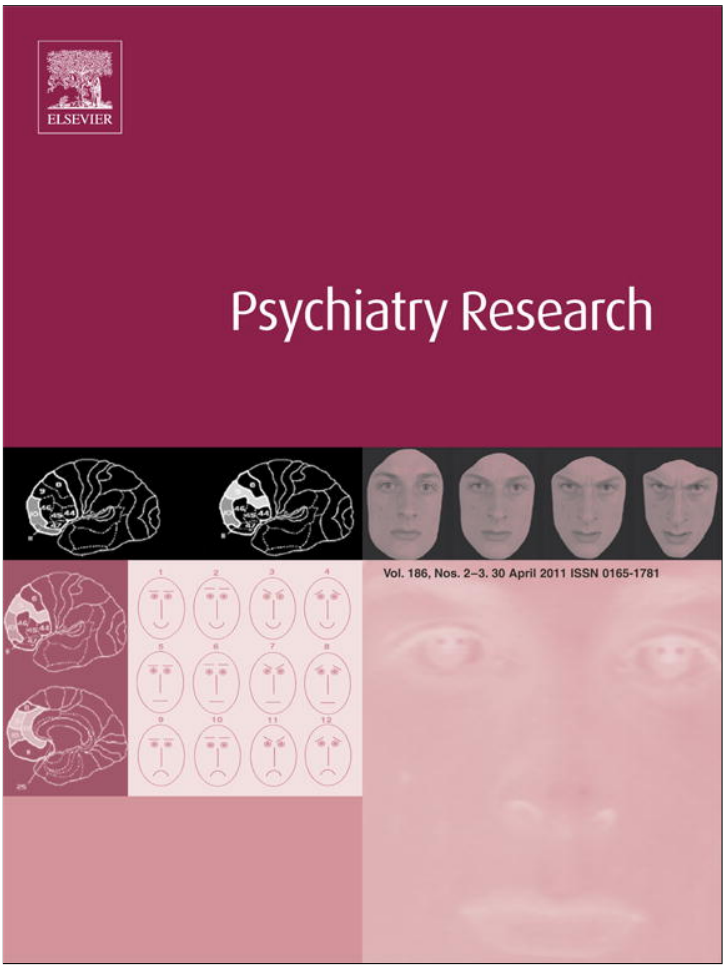

Psychiatry Research 186 (2011) 261–266

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Neuropsychological functioning in adult bipolar disorder and ADHD patients: A comparative study

Teresa Torralva [a,b,*], Ezequiel Gleichgerrcht [a], Fernando Torrente [a,b], María Roca [a,b], Sergio A. Strejilevich [a,b], Marcelo Cetkovich [a,b], Alicia Lischinsky [a,b], Facundo Manes [a,b,*]

[a] Institute of Cognitive Neurology (INECO), Buenos Aires, Argentina
[b] Institute of Neurosciences, Favaloro University, Buenos Aires, Argentina

ARTICLE INFO

Article history:
Received 2 December 2009
Received in revised form 5 August 2010
Accepted 12 August 2010

Keywords:
Memory
Recognition
Executive functions

ABSTRACT

Bipolar disorder (BD) and adult attention deficit hyperactivity disorder (ADHD) usually manifest with shared clinical symptoms, proving quite challenging to thoroughly differentiate one from another. Previous research has characterized these two disorders independently, but no study compared both pathologies from a neuropsychological perspective. The aim of this study was to compare the neuropsychological profile of adult ADHD and BD with each other and against a control group, in order to understand the way in which comprehensive cognitive assessment can contribute to their discrimination as distinct clinical entities as well as their differential diagnosis. All groups were successfully matched for age, sex, years of education, and premorbid IQ. Participants were assessed with an extensive neuropsychological battery evaluating multiple domains. Compared to controls, BD patients had a poorer performance on immediate verbal memory tasks. Both clinical groups exhibited significantly lower scores than controls on the recognition phase of verbal and non-verbal memory tasks, as well as on a task of executive functioning with high working memory demand. Noticeably, however, ADHD had significantly better performance than BD on the recognition phase of both the Rey list memory task and the Rey Figure. The better performance of ADHD patients over BD may reflect the crucial role of the executive component on their memory deficits and gives empirical support to further differentiate the neuropsychological profile of BD and adult ADHD patients in clinical practice.

