**Universidade Federal do Rio de Janeiro**

# ALTERAÇÕES DA ATENÇÃO NO TRANSTORNO BIPOLAR

**Evelyn Vieira Miranda Camelo**

**Rio de Janeiro**

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# Alterações da atenção no transtorno bipolar

Evelyn Vieira Miranda Camelo

Dissertação de Mestrado apresentada aoPrograma de Pós-Graduação emPsiquiatria e Saúde Mental (PROPSAM)do Instituto de Psiquiatria da Universidade Federal do Rio de Janeiro (IPUB/UFRJ),como parte dos requisitos necessários à obtenção do Título de Mestre em Psiquiatria.

Orientador: Prof. Dr. Elie Cheniaux

Co-orientadora: Profa. Dra.Tânia Netto

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# RESUMO


ALTERAÇÕES DA ATENÇÃO NO TRANSTORNO BIPOLAR

Evelyn Vieira Miranda Camelo

Orientador: Elie Cheniaux

Resumo da Dissertação de Mestrado submetida ao Programa de Pós-graduação em Psiquiatria e Saúde Mental, Instituto de Psiquiatria, da Universidade Federal do Rio de Janeiro - UFRJ, como parte dos requisitos necessários à obtenção do título de Mestre em Saúde Mental**.**

Atualmente, diversas pesquisas vêm demonstrando que o transtorno bipolar (TB) cursa com prejuízos cognitivos em todas as fases da doença, até mesmo na eutimia. Essas alterações ocorrem nas áreas da atenção, fluência verbal, funções executivas, e se correlacionam com um maior prejuízo no insight. Acredita-se que grande partedos prejuízos cognitivos no TB sejam, pelo menos em parte, secundários às alterações da atenção. O objetivo do presente estudo é aprofundar o conhecimento sobre a atenção no TB, tema ainda pouco explorado na literatura científica. Realizamos uma revisão sistemática e três estudos clínicos sobre a atenção no TB. Os estudos clínicos foram realizados com pacientes com o diagnóstico de TB, acompanhados no ambulatório de pesquisa do Instituto de Psiquiatria da Universidade Federal do Rio de Janeiro. Foram utilizadas instrumentos de avaliação de sintomas maníacos e depressivos, da gravidade global do TB, de sintomas psicóticos ou positivos, do insight e de incapacitação, além de testes de atenção. Os nossos resultados indicam que: os pacientes com TB apresentam um desempenho nos testes de atenção inferior ao de controles normais; nas fases de mania a atenção está mais comprometida do que nas fases de eutimia e de depressão; sintomas maníacos graves e déficits na atenção são preditores de níveis mais baixos de insight; eumbaixo nível de insight está relacionado a uma maior grau de incapacitação na vida familiar e social.



Palavras-chave: bipolar; atenção; cognição.

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# ABSTRACT


ATTENTION IMPAIRMENT IN BIPOLAR DISORDER

Evelyn Vieira Miranda Camelo

Orientador: Elie Cheniaux

*Abstract* da Dissertação de Mestrado submetida ao Programa de Pós-graduação em Psiquiatria e Saúde Mental, Instituto de Psiquiatria, da Universidade Federal do Rio de Janeiro - UFRJ, como parte dos requisitos necessários à obtenção do título de Mestre em Saúde Mental**.**

Currently, several studies have shown that bipolar disorder (BD) courses with cognitive impairments in all stages of the disease, even in euthymia. These changes occur in the areas of attention, verbal fluency, executive functions, and correlate with a greater loss in insight. It is believed that the cognitive impairments in BD is secondary to changes in attention. The aim of this study is to deepen the knowledge of the attention on BD, subject still little explored in the scientific literature. We conducted a systematic review and three clinical studies of attention on BD. Clinical studies were conducted with patients diagnosed with BD, followed at research clinic of Psychiatry Institute of the Federal University of Rio de Janeiro. Clinical evaluations were used in manic and depressive symptoms, we measure the clinical global impressions of BD, positive or psychotic symptoms, insight and disability, as well as tests of attention. Our results indicate that BD patients exhibit a performance in tests of attention lower than the normal controls; the manic phases attention is more impaired than in the phases of euthymia and depression; severe manic symptoms and deficits in attention are predictors of lower levels of insight; and a low level of insight is related to a higher degree of disability in family and social life.



Keywords: bipolar; attention;cognition.


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**LISTA DE SIGLAS**

CGI-BP do inglês, Clinical Global Impressions Scale for use in bipolar illness

DSM do inglês, Diagnostic and Statistical Manual

GAF do inglês, Global Assessment of Functioning

HAM-D do inglês, Hamilton Depression Scale

ISAD do inglês, Insight Scale for Affective Disorders

PANSS-p do inglês, Positive and Negative Syndrome Scale

YMRS do inglês, Young Mania Rating Scale

TMT do inglês, Trail Making Test

CPTdo inglês, Continuous Performance Test

CPTII do inglês, Continuous Performance Test II, version 5

PCTPdo inglês, Penn Continuous Performance Test

CPT-IP do inglês, Continuous Performance Test, identical pairs version

DS-CPT do inglês, Degraded Stimulus Continuous Performance Test

CPT-AX do inglês, Continuous Performance Test-AX

RVIPdo inglês, Rapid Visual Information Processing

SCWTdo inglês, Stroop Color Word Test

CT do inglês, Cancellation Test

SAT do inglês, Shifting Attention Test

CB do inglês, conditioned blocking

CVLT-II do inglês, California Verbal Learning Test

TAP do inglês, Attentional Performance Test

TL do inglês, Tower of London

COWA do inglês, Controlled Oral Word Association Test

PGIMS do inglês, PGI memory scale

PASAT do inglês, Paced Auditory Serial Addition.

# SUMÁRIO

# 1. INTRODUÇÃO



Déficits cognitivos foram estudados, primeiramente, em pacientes com lesões cerebrais e demência, e depois em pacientes esquizofrênicos. No entanto, desde 1970, muitos autores têm dado atenção aos estudos que avaliam a cognição nos pacientes com transtorno bipolar (TB) (Caligiuri, & Ellwanger, 2000). Um número expressivo de pesquisadores vem se dedicando a identificar as alterações neuropsicológicas nos episódios da doença. Nesse sentido, algumas pesquisas procuraram investigar o desempenho de pacientes em mania, depressão e eutimia, verificando diferenças importantes no funcionamento cognitivo dependendo do estado de humor (Rocca et al., 2006).

De acordo com a revisão de literatura, é possível inferir que os pacientes bipolares apresentamprejuízos cognitivos estáveis e persistentes em todas as fases do TB, incluindo eutimia, nomeadamente nos seguintes domínios: a atenção, aprendizagem, memória, habilidade visuo-espacial e função executiva (Caligiuri, & Ellwanger, 2000; Latalova, Jan, Tomas, Dana, e Hana, 2011).

A atenção é uma função complexa, alguns estudiosos acreditam que, existam três redes de atenção diferenciadas: (1) uma rede atencional posterior, (2) uma rede atencional anterior e (3) uma rede de alerta. A rede posterior envolve o córtex parietal, o pulvinar e o colículo superior, áreas cerebrais que cooperam entre si para o desempenho de operações necessárias à orientação ou desvio da atenção para uma localização espacial determinada. O córtex parietal teria aqui a função específica de “desligar” o foco atencional do estímulo-alvo presente, e o colículo superior se encarregaria de deslocar esse foco para um estímulo esperado (amplificando o alvo indicado pela pista) e o pulvinar se envolveria no “ligar” do foco atencional ao novo estímulo-alvo atendido (Posner e Petersen, 1990) .

A atenção é um processo que necessita de divisão em múltiplas operações. Ela é parte fundamental da atividade sensorial (Caldas, 2000; Mesulam, 1998), é imprescindível à linguagem (Fischler, 1998), à aprendizagem (Trabasso e Bower, 1975) e à memória (Awh, Anllo-Vento e Hillyard, 2000; Cermak e Wong, 1999; Corbetta, Kincade e Shulman, 2002; Norman, 1968) e ainda participa como um distribuidor da atividade sensorial pelos vários níveis de consciência que em paralelo processam a informação (Fernandez-Duque, Baird e Posner, 2000; Posner, 1994; Posner e Rothbart, 1998). Sendo assim, as alterações de atenção são muito relevantes, pois podem afetar outras funções cognitivas, como memória, aprendizado e função executiva (Goodwin, Jaminson , & Ghaemi , 2007).

O comprometimento cognitivo é uma das características dos perfis neuropsicológicos de pacientes bipolares, os déficits cognitivos podem preceder a doença. No entanto, de acordo com alguns autores, tais déficits pioram ao longo do tempo e estão associados com um maior número de episódios afetivos (Vieta et al., 2012).

Mais de 100 estudos compararam pacientes bipolares com controles normais ou em indivíduos com outros transtornos mentais relacionados com o desempenho em testes de atenção (Camelo, et al., 2013). A atenção é geralmente menos prejudicada no TB do que na esquizofrenia, mas mais afetada na depressão unipolar do que em controles normais (Camelo, et al., 2013). No entanto, esses estudos geralmente não discriminam a fase (mania, depressão e eutimia) que o paciente se apresenta no momento da avaliação (Bonnín et al., 2012; Burdick et al., 2009; Clark et al., 2004; Maalouf et al., 2010).

Outro problema recorrente no TB, é a diminuição da capacidade de insight, ou seja, a dificuldade de ter consciência sobre a própria doença.O insight tradicionalmente era definido como uma “correta atitude para mudanças mórbidas em si mesmo”. Uma maior ou menor consciência quanto a estar doente ou apresentar sintomas ou até mesmo algum dano psicossocial pode influenciar significativamente a evolução da própria doença (Cely et al., 2001;Yen et al., 2005).

A falta de insight afeta diretamente a adesão ao tratamento e a vida do paciente com TB (Grinberg LP, et al. 2009). Vários estudos que investigam a relação entre insight e alterações cognitivas foram realizados em pacientes neurológicos primeiramente e mais tarde em pacientes esquizofrênicos. Nos estudos com pacientes neurológicos, incluindo indivíduos com demência, observou-se que o prejuízo cognitivo está associado com pobre insight (Amanzio et al. , 2013, Morris & Mograbi , 2013). Em relação a pacientes esquizofrênicos, não está claro se a sua falta de insight é mais fortemente associado com a gravidade dos sintomas ou déficits neuropsicológicos ( Zhou et al. , 2015) . Mais recentemente, o insight tem sido estudado nos pacientes com TB, tendo sido observda uma correlação entre os níveis mais baixos de insight e maior comprometimento da atenção, função executiva, fluência verbal ( Dias et al., 2008 ).

A justificativa para o nosso estudo é baseada na escassez de pesquisas sobre a atenção no TB comparando as diferentes fases da doença. Outro aspecto importante, diz respeito às alterações cognitivas encontradas nos bipolares, que são decorrentes do prejuízo da atenção, e que estão correlacionadas com níveis mais baixos de insight.

## 1. OBJETIVOS

Objetivo geral: estudar a atenção no TB.

Os objetivos específicos são:

1. Revisar a literatura científica sobre as alterações da atenção em pacientes com TB atualizando o conhecimento sobre o assunto.

2. Avaliar se o desempenho de pacientes com TB em testes de atenção varia de acordo com cada fase da doença e verificar se existem diferenças na atenção ao comparar pacientes bipolares com controles normais.

3. Investigar os preditores clínicos e cognitivos para a perda de insight no TB.

4. Estudar a relação entre a cognição, prejuízo de insight e incapacidade sócio-ocupacional nos pacientes com TB.

## 3. METODOLOGIA

A pesquisa foi realizada no Laboratório de Transtorno Bipolar do Humor do Instituto de Psiquiatria da Universidade Federal do Rio de Janeiro. O ambulatório é coordenado pelo professor Elie Cheniaux. Atualmente, atende cerca de 170 pacientes com o diagnóstico de transtorno bipolar tipo I e tipo II. As escalas clínicas psiquiátricas são usadas regularmente em todas as consultas. As outras três avaliações (avaliação da atenção, escala de insight e incapacidade), foram usadas para essa pesquisa. A aplicação da escala de insight foi adaptada e validada pelo mestre Rafael Assis ( Silva RA et al., 2015).

Importante ressaltar que, não houve interferência no tratamento dos pacientes. E a neuropsicóloga estava cega quanto ao estado afetivo que o paciente se apresentava no momento da avaliação.

Nos estudos clínicos, os únicos critérios de inclusão foram: idade igual ou superior a 18 anos; adequação aos critérios do DSM-IV-TR para os diagnósticos de transtorno bipolar tipo I ou transtorno bipolar tipo II; e assinatura do termo de consentimento livre e esclarecido (Anexo I). Como critérios de exclusão estavam a não aceitação em participar da pesquisa, a não cooperação na aplicação dos instrumentos de avaliação.

Foram elaborados quatro manuscritos sobre as alterações da atenção no TB: uma revisão sistemática e três estudos clínicos. Os estudos clínicos possuem instrumentos clínicos e neuropsicológicos comuns. Como instrumentos de avaliação neuropsicológica, utilizamos: Digit Span (ordem direta e indireta), da bateria Wechsler Adult Intelligence Scale (Wechsler et al., 2005); Letter-Number Sequencing, da bateria Wechsler Adult Intelligence Scale (Wechsler et al., 2005); The Stroop Color and Word Test (SCWT) (Stroop, 1935); Search Symbol, da bateria Wechsler Adult Intelligence Scale (Wechsler et al., 2005); Trail Making Test Part A e B (TMT-A and B; Gaudino et al.,1995), e o teste de Fluência Verbal, da Bateria Montreal de Avaliação da Comunicação-Bateria MAC (Fonseca et al., 2008). E como instrumentos de avaliação clínica, utilizamos: Young Mania Rating Scale (YMRS) (Young et al., 1978), Hamilton Depression Scale (HAM-D) (Hamilton et al., 1960), Clinical Global Impressions Scale for use in bipolar illness (CGI-BP) (Spearing et al. 1997), Positive and Negative Syndrome Scale (PANSS-p) (a subescala de sintomas positivos) (Chaves et al., 1998), escala de insight (De Assis, R et al., 2015) e de incapacidade (Sheehan et al., 1996). Os instrumentos de avaliação clínica foram utilizados durante as consultas pelos médicos assistentes e, após as consultas, os pacientes foram submetidos à avaliação neuropsicológica e à escala de incapacidade pela neuropsicóloga.

## 4. RESULTADOS

O presente estudo resultou em quatro manuscritos, todos submetidos a periódicos internacionais. A revisão sistemática (“Attention impairment in bipolar disorder: a systematic review”) foi publicada na revista Psychology and Neuroscience em 2013. Os outros três manuscritos ainda não foram publicados: “Performance of bipolar disorder patients in attention testing: comparison with normal controls and among manic, depressive, and euthymic phases” foi submetido à revista Psychiatric Quarterly; “Clinical and cognitive

correlates of insight in bipolar disorder" à Journal of Affective Disorders e "Loss of insight and depression contribute to increased disability in bipolar disorder", à Psychiatry and Clinical Neurosciences.

