdalar response to fearful affect. BD: impaired ability to correctly identify fearful affect. |
| Harmer et al. (2002) ²² | 20 euthymic BD; 20 HC | National Adult Reading Test; Premorbid Verbal IQ; Block Design WAIS; Ekman and Friesen Pictures of Affect Series; MORPHED; Famous Face Classification Task | BD: slight but significant impairment in classification of famous faces. BD: facilitated recognition of disgust due to increased target sensitivity. |
| Loughland et al. (2002) ¹⁷ | 65 SCH; 52 affective disorder; 61 HC | Face Recognition Task; Facial Affect Recognition Task (selected from Mazurski & Bond 1993 series); Visual scan paths were recorded using a CEDRIC Mark II | SCH: impaired scan paths not due to lack of foveal attention to stimuli (especially in non-degraded face stimuli). SCH: more behavioural impairments compared to affect and control groups. Affective disorder: impairment in allocating attention to spatial features (especially salient features). All subjects: fewer and shorter fixations for non-degraded versus degraded faces. SCH: path impairments not exacerbated by emotional content. |
| Lembke and Ketter (2002) ²¹ | 8 BD I; 8 euthymic BD I; 8 BD II; 10 HC | Matching of pictures of faces to the words: "fear," "disgust," "anger," "sadness," "surprise," and "happiness" | Manic BD: worse overall recognition of facial emotion, and worse recognition of fear and disgust than controls. Euthymic BD II: greater recognition for fear than manic and euthymic BD I. |
| Getz et al. (2003) ²³ | 25 manic BD; 25 HC | Benton Face Recognition; Computerized Face Recognition; Facial Affect Labelling Task (at 3 time durations: 500 ms, 750 ms, 1000 ms) | Controls and patients did not differ on facial tasks. BD: performed more poorly on facial affect task. BD: slower in responding on all tasks, but presentation time did not effect their performance. BD: impaired in recognizing affective cues. |
| Kucharska-Pietura and David (2003) ²⁰ | 30 BD (mania); 30 MDD; 30 right-hemisphere lesion; 30 left-hemisphere lesion; 30 HC | Chimeric Face Test; Mini Mental State Examination; Annett Handedness Inventory | MMSE scores were higher for controls and manic patients than other groups. Right-hemisphere and MDD: ↓ LHB. Right hemisphere and MDD: difficulty recognizing happy faces. |
| McClure et al. (2003) ³⁶ | 11 pediatric BD; 10 children with anxiety disorder; 25 HC | Facial Memory Test; Facial Emotion Identification | BD children: more errors on identification of low-intensity expressions, and more errors on recognition of child faces, misidentifying them as angry. No differences on facial memory test. |
| Voelbel et al. (2003) ³⁸ | 35 pediatric BD; 23 HC | Cognitive battery; Sainsbury-Butler Faces Test - Sorting | Pediatric BD: impairments in visual and emotional processing. |
| Chang et al. (2004) ³⁹ | 12 male BD with at least one BD parent; 10 HC | Functional magnetic resonance imaging; Visuospatial working memory task; International Affective Picture System (IAPS) | BD: in viewing negatively valenced pictures, had greater activation in the bilateral dorsolateral PFC, inferior frontal gyrus and right insula. For positively valenced pictures, BD had greater activation in the bilateral caudate and thalamus, left middle/superior frontal gyrus, and left ACC. |

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Table 1 - Results from the studies included in this review