1. Introduction

In recent years, the distinction between bipolar disorder (BD) and attention deficit hyperactivity disorder (ADHD) became a topic of growing interest (Kent and Craddock, 2003; Galanter and Leibenluft, 2008). The knowledge about the extension throughout life of both disorders has changed considerably. Initially regarded as a disorder of childhood, ADHD has been shown to persist in adulthood in 10 to 60% of cases (Zametkin, 1995). In parallel, childhood-onset BD has been acknowledged despite of the controversies about its characterization (Youngstrom et al., 2008). Thus, the natural course of ADHD and BD expanded all along the life span. In addition, the two disorders often coexist. In adulthood, comorbidity rates of ADHD in BD samples fluctuate from 9.5% to 21.2%. Inversely, comorbidity rate of BD in adult ADHD samples ranges from 5.1% to 47.1% (Wingo and Ghaemi, 2007). Moreover, the overlap of symptoms between euphoric phases of BD and ADHD – such as distractibility, talkativeness, restlessness, and loss of social inhibition – represents another direct source of potential confusion in diagnosis (Milberger et al., 1995; Carlson, 1998; Galanter et al., 2005).

Certainly, there are also recognizable differences between BD and ADHD. As Wingo and Ghaemi (2007) emphasize, ADHD symptoms tend to be stable, in contrast with the episodic nature of BD troubles. Moreover, increased productivity, inflated self-esteem and psychotic features that might be present in the euphoric periods of BD, rarely appear in ADHD patients. As well, BD patients – excluding subjects with childhood-onset or psychotic features – usually have adequate premorbid functioning, as evidenced by intellectual tests, reading/writing, and different behavioral measures (Reichenberg et al., 2002). Meanwhile, ADHD patients show a pervasive history of problematic functioning since childhood (Brassett-Harknett and Butler, 2007).

Nevertheless, beyond these differences, some questions regarding the distinction of the two entities remain unanswered. In fact, discrepancies related with the course of the disorders are not always easy to discern retrospectively upon current examination. Similarly, the clinical differences with ADHD are neat when considering the more severe or extreme disturbances of BD, but the risk of diagnostic inaccuracy increases when its clinical expressions are mild or diffuse – as in BD type II patients – or when preceding temperamental traits

* Corresponding authors. Castex 3293, Capital Federal, Buenos Aires, Argentina. Tel. +54 11 4807 4748.
E-mail addresses: ttorralva@ineco.org.ar (T. Torralva), fmanes@ineco.org.ar (F. Manes).

0165-1781/$ – see front matter © 2010 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.psychres.2010.08.007

(Hantouche et al., 1998) and subsyndromal manifestations (Judd et al., 2003) create a more continuous course of the disorder. In the same direction, it is worth to point out that the symptom commonalities between BD and ADHD are not restricted to the manic phase. Affective lability has been documented as a characteristic trait of adult ADHD (Wender et al., 2001; Davidson, 2008) and the intercourse of depressive episodes is not infrequent in this disorder (Biederman et al., 1993; Kessler et al., 2006). For this reason, subclinical depressive symptoms and "soft" mood fluctuations of BD patients (Judd et al., 2003) could be difficult to distinguish from intercurrent depressive symptoms and mood instability in ADHD patients, as well as BD mixed episode symptoms could be easily confounded with the irritability and "hot temper" outbursts of ADHD subjects. Likewise, impulsivity – a core symptomatic dimension of ADHD Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) diagnostic criteria – has been found to be present as a stable trait in bipolar euthymic patients (Najt et al., 2007; Peluso et al., 2007). Finally, even if premorbid functioning is mostly preserved in BD subjects, considerable disability and disturbed functioning pervade in remission phases (Huxley and Baldessarini, 2007).

In the scheme of these overlapping features, few empirical studies until now have intended to delimitate ADHD and BD through direct comparison. Most of the existent research has evaluated clinical differences between patients with ADHD/BD comorbidity and patients with the single diagnosis of ADHD or BD (Milberger et al., 1995; Wilens et al., 2003; Nierenberg et al., 2005; Tamam et al., 2006; Tamam et al., 2008). Remarkably, there are no neuropsychological studies contrasting ADHD and BD patients yet, even if cognitive variables could be, at least in advance, an important source of information about underlying neurobiological differences between the two disorders. It is nowadays well established that cognitive functions seem to be impaired in BD patients. This can be reflected in recent neuropsychological studies showing that cognitive deficits are more severe and pervasive in states of symptomatic exacerbation (Fleck et al., 2003; Martinez-Aran et al., 2004), and that such deficits seem to persist throughout the euthymic state (Robinson et al., 2006; Bora et al., 2009; Thompson et al., 2009). This suggests that the absence of symptoms is not necessarily indicative of full cognitive 'recovery'. For instance, deficits in verbal memory and executive functions are the most clinically reliable symptoms during the euthymic state across different studies in BD (Robinson et al., 2006).