Os quatro artigos são apresentados a seguir:

# Attention impairment in bipolar disorder: a systematic review

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**Abstract**

Bipolar disorder (BD) has been associated with marked cognitive impairment, including euthymic periods. Attention is among the most compromised functions in BD. Changes related to learning, memory, and visuospatial abilities can be derived from these attention impairments. The objective of this article is to review the scientific literature on the performance of BD patients in attention tests. A systematic review was performed of controlled studies that assessed attention in patients diagnosed with BD aged between 18 and 65 years. The databases included Medline, LILACS, Cochrane Library, Institute for Scientific Information Web of Knowledge, and Scientific Electronic Library Online (SciELO), and the search encompassed the period from 2008 to 2013. Only studies that had a minimum sample

of 10 patients were included. A total of 110 articles fulfilled the inclusion criteria. Compared with healthy control subjects, bipolar patients showed poorer attention performance. Compared with other mental disorders, BD was associated with poorer performance than unipolar depression but better performance than schizophrenia. When bipolar patients in different phases of the disease were compared with one another, the performance of euthymic patients was similar to or better than patients in a depressive state; moreover, manic patients performed worse than depressive patients. Attention is significantly impaired in BD. Attention impairment in BD is milder than in schizophrenia but greater than in unipolar depression. Attention impairment is possibly more severe in manic and depressed episodes than in euthymic periods.

**Keywords:** attention, cognition, neuropsychological tests, bipolar disorder.

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Cognitive deficits were first studied in brain injury and dementia and later in schizophrenia. However, since the 1970s, much effort has been devoted to understanding cognitive function in mood disorders, particularly bipolar disorder (BD; Caligiuri, & Ellwanger, 2000). The literature has provided evidence of stable and persistent cognitive impairments across the phases of BD, including euthymia, particularly in the following domains: sustained attention, learning, memory, visuospatial ability, and executive function (Caligiuri, & Ellwanger, 2000; Latalova, Jan, Tomas, Dana, & Hana, 2011). In BD, attentional changes are very relevant and can affect other cognitive functions, such as memory, learning, and executive function (Goodwin, Jaminson, & Ghaemi, 2007).

Numerous review articles have been published on cognitive impairments in BD, but these studies did not specifically address attention impairments (Sachs, Schaffer, & Winklbaur, 2007; Latalova et al., 2011; Kałwa, 2010; Quaishi & Frangou, 2002). To our knowledge, only one review article published 9 years ago (Clark, & Goodwin, 2004) focused specifically on attentional changes in bipolar patients. The present study provides an update on the knowledge of attention impairments in patients with BD by systematically reviewing controlled studies published in the past 5 years.

## Methods

We performed a systematic review of the scientific literature on attention impairments in BD. References were identified in five databases (i.e., Medline, Institute for Scientific Information [ISI] Web of Knowledge, Cochrane Library, Scientific Electronic Library Online [SciELO], and LILACS) from 2008 to May, 27, 2013. The following search terms were used: "bipolar" and "attention" or "neuropsychological" or "cognition" or "cognitive." The inclusion criteria were the following: samples with at least 10 patients diagnosed with BD, aged 18 and 65 years, and evaluations that used neuropsychological tests that assessed attention. Only controlled trials (e.g., comparisons with healthy controls, with other mental disorders, or among BD patients in different affective states) were considered. Review articles, case reports, letters to the editor, and book chapters were excluded. No search of unpublished work was performed. Citations within a paper were also included as an additional source of references.

## Results

The initial search retrieved 7,885 citations from Medline, 7396 from the ISI Web of Knowledge, 328 from Cochrane Library, 113 from SciELO, and 148 from LILACS, with some overlap among the databases. A total of 879 abstracts were classified as potentially relevant according to our criteria. After the appraisal of the full-text articles, 110 citations were selected.

### *Studies that compared BD patients with healthy control subjects*

As shown in Table 1, 91 studies compared patients with a diagnosis of BD with healthy control subjects. In 80 of these studies, bipolar patients performed significantly worse in attention tests compared with healthy controls. In 11 studies, however, no significant difference was found between groups. In 53 of the 91 studies, the patients were not differentiated according to their mood state. In 36 of the 38 studies that incorporated such discrimination, both euthymic patients and patients in a manic or depressed state performed worse on attention tests than controls. One of these 38 studies found no significant difference between euthymic bipolar patients and healthy controls. Among the 80 studies in which the bipolar patients had poorer results compared with controls, sustained attention was evaluated in 40 studies, divided attention was evaluated in 42 studies, and selective attention was evaluated in 18 studies. Some of the studies evaluated more than one modality of attention.

### *Studies that compared BD with other mental disorders*

As shown in Table 2, 15 studies compared BD patients with other mental disorders. In ten of these studies, comparisons were made with schizophrenia. The performance of bipolar

patients on attention tests was significantly superior in seven of the ten studies. Among these seven studies, sustained attention was evaluated in four studies, and divided attention was evaluated in three studies. In two studies that evaluated divided and selective attention, no significant differences were found between the two groups. In only one study, patients with schizophrenia outperformed bipolar patients. In this study, sustained attention was assessed.
Five studies compared bipolar patients with unipolar depression patients. Sustained attention was evaluated in four of these studies. Selective attention was evaluated in two of these studies, and divided attention was evaluated in one of these studies. Unipolar depression patients had better attention performance in four of the five studies. No significant differences were found between the two groups in one study in measures of sustained and selective attention.

***Studies that compared the different phases of BD***

As seen in Table 3, four studies compared BD patients in different mood states. In two studies that evaluated sustained attention, euthymic bipolar patients were contrasted with patients in a depressed state. In one of these studies, euthymic patients had superior performance on attention tests, whereas no significant differences were found between groups in the other study. In the other two studies, depressive bipolar patients performed better than manic patients on tests that evaluated divided and selective attention.

## Discussion

The present systematic review described controlled studies with bipolar patients who underwent neuropsychological evaluation using attention tests. Our aim was to provide an update on the body of knowledge about attention impairment in patients with BD based on studies published over the past five years.

According to our review, compared with health controls, patients with BD presented worse performance. Recently, other reviews that compared BD patients with healthy controls with regard to cognitive performance have been published (Thompson et al., 2005; Borges, Trentini, Bandeira, & DellÁglio, 2008; Burdick, Gunawardane, Goldberg, Halperin, Garno, & Malhotra, 2007; Rocca & Lafer, 2006). Our results on attention impairment in BD were very similar to those found in these reviews. These studies showed that cognitive impairment is part of the neuropsychological profile of BD patients. Specifically, these findings showed that these individuals have impairments in attention performance compared with healthy controls, regardless of whether the patients are euthymic, manic, or depressed. For example, Bora,

Yücel, & Pantelis (2010) reviewed 12 studies that had samples with at least 10 subjects in each group, including patients with BD and healthy individuals, which were neurocognitively compared. All of these studies showed that patients with BD had inferior performance in tasks that measure executive function, memory, and attention.

According to our review, in seven of the ten studies that compared BD with schizophrenia, bipolar patients performed better in attention tests. Indeed, most of the review articles identified in the present study showed that patients cognitive deficits are more pronounced in patients with schizophrenia than in patients with BD in several cognitive functions, including psychomotor speed, verbal and visual memory, attention, and executive function (Goldberg et al., 1993; Evans, Heaton, Paulsen, McAdams, Heaton, & Jeste, 1999; Hawkins, Hoffman, Quinlan, Rakfeldt, Docherty, &Sledge, 1997; Rocca & Lafer, 2006; Quaishi & Frangou, 2002). For example, Daban et al. (2006) selected 38 studies that compared BD and schizophrenia patients during the execution of neuropsychological tasks. Patients with BD performed better on tasks that measured Intelligence Quotient (IQ), attention, memory, and executive function. The authors proposed that the poor performance in schizophrenia patients occurred because of the presence of psychotic symptoms, the duration of the illness, and hospitalization. Simonsen et al. (2008) found that BD patients with psychotic symptoms have similar performance as schizophrenia patients in some neurocognitive tasks, such as verbal memory and processing speed. Some authors (Andreasen, & Powers, 1974; Strauss, Bohannon, Stephens, & Pauker, 1984; Goldberg et al., 1993; Evans et al., 1999) believe that defining the mood state in samples of BD patients is important because manic patients perform worse than depressive or euthymic patients in working memory, selective attention, and divided attention tasks, and manic patients perform similarly to schizophrenia patients.

We found only five studies that compared BD patients with unipolar depression patients by applying attention tests. In four of these studies, BD patients had worse performance (Benson et al., 2008; Xu et al., 2012; Maalouf et al., 2010). According to other review articles (Rocca & Lafer., 2006; Murphy & Sahakian, 1999), patients with BD present worse performance than unipolar depression patients not only in attention tests but also in several other cognitive tasks, such as executive function and working memory.

Our search found only four studies that compared BD patients in different mood states (i.e., euthymia, mania, and depression). In two studies, manic patients presented worse performance than depressed patients. However, the distinction between depressed and euthymic patients was less evident. Two articles (Martínez-Arán et al., 2009; Rocca & Lafer,

2006) showed that euthymic patients had difficulty in cognitive tasks, but this impairment was less severe compared with depressive and manic patients. Some review articles (Van Gorp, Altshuler, Theberge, Wilkins, & Dixon, 1998; Cavanagh, Van Beck, Muir, & Blackwood, 2002; Clark, Iversen, & Goodwin, 2002; Deckersback, McMurrich, Ogutha, Savage, Sachs, & Rauch, 2004) reported consistent deficits in sustained attention, verbal memory, and executive function in mania. Moreover, patients with BD in the depressive or euthymic phase performed better than manic patients in attention tasks (Zubieta, Huguelet, O'Neil, & Giordani, 2001; Clark et al., 2002; Thompson et al., 2005; Xu et al., 2012), verbal learning (Clark et al., 2002; Deckersbach et al., 2004), and visual memory (MacQueen & Young, 2003; Deckersbach et al., 2004).

One hypothesis that may explain the worse performance in manic patients in sustained attention tests is related to the typical impulsivity exhibited by these patients. They answer quickly and incorrectly before the stimulus appears, thus impairing their performance. Impairments in sustained attention were observed in the Continuous Performance Test (CPT), which represents a central neuropsychological deficit associated with mania (Murphy et al., 1999).

Attention is a complex system related to the activation of other cognitive functions; thus, attention impairments in BD patients can be primarily related to other cognitive dysfunctions (Van Gorp et al., 1998; Martínez-Arán et al., 2009). In BD, alterations in attention are highly relevant and can affect other cognitive functions, such as learning, executive function, and memory (Goodwin et al., 2007).

Cognitive deficits become worse over the course of BD (Vieta, 2012; Levy et al., 2009) and are associated with a greater number of disease episodes (Vieta et al., 2012). Selva et al. (2007) failed to find differences between psychotic and non-psychotic subjects on a series of memory, executive function, and attention tests. Harkavy-Friedman et al. (2006) found that suicide attempters with BD had worse performance than non-suicidal bipolar patients in psychomotor performance, working memory, attention, and impulse control.

Patients with BD generally exhibit typical cognitive development premorbidly but exhibit deficits by the first episode that are amplified as the symptoms worsen. Some data suggest that cognitive deficits may precede the onset of mania; therefore, identifying cognitive predictors of bipolar disorder would be beneficial to facilitate early intervention (Lewandowski, Cohen, Keshavan, & Ongür, 2011; Olvet, Burdick, & Cornblatt, 2013).

First-episode mania patients were found to have less neurocognitive deficits in psychomotor speed, attention, learning and memory, executive function, and IQ compared with multiple-episode patients (Hellvin et al., 2012; Van Gorp et al., 1998).

Psychiatric medications commonly used in BD can affect cognition. According to some review articles (Honig, Arts, Ponds, & Riedel, 1999; Pachet, & Wisniewski, 2003), lithium may exert mild negative effects in tasks of verbal memory and psychomotor speed, whereas visuo-spatial performance, attention, and executive performance are spared. Lithium has also been shown to exert a neuroprotective effect and be related to better cognitive performance in patients with BD (Bauer, Alda, Priller, & Young, 2003). Atypical antipsychotics have shown more negative effects on cognition compared with lithium and anticonvulsants (Arts, Jabben, Krabbendam, & van Os, 2011; Macqueen, & Young, 2003; Torrent et al., 2011; Yurgelun-Todd et al., 2002).

Some studies have reported that cognitive impairment in patients with BD represents a trait marker of the disease (Clark et al., 2004). These studies have proposed a neurodegenerative hypothesis to explain the cognitive deficits associated with BD (McKinnon, Cusi, & Macqueen, 2012). Cognitive damage would be an endophenotype of the disorder and a marker associated with this mental disorder. The term “endophenotype” was used by Gottesman (2003) to describe a trait that may be intermediate on the chain of causality from genes to diseases. Some family relatives of affected patients also carry the endophenotype, although not the disorder phenotype (i.e., affective symptoms) in the case of BD (Adida et al., 2012). In fact, some studies also described attention deficits in unaffected relatives of individuals with mood disorders (Bora, Yucel, & Pantelis, 2009; Brotman, Rooney, Skup, Pine, & Leibenluft, 2009; Grunebaum, Cohler, Kauffman, & Gallant, 1978; Klimes-Dougan, Ronsaville, Wiggs, & Martinez, 2006; Zalla et al., 2004).

Gottesman, & Gould (2003) discussed endophenotypes and suggested five criteria that should be characteristic of a trait to qualify it as an endophenotype. These five criteria are used to assess the viability of using measures of neuropsychological dysfunction as endophenotypes for genetic studies of BD (Savitz, Solnes, & Ramesar, 2005). The importance of early interventions in BD have been extensively studied, and recent efforts have been made to identify individuals who are at increased risk; e.g., relatives of bipolar patients (Bora et al., 2009; Olvet et al., 2013). For this reason, some researchers have recently begun to focus on the genetic contributions to discrete (as opposed to global) cognitive processes, such as executive function, working memory, and attention. For example, a version of executive

function evaluated by selective and sustained attention tests, e.g., WCST and CPT (Conners, 2000) was reported to have a degree of heritability (Savitz et al., 2005).

To demonstrate that a trait is an endophenotype, the trait must be shown to be mood state-independent and heritable (Gottesman, & Gould, 2003). Thus, studies that examine neurocognitive aspects and neuroanatomic changes, together with genetics studies, are important to improve our understanding of the neural basis of BD (Kurnianingsih, Kuswanto, McIntyre, Qiu, Ho, & Sim, 2011).

Considering the neuroanatomic changes that occur in BD, a correlation has been found between a longer disease duration and more pronounced atrophy in the frontal cortex, an area that is closely related to attention (Stoll, Renshaw, Yurgelun-Todd, & Cohen, 2000; Kemptom, Geddes, Ettinger, Williams, & Grasby, 2008). Studies of bipolar patients tested attentional impairment using the CPT and structural and functional magnetic resonance imaging and reported changes in the dorsolateral prefrontal cortex (Rocca & Lafer, 2006), prolonged amygdala overactivation, and prefrontal cortex atrophy (Sax, Strakowski, Zimmerman, DelBello, Keck, & Hawkins, 1999). In addition to these findings, other studies have reported that certain neuroanatomic structures are associated with attention dysfunction during mania (Sax et al., 1999). One such structure is the right prefrontal cortex, which appears to be involved in sustained attention (Manly, & Robertson, 1997).