| Authors and year | Subjects | Neuropsychological tests | Results |
|---------------------------------------|--|---|---|
| Lawrence et al. (2004) ³ | 12 BD I; 9 MDD; 11 HC | Three 6-minute experiments of face emotion recognition using sad, happy and fearful expressions of 100, 50 or 0%; Either Recognition Memory of Short Recognition Memory Test for faces (Warrington, 1996); Scanning in fMRI | As the intensity of emotional expression ↑ so did activation of the cerebellum, fusiform gyri, middle and temporal gyri. |
| Lennox et al. (2004) ²⁸ | 10 manic BD I; 12 HC | Functional MRI and a explicit facial affect recognition task | BD: attenuated subjective rating of the intensity of sad facial expressions, and associated attenuation of activation in subgenual ACC and bilateral amygdale, with ↑ activation in posterior cingulate and posterior insula. No neurocognitive abnormalities in response to happy facial expressions. |
| Malhi et al. (2004) ³⁰ | 10 right handed female BD I; 10 female HC | fMRI scanning while viewing emotional faces | BD: needed more time to respond to fear and disgust. Euthymic BD: facial expressions to fear produced ↑ neural activation in hippocampus, inferior parietal, superior temporal cortices and cerebellum. HC: disgust faces produced ↑ neural activation in frontal cortex, right insula and visual processing regions. |
| Venn et al. (2004) ²⁴ | 17 euthymic BD; 17 HC | Interactive computer test, accuracy of emotion recognition and sensitivity to 6 different facial expressions | BD and controls: no difference for any of the facial expressions. Initial analysis: impairment in recognition of fear. |
| Bora et al. (2005) ²⁵ | 43 euthymic BD; 30 HC | Eyes and Hinting Task Emotion Recognition; Face Recognition | The patient group was impaired on both tasks, including euthymic patients. |
| Bozicas et al. (2006) ²⁶ | 19 BD I (remitted); 30 HC | Kinney's Identity Matching Test (KIMT); Kinney's Affect Matching Test (KAMT) | BD: worse than HC on the KAMT, but not on the KIMT. |
| Chen et al. (2006) ³² | 8 depressed BD; 8 manic BD; 8 HC | Explicit facial affect recognition task; Implicit facial affect recognition task | Depressed and manic BD: overactivate brain regions in response to facial expressions of happiness and sadness, and they ↑ neural response to fear faces. Manic BD: response to sad faces was modulated by attentional level of processing. Implicit recognition was associated with overactivation and explicit recognition was associated with underactivation of limbic and frontal regions. All 3 groups: implicit recognition engendered stronger activation by all emotional types. |
| Rich et al. (2006) ⁴⁰ | 22 BD youths; 21 HC | Emotional and non emotional tasks during fMRI | BD perceived greater hostility in neutral faces and reported more fear when viewing them. BD: greater activation in the left amygdale, accumbens, putamen, and ventral PFC when rating face hostility, and greater activation in the left amygdale and bilateral accumbens when rating their fear of face. |
| Brotman et al. (2007) ³⁷ | 20 pediatric BD with lifetime anxiety; 11 pediatric BD without lifetime anxiety; 14 HC | Visual probe paradigm | Pediatric BD with lifetime anxiety: bias toward threatening faces. |
| Dickstein et al. (2007) ⁴¹ | 23 pediatric BD; 22 HC | fMRI scanning while viewing emotional faces | BD: ↓ memory for emotional faces and ↑ neural activation in the striatum and ACC for happy faces and orbitofrontal for angry faces. |
| Pavuluri et al. (2007) ⁴³ | 10 euthymic, unmedicated pediatric BD; 10 HC | Affective face processing task | BD: ↓ activation in right ventrolateral PFC and ↑ activity in right pregenual ACC, amygdale and paralimbic cortex in response to both angry and happy faces. |
| Malhi et al. (2007) ³¹ | 10 female euthymic BD; 10 HC | fMRI; Explicit facial emotion recognition task | BD: they were equally accurate in identifying facial expressions as HC, but they were slower to respond to fear and disgust. Within-group analyses: responses to fear and disgust resulted in activation of anticipated brain regions such as amygdala and insula, respectively. Between-group random effects analysis: revealed differential responses to both disgust and fear in both HC and BD, but patients responded largely to fear and HC responded more to disgust (differential activation involving the hippocampus and amygdala). |
| Schenkel et al. (2007) ⁴⁴ | 29 PBD unmedicated /acutely; 29 PBD medicated/clinical stabilized; 28 HC | Tasks of facial affect identification and differentiation | PBD showed marked impairments in the ability to correctly identify emotionally intense happy and sad facial expressions. Unmedicated PBD performed more poorly than HC. PBD with ADHD performed more poorly than PBD without ADHD. |