In a recent meta-analysis of cognitive deficits in BD, Kurtz and Gerraty (2009) reported findings from a large number of studies over the past two decades, revealing that individuals with BD present deficits on standardized neuropsychological measures, with particularly marked impairment in executive functions and verbal learning (Robinson et al., 2006; Arts et al., 2008; Bora et al., 2009) independently of the psychiatric symptom reduction (Joffe et al., 1988) and the intensity of the disease process in and of itself (Ferrier et al., 1999). These results suggest that BD during euthymia is characterized by generalized moderate levels of neuropsychological impairment, with a particular impairment of verbal learning and memory. Executive functions, such as response inhibition and set shifting, have also been reported to be impaired in the euthymic bipolar population (Kolur et al., 2006). In fact, a subset of these deficits (namely, impaired visual and verbal memory, decreased phonemic fluency, and motor slowing) moderately worsens during acute disease states.

Regarding ADHD, the investigation of its neuropsychology is a relatively young area of research, especially in adult populations, and most studies are descriptive in nature rather than designed to evaluate specific hypotheses. Nevertheless, neuropsychological research has consistently identified stable dysfunctions in the cognitive domains of attention (sustained and focused), inhibition, processing speed, motor speed, and verbal declarative memory (Barkley, 1997; Hervey et al., 2004). Yet, the most severely impaired cognitive domain seems to be executive functioning, affecting planning, self-monitoring, working memory, flexibility, and set shifting, among others.

Even if executive and declarative memory deficits appear to be shared symptoms of both disorders in comparison with healthy subjects, at present, there is a lack of relevant data to discern whether those difficulties are identical in BD and adult ADHD, or else, if the nature and extension of the cognitive deficits differ between the two conditions.

Accordingly, the aim of this study was to compare the neuropsychological profile of these two psychiatric disorders that show considerable clinical overlap at the phenomenological level in order to understand the way in which comprehensive cognitive assessment can contribute to differentiate BD and adult ADHD.

2. Methods

2.1. Participants

ADHD and bipolar patients were evaluated during admission interviews to the specialized Clinics of Adult ADHD and BD at our Institute. All participants (patients and controls) went through a standard assessment process including neurological, neuropsychiatric and neuropsychological examinations as needed for diagnosis. Patients in the BD group (BD, $n=15$) and the attention deficit hyperactivity disorder group (ADHD, $n=16$) were consecutively selected from the outpatients population with the following inclusion criteria: age between 18 and 60 years old; diagnosis of BD I or adult ADHD according to DSM-IV criteria, using a Structured Clinical Interview for DSM-IV (SCID) (First et al., 1996). Additionally, BD patients were all euthymic (determined by Hamilton Depression Rating Scale ≤ 8 and Young Mania Rating Scale ≤ 6) for at least 8 weeks with no change of medication type or dose over a period of 4 months. Exclusion criteria were: other diagnosis in axis I except from generalized anxiety disorder; and history of mental retardation, neurological disease, or any clinical condition that could affect cognitive performance. The attention deficit hyperactivity disorder group received relevant pharmacological treatment with no change of dose over a period of 6 months. Eleven (69%) were of the hyperactive subtype, and five (31%) were of the inattentive subtype.

Healthy controls (CTR, $n=15$) were randomly recruited from a larger pool of volunteers who had neither a history of abuse of recreational drugs nor a family history of neurodegenerative or psychiatric disorders. The study was approved by the Ethics Committee at our Institute in accordance with the Declaration of Helsinki. All participants gave written informed consent for their participation after receiving a complete description of the study.