Furthermore, functional neuroimaging studies of bipolar patients have detected activation in the right prefrontal cortex during the assessment of sustained attention (Coull, Frith, Frackowiak, & Grasby, 1996; Paus, Zatorre, & Hofle, 1997). Other modalities of attention, such as selective and divided attention, have also been associated with functional or structural alterations. In patients with BD, a reduction of neural responsiveness was observed in regions involved in selective attention within the posterior and inferior parietal lobes (Pompei et al., 2011). Additionally, impairment in divided attention in patients with bipolar depression has been attributed to a reduction of attentional resources by the central executive (i.e., the working memory component) and impaired activation in the frontal lobe (Paus, Zatorre, & Hofle, 1997). According to the results of the present review, all types of attention are significantly impaired in BD (Ancín et al., 2011; Andersson, Barder, Hellvin, Løvdahl, & Malt, 2008; Barrett, Mulholland, Cooper, & Rushe, 2009; Bonnín et al., 2012; Burdick et al., 2009; Iverson, Brooks, & Young, 2009). Specifically, sustained attention and divided attention are more severe in mania and in depression, respectively (Murphy et al., 1999).

Attentional impairment in BD is less severe than in schizophrenia but greater than in unipolar depression and possibly more severe in the mania and depression phases of BD than

in the euthymia phase. These findings have prompted us to propose the development of cognitive rehabilitation techniques for individuals with BD that are similar to those used for persons with frontal lobe dysfunction (Levine, Turner, & Stuss, 2008) or brain injury (Ponsford, 2008). Attention is directly related to other cognitive functions, such as learning, memory, and executive function. Alterations in these and other cognitive functions could at least partially derive from attention deficits. Further studies are needed to investigate the attention alterations in BD, especially longitudinal studies that would allow an enhanced understanding of the progressive character of attention deficits in BD.

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**Table 1.** Studies that compared bipolar patients with normal controls with regard to attention performance.

| Study | Sample and design | Instruments | Type of attention | Results |
|---|---|---|---|---|
| Trivedi, Goel, Sharma, Singh, & Tandon, 2008 | 15 BD-e *vs.* 15 NC | CPT | Sustained attention | BD = NC |
| Morisano, Wing, Sacco, Arenovich, & Goerge, 2013 | 16 BD *vs.* 17 NC | CPT | Sustained attention | BD = NC |
| Gualtieri & Morgan, 2008 | 96BD *vs.* 907 NC | SCWT, CPT, SAT | Selective, sustained, divided attention | BD = NC |
| Frantom, Allen, & Cross, 2008 | 19 BD *vs.* 19 NC | SCWT, CPT, TMT | Selective, sustained, divided attention | BD = NC |
| Aydemir & Ender, 2009 | 38 BD *vs.* 19 NC | SCWT | Selective attention | BD = NC |
| Antila et al., 2009 | 39 BD *vs.* 55 NC | Digit Span, TMT | Divided attention | BD = NC |
| Torralva et al., 2011 | 15 BD *vs.* 15 NC | Digit Span, TMT | Divided attention | BD = NC |
| Tuulio-Henriksson et al., 2011 | 17 BD *vs.* 66 NC | Digit Span | Divided attention | BD = NC |
| Xu et al., 2012 | 223 BD *vs.* 202 NC | Digit Span | Divided attention | BD = NC |
| Wu et al., 2011 | 40 BD *vs.* 19 NC | Digit Symbol | Divided attention | BD = NC |
| Li et al., 2012 | 34 BD *vs.* 17 NC 80 | Go/No-Go CPT | Divided attention Sus- | BD = NC BD < NC |
| Burdick et al.,2011 | BD-e *vs.*149 NC | CPT | tained attention | BD < NC |
| Schretlen et al.,2013 | 126 BD *vs*.340 NC | | Sustained attention | |
| Sanchez-Moreno et al., 2009 | 65 BD *vs.* 35 NC | Digit Span, TMT | Divided attention | BD < NC |
| Martino, Strejilevich, Torralva, & Manes, 2010 | 85 BD-e *vs.* 34 NC<br>100 BD-e *vs*. 50 NC | Digit Span, TMT<br>TMT | Divided attention<br>Divided attention | BD < NC BD < NC |
| Elshahawi,Essawi,Rabie,Mansour,Beshry,&Mansour,2011 | | | | |
| Normala, Abdul, Azlin, | 40 BD *vs.* 40 NC | Digit Span, TMT | Divided attention | BD < NC |
| Nik, Hazli, & Shah, 2010 | 103 BD-e *vs.* 35 NC | Digit Span, TMT | Divided attention | BD < NC |
| Burdick et al.,2011 | | | | |
| Torrent et al., 2011 | 79 BD-e *vs.* 35 NC | Digit Span, TMT | Divided attention | BD < NC |
| Martino et al., 2011[a] | 87 BD-e *vs.* 39 NC | Digit Span, TMT | Divided attention | BD < NC |
| Martino et al., 2011b | 81 BD-e *vs.* 34 NC | Digit Span, TMT | Divided attention | BD < NC |
| Bonnín et al., 2012 | 103 BD-e *vs.* 30 NC | Digit Span, TMT | Divided attention | BD < NC |
| Torrent et al., 2012 | 68 BD-e *vs.* 45 NC | Digit Span, TMT | Divided attention | BD < NC |
| Pattanayak, Sagar, & Mehta, 2012 | 30 BD-e *vs.* 20 NC | Digit Span, TMT | Divided attention | BD < NC |
| Martino et al., 2008 | 50 BD *vs.* 30 NC | Digit Span, TMT, | Divided, sustained | BD < NC |

| | | | | |
|---|---|---|---|---|
| | | CPT | attention | |
| Soeiro-de-Souza, Machado-Vieira, Soares Bio, Do Prado, & Moreno, 2012 | 66 BD *vs.* 78 NC | Digit Span, TMT, SCWT | Divided, selective attention | BD < NC |
| Soeiro-de-Souza et al., 2012 | 72 BD *vs.* 76 NC | Digit Span, TMT, SCWT | Divided, selective attention | BD < NC |
| Hill et al., 2009 | 22 BD *vs.* 41 NC | Digit Span, CPT | Divided, sustained attention | BD < NC |
| Jabben, Krabbendam, & van Os, 2009 | 76 BD *vs.* 61 NC | Digit Span, CPT | Divided, sustained attention | BD < NC |
| Thompson, Gray, Crawford, Hughes, Young, & Ferrier, 2009 | 63 BD-e *vs.* 63 NC | Digit Span, CPT, TMT SCWT, COWA, TL | Divided, sustained, selective attention | BD < NC |
| Mur et al., 2008b | 15 BD *vs.* 15 NC | Digit Span, SCWT | Divided, selective attention | BD < NC |
| Simonsen et al., 2008 | 73 BD *vs.* 124 NC | Digit Span | Divided attention | BD < NC |
| Barrett et al., 2009 | 32 BD-m *vs.* 67 NC | Digit Span | Divided attention | BD < NC |
| Gogos, Joshua, & Rossell, 2010 | 40 BD *vs.* 43 NC | Digit Span | Divided attention | BD < NC |
| Vaskinn, Sundet, Simonsen, Hellvin, Melle, & Andreassen, 2011 | 106 BD *vs.* 340 NC | Digit Span | Divided attention | BD < NC |
| Yates, Dittmann, Kapczinski, & Trentini, 2011 | 65 BD *vs.* 34 NC | Digit Span | Divided attention | BD < NC |
| Dickerson et al., 2011 | 60 BD *vs.* 312 NC | Digit Span | Divided attention | BD < NC |
| Gerber et al., 2012 | 30 BD-e *vs.* 20 NC | Digit Span | Divided attention | BD < NC |
| Chou et al., 2012 | 23 BD-e *vs.* 33 NC | Digit Span | Divided attention | BD < NC |
| Soeiro-de-Souza, Bio, Dias, Vieta, Machado-Vieira, & Moreno, 2013 | 109 BD *vs.* 96 NC | Digit Span | Divided attention | BD < NC |
| Burdick et al., 2009 | 24 BD *vs.* 24 NC | SCWT | Selective attention | BD < NC |
| Pompei et al., 2011 | 39 BD-e *vs.* 48 NC | SCWT | Selective attention | BD < NC |
| Lewandowski et al., 2011 | 31 BD *vs.* 20 NC | SCWT | Selective attention | BD < NC |
| Juselius, Kieseppa, Kaprio, Lonnqvist, & Tuulio-Henriksson, 2009 | 26 BD-e *vs.* 114 NC | TMT | Divided attention | BD < NC |
| Solé et al., 2012 | 43 BD *vs.* 42 NC | TMT | Divided attention | BD < NC |
| Chang et al., 2012 | 94 BD *vs.* 29 NC | TMT | Divided attention | BD < NC |
| Benson et al., 2008 | 30 BD *vs.* 66 NC | CPT | Sustained attention | BD < NC |
| Mur et al., 2008[a] | 33 BD *vs.* 33 NC | CPT | Sustained attention | BD < NC |
| Tabarés-Seisdedos et al., 2008 | 43 BD *vs.* 25 NC | CPT | Sustained attention | BD < NC |
| Malloy-Diniz, Neves, Abrantes, Fuentes, & Correa, 2009 | 39 BD *vs.* 53 NC | CPT | Sustained attention | BD < NC |
| Strakowski et al., 2009 | 70 BD-m *vs.* 34 NC | CPT | Sustained attention | BD < NC |
| Lahera et al., 2009 | 24 BD-e *vs.* 38 NC | CPT | Sustained attention | BD < NC |
| Swann, Lijffijt, Lane, Steinberg, & Moeller, 2009 | 112 BD *vs.* 71 NC | CPT | Sustained attention | BD < NC |
| Sanchez-Morla et al., 2009 | 73 BD-e *vs.* 67 NC | CPT | Sustained attention | BD < NC |
| Brooks, Bearden, Hoblyn, Woodard, & Ketter, 2010 | 16 BD-e *vs.* 11 NC | CPT | Sustained attention | BD < NC |
| Van der Wer-Eldering, Burger, Holthausen, Aleman, & Nolen, 2010 | 110 BD *vs.* 75 NC | CPT | Sustained attention | BD < NC |
| Ancín et al., 2011 | 143 BD-e *vs.* 101 NC | CPT | Sustained attention | BD < NC |
| Van der Wer-Eldering, Burger, Jabben, Holthausen, Aleman, & Nolen, 2011 | 108 BD *vs.* 75 NC | CPT | Sustained attention | BD < NC |
| Arts et al., 2011 | 76 BD *vs.* 61 NC | CPT | Sustained attention | BD < NC |
| Pan, Hsieh, & Liu, 2011 | 32 BD-e *vs.* 39 NC | CPT | Sustained attention | BD < NC |
| Howells, Ives-Keliperi, Horn, & Stein, 2012 | 12 BD-e *vs.* 9 NC | CPT | Sustained attention | BD < NC |
| Sepede et al., 2012 | 24 BD-e *vs.* 24 NC | CPT | Sustained attention | BD < NC |

| | | | | |
|---|---|---|---|---|
| Donohoe et al., 2012 | 110 BD *vs.* 163 NC | CPT | Sustained attention | BD < NC |
| Fleck et al., 2012 | 50 BD *vs.* 34 NC | CPT | Sustained attention | BD < NC |
| Lee, Altshuler, Glahn, Miklowitz, Ochsner, & Green, 2013 | 68 BD *vs.* 36 NC | CPT | Sustained attention | BD < NC |
| Cummings et al., 2013 | 125 BD *vs.* 171 NC | CPT | Sustained attention | BD < NC |
| Strakowski et al., 2010 | 108 BD-m *vs.* 48 NC | DSCPT | Sustained attention | BD < NC |
| Hellvin et al., 2012 | 55 BD-m *vs.* 110 NC | DSCPT | Sustained attention | BD < NC |
| Holmes et al., 2008 | 65 BD-d *vs.* 52 NC | RVIP | Sustained attention | BD < NC |
| Roiser et al., 2009 | 49BD-d *vs.* 55 NC | RVIP | Sustained attention | BD < NC |
| Maalouf et al., 2010 | 52 BD *vs.* 28 NC | RVIP | Sustained attention | BD < NC |
| Yoram et al., 2013 | 47 BD *vs.* 31 NC | RVIP | Sustained attention | BD < NC |
| Vierck et al., 2013 | 96 BD *vs.* 24 NC | RVIP | Sustained attention | BD < NC |
| Chaves et al., 2011 | 29 BD *vs.* 30 NC | IP-CPT, Digit Span | Sustained, divided attention | BD < NC |
| Mora, Portella, Forcada, Vieta, & Mur, 2012 | 28 BD-e *vs.* 26 NC | CPT, Digit Span, SCWT | Sustained, divided, selective attention | BD < NC |
| Iverson et al., 2011 | 43 BD *vs.* 659 NC | CPT, SCWT | Sustained, selective attention | BD < NC |
| Levy, 2013 | 30 BD-e *vs.* 22 NC | CPT, SCWT | Sustained, selective attention | BD < NC |
| Iverson et al., 2009 | 47 BD *vs.* 47 NC | CPT, SCWT, SAT | Sustained, selective, divided, attention | BD < NC |
| Martinez-Aran et al., 2008 | 65 BD-e vs. 35 NC | TMT, SCWT | Divided, selective attention | BD < NC |
| López-Jaramillo et al., 2010b | 40 BD-e vs. 20 NC | TMT, SCWT | Divided, selective attention | BD < NC |
| Marshall et al., 2012 | 256 BD vs. 97 NC | TMT, SCWT | Divided, selective attention | BD < NC |
| Doğanavşargil, Bokmen, Akbas, Cinemre, Metin, & Karaman, 2013 | 60 BD-e vs. 20 NC | TMT, SCWT | Divided, selective attention | BD < NC |
| López-Jaramillo et al., 2010[a] | 98 BD-m vs. 66 NC | TMT, SCWT, CT | Divided, selective attention | BD < NC |
| Torres et al., 2010 | 45 BD vs. 25 NC | TMT, SCWT, RVIP, CVLT-II | Divided, selective, sustained attention | BD < NC |
| Cuesta et al., 2011 | 65 BD *vs.* 76 NC 60 | TMT, Digit Span | Divided attention | BD < NC BD < NC |
| Watson et al.,2012 | BD-d *vs.*55 NC | Digit Symbol | Divided attention | |
| Pradhan, Chakrabarti, Nehra, & Mankotia, 2008 | 48 BD-e *vs.* 23 NC | PGIMS | Selective attention | BD < NC |
| Wobrock et al., 2009 | 18 BD *vs.* 23 NC | TMT | Divided attention | BD > NC |
| Mahlberg, Adli, Bschor, & Kienast, 2008 | 28 BD-m *vs.* 30 BD-d | TMT | Divided attention | BD > NC |
| Liu, Chen, Hsieh, Su, Yeh, & Chen, 2010 | 27 BD *vs.* 21 NC | TAP | Divided attention | BD < NC |
| Shan et al., 2011 | 69 BD *vs.* 22 NC | Digit Symbol | Sustained attention | BD < NC |

>, better performance; <, worse performance; =, similar performance. BD, bipolar disorder; NC, normal control; SZ, schizophrenia; UP, unipolar depression; BD-e, bipolar disorder, euthymic; BD-d, bipolar disorder, depressive; BD-m, bipolar disorder, manic; TMT, Trail Making Test; CPT, Continuous Performance Test ; CPTII, Continuous Performance Test II, version 5; PCTP, Penn Continuous Performance Test; CPT-IP, Continuous Performance Test, identical pairs version; DS-CPT, Degraded Stimulus Continuous Performance Test; CPT-AX, Continuous Performance Test-AX (a character or number preceded by another character or number as a target); RVIP, Rapid Visual Information Processing; SCWT, Stroop Color Word Test; CT, Cancellation Test; SAT, Shifting Attention Test; CB, conditioned blocking; CVLT-II, California Verbal Learning Test; TAP, Attentional Performance Test; TL, Tower of London; COWA, Controlled Oral Word Association Test; PGIMS, PGI memory scale; PASAT, Paced Auditory Serial Addition.