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Table 1 - Results from the studies included in this review

| Authors and year | Subjects | Neuropsychological tests | Results |
|-------------------------------------|--|--|--|
| Vaskinn et al. (2007) ¹⁸ | 31 SCH; 21 BDI; 31 HC | Visual facial pictures; Auditory sentences emotional stimuli | Visual emotion perception was unimpaired in both clinical groups. Only SCH showed reduced auditory emotion perception. Differences in gender was observed in SCH and HC, because males performed worse than females. |
| Brotman et al. (2008) ⁴⁶ | 52 BD patients; 24 at risk youths; 78 HC | Facial expressions subtests of the Diagnostic Analysis of Nonverbal Accuracy Scale | BD patients and children at risk made more errors than control subjects when identifying emotion on child and adult faces. |
| Foland et al. (2008) ²⁹ | 9 BD I in mania; 9 HC | fMRI; Emotional labelling task; Emotional perception task | Compared with healthy controls, manic BD patients had a significantly reduced VLPFC regulation of amygdale response during the emotion labelling task. |
| Rich et al. (2008) ⁴⁵ | 39 NP-PBD; 31 SMD; 36 HC | Emotional expression multimorph task | NP-PBD and SMD required significantly more morphs than HC to label correctly faces. They require more intense facial emotion to do the recognizing. |

ACC = anterior cingulate cortex; ADHD = attentional deficit hyperactivity disorder; BD = Bipolar disorder; fMRI = functional MR; HC = healthy controls; LHB = left hemi-face bias; MDD = Major depressive disorder; NP-PBD = narrow phenotype pediatric bipolar; PFC = prefrontal cortex; RHB = right hemi-face bias; SCH = Schizophrenia; SMD = severe mood dysregulation; STP = schizotypal personality disorder; VLPFC = ventrolateral prefrontal cortex
 †: increased or greater
 ‡: reduced;

Control subjects and depressed BD patients judged chimeric faces correctly. Schizophrenic patients with negative symptoms judged positive faces as negative and vice versa, while schizophrenics with positive symptoms and manic BD judged all faces as positive. For composite faces all groups judged appropriately. Considering that 90% of control subjects displayed left hemi-face bias (LHB), emotional stimuli are likely to be processed by the right hemisphere. All patients showed only a weak LHB. In fact, negative schizophrenics showed a right hemi-face bias (RHB) instead. Since deficits were only found for chimeric face interpretation, the author suggests that hemispheric disruptions may only be seen using complex stimuli.

Loughland et al. conducted a visual scan-path study on facial emotion perception in 63 schizophrenics, 27 MDD, 17 BD and 61 control subjects.¹⁷ Subjects were tested on Face and Facial Affect Recognition Tasks. For the Facial Affect Task, which consisted of stimuli from the *Ekman and Friesen Series of Facial Affect*, subjects were asked to match the stimulus face to one of either 3 (happy, sad or neutral) or 7 (happy, sad, angry, fearful, disgusted, surprised or neutral) emotions. For the Face Task, they had to match the stimulus face to one of 3 or 7 possible answer faces. Each task consisted of identifiable (non-degraded) and non-identifiable (degraded) faces. For facial recognition, groups differed only in their performance on the 7-choice designs.

Affective and schizophrenic patients were both less accurate at matching non-degraded faces than control subjects. For facial affect recognition groups differed only for the recognition of happiness in a 7-choice design. Schizophrenic patients were less accurate at labeling happy faces than both affective patients and controls. Visual scan-path data showed that for degraded faces schizophrenic patients suffered from restricted scanning strategies, while BD patients tended to avoid specific facial features (eyes, nose, and mouth) and made a significantly reduced number of fixations.

Schizophrenic patients may suffer from fundamental deficits in visuo-cognitive strategies of face perception, which is likely to be trait-based, whereas, the avoidance of salient facial features found in BD patients may be due to dysthymic mood states at time of testing, reflecting state-based attentional disturbances in the perception of socially relevant stimuli.

In a recent research, Vaskinn et al. verified that schizophrenic and BD patients had no difficulty to recognize emotions in facial pictures in comparison with healthy controls, however, only schizophrenic patients presented reduced auditory emotion perception. Comparing by gender, only healthy and schizophrenic males performed worse than their female counterparts.¹⁸

Taken together, these studies suggested that BD patients may suffer from specific deficits in facial emotion recognition, but schizophrenic patients were less accurate in recognition emotions in faces than BD or MDD.