2.2. Materials and procedure

The procedures were initially approved and supervised by the ethics committee at the Institute of Cognitive Neurology. Patients completed a series of psychiatric and behavioral questionnaires, incorporated as part of the regular neuropsychiatric examination, in order to establish a profile of clinical symptoms. Relatives or significant others were usually present throughout assessment interviews, during which they completed the informant-based version of questionnaires. Depression and mania were rated in BD using the Hamilton Depression Rating Scale (HDRS; Hamilton, 1960) and the Young Mania Rating Scale (YMRS; Young et al., 1978), respectively. Symptomatic profile of ADHD was obtained from the inattention and hyperactivity/impulsivity scores of the ADHD Rating Scale for Adults (Barkley and Murphy, 1998). The ADHD Rating Scale for Adults is a self-report questionnaire that contains 18 items based on the diagnostic criteria for ADHD in the DSM-IV. Respondents rate the intensity of current ADHD symptoms on a 4-point Likert scale, ranging from 0 to 3 ("rarely or never," "sometimes," "often," or "very often," respectively). In line with the DSM-IV view of the disorder, the scale is organized in two subscales, one for the inattention symptoms and the other for the hyperactive–impulsive symptoms. The ADHD-RS allows two different interpretations. One represents the total score for each subscale, which gives a measure of the frequency of the symptoms, and the other is the symptom count, which is the number of items answered as "Often" or "Very Often". In this study we report the total score for each subscale. Participants completed two versions of this scale, one targeting current symptoms and the other for childhood symptoms between ages 5 to 12 years. For the two clinical groups in this study, these same rating scales were obtained from parents or spouses, but only participants' self-report ratings of current symptoms were taken into account for the present study. Thus, for each participant, the scale provides three different scores: the sum of ADHD item ratings on the total scale (ADHD-RS-T), the sum of inattention items (ADHD-RS-I), and the sum of hyperactive–impulsive items (ADHD-RS-HI). The Beck Depression Inventory II (BDI-II; Beck, Steer, & Brown, 1996) was used to control for mood disturbances in adult ADHD. The BDI-II was also administered to BD patients and controls in order to obtain a scale for depression comparable across the clinical groups.

Participants in all groups completed a thorough neuropsychological battery assessing (1) estimated premorbid IQ with the Word Accentuation Test — Buenos Aires (WAT-BA; Burin et al., 2000), which presents a list of words which participants

must read aloud with proper accentuation without considering the word's meaning; (2) attention with the forward digits span task of the Wechsler Adult Intelligent Scale III (WAIS III; Wechsler, 1997) and the Trail Making Test Part A (TMT-A; Partington and Leiter, 1949); (3) verbal memory through the Rey auditory verbal learning test (RAVLT; Rey, 1941) and the logical memory subtest of the Weschler Memory Scale – Revised (WMS-R; Weschler and Stone, 1987), and non-verbal memory with the Rey Complex Figure test (Rey, 1941); (4) executive function using the backward digits span test (Wechsler, 1997), part B of the Trail Making Test (TMT-B; Partington and Leiter, 1949), the Letter-Number Sequencing Test (LNST; Wechsler, 1997), the modified version of the Wisconsin Card Sorting Test (WCST; Nelson, 1976), the Frontal Assessment Battery (FAB; Dubois et al., 2000), which is an executive screening test that consists of six subtests assessing conceptualization, cognitive flexibility, motor programming, sensitivity to interference, motor inhibitory control, and prehension behavior.

2.3. Statistical analysis

Demographic and neuropsychological data were compared between the three groups using a one-way ANOVA design followed by Bonferroni *post hoc* tests when appropriate. For variables with a non-homogenous distribution, the Kruskal Wallis *H* test was used, followed by Mann Whitney *U* tests to contrast two groups at a time. When analyzing categorical variables (e.g. gender, recognition), the Freeman–Halton extension of the Fisher exact probability test for 2×3 contingency tables was used. The relationship between different variables was calculated using Spearman's correlation coefficient. The α value was set at 0.05, two-tailed for all analyses.

3. Results

General demographic information, as well as psychiatric and neuropsychological test results is summarized for the BD, ADHD, and control groups in Table 1. Groups were successfully matched for their age ($F_{2,43}=0.49$, $P=0.61$), years of education ($F_{2,43}=0.80$, $P=0.92$), sex ($\chi^2=1.38$, d.f.$=2$, $P=0.50$), and estimated premorbid IQ, as measured by the WAT-BA ($F_{2,43}=0.35$, $P=0.71$). As expected, a significant difference was found between the groups on BDI-II scores ($F_{2,43}=9.35$, $P<0.01$), with controls significantly differing from ADHD and BD (both, $P<0.01$) but no significant differences observed between the clinical groups ($P=0.96$).

3.1. Attention

No significant differences were found between the groups for their performance on the digits forward span task ($\chi^2=1.84$, d.f.$=2$, $P=0.396$) and the TMT-A ($F_{2,43}=1.43$, $P=0.25$).