**Table 2.** Studies that compared attention performance in bipolar disorder and other mental disorders.

| Study | Sample and design | Instrument | Type of attention | Results |
|---|---|---|---|---|
| Gogos et al., 2009 | 12 BD-e *vs.* 28 SZ | Digit Span | Divided attention | BD > SZ |
| Barret et al., 2009 | 32 BD-m *vs.* 44 SZ | Digit Span, CB | Divided attention | BD > SZ |
| Cuesta et al., 2011 | 65 BD *vs.* 86 SZ | Digit Span, TMT | Divided attention | BD > SZ |
| Tabarés-Seisdedos et al., 2008 | 43 BD *vs.* 47 SZ | Asarnow CPT | Sustained attention | BD > SZ |
| Lee et al., 2013 | 68 BD *vs.* 38 SZ | CPT | Sustained attention | BD > SZ |
| Schretlen et al.,2013 | 126 BD vs.110 SZ | CPT | Sustained attention | BD > SZ |
| Cummings et al., 2013 | 125 BD *vs.* 573 SZ | CPT | Sustained attention | BD > SZ |
| Pradhan et al., 2008 | 48 BD-e *vs.* 32 SZ | PGIMS | Selective attention | BD = SZ |
| Wobrock et al., 2009 | 18 BD *vs.* 24 SZ | TMT | Divided attention | BD = SZ |
| Donohoe et al., 2012 | 110 BD *vs.* 487 SZ | CPT | Sustained attention | BD < SZ |
| Benson et al., 2008 | 30 BD *vs.* 34 UP | CPT | Sustained attention | BD < UP |
| Iverson et al., 2011 | 43 BD *vs.* 143 UP | CPT, SCWT | Sustained, selective attention | BD < UP |
| Xu et al., 2012 | 223 BD *vs.* 293 UP | Digit Span | Divided attention | BD < UP |
| Maalouf et al., 2010 | 18 BD-e *vs.* 14 BD-d *vs.* 20 UP | RVIP | Sustained attention | BD-e < UP BD-d < UP |
| Gualtieri & Morgan, 2008 | 96 BD *vs.* 285 UP | CPT, SCWT | Sustained, selective attention | BD = UP |

See Table 1 for abbreviations

**Table 3.** Studies that compared attention performance in the different phases of bipolar disorder.

| Study | Sample and design | Instruments | Types of attention | Results |
|---|---|---|---|---|
| Maalouf et al., 2010 | 18 BD-e *vs.* 14 BD-d | RVIP | Sustained attention | BD-e = BD-d |
| Van der Wer-Eldering et al., 2011 | 45 BD-e *vs.* 63 BD-d | CPT | Sustained attention | BD-e > BD-d |
| Mahlberg et al., 2008 | 28 BD-m *vs.* 30 BD-d | TMT | Divided attention | BD-d > BD-m |
| Soeiro-de-Souza et al., 2012 | 41 BD-m *vs.* 25 BD-d | Digit Span, TMT, SCWT | Divided, selective attention | BD-d > BD-m |

See Table 1 for abbreviations

# Performance of bipolar disorder patients in attention testing: comparison with normal controls and among manic, depressive, and euthymic phases.

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**Abstract**

*Background:*Several studies on cognition in bipolar disorder (BD) have been developed on the last decade. Neuropsychological evaluation of attention in BD patients is fundamental since alterations in attention affect other cognitive functions.

*Objective***:** Evaluate if performance of BD patients in attention tests varies according to each phase of the disease and verify if there are differences in attention when comparing BD patients with normal controls.

*Method:*The study included 101 BD patients, with ages between 18 to 65 years, being 52 euthymic, 22 manic and 27 depressive, besides 30 normal controls. All subjects were evaluated though Hamilton Depression Scale, Young Mania Rating Scale and Global Assessment of Functioning, bipolar version (CGI-BP). Attention was evaluated through a neuropsychological battery.

*Results:* Normal controls had a better performance in selective attention tests than BD patients. No differences were found among manic, depressive and euthymic phases.

*Conclusion:*Attention is markedly impaired in BD. Nevertheless, the results of this study do not imply that the severity of the attention deficit in BD patients varies according to decease phase.

*Keywords:* attention, bipolar disorder, cognition, mania, depression, euthymia.

## Introduction

Bipolar disorder (BD) is associated to significant cognitive impairment observed not only in manic and depression phases, but also in euthymia [35]. In BD, changes in attention are relevant since impairment in attention may affect the remaining cognitive functions – memory, learning and executive functions [13].

Over 100 studies have compared BD patients with normal controls or subjects with other mental disorders regarding performance in attention testing [4]. Attention is usually less impaired in BD than in schizophrenia but more affected in unipolar depression than in normal controls [4]. However, such studies usually do not discriminate the disorder phase affecting the patient at the moment the evaluation [2,3,5,18, 23,29,30]. Performance in attention tests seems to be worse in manic phases. Nevertheless, few studies have compared bipolar patients in different mood states [16, 26].

This study aims at evaluating if performance of BD patients in attention tests varies according to their mood state and if significant difference can be found when comparing performance of BD patients in attention tests with that of normal controls.

## Materials and method

### Participants and setting

This study was performed in the bipolar disorder outpatient research clinic in the Institute of Psychiatry of the Federal University of Rio de Janeiro (Instituto de Psiquiatria da Universidade Federal do Rio de Janeiro - UFRJ), Brazil. The local Ethics Comitee approved the study. All the patients in treatment in the outpatient clinic were invited to take part in the study. Those who accepted gave their written informed consent.

Socioeconomic data were collected as well as information on educational level, sex and age of each patient [6]. Inclusion criteria were: diagnosis of bipolar disorder type I or type II according to DSM-IV-TR criteria [1] and age between 18 and 65 years. Exclusion criteria were: serious non-psychiatric disease and refusal to give written informed consent.

The sample was composed of 101 bipolar patients: 52 in euthymia, 22 in mania and 27 in depression. Thirty (30) normal controls, employees of the Institute of Psychiatry of UFRJ, were also evaluated. The study took place between January, 2013 and December, 2014.

**Instruments**

*Psychiatric evaluation*

A structured clinical interview according to DSM-IV-TR axis, SCID-I, I was performed in order to establish a BD diagnosis [8]. Patients were classified regarding their mood state – mania, depression or euthymia – according to DSM-IV-TR criteria [1].

A psychiatric evaluation of each patient was performed by their physician through the following instruments: Young Mania Rating Scale (YMRS) [37] for manic symptoms, Hamilton Depression Scale (HAM-D17) [14] for depressive symptoms and the Global Assessment of Functioning, bipolar version (CGI-BP) [28] to assess bipolar disorder as a whole. Each physician was previously trained by the research coordinator (EC) regarding the usage of the above-mentioned scales in order to ensure reliability.

*Neuropsychological tests*

After the application of the psychiatric scales, patients went through a neuropsychological evaluation by a neuropsychologist who was not aware of the patients' mood states. The normal controls were submitted to the same evaluation. The neuropsychological instruments were applied in a pre-established pattern for each patient. The testing lasted approximately 30 minutes and evaluated selective and divided attention. Initially a socio-demographic questionnaire was applied. Next a neuropsychological battery was used to evaluate selective attention. It included the following instruments: ***Digit Span*** (direct and reverse orders), Wechsler Adult Intelligence Scale-Revised (WAIS-III) [22,35]; ***Letter-Number Sequencing***, part of Wechsler Adult Intelligence Scale-Revised [35]; ***The Stroop Color and Word Test (SCWT)*** [29]; and ***Search Symbol***, part of Wechsler Adult Intelligence Scale-Revised [35]. ***Trail Making Test Part A e B (TMT-A e B)*** were used to evaluate divided attention [12]. The Verbal Fluency Test, part of the Montreal Communication Evaluation Battery (MAC, in BRAZIL) was used to evaluate the executive functions [9] in order to clarify whether attention problems possibly found could derive from executive function impairment.

Attention performance was tested in BD patients against the same testing in normal controls. Besides, a comparison among mania, depression and euthymia in those patients was also performed.

## Statistical analysis

Data analysis was carried out using SPSS software (version 20.0). Descriptive statistics were used to illustrate the sample characteristics. Differences in socio-demographic and clinical characteristics according to mood state were tested with one-way ANOVAs, followed by pairwise comparisons with t-tests; for non-parametric variables chi-square or Kruskal-Wallis tests were used as an alternative. For clinical characteristics, the comparisons were restricted to BD patients.

A similar approach was used to explore differences in cognitive tests between patient groups, with one-way ANOVAs comparing the four groups being followed by pairwise comparisons with t-tests. To control for the effect of multiple testing, Bonferroni corrections were used. In order to reduce the number of tests, summary measures were used in the case of some tests. Specifically, summary scores were used for the TMT ((Time taken to complete Part B – Time taken to complete Part A)/ Time taken to complete Part A), and for the Stroop test (Correct answers of the interference phase – Correct answers of the color naming phase).

## Results

### Sample characteristics

Clinical and socio-demographic characteristics of the sample can be seen in Table 1. There were no significant group differences in terms of demographic variables ($p > .05$). By contrast, as expected, there were significant differences in YMRS ($F (2, 98) = 70.71$, $p < .001$) and HAM-D scores ($F (2, 98) = 105.36$, $p < .001$), with higher scores in YMRS during mania ($p < .001$) and in HAM-D during depression ($p < .001$). There was also a difference in CGI-BP global scores ($F (2, 98) = 120.90$, $p < .001$), with less severity in euthymia in comparison with the other groups ($p < .001$), and higher severity in depression relative to mania ($p = .010$).

### Performance differences in cognitive tests

Performance of participants in the cognitive tests can be seen in Table 2. There were no significant differences in performance between groups in the digit span (forward: ($F(3, 127) = 0.70$, $p = .555$), backward: ($F(3, 127) = 0.31$, $p = .818$)), TMT ($F(3, 127) = 0.70$, $p = .551$), Letter – Number Sequencing ($F(3, 127) = 0.54$, $p = .654$), phonemic ($F(3, 127) = 0.20$, $p = .894$) and semantic fluency ($F(3, 127) = 1.07$, $p = .367$). There were significant differences for the Stroop test ($F(3, 127) = 5.28$, $p = .002$) and Symbol Search test ($F(3, 127) = 4.18$, $p = .007$). Pairwise comparisons indicated that for the Stroop test, normal controls performed better than all 3 patient groups ($p < .05$), while in the Symbol Search test normal controls outperformed patients in mania only ($p = .005$).

**Discussion**

Since attention consists of a complex system associated with the activation of other cognitive functions, alterations in it jeopardize the remaining executive functions. [20 33]. In this study, bipolar patients in different phases were compared with normal controls regarding their performance in neuropsychological tests of attention. The objective was to verify if there is significant difference in attention performance between BD patients and normal subjects and among the different BD phases. Bipolar patients had worse performance than normal controls in two tests evaluating selective attention. More specifically, in one of the tests the difference was found only in manic patients. No significant difference was found in attention tests among BD phases.

Similarly to our results, several other studies found worse performance in tests of selective attention in BD patients in mania, depression and euthymia when compared with normal controls [4,26]. Selective attention in BD patients is associated with structural and functional impairment in posterior and inferior parietal lobes [25].

Regarding divided attention (digit span), a few studies [10, 11] besides this found no significant difference when comparing bipolar patients with normal controls. However, Rocca et al. [26] observed worse performance in tests of BD patients.

Not many studies have compared the performance on attention tests among the BD mood states. Three of them [17, 27, 32] found more severe attention impairment in mania and depression than in euthymia. However, two other studies [18,19] found no significant differences when comparing euthymia, mania and depression, what is in accordance with the

results in this study. It is possible that the sample size in this study has weakened the statistical power to detect differences among groups.

Cognitive impairment is one of the characteristics of the neuropsychological profiles of BD patients. Cognitive deficits may precede the disease [16, 23]. However, according to a few authors, such deficits get worse along time [15] and are associated with a higher number of affective episodes [34].

Therefore, the development of techniques of cognitive rehabilitation of BD patients are of utmost importance. A few studies [7, 21] have noted that it is possible to observe improvement in cognitive performance and psychosocial functioning in BD patients after just a few sessions of cognitive rehabilitation. Nevertheless, studies in the area are still too few.

## Conclusion

The results in this study show clear impairment in attention in BD, especially in selective attention. Conversely, it is unclear whether the severity of such impairment increases or decreases according to patients' mood states.

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## Tables

Table 1 – Socio-demographic and clinical characteristics of participants

| Variable | Euthymia (n =52) Mean (SD) / Range | Mania (n = 22) Mean (SD) / Range | Depression (n = 27) Mean (SD) / Range | Controls (n = 30) Mean (SD) / Range | Group differences |
|---|---|---|---|---|---|
| Age | 44.5 (10.5) / 23–65 | 46.6 (10.9) / 26–64 | 45.4 (12.2) / 19–65 | 39.3 (13.4) / 20–65 | – |
| Gender* | | | | | |
| Female | 36 (69.2) | 14 (63.6) | 23 (85.2) | 18 (60.0) | – |
| Male | 16 (30.8) | 8 (36.4) | 4 (14.8) | 12 (40.0) | |
| Years of education | 11.9 (4.3) / 2–19 | 12.6 (3.5) / 4–18 | 12.9 (3.1) / 6–19 | 10.6 (3.4) / 2–17 | – |
| Socio -economic status** | | | | | |
| Low incon | 13 (25.0) | 3 (13.7) | 5 (18.5) | 8 (25) | – |
| Medium incon | 30 (57.7) | 14 (63.6) | 20 (74.1) | 17 (57.7) | |
| High incon | 9 (17.3) | 5 (22.7) | 2 (7.4) | 5 (17.3) | |
| YMRS | 1.3 (2.4) / 0–14 | 16.2 (9.2) / 0–41 | 4.0 (3.6) / 0–11 | – | M>E=D |
| HAM-D | 2.7 (2.4) / 0–8 | 4.9 (3.9) / 0–14 | 15.4 (5.4) / 4–25 | – | D>E=M |
| CGI global | 1.3 (0.5) / 1–2 | 3.3 (1.2)/ 1–7 | 4.0 (0.9) / 3–6 | – | D>M>E |

*#(%) Female/Male;** #(%) low/ medium/ high incon; YMRS – Young Mania Rating Scale; HAM-D – Hamilton Depression Rating Scale; CGI – Clinical Global Impression scale.