2. BD vs major depressive disorder

It has been hypothesized that deficits related to the right hemisphere were responsible for the difficulties in the recognition of emotions in patients with MDD.¹⁹

In 1992, Rubinow and Post applied a photograph-matching and a sentence-matching test to 7 patients with BD type I, 5 with BD type II, 5 with MDD and 31 control subjects.¹⁹ All patients were medication-free. Subjects had to match each of 48 photographs to 1 of 7 depicting different emotions (happiness, sadness, fear, anger, surprise, disgust and interest). Similarly, they had to match one of seven affect words to each of 48 sentences. Due to the small

sample numbers, all affect patient data were grouped. Patients were impaired in photograph-matching but not in sentence-matching. Specifically, they made significantly more mistakes for sad faces, and tended to make more mistakes for happy faces in comparison to control subjects.

The deficits of facial emotion labeling in depressed patients were comparable to those found in right-hemisphere lesion patients. Thus, the deficit in facial emotion processing is likely to occur due to dysfunction in the right-hemisphere.

Kucharska-Pietura and David examined whether MDD would be related to a reduction in right-hemispheric arousal and mania to its increase, using a chimeric face test.²⁰ Thirty BD patients, recovering from manic episodes, were compared to 30 MDD, 30 patients with right-hemisphere brain damage, 30 with left-hemisphere brain damage and 30 control subjects. BD patients were maintained on one or more mood stabilizers and additional benzodiazepines, and MDD patients were receiving antidepressants. The chimeric face test consisted of 12 hemi-faces with sad and happy expressions that were each mirror-imaged. On the face task, right-hemisphere damage and depressed patients were impaired in the recognition of happy faces and showed a significant reduction in left-hemisphere bias (LHB). Left-hemisphere damaged patients and manic BD patients showed normal LHB and performed as controls in the recognition of facial expressions. These results suggest that MDD patients are impaired in the ability to direct spatial attention, which is thought to be a right-hemisphere function. However, antidepressant medication may reduce right hemisphere activation while mood stabilizers may not.

3. Facial emotion perception in adults with bipolar disorder

Lembke and Ketter found that manic BD patients had worse overall performance, and especially suffered from deficits in the recognition of fear and disgust.²¹ They tended to label fear faces as surprise; and disgust as anger. In comparison to control subjects, euthymic BD II patients were significantly better at recognizing fear, while BD I patients were numerically better at recognizing fear. The perception of fear is specifically altered in BD considering the increased recognition in euthymic patients and the deficient recognition in mania. The finding that manic patients mistook fear for surprise could explain their aggressive approach behaviour.

Harmer et al. noted that euthymic BD patients showed a slight but significant impairment in the recognition of famous faces and a facilitated recognition of disgust, being more accurate in their recognition than control subjects.²²

Getz et al. compared 25 medicated manic BD patients to 25 control subjects on the Benton Face Recognition Test, and novel computerized tests of face and facial affect recognition.²³ Patients made significantly more errors on the facial affect recognition task than controls. There were no significant performance differences between patients who were on or off mood stabilizers, antipsychotics, antidepressants and benzodiazepines, but the sample size was small. Furthermore, no group differences appeared for either of the face tasks, though BD patients had slower reaction times. These results suggest that BD patients suffer from specific deficits of facial emotion perception.

In 2004, Venn et al. compared 17 euthymic medicated BD patients to 17 control subjects on the Benton Face Recognition Test and a facial emotion recognition task.²⁴ No group differences were found in scores of face recognition. For facial emotion recognition, BD patients were less accurate in recognizing fear. No evidence for trait-like deficits of facial emotion recognition in BD was determined.

Bora et al. examined 43 euthymic medicated BD patients and 30 control subjects through the Eyes Test, the Hinting Test, basic face and emotion recognition tests and tests of sustained attention.²⁵ This study intended to determine whether BD patients suffer from theory of mind (ToM) deficits. Impaired performance of BD patients on both ToM tests (Eyes and Hinting), which were likely due to impairments on tests of emotion recognition and sustained attention, were demonstrated.

Bozikas et al. verified that patients with medicated BD in remission performed worse than controls in a test where they needed to identify emotion in human faces.²⁶ They demonstrated that the impairment was not attributed to problems with facial perception per se, but to perception of the relative valence of facial expressions indicating emotions. The performance of patients was not correlated with age of onset and duration of illness, or with residual manic or depressive symptoms.

