



Neuropsychological profiles of major depressive disorder and bipolar disorder during euthymia. A systematic literature review of comparative studies

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A B S T R A C T

Bipolar disorder and major depressive disorder have been shown to be associated with neurocognitive abnormalities during periods of clinical remission. However, at present, there is no consensus on whether these disorders have distinctive cognitive profiles. The aim of this study was to provide an updated systematic review of studies comparing neuropsychological functioning between bipolar disorder and major depressive disorder during remission. Main findings included the following: 1) no differences regarding performances in measures of attention and processing speed, executive functions and theory of mind were found between both patient groups and 2) regarding verbal memory, preliminary evidence points towards a more defective performance in patients with bipolar disorder than those with major depressive disorder. However, several variables with negative impact on cognition (medication status, age at onset, premorbid IQ, bipolar subtype, among others) were not adequately controlled in most studies. In conclusion, evidence from studies exploring neuropsychological profiles in bipolar disorder and major depressive disorder could not provide clues to differentiate these mood disorders. Larger studies with adequate control of confounding variables would be necessary to elucidate if the finding of more defective verbal memory performance in bipolar disorder is truly explained by distinct underlying mechanisms.

1. Introduction

Major Depressive Disorder (MDD) and Bipolar Disorder (BD) are complex chronic illnesses that affect mood and other biological rhythms, causing distortions of normal behavior that carry varying levels of burden and even disability in many cases (Ustün et al., 2004; Whiteford et al., 2013). Recent data suggest that the prevalence of these disorders is higher than previously reported, reaching 17–30% for MDD (Kessler et al., 2005; Angst et al., 2016) and 2–4% for BD when broad diagnostic criteria are applied (Kessler et al., 2005; Merikangas et al., 2011). Thus, mood disorders represent a major public health concern (WHO, 2012). Several studies (Fennig et al., 2002; Martino et al., 2008; Yen et al., 2011; Gilbert and Marwaha, 2013; Mackala et al., 2014; Baune and Malhi, 2015) have linked poor

functional outcomes in subjects suffering from both mood disorders to neuropsychological abnormalities, which involve a broad array of domains and persist even during periods of clinical remission (Torres et al., 2007; Arts et al., 2008; Mann-Wrobel et al., 2011; Bora et al., 2013; Rock et al., 2014; Porter et al., 2015; Bora et al., 2016). Cognitive disturbances in these patients appear to be, at least partly, independent of medication status and other illness-related variables, as similar abnormalities, though of smaller magnitude, have been found in healthy relatives of affected subjects (Christensen et al., 2006; Arts et al., 2008; Balanzá-Martinez et al., 2008; Bora et al., 2009).

In recent years, great emphasis has been placed on characterizing cognitive aspects of mood disorders. In this scenario, a number of studies comparing cognitive performance between MDD and BD have been published. However, their results were contradictory and incon-

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Table 1
Summary of studies comparing neuropsychological performance between MDD and BD during euthymia.

Primary Study	Sample	Criteria of euthymia	Matched	Neuropsychological Domain	Main Results
Albus et al. (1996) ^a	Adult first-episode inpatients: MDD (n= 10), BD I (n=17) and HC (n=27).	NA	Age Sex Education Socio-economic status	Executive function Episodic memory (verbal and visual)	BD and MDD underperformed HC on processing speed and memory. Only subgroups of MDD and BD with psychotic features underperformed HC on executive functions and attention.
Paradiso et al. (1997)	Adult recurrent MDD (n=20), BD (n=11) and HC (n=19).	HDRS < 15 MBRS < 17	Age Sex Education Severity of depressive symptoms* Duration of illness* General cognitive status (MMSE)* Remission time* Sex	Attention and processing speed Attention (sustained attention) Attention and Processing speed Executive function Episodic memory (verbal)	BD and MDD performed equally on all measures. Only MDD presented with more defective performance than HC in all measures. MDD underperformed BD in executive function.
Robertson et al. (2003)	Young, adolescent-onset MDD (n=30), BD I (n=44), and HC (n=45)	BDI < 13	Sex	Attention (sustained) and processing speed	There were no differences between patient groups and HC. Performance of BD was not significantly different from MDD.
Clark et al. (2005b)	Adult BD (n=13), MDD (n=15) and HC (n=46)	HDRS < 9 YMRS < 9	Age Crystallized IQ	Attention (sustained) and processing speed	No differences were found between patient groups in sustained attention, but BD underperformed HC on this measure, while MDD did not. There were no differences in processing speed between MDD and BD performance, while both underperformed HC.
Smith et al. (2006)	Young adult patients with recurrent depressive episodes: MDD (n=42), BD-NOS (n=21), and HC (n=33).	HDRS < 9	Age Sex Premorbid IQ Severity of depressive symptoms Age at onset* Number of depressive episodes* History of deliberate self-harm* Education General physical status	Episodic memory (verbal) Executive function Attention and Processing speed	BD were significantly more impaired than MDD and HC on tests of executive function and verbal memory. MDD did not differ significantly from HC on verbal memory function but performed less well on a test of executive function. BD underperformed HC in all measures.
Canuto et al. (2010)	Elderly with early-onset mood disorders: MDD (n=36), BD (n=22: 11 BD I and 11 BD II), and HC (n=62).	GDS < 5 YMRS < 5	Age Sex Premorbid IQ Severity of depressive symptoms Age at onset* Number of depressive episodes* History of deliberate self-harm* Education General physical status	Episodic memory (verbal) Attention and Processing speed Executive function	BD underperformed MDD and HC on processing speed, working and episodic memory. No differences were found between MDD and HC performances.
Gidengers et al. (2012)	Elderly MDD (n=122), BD (n=43: 33 BD I and 10 BD II), and HC (n=92).	HDRS < 11 YMRS < 11	Age	Executive function Episodic memory (verbal) Processing speed Executive function	BD and MDD underperformed HC across all measures. BD had worse cognitive performance than MDD across all measures.
Xu et al. (2012) ^b	Adult MDD (n=100), BD (n=94, 42 BD I and 52 BD II), and HC (n=202)	HDRS < 8 YMRS < 6	NA	Attention and processing speed Episodic memory (visual)	Both BD and MDD underperformed HC on processing speed and visual memory. MDD underperformed BD and HC groups on executive functions. (continued on next page)

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