Table 2 – Cognitive performance of participants

| Variable | Euthymia (n =52) Mean (SD) / Range | Mania (n = 22) Mean (SD) / Range | Depression (n = 27) Mean (SD) / Range | Controls (n = 30) Mean (SD) / Range | Group differences |
|---|---|---|---|---|---|
| Digit Span | | | | | |
| Forward | 7.2 (1.9) / 4–12 | 7.0 (1.7) / 4–11 | 7.2 (2.1) / 4–12 | 6.6 (1.6) / 4–10 | – |
| Backward | 4.0 (2.3) / 1–13 | 3.5 (1.6) / 2–8 | 3.8 (1.7) / 1–9 | 3.7 (2.5) / 0–14 | – |
| Symbol Search | 22.5 (10.3) / 2–41 | 19.0 (8.1) / 6–41 | 22.1 (8.7) / 8–43 | 27.6 (7.2) / 10–43 | C>M; M=D=E |
| TMT* | 1.2 (0.8) / -.55–3.5 | 1.0 (1.1) / -.9–4.3 | 1.1 (0.9) / -.2–3.1 | 1.4 (1.0) / -.8–4 | – |
| Stroop test** | -17.3 (19.1) / -47–36 | -13.6 (15.2) / -33–23 | -11.4 (19.0) / -37–32 | -27.8 (11.0) / -45–-8 | C>E=M=D |
| Phonemic fluency | 17.1 (10.6) / 1–52 | 16.6 (8.2) / 5–37 | 15.6 (6.7) / 2–26 | 16.2 (5.8) / 6–29 | – |
| Semantic fluency | 17.8 (8.0) / 5–43 | 15.0 (8.2) / 0–32 | 15.8 (5.1) / 6–26 | 16.2 (5.0) / 7–30 | – |
| Letter–Number Sequencing | 4.8 (3.0) / 1–13 | 4.4 (2.4)/ 1–11 | 5.4 (2.8) / 1–12 | 5.2 (7.2) / 1–10 | – |

TMT – Trail making test.

*((Time taken to complete Part B – Time taken to complete Part A)/ Time taken to complete Part A); ** (Correct answers of the interference phase – Correct answers of the color naming phase).

# Clinical and cognitive correlates of insight in bipolar disorder

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## Abstract

Background: Insight is greatly impaired in Bipolar Disorder (BD), especially during mania. Cognitive impairment is also present in BD. Despite that, few studies have investigateda possible association between these two aspects.

Objective**:**Compare BD affective states regarding performance in cognitive testing and investigate clinical and cognitive predictors for insight loss in BD.

Methods:The study investigated a sample of 65 patients who were evaluated in one of the BD phases (mania, euthymia or depression). All the subjects were submitted to neuropsychological evaluation and completed theInsight Scale for Affective Disorders (ISAD).The relationship between level of insight and clinical/cognitive variables was analyzed through multiple regression models.

Results:No significant differences were found among BD phases regarding performance in cognitive testing. Insight was more impaired in mania then in depression or euthymia. Predictors for loss of insight were: severity of manic symptoms and impairments in selective attention (Symbol search test), divided attention (Trail making test) and inhibition (Stroop test).

Limitations: The sample size is a potential limitation of the current study. Nevertheless, the results suggest this had limited impact, with group differences being detected for a number of variables; when differences were not found, effect sizes were small.

Conclusion:The results found have important clinical importance, suggesting, for example, that rehabilitation of specific cognitive skills may improve insight in BD.


Keywords:insight, cognition, bipolar disorder, awareness.

## Introduction

Insight is frequently impaired in bipolar disorder (BD), especially in mania (Silva RA et al., 2014). Limited awareness about being ill or specific symptoms may interfere significantly in patient self-evaluation. Poor insight is also associated with reduced treatment compliance and deterioration along the course of the disease. A number of clinical characteristics have shown associations with insight, including level of manic and depressive symptomatology and illness duration, but the predictors may vary according to the phase of BD (Silva RA et al., 2014).

Cognitive changes in BD are relevant and clinically significant. They can affect attention, memory, learning and executive functions (Goodwin, Jamison et al., 2007). Few studies have compared BD phases regarding cognitive performance (Camelo et al., 2013). More specifically, only 4 studies have made such comparison so far, all focused on attention (Van der Wer-Eldering et al., 2011; Maalouf et al., 2010; Mahlberg et al., 2008; Soeiro-de-Souza et al., 2012).

Several studies investigating the relationship between insight and cognitive changes have been conducted in neurological patients and later in schizophrenic patients. Research with neurological patients, including individuals with dementia, has shown that cognitive impairment is associated with poor *insight (*Amanzio et al., 2013, Morris & Mograbi, 2013). Regarding schizophrenic patients, it is unclear whether their lack of insight is more strongly associated with symptom severity or neuropsychological deficits (Zhou et al., 2015). The issue has been lately considered with respect to BD and correlations between lower levels of insight and higher impairment in executive function, verbal fluency and attention have been observed (Dias et al., 2008). Attention has been addressed in only two studies that investigated its relationship with insight in BD. Braw et al.(2010) found a significant correlation between poor insight and attention deficit, but Yen et al., 2008 failed to find a relationship.

In summary, few studies have investigated the relationship between cognitive impairment in BD and loss of insight. Their findings show discrepancies and therefore demand further investigation. Accordingly, the objectives of the present study are to compare BD affective states in terms of performance in cognitive tests and to investigate the relationship between such neuropsychological results and insight in BD.

# Materials and methods

## Participants and setting

This study was performed in the BD outpatient research clinic in the Institute of Psychiatry of the Federal University of Rio de Janeiro (UFRJ), Brazil. The local Research Ethics Committee approved the study. All the patients in treatment in the outpatient clinic were invited to take part in the study. Those who accepted gave their written informed consent.

Inclusion criteria were: diagnosis of bipolar disorder type I or type II according to DSM-V criteria (American Psychiatric Association, 2013) and age between 18 and 65 years. Exclusion criteria were: serious non-psychiatric disease (e.g. vascular disorder, organ failure) and fewer than 4 years of formal education.

The sample was comprised of 65 bipolar patients: 34 in euthymia, 11 in mania and 20 in depression phases. The study was performed between June, 2014 and February, 2015.

## Instruments

### *Clinical and demographic variables*

Socioeconomic data were collected as well as information on educational level, sex and age of each patient. A structured clinical interview according to DSM-V, was performed in order to establish a BD diagnosis. Patients were classified regarding their mood state – mania, depression or euthymia – according to DSM-V criteria (American Psychiatric Association, 2013).

A psychiatric evaluation of each patient was performed by their physician through the following instruments: Young Mania Rating Scale (YMRS) (Young et al., 1978) for manic symptoms, Hamilton Depression Scale (HAM-D17) (Hamilton et al., 1960) for depressive symptoms and the Global Assessment of Functioning, bipolar version (CGI-BP) (Spearing et al. 1997) to assess bipolar disorder severity as a whole. The Insight Scale for Affective Disorders – ISAD – (Olaya et al., 2012) was applied following translation and validation to Brazilian Portuguese (RA da Silva et al., 2015). Each item of ISAD is scored from 1 to 5,

with 1 representing fully preserved insight and 5 indicating the most compromised insight.

Each physician was previously trained by the research coordinator with respect to the usage of the above-mentioned scales in order to ensure reliability. After the application of each scale, patients were individually submitted to cognitive evaluationby a neuropsychologist.

*Cognitive variables*

The neuropsychological instruments were applied in a pre-established order for each patient. The testing took 30 minutes and evaluated several cognitive skills. The neuropsychological battery was comprised of: Digit Span (direct order and backwards), Letter-Number Sequencing and Search Symbol from the Wechsler Adult Intelligence Scale-Revised (Wechsler et al., 2005); The Stroop Color and Word Test (SCWT) (Stroop, 1935), Trail Making Test Part A e B (TMT-A and B; Gaudino et al.,1995), and the verbal fluency test from Montreal Communication Evaluation Battery (Fonseca et al., 2008).

**Statistical analysis**

Data analysis was carried out using SPSS software (version 20.0). Descriptive statistics were used to illustrate the sample characteristics. Differences in socio-demographic, cognitive variables and clinical characteristics according to mood state were tested with one-way ANOVAs, followed by pairwise comparisons with t-tests; for non-parametric variables, such as gender, the chi-square test was used as an alternative.

Differences in insight were explored with one-way ANOVAs, followed by post-hoc t-tests. These were calculated for total insight scores and also specifically for the first three items of the scale, concerning insight about having an illness and its consequences.

Stepwise regression models were calculated to investigate predictors of loss of insight in BD. To keep collinearity low, variables highly correlated with others (such as CGI score) were not included. For similar reasons, in the case of tests measuring related constructs (e.g. forward and backward digit span), the most representative test for each cognitive function was chosen. In the case of some tests (e.g. TMT), summary measures were used. These procedures were also done to reduce the number of predictor variables in the regression models, considering the size of our sample.

The following variables were included: mania symptoms (YMRS total score), depression symptoms (HAM-D total score), semantic fluency (total number of clothes named

in one minute), verbal working memory (backward digit span), attention and speed of processing (Symbol Search), task shifting (Time taken to complete TMT Part B – Time taken to complete TMT Part A)/ Time taken to complete TMT Part A) and inhibition (Stroop test; correct answers of the interference phase – correct answers of the color naming phase).

To avoid inflation of type II error and exclusion of predictors involved in suppressor effects, a backward regression method was used. In this procedure, all the predictors are initially included, and then one variable is deleted in each iteration considering the (lack of) contribution it gives to the model. This is done until no further improvement can be achieved by deleting predictors. The models were evaluated on the basis of the highest explained variance ($R^2$), highest cross-validity (adjusted $R^2$) and best Akaike's Information Criterion (AIC).

## Results

### Sample characteristics

Clinical, cognitive and socio-demographic characteristics of the sample can be seen in Table 1. There were no significant group differences in terms of demographic variables or any cognitive test ($p > .05$). By contrast, as expected, there were significant differences in YMRS ($F (2, 62) = 60.92$, $p < .001$) and HAM-D scores ($F (2, 62) = 70.29$, $p < .001$), with higher scores in YMRS during mania ($p < .001$) and in HAM-D during depression ($p < .001$). There was also a difference in CGI-BP scores ($F (2, 62) = 79.52$, $p < .001$), with less severity in euthymia in comparison with the other groups ($p < .001$).

### Differences in insight

There were significant group differences in total insight scores ($F (2, 62) = 22.59$, $p < .001$), with poorer insight in mania in relation to both euthymia and depression ($p < .001$). Exploring specifically the three first items of the scale, significant differences were found for item #2 ("Awareness of treatment efficacy for current symptoms or preventing relapses"); $F (2, 62) = 7.58$, $p = .001$), with patients in mania showing poorer insight than patients in euthymia ($p = .001$) or depression ($p = .013$). There were no significant group differences for ISAD items #1 ("Awareness of suffering from a affective disorder"); $F (2, 62) = 1.06$, $p = .353$) and #3 ("Awareness of consequences of the illness on work, family and social life"); F

(2, 62) = 2.13, p = .128).

**Regression models**

The regression models can be seen in Table 3. There was no evidence of collinearity in the data, with VIF and tolerance values within the recommended range (Field, 2013). All regression models significantly predicted insight in bipolar disorder ($p < .001$ in all models). The models had high explained variance ($R^2$) and cross-validity (adjusted $R^2$), with minimal decreases in these values with the exclusion of variables. There was marginal improvement of the AIC in model 4, which included four predictors for compromised insight: severity of manic symptoms ($p < .001$), poorer performance in the Symbol Search ($p = .029$) and Stroop ($p = .171$), and longer time completing the TMT ($p = .094$).

## Discussion

In this study, patients with BD were submitted to cognitive and insight evaluation with the aim of verifying if performance on the tests varied according to patient mood state as well as if there was a significant relationship between cognitive deficit and insight impairment. Patients in mania had poorer global insight and insight about treatment efficacy. No significant difference in cognitive performance was found when comparing mania, depression and euthymia. Regression models indicated that the best predictors for loss of insight in BD are severity of manic symptoms and cognitive performance in the TMT, Symbol search and Stroop test.

To the best of our knowledge, only four studies have so far compared BD mood states in relation to attention skills. In two of these studies, evaluating sustained attention, depressed patients had worse(Van der Wer- Eldering et al., 2011)or similar performance (Maalouf et al., 2010) when compared with bipolar patients in euthymia. In the two other studies, evaluating divided and selective attention (Mahlberg et al., 2008; Soeiro-de-Souza et al., 2012), depressed patients had better performance than those in mania. It is possible that no differences were found in the current study because of small subsamples for each BD phase. That is unlikely though, since effect sizes for differences in the cognitive tests were so low that very large samples would be needed to detect differences assuming similar effect sizes. A

more likely explanation is that the severity of BD in the sample was mild, with reduced cognitive impairment in participants.

Regarding insight, the results in this study were similar to those of several others that found higher impairment in mania than in euthymia or depression (Cassidy et al., 2010; Silva RA, et al. 2014). Furthermore, severity of manic symptomatology was a predictor of loss of insight in the regression models. In addition to the overall score, impairments during mania were found for insight about treatment efficacy. This highlights the potential effect of insight in treatment compliance, impacting on the prognosis of the illness (Silva RA et al., 2014).

It was also noted that impaired performance in Symbol Search, Stroop and TMT testing is related to poorer insight. Not many studies investigate the relationship between insight level and cognitive skills in BD. The association with the TMT confirms previous findings by Dias et al. (2008). To the best of our knowledge, no other study has indicated a relationship between performance in the Stroop and Symbol search tasks with insight into BD. These three tasks have in common the measurement of executive functions, which are thought to give an important contribution for awareness (Amador & David, 2004). Models of awareness have suggested that mechanisms based on executive functions are essential for the monitoring of performance, including detection and response to errors (Morris and Mograbi, 2013). Frontal lobe dysfunction has been proposed as an important pathological mechanism in BD, and it has been suggested that prefrontal cortex (Miller & Cohen 2001) and frontoparietal dysfunction *(Dias et al., 2008; Varga et al., 2006) are related to poor insight in BD.*

It is notable that in terms of the specific abilities measured by these tasks, attention, cognitive flexibility and inhibition feature prominently. This may suggest that patients during mania have poor abilities to appropriately select and encode information about their condition. Some authors suggest that there is no difference between attention and awareness, with both corresponding to the same cognitive phenomenon (Posner, 1994; Merikle and Joordens, 1997; Mole, 2008; De Brigard and Prinz, 2010), In addition, impairments in cognitive flexibility may indicate poor ability to incorporate new information, discrepant with previous self-knowledge. Altogether, these would lead to a distorted sense of self ability, with personal information about ability being compromised (Morris & Mograbi, 2013).

A potential limitation of the current study refers to the sample size. However, the results suggest that sample size had limited impact, with group differences being detected for a number of variables; as indicated, when differences were not found, effect sizes were small, such that significant group differences would only be found with much larger samples. In

addition, the regression models were robust, explaining a very high proportion of variance in insight.

## Conclusion

The results in this study show that insight is worse in the manic phase and that there is a correlation between lower levels of insight and higher impairment in performance of attention, inhibition and cognitive flexibility testing. Identifying such predictors allows planning cognitive rehabilitation so as to target insight improvement, leading to better treatment compliance and prognosis.

Conflict of interest:

The authors declare no conflict of interest.