1) Imaging studies of facial affect recognition in adults with bipolar disorder

In 2000, Yurgelun-Todd et al. conducted the first imaging study on facial affect perception in BD.²⁷ They hypothesized that if BD patients have functional deficits of the dorsolateral prefrontal cortex, they would show altered responses to facial stimuli. The prefrontal cortex is essential for assimilating and integrating information, and planning, inhibiting or initiating emotional responses. The authors chose to evaluate only happy and fearful affect as fearful affect was shown to elicit the largest orienting response in previous studies. Fourteen stable BD and 10 control subjects were scanned while passively viewing faces. Only 10 of the 14 BD patients were able to accurately identify fear. fMRI data for BD patients, in response to fear, showed a decrease in neural activation of the right prefrontal area and an increase in activation of the left amygdala in comparison to control subjects, suggesting alterations in the fronto-limbic circuitry. Nevertheless, cognitive as well as affective abilities were necessary to complete the task (concentration, attention, affect recall and affective labelling) making it difficult to draw specific conclusions from this study.

In accordance to findings in adults showing abnormalities in both memory and face-emotion processing, Lawrence et al. compared neural activation to emotional faces in 12 BD type I (3 euthymic, 7 had mild depression and 2 moderate to severe depression), 9 MDD and 11 control subjects.³ Although there were no behavioural differences in performance, functional abnormalities in sub-cortical, ventral and dorsal prefrontal regions in both patient groups were detected. In response to fear, BD patients showed an increased neural response in the right globus pallidus, the anterior thalamus, the left amygdala and the ventrolateral prefrontal cortex. Control subjects showed increased response in the right amygdala and hippocampus, and right dorsolateral prefrontal cortex. In response to happy faces, BD patients showed increased responses in a large cluster extending from the left uncus, ventrally to the amygdala and caudate nucleus, and in the ventromedial prefrontal cortex and right ventrolateral prefrontal cortex. Control subjects showed an increased response in the right parahippocampal gyrus and thalamus, the midbrain, caudate nucleus and left amygdala, while MDD patients showed decreased responses in these areas. In response to sad faces, BD patients showed increased activity of the left hippocampus and the ventral prefrontal cortex, while controls showed increased responses in the orbitofrontal and dorsolateral prefrontal cortices. Severity of depression was not correlated to the magnitude of neural response in BD patients, suggesting that differential activity is not likely to be symptom related. Instead it

would reflect trait-like differences between BD, MDD and healthy controls in response to facial expressions.

Lennox et al. were the first group to scan patients in mania while viewing happy and sad faces from the Face and Emotion Expression: Series and Tests (FEEST).²⁸ Ten manic BD patients and 12 control subjects performed the Benton Facial Memory Test. An attenuated subjective rating for sad faces in BD patients, which was linked to decreased activation of the subgenual anterior cingulate and amygdala, and an increased activation of the posterior cingulate and posterior insula were found. Neural response to happy faces was comparable for BD patients and controls. Results may reflect a positive bias for facial emotion perception in mania.

Corroborating this previous finding, Foland et al. showed that manic patients had a reduced ventrolateral prefrontal cortex (VLPFC) regulation of amygdala response during the emotion labelling task.²⁹ The authors discussed that the reductions in inhibitory frontal activity in mania may lead to an increased reactivity of amygdala.

Finally, Malhi et al. scanned 10 hypomanic BD patients and 10 controls while viewing captioned pictures from the *Teasedale Video-playback series*.³⁰ In these experiments negative or positive affect was evoked by the caption rather than the picture. Subjective ratings of affect were similar for controls and patients, but fMRI data showed significant differences in areas of activation. In response to negative affect patients showed much less cortical activation than controls, while presenting activation in similar areas for positive affect. These results offer supporting evidence for a positive bias in mania.

Malhi et al. showed that 10 female BD patients in remission were as equally accurate in identifying facial expression as 10 female healthy controls but were slower to respond to fear and disgust, which resulted in activation by amygdala and insula.³¹ However, facial expressions to fear produced greater activation in euthymic BD patients in hippocampal structures, the inferior parietal and superior temporal cortices and the cerebellum, and disgust faces produced greater activation in healthy subjects with significant differences in frontal cortex, right insula and visual processing regions. It is possible that in BD prefrontal subcortical network dysfunction that relegates neural processing to limbic regions is impaired.

Chen et al. verified that depressed and manic patients exhibited abnormal neural responses to sad, fearful, and happy facial expressions. They exhibited overactivated responses to fearful faces, as well as to mood incongruent facial expressions, with the depressed group exhibiting overactivity in the fusiform gyrus in response to sad faces.³² Manic patients also showed an altered response to sad faces, their corticolimbic regions were overactivated for implicit processing and underactivated for explicit processing.³² The activation pattern observed in this study for depressed patients was similar to the one found in previous fMRI studies which demonstrated, that depressed and euthymic BD patients overactivated specific brain regions in response to positive affective stimuli.^{3,30}

4. Clinical and imaging studies in children with BD

The study of pediatric BD is a field of investigation that only recently became the focus of BD researchers. The clinical presentation of pediatric BD includes symptoms that can be confounded by those of other childhood disorders, mainly Attention Deficit/Hyperactivity Disorder (ADHD) and Conduct disorder. These symptoms' overlap imposes important complications regarding clinical and psychological evaluations. Pediatric BD carries high morbidity and psychosocial dysfunction because of its chronic

and frequently rapid-cycling symptoms and relative treatment resistance.³³ Thus, efforts have been directed towards understanding the cognitive and emotional characteristics of these children. BD children present deficits in executive functions, including attention, working memory and organization/problem solving skills, similar to adults.^{34,35} The emotional recognition is another area of interest to be studied in this population.

McClure et al. examined 11 BD children (mean age 13.7 years), 10 anxiety disorder children (mean age 12.9y) and 25 control subjects (mean age 13.5y) on tests of facial memory and emotion identification.³⁶ Lifetime rates of ADHD were higher in the BD group (82%) than in the anxiety (10%) or comparison (0%) groups. Lifetime oppositional defiant disorder was present in 36% of the BD group and 50% of the anxious group and in none of the comparison subjects. Of the anxious group, 40% had comorbid MDD. All anxious and comparison subjects were medication-free; all BD subjects were receiving medication. The emotion identification task consisted of 24 photographs of adults and 24 photographs of children in both high and low intensities of happiness, sadness, anger and fear. BD patients made more errors in the identification of low-intensity faces than control and anxiety disorder subjects. They also made more errors in the recognition of child faces, over-identifying faces as angry. Furthermore, Brotman et al. showed that pediatric BD with anxiety demonstrated a bias toward recognizing threatening faces in relation to pediatric BD without anxiety.³⁷

Voelbel et al. described that BD children had difficulties to identify emotion in faces, but they did not specify which emotion was more inaccurately identified.³⁸

In 2004, Chang et al. assessed functional magnetic resonance imaging using cognitive and affective tasks, but the affective task was not affective emotion in faces, otherwise it was composed of pictures which were negatively or positively valenced.³⁹ They evaluated 12 euthymic male subjects who had at least one parent with BD, children taking stimulants were asked to discontinue these medications for at least 24 hours before testing but other types of medications were not asked to be discontinued. Subjects with BD presented abnormalities in the regulation of prefrontal – subcortical circuits, as they had greater activation in the bilateral dorsolateral prefrontal cortex, inferior frontal gyrus, and right insula when they were viewing negatively valenced pictures, but the control group presented greater activation only in the right posterior cingulate gyrus. For positively valenced pictures, BD patients had greater activation in the bilateral caudate and thalamus, left middle/superior frontal gyrus, and left anterior cingulate cortex, whereas controls had no areas of greater activation.

Rich et al. studied amygdala dysfunction examining neural mechanisms mediating face processing.⁴⁰ Compared with healthy controls (n = 21), BD adolescents (n = 22) perceived greater hostility in neutral faces and reported more fear. Furthermore, BD patients had greater activation in the left amygdala, accumbens, putamen and ventral prefrontal cortex when rating face hostility and greater activation in the left amygdala and bilateral accumbens when rating their fear of the face. There were no between-group differences in the non emotional conditions. These results were consistent with prior studies in adult BD patients.²⁷

Dickstein et al. showed that pediatric BD subjects have reduced memory for emotional faces, particularly on fearful faces.⁴¹ Besides, fMRI analyses showed that these patients, compared to a control group, had increased activation in the striatum and anterior cingulate cortex when successfully encoding happy faces and in the orbitofrontal cortex when successfully encoding angry faces.