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## Tables

| Variable | Euthymia (n =34) Mean (SD) / Range | Mania (n = 11) Mean (SD) / Range | Depression (n = 20) Mean (SD) / Range | Group differences |
|---|---|---|---|---|
| Age | 44.5 (9.6) / 29–64 | 46.5 (11.5) / 31–63 | 45.1 (12.1) / 19–63 | – |
| Gender* | 24/10 | 6/5 | 17/3 | – |
| Years of education | 11.0 (4.0) / 2–19 | 13.4 (4.2) / 4–17 | 12.6 (3.1) / 6–18 | – |
| YMRS | 1.3 (2.6) / 0–14 | 20.3 (10.3) / 8–41 | 4.3 (3.6) / 0–10 | M>E=D |
| HAM-D | 2.5 (2.3) / 0–8 | 4.3 (2.8) / 0–8 | 15.0 (5.8) / 4–25 | D>E=M |
| CGI-BP global | 1.3 (0.5) / 1–2 | 3.4 (1.2)/ 1–7 | 4.0 (0.9) / 3–6 | E <M=D |
| Digit Span | | | | |
| Forward | 6.9 (1.9) / 4–11 | 7.4 (2.1) / 4–11 | 6.8 (2.2) / 4–12 | – |
| Backward | 3.8 (2.5) / 1–13 | 3.5 (2.0) / 2–8 | 4.0 (1.7) / 2–9 | – |
| Symbol search | 22.1 (10.3) / 5–41 | 20.4 (10.1) / 6–41 | 21.6 (8.8) / 8–43 | – |
| TMT* | 1.3 (0.9) / -0.5–3.5 | 1.5 (1.1) / 0.4–4.3 | 1.3 (1.0) / -0.2–3.3 | – |
| Stroop test** | -22.8 (13.9) / -47–27 | -17.2 (8.0) / -31–-4 | -15.6 (16.7) / -37–28 | – |
| Phonemic fluency | 18.0 (10.3) / 2–52 | 15.2 (9.2) / 5–37 | 15.0 (6.6) / 2–23 | – |
| Semantic fluency | 17.2 (7.5) / 5–43 | 14.0 (8.0) / 3–32 | 15.6 (5.0) / 7–26 | – |

Table 1 – Socio-demographic, clinical and cognitive characteristics of participants

*# Female/Male; YMRS – Young Mania Rating Scale; HAM-D – Hamilton Depression Rating Scale; CGI-BP– Clinical Global Impression scale–bipolar version;TMT – Trail making test.

*(Time taken to complete Part B – Time taken to complete Part A)/ Time taken to complete Part A); ** (Correct answers of the interference phase – Correct answers of the color naming phase).

| Variable | Euthymia (n =34) Mean (SD) / Range | Mania (n = 11) Mean (SD) / Range | Depression (n = 20) Mean (SD) / Range | Group differences |
|---|---|---|---|---|
| ISAD item #1 | 1.7 (1.2), 1–5 | 2.0 (1.7), 1–5 | 1.3 (1.1), 1–5 | – |
| ISAD item #2 | 1.1 (0.2), 1–2 | 2.2 (1.7), 1–5 | 1.2 (0.8), 1–4 | E = D < M |
| ISAD item #3 | 1.7 (1.3), 1–5 | 2.4 (1.8), 1–5 | 1.3 (1.0), 1–5 | – |
| ISAD total score | 18.8 (2.4), 17–27 | 32.4 (12.8), 17–63 | 20.4 (4.3), 17–32 | E = D < M |

Table 2 – Insight scores of participants

Table 3 – Regression models with predictors for ISAD total scores

| | Model 1 | | Model 2 | | Model 3 | | Model 4 | | Model 5 | |
|---|---|---|---|---|---|---|---|---|---|---|
| Variable | *B* | p-value | *B* | p-value | *β* | p-value | *β* | p-value | *B* | p-value |
| YMRS | .71 | <.001 | .71 | <.001 | .72 | <.001 | .74 | <.001 | .73 | <.001 |
| Symbol search | -.12 | .181 | -.13 | .155 | -.13 | .153 | -.18 | .029 | -.15 | .060 |
| TMT* | .13 | .099 | .13 | .100 | .13 | .094 | .13 | .094 | .13 | .096 |
| Stroop** | -.10 | .244 | -.11 | .187 | -.10 | .221 | -.11 | .171 | | |
| Semantic fluency | -.17 | .099 | -.16 | .108 | -.11 | .225 | | | | |
| Backward digit span | .11 | .209 | .11 | .222 | | | | | | |
| HAM-D | -.04 | .648 | | | | | | | | |
| Model p-value | <.001 | | <.001 | | <.001 | | <.001 | | <.001 | |
| $R^2$ | .66 | | .66 | | .65 | | .64 | | .63 | |
| $Adjusted R^2$ | .62 | | .62 | | .62 | | .62 | | .61 | |

YMRS – Young Mania Rating Scale; HAM-D – Hamilton Depression Rating Scale; TMT – Trail making test.

*(Time taken to complete Part B – Time taken to complete Part A)/ Time taken to complete Part A); ** (Correct answers of the interference phase – Correct answers of the color naming phase).

# Loss of insight and depression contribute to increased disability in bipolar disorder

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Increasingly, evidence suggests that bipolar disorder (BD) may contribute to significant disability and reduced functioning in work, family and social life[1]. Previous studies explored factors related to disability in BD but few investigated cognitive correlates and, to the best of our knowledge, the relationship between loss of insight and disability has never been studied in BD.

Forty patients with BD (19 in euthymia, 5 in mania and 16 in depression; DSM-IV criteria) were recruited in the outpatient unitof the Institute of Psychiatry of the Federal University of Rio de Janeiro (the project received ethics approval and participants provided written informed consent). Participants completedthe Sheehan Disability Scale (SDS)[2], a battery of cognitive tests (Digit Span, Letter-Number Sequencing, Stroop Test, Symbol Search, Trail Making Test) and a clinical examination including measures of illness severity (CGI-BP), manic and depressive symptoms (YMRS and HAM-D, respectively), insight (ISAD) and positive psychotic symptoms (PANSS-p). Pearson correlations were calculated to identify factors linked to disability, and significant variables were included instepwisemultiple regression models investigating predictors of disability in BD.

Illness severity correlated with total SDS scores ($r$ =.33, p =.037) and the social life disability subscale ($r$ =.34, p =.031). Depressive symptoms correlated with total SDS scores ($r$ =.42, p =.007), social life disability ($r$ =.41, p =.007) and family life disability ($r$ =.35, p =.028). Loss of insight correlated with total SDS scores ($r$ =.48, p =.003), social life disability ($r$ =.51, p =.001), family life disability ($r$ =.37, p =.026) and showed a trend for a relationship with work disability ($r$ =.31, p =.065). There were no significant correlations between disability and cognitive abilities or other clinical variables (p >.05). A multiple regression analysis with total SDS scores as the dependent variable and depressive symptoms, loss of insight and BD severity as predictors was calculated. A model including depressive symptoms (standardized β =.34, p =.033) and loss of insight (standardized β =.36, p =.022) significantly predicted (p =.001) disability in BD, with moderate explained variance ($R^2$ =.33) and cross-validity (adjusted $R^2$ =.29).

The results highlight the pervasive role of loss of insight, indicating that it may also lead to increased disability, in particular of social and family life. One potential explanation is that loss of insight may interfere in interpersonal relationships. Additionally, loss of insight

impacts on treatment compliance[3], which can also lead to increased disability. The relationship between depressive symptoms and disability has been reported consistently in previous studies[1]. The results emphasize the need to manage these symptoms, even outside the acute stages of the illness, avoiding excessive disability in BD patients.

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## 5.CONCLUSÕES

A partir dos dados apresentados nos artigos presentes nesta dissertação, podemos concluir que os pacientes bipolares apresentam déficits na atenção em todas fases da doença, porém esse prejuízo é mais grave na fase de mania do que em depressão e eutimia. Quando comparados aos controles normais, os pacientes com TB apresentam um maior prejuízo significativo na atenção seletiva. Além disso, evidenciou-se que sintomas maníacos mais graves e performance prejudicada em testes de atenção seletiva, atenção dividida e controle inibitório correlacionam-se com níveis mais baixos de insight. Por fim, nossos resultados indicaram que a falta de insight contribui para uma maior incapacitação sócio-ocupacional no TB.

O planejamento futuro é de estudar a reabilitação cognitiva de pacientes com TB, tema ainda muito incipiente na literatura científica.

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# 7. ANEXOS

## 7.1. Anexo I

### Termo de Consentimento Livre e Esclarecido

O sr.(a) está sendo assistido num setor de pesquisa do ambulatório do Instituto de Psiquiatria da Universidade Federal do Rio de Janeiro. A linha de pesquisa que estuda o transtorno bipolar é coordenada pelo prof. Elie Cheniaux. As consultas médicas e psicológicas realizadas aqui, assim como as prescrições terapêuticas, são idênticas às que acontecem no ambulatório geral desta instituição. Todavia, durante as consultas, o sr.(a) é submetido a uma avaliação mais detalhada (avaliação neuropsicológica) através do uso de instrumentos de pesquisa, como questionários e escalas que avaliam sua atenção durante o período de 30 minutos. Após a avaliação da atenção pela psicóloga Evelyn Miranda Camelo, o Sr. será submetido ao exame de eletroencefalografia (EEG) realizado pela psicóloga Bruna Velasques e pela fisioterapeuta Juliana Bittencourt. Esta avaliação tem como o objetivo a ampliação do conhecimento científico sobre o transtorno bipolar.Esta avaliação tem como o objetivo a ampliação do conhecimento científico sobre o transtorno bipolar.

Essa pesquisa está de acordo com os procedimentos éticos estabelecidos pela Resolução 96/96, do Conselho Nacional de Saúde. Ressalta-se que a identidade dos participantes será mantida em sigilo e que os dados obtidos serão de uso exclusivo para fins de pesquisa, podendo os participantes receber resultados dos instrumentos aplicados, se assim desejarem.

A pesquisa pode causar um risco mínimo que está relacionado ao desconforto com a aplicação da bateria de testes. Com isso, a qualquer momento, o sr.(a) poderá desistir de sua participação na pesquisa, sendo então encaminhado para o ambulatório geral desta instituição.

Eu, _____, identidade nº _____, declaro que li e compreendi o que me foi explicado e, dessa forma, concordo em participar do estudo.

Rio de Janeiro, ____ de _____ de _____.

Dados da Pesquisadora Responsável: Evelyn V.M.Camelo

End: Barão de Mesquita, 595/203- Tijuca.

Contato: 94723522

E-mail:evypsi@gmail.com

Dados do Comitê de Ética e Pesquisa –IPUB

End: Rua Venceslau Brás, 71 fds. Prédio da Direção – 2º andar – sala do CEP. 22.290-140 – Campus Praia Vermelha - Botafogo – Rio de Janeiro.**Telefone/fax:** 55 (21) 3873-5510

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Pesquisador Sujeito

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## 7.2. Anexo II

**YMRS – Escala de avaliação de mania de Young**
**Item - definição**

*01. Humor e afeto elevados*

Este item compreende uma sensação difusa e prolongada, subjetivamente experimentada e relatada pelo indivíduo, caracterizada por sensação de bem-estar, alegria, otimismo, confiança e ânimo. Pode haver um afeto expansivo, ou seja, uma expressão dos sentimentos exagerada ou sem limites, associada à intensa relação com sentimentos de grandeza (euforia). O humor pode ou não ser congruente ao conteúdo do pensamento.

(0) Ausência de elevação do humor ou afeto.

(1) Humor ou afeto discreta ou possivelmente aumentados, quando questionado.

(2) Relato subjetivo de elevação clara do humor; mostra-se otimista, autoconfiante, alegre; afeto apropriado ao conteúdo do pensamento.

(3) Afeto elevado ou inapropriado ao conteúdo do pensamento; jocoso.

(4) Eufórico; risos inadequados, cantando.

(X) Não avaliado.

*02. Atividade motora - energia aumentada*

Este item compreende a psicomotricidade - e expressão corporal - apresentada pelo paciente, incluindo a sua capacidade em controlá-la, variando desde um grau de normalidade, até um estado de agitação, com atividade motora sem finalidade, não influenciada por estímulos externos. O item compreende ainda o relato subjetivo do paciente, quanto à sensação de energia, ou seja, capacidade de produzir e agir.

(0) Ausente.

(1) Relato subjetivo de aumento da energia ou atividade motora.

(2) Apresenta-se animado ou com gestos aumentados.

(3) Energia excessiva; às vezes hiperativo; inquieto (mas pode ser acalmado).

(4) Excitação motora; hiperatividade contínua (não pode ser acalmado).

(X) Não avaliado.

*03. Interesse sexual*

Este item compreende idéias e/ou impulsos persistentes relacionados a questões sexuais, incluindo a capacidade dopaciente em controlá-los. O interesse sexual pode restringir-se a pensamentos e desejos não concretizados, em geral verbalizados apenas após solicitação, podendo chegar até a um comportamento sexual frenético e desenfreado, sem qualquer controle ou crítica quanto a riscos e normas morais.

(0) Normal; sem aumento.

(1) Discreta ou possivelmente aumentado.

(2) Descreve aumento subjetivo, quando questionado.

(3) Conteúdo sexual espontâneo; discurso centrado em questões sexuais; auto-relato de hipersexualidade.

(4) Relato confirmado ou observação direta de comportamento explicitamente sexualizado, pelo entrevistador ou outras pessoas.

(X) Não avaliado.

*04. Sono*

Este item inclui a redução ou falta da capacidade de dormir, e/ou a redução ou falta de necessidade de dormir, parasentir-se bem-disposto e ativo.

(0) Não relata diminuição do sono.

(1) Dorme menos que a quantidade normal, cerca de 1 hora a menos do que o seu habitual.

(2) Dorme menos que a quantidade normal, mais que 1 hora a menos do que o seu habitual.

(3) Relata diminuição da necessidade de sono.

(4) Nega necessidade de sono.

(X) Não avaliado.

*05. Irritabilidade*

Este item revela a predisposição afetiva para sentimentos/emoções como raiva ou mau-humor apresentados pelo paciente frente a estímulos externos. Inclui baixo-limiar à frustração, com reações de ira exagerada, podendo chegar a um estado constante de comportamento desafiador, querelante e hostil.

(0) Ausente.

(2) Subjetivamente aumentada.

(4) Irritável em alguns momentos durante a entrevista; episódios recentes (nas últimas 24 horas) de ira ou irritação na enfermaria.

(6) Irritável durante a maior parte da entrevista; ríspido e lacônico o tempo todo.

(8) Hostil; não cooperativo; entrevista impossível.

(X) Não avaliado.

*06. Fala* (*velocidade e quantidade*)

Este item compreende a velocidade e quantidade do discurso verbal apresentado pelo paciente. Inclui sua capacidade de percebê-lo e controlá-lo, por exemplo, frente a solicitações para que permaneça em silêncio ou permita que o entrevistador fale.

(0) Sem aumento.

(2) Percebe-se mais falante do que o seu habitual.

(4) Aumento da velocidade ou quantidade da fala em alguns momentos; verborréico, às vezes (com solicitação, consegue-se interromper a fala).

(6) Quantidade e velocidade constantemente aumentadas; dificuldade para ser interrompido (não atende a solicitações; fala junto com o entrevistador).

(8) Fala pressionada, ininterruptível, contínua (ignora a solicitação do entrevistador).

(X) Não avaliado.

*07. Linguagem - Distúrbio do pensamento*

Este item refere-se a alterações da forma do pensamento, avaliado pelas construções verbais emitidas pelo paciente. O pensamento pode estar mais ou menos desorganizado, de acordo com a gravidade das alterações formais do pensamento, descritas a seguir:

ıı*Circunstancialidade*: fala indireta que demora para atingir o ponto desejado, mas eventualmente vai desde o ponto de origem até o objetivo final, a despeito da superinclusão de detalhes;

ıı*Tangencialidade*: incapacidade para manter associações do pensamento dirigidas ao objetivo - o paciente nunca chega do ponto inicial ao objetivo final desejado;

ıı*Fuga de idéias*: verbalizações rápidas e contínuas, ou jogos de palavras que produzem uma constante mudança de uma idéia para outra; as idéias tendem a estar conectadas e, mesmo em formas menos graves, podem ser difíceis de ser acompanhadas peloouvinte;

ıı*Ecolalia consonante*: repetição automática de palavras ou frases, com entonação e forma que produzem efeito sonoro de rima;

ıı*Incoerência*: fala ou pensamento essencialmente incompreensíveis aos outros, porque as palavras ou frases são reunidas sem uma conexão com lógica e significado.

(0) Sem alterações.

(1) Circunstancial; pensamentos rápidos.

(2) Perde objetivos do pensamento; muda de assuntos freqüentemente; pensamentos muito acelerados.

(3) Fuga de idéias; tangencialidade; dificuldade para acompanhar o pensamento; ecolalia consonante.

(4) Incoerência; comunicação impossível.

(X) Não avaliado.

*08. Conteúdo*

Este item compreende idéias e crenças apresentadas pelo paciente, variando, de acordo com a intensidade, de idéias novas e/ou incomuns ao paciente, ideação supervalorizada (ou seja, crença falsa, intensamente arraigada, porém susceptível à argumentação racional), a delírios (crenças falsas, baseadas em inferências incorretas sobre a realidade, inconsistentes com a inteligência e antecedentes culturais do paciente, e que não podem ser corrigidas pela argumentação). Conteúdos comumente encontrados no paciente maníaco, incluem:

ıı*Idéias místicas*: de conteúdo religioso;

ıı*Idéias paranóides*: crença de estar sendo molestado ou perseguido;

ıı*Idéias de grandeza*: concepção exagerada da própria importância, poder ou identidade, incluindo posses materiais, qualidades incomuns e relacionamentos especiais com personalidades famosas ou entidades místicas;

ıı*Idéias de referência*: crença de que o comportamento dos outros tem relação consigo próprio ou de que eventos, objetos ou outras pessoas possuem um significado particular e incomum para si.

(0) Normal.

(2) Novos interesses e planos compatíveis com a condição sócio-cultural do paciente, mas questionáveis.

(4) Projetos especiais totalmente incompatíveis com a condição sócio-econômica do paciente; hiper-religioso.

(6) Idéias supervalorizadas.

(8) Delírios.

(X) Não avaliado.

*09. Comportamento disruptivo agressivo*

Este item compreende a atitude e as respostas do paciente ao entrevistador e à situação da entrevista. O paciente pode apresentar-se desconfiado ou irônico e sarcástico, mas ainda assim respondendo aos questionamentos, ou então não cooperativo e francamente agressivo, inviabilizando a entrevista.

(0) Ausente, cooperativo.

(2) Sarcástico; barulhento, às vezes, desconfiado.

(4) Ameaça o entrevistador; gritando; entrevista dificultada.

(6) Agressivo; destrutivo; entrevista impossível.

(X) Não avaliado.

*10. Aparência*

Este item compreende a apresentação física do paciente, incluindo aspectos de higiene, asseio e modo de vestir-se.

(0) Arrumado e vestido apropriadamente

(1) Descuidado minimamente; adornos ou roupas minimamente inadequados ou exagerados.

(2) Precariamente asseado; despenteado moderadamente; vestido com exagero.

(3) Desgrenhado; vestido parcialmente; maquiagem extravagante.

(4) Completamente descuidado; com muitos adornos e adereços; roupas bizarras.

(X) Não avaliado

*11. Insight* (*discernimento*)

Este item refere-se ao grau de consciência e compreensão do paciente quanto ao fato de estar doente. Varia de um entendimento adequado (afetivo e intelectual) quanto à presença da doença, passando por concordância apenas frente à argumentação, chegando a uma negação total de sua enfermidade, referindo estar em seu comportamento normal e não necessitando de qualquer tratamento.

(0) Insight presente: espontaneamente refere estar doente e concorda com a necessidade de tratamento

(1) Insight duvidoso: com argumentação, admite possível doença e necessidade de tratamento.

(2) Insight prejudicado: espontaneamente admite alteração comportamental, mas não a relaciona com a doença, ou discorda da necessidade de tratamento.

(3) Insight ausente: com argumentação, admite de forma vaga alteração comportamental, mas não a relaciona com a doença e discorda da necessidade de tratamento.

(4) Insight ausente: nega a doença, qualquer alteração comportamental e necessidade de tratamento.

(X) Não avaliado.

## 7.3. Anexo III

### Guia da entrevista estruturada para a escala de avaliação de depressão de Hamilton

Nome do paciente: _____

Entrevistador: _____

Data: ____/____/____

**Introdução:**

Gostaria de lhe fazer algumas perguntas sobre a última semana. Como você tem se sentido desde a última (dia da semana)? Sepaciente ambulatorial: Você tem trabalhado? Se não: Especifique por que não?

**1.** Como tem estado seu humor na última semana?

Você tem se sentido para baixo ou deprimido?

Triste? Sem esperança?

Na última semana, com que freqüência você se sentiu (utilize a palavra referida pelo paciente)? Todos os dias? O dia inteiro?

Você tem chorado?

***Humor depressivo (tristeza, desesperança, desamparo, inutilidade)***

0- ausente.

1- sentimentos relatados somente se perguntados.

2- sentimentos relatados espontaneamente, com palavras.

3- comunica os sentimentos não com palavras, mas com expressão facial, postura, voz e tendência ao choro.

4- o paciente comunica quase que exclusivamente esses sentimentos, tanto em seu relato verbal como na comunicação não-verbal.

*Se pontuou de 1 a 4, pergunte:* ***Há quanto tempo você tem se sentido desta maneira?***

**2.** Você tem se sentido especialmente autocrítico nesta última semana, sentindo que fez coisas erradas ou decepcionou outraspessoas?

SE SIM: quais foram esses pensamentos?

Você tem se sentido culpado em relação a coisas que fez ou não fez?

Você tem pensado que, de alguma forma, você é responsável pela sua depressão?

Você sente que está sendo punido ficando doente?

***Sentimentos de culpa:***

0- ausente.

1- auto-recriminação, acha que decepcionou outras pessoas.

2- idéias de culpa ou ruminações de erros ou ações pecaminosas (más) no passado.

3- paciente acha que a doença atual é uma punição (castigo). Delírio de culpa.

4- ouve vozes que o acusam ou denunciam e/ou tem alucinações visuais ameaçadoras.

**3.** Nessa última semana, você teve pensamentos de que não vale a pena viver ou que você estaria melhor morto? ou pensamentosde se machucar ou até de se matar?

SE SIM: o que você tem pensado sobre isso? Você já se machucou?

***Suicídio:***

0- ausente.

1- acha que não vale a pena viver.

2- deseja estar morto ou pensa em uma possível morte para si.

3- idéias ou atitudes suicidas.

4- tentativas de suicídio.

**4.** Como tem sido seu sono na última semana?

Você teve alguma dificuldade em iniciar o sono? Após se deitar, quanto tempo leva para conseguir dormir?

Em quantas noites nesta última semana você teve problemas para iniciar o sono?

***Insônia inicial:***

0- sem dificuldades para iniciar o sono.

1- queixa de dificuldade ocasional para iniciar o sono, ou seja, mais que meia hora.

2- queixa de dificuldade para iniciar o sono todas as noites.

**5.** Durante essa última semana, você tem acordado no meio da noite?

SE SIM: você sai da cama? o que você faz? (somente vai ao banheiro?)

Quando volta para a cama, você volta a dormir logo?

Você sente que seu sono é agitado ou perturbado em algumas noites?

***Insônia intermediária:***

0- sem dificuldade.

1- queixa de agitação e perturbação durante a noite.

2- acorda durante a noite – qualquer saída da cama (exceto por motivos de necessidade fisiológica).

**6.** A que horas você tem acordado pela manhã na última semana?

Se cedo: acorda com despertador ou sozinho? A que horas você normalmente acordava (ou seja, antes de ficar deprimido)?

***Insônia tardia:***

0- sem dificuldade.

1- acorda durante a madrugada, mas volta a dormir.

2- não consegue voltar a dormir se levantar da cama durante a noite.

**7.** Como você tem passado seu tempo na última semana (quando não está no trabalho)?
Você se sente interessado em fazer (essas atividades) ou você tem de se forçar?
Você parou de fazer atividades que costumava fazer? SE SIM: Por quê?
Há alguma coisa que você aguarda ansiosamente?
(no seguimento): Seu interesse voltou ao normal?

***Trabalho e atividades:***

0- sem dificuldades.

1- pensamentos e sentimentos de incapacidade, fadiga ou fraqueza, relacionados a atividades, trabalho ou passatempos.

2- perda de interesse em atividades, passatempos ou trabalho, quer relatado diretamente pelo paciente, quer indiretamente por desatenção, indecisão ou vacilação (sente que precisa se esforçar para o trabalho ou outras atividades).

3- diminuição no tempo gasto em atividades ou queda de produtividade. No hospital, o paciente ocupa-se por menos de três horas por dia em atividades (trabalho hospitalar ou passatempos) com exceção das tarefas rotineiras da enfermaria.

4- parou de trabalhar devido à doença atual. No hospital, sem atividades, com exceção das tarefas rotineiras da enfermaria, ou se não consegue realizá-las sem ajuda.

**8.** Avaliação baseada na observação durante a entrevista:

***Retardo (lentificação do pensamento e da fala, dificuldade de concentração, diminuição da atividade motora):***

0 pensamentos e fala normais.

1 lentificação discreta à entrevista.

2 lentificação óbvia durante à entrevista.

3 entrevista difícil.

4 estupor completo.

**9.** Avaliação baseada na observação durante a entrevista:

***Agitação:***

0 nenhuma.

1 inquietação.

2 mexe as mãos, cabelos etc.

3 movimenta-se bastante, não consegue permanecer sentado durante a entrevista.

4 retorce as mãos, rói as unhas, puxa os cabelos, morde os lábios.

**10.** Você tem se sentido especialmente tenso ou irritado nesta última semana?

Você tem estado preocupado com coisas pouco importantes com as quais normalmente não se preocuparia? SE SIM: Como com o quê, por exemplo?

***Ansiedade psíquica:***

0 sem dificuldade.

1 tensão e irritabilidade subjetivas.

2 preocupa-se com trivialidades.

3 atitude apreensiva aparente no rosto ou na fala.

4 paciente expressa medo sem ser perguntado.

**11.** Na última semana, você sofreu de alguns dos seguintes sintomas físicos?

*Leia a lista, parando após cada sintoma para resposta.*

O quanto esses sintomas o incomodaram na última semana? Quão intensos foram? Quanto tempo ou com que freqüência os teve?

*Nota: não considerar se claramente relacionados à medicação (por exemplo, boca seca e imipramina).*

***Ansiedade - somática:***

Concomitantes fisiológicos da ansiedade, como:

GI: boca seca, flatulência, indigestão, diarréias, cólicas, eructações.

CV: palpitação, cefaleias.

Respiratórios: hiperventilação, suspiros.

Ter de urinar frequentemente.

Sudorese.

0 ausente.

1 duvidoso ou trivial: sintomas menores, relatados quando questionados.

1 leve: paciente descreve espontaneamente os sintomas, que não são acentuados ou incapacitantes.

3 moderado: mais do que 2 sintomas e com maior freqüência. São acompanhados de estresse subjetivo e prejudicam o funcionamento normal.

4 grave: numerosos sintomas, persistentes e incapacitantes na maior parte do tempo, ou ataques de pânico quase diariamente.

**12.** Como tem estado seu apetite nesta última semana? (Como se compara ao seu apetite habitual?).

Você tem tido que se força a comer?

As outras pessoas têm insistir para você comer?

***Sintomas gastrointestinais – somáticos:***

0 nenhum.

1 perda de apetite, mas come sem necessidade de insistência.

2 dificuldade para comer se não insistirem.

**13.** Como tem estado sua "energia" nesta última semana?

Você se sente cansado o tempo todo?

Nesta última semana, você teve dor nas costas, dor de cabeça ou dor muscular?

Nesta última semana, você tem sentido um peso nos membros, nas costas ou na cabeça?

***Sintomas somáticos gerais:***

0 nenhum.

1 peso em membros, costas ou cabeça; dor nas costas, na cabeça ou nos músculos. Perda de energia e fatigabilidade.

2 qualquer sintoma bem caracterizado e nítido.

**14.** Como tem estado seu interesse por sexo nesta semana? (não estou lhe perguntando sobre seu desempenho, mas sobre seu interesse por sexo- o quanto você tem pensado nisso?

Houve alguma mudança em seu interesse por sexo (em relação à época em que você não estava deprimido)?

Isso é algo em que você tem pensado muito? Se não: isso é pouco habitual para você?

***Sintomas Genitais – (como perda de libido, distúrbios menstruais):***

0 ausentes.

1 leves ou infreqüentes: perda de libido, desempenho sexual prejudicado.

2 óbvio e graves: perda completa do interesse sexual.

**15.** Na última semana, o quanto seus pensamentos têm focalizado na sua saúde física ou no funcionamento de seu corpo (comparado ao seu pensamento habitual).

Você se queixa muito de sintomas físicos?

Você tem-se deparado com situações em que você pede ajuda para fazer coisas que poderia fazer sozinho?

SE SIM: Como o quê, por exemplo? Com que freqüência isso tem ocorrido?

***Hipocondria:***

0 ausente.

1 auto-observação aumentada (com relação ao corpo).

2 preocupação com a saúde.

3 queixas freqüentes, pedidos de ajuda etc.

4 delírios hipocondríacos.

**16.** Você perdeu algum peso desde que essa (DEPRESSÃO) começou? SE SIM: Quanto?

SE INCERTO: Você acha que suas roupas estão mais folgadas?

No Seguimento: Você voltou a ganhar peso?

**Perda de Peso (desde o início da doença ou da última avaliação)**

0 sem perda de peso ou perda de peso NÃO causada pela doença atual.

1 perda de peso provavelmente causada pela doença atual. Perda de menos de meio quilo.

2 perda de peso definitivamente causada pela doença atual. Perda de meio quilo ou mais.

**17.** Avaliação baseada na observação.

***Crítica (Conseqüência da doença):***

0 reconhece estar deprimido e doente OU não estar deprimido no momento.

1 reconhece estar, mas atribui a causa à má alimentação, ao clima, ao excesso de trabalho, a um vírus, à necessidade de descansoetc.

2 nega estar doente.

### 7.4. Anexo IV

**Escala de impressão clínica global - versão bipolar (CGI-BP)**

(Spearing et al., 1997)

**Item I – Gravidade da doença**

Considerando sua experiência clínica total com pacientes bipolares, quão gravemente doente tem estado o paciente durante a última semana?