There were no between-group differences in neural activation during fearful face encoding. A study conducted by Nelson et al. showed that healthy adolescents displayed more activity in the subgenual anterior cingulate when viewing subsequently remembered happy faces and more activity in the right posterior hippocampus when viewing subsequently remembered neutral faces.⁴²

Pavuluri et al. also demonstrated that medication-free BD adolescents had disturbance in prefrontal cortex affect modulation systems and atypical responses in posterior perceptual processing systems.⁴³ BD type I patients, who were euthymic for a minimum of 4 months, presented reduced activation of right rostral ventrolateral prefrontal cortex together with increased activity in right pregenual anterior cingulate, amygdala, and paralimbic cortex in response to both angry and happy faces in relation to neutral faces. They also showed reduced activation of visual areas in occipital cortex together with greater activation in higher-order visual perceptual areas, including superior temporal sulcus and fusiform gyrus with angry faces and posterior parietal cortex with happy faces. According to the authors, disturbances in affect processing circuitry could contribute to emotional dysregulation and social cognitive difficulties in BD youth.

Schenkel et al. showed that deficits in emotion processing could be considered state of illness and trait-related of illness, because both children with PBD medicated and clinically stabilized, and unmedicated patients in acute phase had impairment in the ability to correctly identify emotionally intense happy and sad facial expressions, tending to misjudge extreme facial expressions as being moderate to mild in intensity.⁴⁴ However, only unmedicated group performed more poorly than healthy subjects to differentiate subtle variations of happy or sad expressions.

Rich et al. evaluated children with narrow phenotype BD (i.e., history of at least one hypomanic or manic episode with euphoric mood) and children with severe mood dysregulation (i.e., chronic irritability and hyperarousal without episodes of mania) in a task of emotional recognition which presented gradients from 100% neutrality to 100% emotional expression.⁴⁵ They found that both patient groups needed significantly more clear expressions of emotion than controls to label faces correctly.

Finally, Brotman et al. confirmed their hypothesis that children with family history of BD would have facial emotion processing deficits similar to those seen in pediatric BD.⁴⁶ Compared with the control group, both the BD and at-risk groups made more errors in identifying emotions in child and adult faces. It means that deficits in facial emotional labeling may be a risk marker for developing bipolar disorder in the future. The authors propose that these deficits may be considered as an endophenotype of the disease since they are also presented in the unaffected relatives of BD patients.

Discussion

BD patients, even during remission, have psychosocial problems caused not only by residual symptoms, but also by cognitive deficits and difficulties to recognize emotions in human faces.

The literature presents a variation of results concerning facial emotion perception in BD. The comparison between schizophrenic and mood disorder patients demonstrated that schizophrenic patients were less accurate in recognition emotions than BD or MDD.

MDD patients seem to present deficits of facial emotion labelling comparable to those found in right-hemisphere lesion patients.^{19,20} However, the theory about right hemisphere impairment does not explain all cognitive deficits found in BD.⁴⁷

Right hemisphere is dominant in the perception of affect. This was demonstrated using the chimeric face task, in which subjects

were asked to determine which was the happier of two composite facial photographs, and it reliably elicited a RH advantage. David and Cutting¹³ and Kucharska-Pietura and David²⁰ found that manic patients showed greater LH bias than healthy controls; depressives (predominantly unipolar) showed reduced LH bias compared to healthy controls; schizophrenia showed no bias to either side. They interpret this finding as suggestive of RH hyperfunction in mania and RH hypofunction in depression and schizophrenia. This result showed that the notion of a stable RH dysfunction or 'lesion' in BD is inconsistent and can be dependent of mood states.⁴⁷

Two studies showed that BD patients did not have problems to recognize faces, but they were impaired on a task of facial affect labelling, specifically, they were less accurate in recognizing fear, even in euthymia.^{23,24} In mania, they have an impaired capacity to recognize fear and disgust,²¹ and when euthymic, they recognized disgust better than when manic.²²

BD children presented a trend to misjudge extreme facial expressions as being moderated or mild in intensity. It is important to consider that these deficits are associated with psychosocial impairments and subsequently they should be evaluated in interventional studies.^{40,44}

Follow-up studies re-testing the patients after recovery or testing manic and depressive patients during euthymia are needed. These studies can better investigate if these abnormalities in emotion recognition reflect a state or trait marker of mood disorder.