MANIA: _____

DEPRESSÃO: _____

TR. BIPOLAR GLOBAL: _____

*Em caso de tanto mania como depressão terem escore igual ou superior a 3, discriminar:*

*( ) estado misto ( ) virada para mania ( ) virada para depressão*

Escores:

**1** – **Normal, não doente** (sem sintomas).

**2** – **Minimamente doente** (sintomas mínimos, manteve funcionamento eficiente).

**3** – **Levemente doente** (baixo nível de sintomas, sofrimento subjetivo, pouco ou nenhum prejuízofuncional).

**4** – **Moderadamente doente** (alguns sintomas proeminentes, prejuízo funcional moderado).

**5** – **Acentuadamente doente** (sintomas significativos, prejuízo funcional muito substancial).

**6** – **Gravemente doente** (sintomas muito evidentes, incapaz de funcionar na maioria das áreas).

**7** – **Muito gravemente doente** (sintomas extremos, completamente incapacitado, requerendo cuidadosextra).

## 7.5. Anexo V

**PANSS – Positive Scale**

**P1 – DELÍRIOS**: Crenças que são infundadas, irrealistas, e idiossincráticas.

Base para avaliar: conteúdo do pensamento expresso na entrevista e sua influência nas relações sociais e no comportamento.

**1 – Ausente** – A definição não se aplica.

**2 – Mínimo** – Patologia questionável: pode estar no extremo superior dos limites normais.

**3 – Leve** – Presença de um ou dois delírios que são vagos, não cristalizados e não tenazmente mantidos. Os delírios não interferem com o pensamento, relações sociais ou comportamento.

**4 – Moderado** – Presença de uma série de delírios instáveis, pobremente formados, ou de alguns delírios bem formados que ocasionalmente interferem com o pensamento, relações sociais ou comportamento.

**5 - Moderado grave** – Presença de numerosos delírios bem formados que são tenazmente mantidos e ocasionalmente interferem com o pensamento, relações sociais ou comportamento.

**6 – Grave** – Presença de um conjunto estável de delírios que são cristalizados, possivelmente sistematizados, tenazmente mantidos, e claramente interferem com o pensamento, relações sociais ou comportamento.

**7 – Extremo** - Presença de um conjunto estável de delírios que são altamente sistematizados ou muito numerosos e que dominam a maior parte das áreas da vida do paciente. Isso freqüentemente resulta em ação inapropriada ou irresponsável, a qual pode até mesmo ameaçar a segurança do paciente ou de outros.

**P2 – DESORGANIZAÇÃO CONCEITUAL**: Processo desorganizado de pensamento caracterizado pela ruptura do seqüenciamento direcionado a um objetivo (por ex.,

circunstancialidade, tangencialidade, afrouxamento das associações, ilogicidade grosseira, ou bloqueio do pensamento).

Base para avaliar: processo cognitivo-verbal observado durante o curso da entrevista.

**1 – Ausente** – A definição não se aplica.

**2 – Mínimo** – Patologia questionável: pode estar no extremo superior dos limites normais.

**3 – Leve** – O pensamento é circunstancial, tangencial ou paralógico. Há alguma dificuldade em direcionar os pensamentos para um objetivo, e algum afrouxamento das associações pode ser evidenciado sob pressão.

**4 – Moderado** – Capaz de focar os pensamentos quando as comunicações são breves e estruturadas, mas se torna frouxo ou irrelevante quando lida com comunicações mais complexas ou quando está sob mínima pressão.

**5 - Moderado grave** – Geralmente tem dificuldade em organizar os pensamentos, como evidenciado por frequentes irrelevâncias, perda da conectividade, ou afrouxamento das associações quando não está sob pressão.

**6 – Grave** – O pensamento está seriamente descarrilado e internamente inconsistente, resultando em irrelevâncias grosseiras e ruptura dos processos de pensamento, o que ocorre quase constantemente.

**7 – Extremo** – Os pensamentos apresentam tal ruptura que o paciente está incoerente. Há um acentuado afrouxamento das associações, o que resulta em total fracasso da comunicação (por ex. “salada de palavras”) ou mutismo.

**P3 – COMPORTAMENTO ALUCINATÓRIO**: Relato verbal ou comportamento indicando percepções que não são geradas por estímulos externos. Isso pode ocorrer nas modalidades auditiva, visual, olfativa ou somática.

Base para avaliar: relato verbal e manifestações físicas durante o curso da entrevista, assim como relatos de comportamento por parte de trabalhadores de cuidados primários ou familiares.

**1 – Ausente** – A definição não se aplica.

**2 – Mínimo** – Patologia questionável: pode estar no extremo superior dos limites normais.

**3 – Leve** – Uma ou duas alucinações claramente formadas porém raras, ou então um número de percepções anormais

vagas que não resultam em distorções do pensamento ou do comportamento.

**4 – Moderado** – Alucinações ocorrem freqüente mas não continuamente, e o pensamento e o comportamento do paciente são afetados apenas em pequena monta.

**5 - Moderado grave** – Alucinações são freqüentes, podem envolver mais de uma modalidade sensorial e tendem a distorcer o pensamento e/ou levam a uma ruptura no comportamento. O paciente pode ter uma interpretação delirante dessas experiências e responder a elas emocionalmente e, às vezes, responder a elas verbalmente também.

**6 – Grave** – Alucinações estão presentes quase continuamente, causando uma grande ruptura no pensamento e no comportamento. O paciente as trata como percepções reais, o funcionamento é impedido pelas frequentes respostas emocionais e verbais a elas.

**7 – Extremo** – O paciente está quase totalmente preocupado com alucinações, as quais virtualmente dominam o pensamento e o comportamento. As alucinações levam a uma rígida interpretação delirante e provocam respostas verbais e comportamentais, incluindo obediência a alucinações imperativas.

**P4 – EXCITAÇÃO**: Hiperatividade como refletida em comportamento motor acelerado, resposta exacerbada a estímulos, hipervigilância, ou excessiva labilidade afetiva.

Base para avaliar: manifestações comportamentais durante o curso da entrevista, assim como relatos de comportamento por parte de trabalhadores de cuidados primários ou familiares.

**1 – Ausente** – A definição não se aplica.

**2 – Mínimo** – Patologia questionável: pode estar no extremo superior dos limites normais.

**3 – Leve** – Tende a ficar levemente agitado ou hipervigilante durante a entrevista, mas sem episódios de excitação ou acentuada labilidade de humor. Pode haver uma leve pressão para a fala.

**4 – Moderado** – Agitação ou hipervigilância é claramente evidente durante a entrevista, afetando a fala e a mobilidade geral, ou episódios de “explosão” ocorrem esporadicamente.

**5 - Moderado grave** – Hiperatividade significativa ou freqüentes “explosões” de atividade motora são observadas, tornando difícil para o paciente permanecer sentado por mais do que alguns minutos num dado período.

**6 – Grave** – Excitação acentuada domina a entrevista, restringe a atenção, e afeta até certo ponto funções pessoais taiscomo alimentar-se e dormir.

**7 – Extremo** - Excitação acentuada interfere seriamente com a alimentação e o sono e faz as interações interpessoais virtualmente impossíveis. A aceleração da fala e da atividade motora podem resultar em incoerência e exaustão.

**P5 – GRANDIOSIDADE**: Auto-opinião exagerada e convicções não realistas de superioridade, incluindo delírios de habilidades extraordinárias, riqueza, conhecimento, fama, poder e correção moral.

Base para avaliar: o conteúdo do pensamento expresso na entrevista e sua influência no comportamento.

**1 – Ausente** – A definição não se aplica.

**2 – Mínimo** – Patologia questionável: pode estar no extremo superior dos limites normais.

**3 – Leve** – Alguma expansividade ou presunção é evidente, mas sem delírios de grandeza bem delineados.

**4 – Moderado** – Sente-se distinta e irrealisticamente superior aos outros. Alguns delírios pobremente formados sobre status ou habilidades especiais podem estar presentes mas não produzem nenhum efeito.

**5 - Moderado grave** – Delírios bem delineados relativos a habilidades notáveis, status, ou poder são expressos e influenciam a atitude mas não o comportamento.

**6 – Grave** – Delírios bem delineados de notável superioridade envolvendo mais de um parâmetro (riqueza, conhecimento, fama, etc.) são expressos, influenciam notavelmente as interações, e podem afetar o comportamento.

**7 – Extremo** – O pensamento, as interações e o comportamento são dominados por múltiplos delírios de assombrosa habilidade, riqueza, conhecimento, fama, poder, e/ou estatura moral, que podem ser bizarros.

**P6 – SUSPICÁCIA / PERSEGUIÇÃO**: Idéias de perseguição não realistas ou exageradas, como refletidas em precaução, uma atitude de desconfiança, hipervigilância suspicaz, ou delírios francos de que outros pretendem prejudicá-lo.

Base para avaliar: o conteúdo do pensamento expresso na entrevista e sua influência no comportamento.

**1 – Ausente** – A definição não se aplica.

**2 – Mínimo** – Patologia questionável: pode estar no extremo superior dos limites normais.

**3 – Leve** – Apresenta uma atitude “defensiva” ou de franca desconfiança, mas pensamentos interações ecomportamento são minimamente afetados.

**4 – Moderado** – A desconfiança é claramente evidente e se impõe na entrevista e/ou no comportamento, mas não há evidência de delírios persecutórios, e não parece afetar a atitude ou as relações interpessoais do paciente.

**5 - Moderado grave** – O paciente mostra acentuada desconfiança, levando a uma extensa ruptura das relações interpessoais, ou então há delírios persecutórios bem delineados que têm um impacto limitado nas relações interpessoais e no comportamento.

**6 – Grave** – Delírios de perseguição penetrantes e bem delineados que podem ser sistematizados e que interferem significativamente nas relações interpessoais.

**7 – Extremo** – Uma rede de delírios persecutórios sistematizados domina o pensamento, as relações sociais e o comportamento do paciente.

**P7 – HOSTILIDADE**: Expressões verbais e não verbais de raiva e ressentimento, incluindo sarcasmo, comportamento passivo-agressivo, insulto verbal e agressão.

Base para avaliar: comportamento interpessoal observado durante a entrevista e relatos por parte de trabalhadores de cuidados primários ou familiares.

**1 – Ausente** – A definição não se aplica.

**2 – Mínimo** – Patologia questionável: pode estar no extremo superior dos limites normais.

**3 – Leve** – Comunicação indireta ou disfarçada de raiva, tal como sarcasmo, desrespeito, expressões de hostilidade, e irritabilidade ocasional.

**4 – Moderado** – O paciente apresenta uma atitude excessivamente hostil, exibindo irritabilidade freqüente e expressão direta de raiva ou ressentimento.

**5 - Moderado grave** – O paciente está altamente irritável e, em certas ocasiões, está verbalmente insultuoso ou ameaçador.

**6 – Grave** – Ausência de cooperação e insultos ou ameaças verbais notavelmente influenciam e seriamente afetam as relações sociais. O paciente pode estar violento e destrutivo, mas não está fisicamente agressivo em relação aos outros.

**7 – Extremo** – Acentuada raiva resulta em extrema falta de cooperação, tornando impossível outras interações, ou episódio(s) de agressão física em relação aos outros.

### 7.6. Anexo VI

**Insight Scale for Affective Disorders**

Indique o escore apropriado com um X: 0= não pode ser avaliado ou item não relevante; 1= consciência; 3= consciência
moderada; 5= sem consciência.

_____

_____

0 1 2 3 4 5

_____

_____

1 Consciência de sofrer de um transtorno afetivo (do humor).

2 Consciência da eficácia do tratamento para os sintomas atuais ou para prevenir recidivas.

3 Consciência das consequências da doença sobre o trabalho, família e vida social.

4 Consciência de apresentar humor deprimido/expansivo ou irritável (conforme apropriado).

5 Consciência de apresentar acentuado(a) aumento/redução de atividades prazerosas (conforme apropriado).

6 Consciência de apresentar ganho/perda significativo(a) de peso (conforme apropriado).

7 Consciência de apresentar insônia ou hipersonia (conforme apropriado).

8 Consciência de apresentar alentecimento ou agitação psicomotor(a) (conforme apropriado).

9 Consciência de apresentar fadiga ou excesso de energia.

10 Consciência de apresentar sentimentos de inutilidade ou culpa, ou autoestima aumentada ou grandiosidade.

11 Consciência de apresentar lentidão da fala ou verborragia/tagarelice (conforme apropriado).

12 Consciência de apresentar bradipsiquismo/fuga de idéias (conforme apropriado).

13 Consciência de apresentar baixo nível de atenção/distração.

14 Consciência de apresentar aparência desleixada.

15 Consciência de apresentar sintomas de confusão-desorientação.

16 Consciência de ter relações sociais pobres.

17 Consciência de apresentar delírios e alucinações (conforme apropriado).

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*A.1. Escala de consciência de morbidade para transtornos afetivos (do humor)*

*A.1.1. Instruções*

Esta escala requer que o indivíduo tenha um transtorno afetivo (do humor) com um dos sintomas detalhados abaixo. Para cada sintoma-item, deve-se confirmar que o indivíduo apresentou esse determinado sintoma durante o período pesquisado. A gravidade do sintoma não é relevante, só é necessário que ele esteja claramente presente. A verificação da lista de sintomas deve ser feita antes do preenchimento da escala para determinar quais sintomas-item são relevantes. Os três itens gerais (números 1, 2 e 3), que não correspondem a sintomas específicos, são normalmente relevantes e devem ser incluídos em todos os casos. Períodos de tempos maiores ou menores podem ser usados para a avaliação da consciência atual, dependendo dos objetivos da pesquisa.

**7.7. Anexo VII**

**Sheehan Disability Scale**

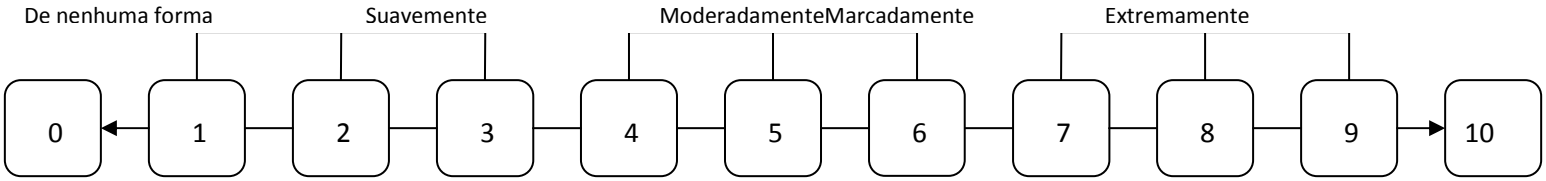
Nome do paciente:

Data: _____/_____/20_____

Responda com base nos <u>últimos 7 (sete) dias</u>:

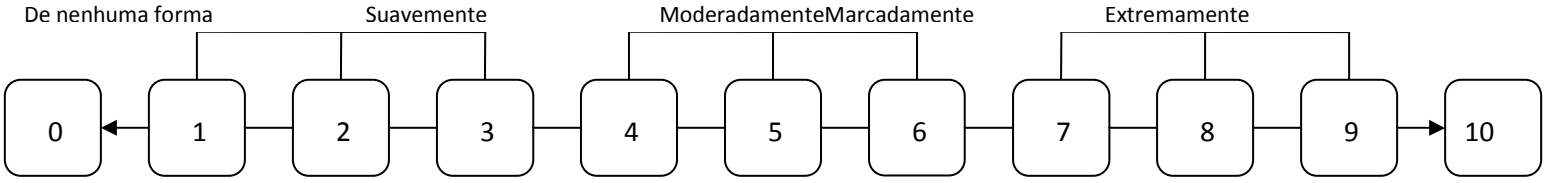
## Trabalho/Escola

**Os sintomas têm interrompido suas atividades no trabalho/escola:**




## Vida Social

**Os sintomas têm interrompido sua vida social:**




## Vida familiar/responsabilidades do lar

**Os sintomas têm interrompido sua vida familiar/responsabilidades do lar:**