Another interesting point is to consider that research groups have used a number of different designs and tasks to evaluate cognitive and emotional performance in BD patients. Standardizing test designs is essential for making results comparisons possible. Furthermore, performing accurately on tests of facial affect requires a compilation of attentional, executive and emotional abilities, making it difficult to determine whether the key deficit is in fact the processing of facial expressions.²⁷ Besides, some studies evaluated small samples (less than 10 subjects in one of the samples), which impairs the generalization of the conclusions.^{19,21,29,32}

Imaging studies were difficult to compare due to different patient group selection and designs applied. The involvement of the ventrolateral prefrontal cortex and amygdala in the pathophysiology of BD was strengthened in many studies: three of them found an increased left amygdala response to fear,^{27,31} even in children;³⁸ and three studies showed that depressed and euthymic BD patients presented overactivation in amygdala in response to positive affective stimuli.^{3,30,39} However, Foland et al. showed that patients in mania presented reduced VLPFC regulation of amygdala response during the emotion labelling task, what could explain the reductions in the inhibitory frontal activity with impact in behaviour and social life.²⁹

A potential limitation in the literature is the impact of psychotropic medications on cognition, specifically on the perception of emotion. Venn et al. showed that among healthy subjects, administration of benzodiazepine impairs cognition of anger, administration of propranolol leads to increase in reaction time to recognize sadness, and administration of citalopram and reboxetine reduces perception of negative expressions.²⁴ It is plausible that other pharmacological agents could have an effect on the neurocircuits underlying some of the different facial affects and this has to be verified in future studies in BD patients.

Conclusion

Despite the methodological deficits found in the literature, the findings allow important conclusions. The deficits found

in BD patients can be differentiated from those found in other psychiatric disorders, such as schizophrenia and MDD. Facial emotion deficits were less severe in BD than in schizophrenia. Furthermore, affective and cognitive deficits vary according to the mood states. Several studies relate a possible positive bias in mania to enhanced recognition of specific emotions, such as fear and disgust.

Future studies should aim at standardizing task designs and differentiating deficits in different mood-associated stages of the

disorder. A suggestion would be to examine patients first in euthymia and prospectively when in full episode of depression and/or mania. Another suggestion would be the follow-up of at-risk individuals, such as offspring of BD patients, which may help to define an endophenotype for this disorder.

Acknowledgements

This study was supported in part by a generous donation from the Thompson Motta family.

Disclosures

| Writing group member | Employment | Research grant ¹ | Other research grant or medical continuous education ² | Speaker's honoraria | Ownership interest | Consultant/ Advisory board | Other ³ |
|-------------------------------------|----------------------|-----------------------------------|---|---------------------|--------------------|----------------------------|---|
| Cristiana Castanho de Almeida Rocca | HC-FMUSP | - | - | - | - | - | - |
| Eveline van den Heuvel | Universiteit Utrecht | - | - | - | - | - | - |
| Sheila C. Caetano | USP** | FAPESP*** CNPq*** NARSAD*** | APA/AstraZeneca Young Minds in Psychiatry International Awards*** | - | - | - | CNPq and FAPESP post-doctoral Scholarship |
| Beny Lafer | USP** | FAPESP*** CNPq*** | APA/AstraZeneca Young Minds in Psychiatry International Awards*** | Astra-Zeneca* | - | - | - |

* Modest

** Significant

*** Significant. Amounts given to the author's institution or to a colleague for research in which the author has participation, not directly to the author.

Note: HC-FMUSP = Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo; USP = Universidade de São Paulo; FAPESP = Fundação de Amparo à Pesquisa do Estado de São Paulo; CNPq = Conselho Nacional de Desenvolvimento Científico e Tecnológico; NARSAD = National Alliance for Research on Schizophrenia and Depression.

For more information, see Instructions for authors.

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