3.2. Memory

The immediate recall on the logical memory subtest of the WMS-R (Table 1) significantly differed between the groups ($F_{2,43}=6.26$, $P<0.01$), with BD performing significantly worse than controls ($P=0.004$). The performance of the three groups on the delayed recall phase, however, was not significantly different ($\chi^2=3.56$, d.f.$=2$, $P=0.17$). No significant differences were found across the group on the recognition phase of this task either ($F_{2,43}=0.84$, $P=0.90$).

Immediate recall performance on the RAVLT differed between the groups ($F_{2,43}=8.55$, $P=0.001$), with controls performing significantly better than both BD ($P=0.01$), and ADHD ($P=0.045$). In fact, a repeated measures ANOVA with trial (1 through 5) as the within-group factor and group (control, ADHD, or BD) as the between-group factor (Fig. 1) revealed a main effect of trial ($F_{4,172}=204.8$, $P<0.001$), a main effect of group ($F_{2,43}=5.04$, $P=0.01$), but a non-significant

Table 1
Demographic information and neuropsychological tests for bipolar, ADHD, and control groups. Values are shown as Mean (S.D.) and statistical comparison test results are shown on the right columns. Bold values are p<0.005.

		BD ($n=15$)	ADHD ($n=16$)	CONTROL ($n=15$)	BD vs. ADHD	BD vs. CTR	ADHD vs. CTR
Demographics	Age (years)	41.3 (8.1)	46.6 (14.2)	43.9 (19.8)	n.s.	n.s.	n.s.
	Gender (M:F)	5:10	6:10	8:7	n.s.	n.s.	n.s.
	Education (years)	14.3 (2.7)	14.1 (4.0)	14.6 (3.0)	n.s.	n.s.	n.s.
Clinical profile	Age at onset (years)	27.7 (12.9)					
	Duration (years)	19.2 (14.6)					
	Barkley						
	Inattention		10.5 (4.5)				
	Hyperactivity		9.32 (4.3)				
	BDI-II	10.6 (4.9)	9.4 (3.7)	1.4 (2.9)	n.s.	<**0.01**	<**0.01**
	Hamilton Scale	5.1 (5.5)					
	YMRS	3.2 (3.5)					
	WAT-BA	37.4 (6.3)	36.2 (7.2)	37.5 (0.6)	n.s.	n.s.	n.s.
Attention	Digits forward	6.93 (1.0)	6.63 (2.2)	7.5 (2.1)	n.s.	n.s.	n.s.
	Trail A	38.5 (15.0)	36.2 (12.2)	31.1 (8.9)	n.s.	n.s.	n.s.
Memory	Logical memory						
	Immediate	17.9 (6.0)	23.4 (7.2)	26.3 (8.0)	n.s.	**0.004**	n.s.
	Recall	16.4 (2.1)	20.3 (6.9)	17.6 (2.5)	n.s.	n.s.	n.s.
	Recognition	17.2 (1.4)	17.1 (1.9)	18.5 (1.5)	n.s.	n.s.	n.s.
	RAVLT						
	Immediate	44.1 (7.7)	48.4 (8.7)	55 (4.6)	n.s.	**0.01**	**0.045**
	Delayed	8.7 (3.3)	9.8 (2.5)	9.6 (4.2)	n.s.	n.s.	n.s.
	Recognition	11.6 (3.4)	13.8 (1.6)	14.3 (0.9)	**0.024**	<**0.01**	n.s.
	Rey Figure						
	Immediate	34.0 (3.5)	35.4 (1.5)	35.1 (1.3)	n.s.	n.s.	n.s.
	Delayed	15.8 (7.6)	20.2 (5.5)	19.4 (7.4)	n.s.	n.s.	n.s.
	Recognition	8/15	14/16	14/15	**0.027**	n.s.	n.s.
Executive functions	Digit backwards	4.13 (0.9)	4.5 (2.1)	5.07 (1.6)	n.s.	n.s.	n.s.
	Trails B	97.9 (42.3)	77.6 (22.4)	78.0 (44.0)	n.s.	n.s.	n.s.
	LNST	8.6 (3.9)	8.25 (2.3)	11.1 (3.1)	n.s.	**0.032**	**0.023**
	WCST	5.7 (0.5)	5.5 (1.2)	5.7 (0.6)	n.s.	n.s.	n.s.
	FAB						
	Motor series	2.8 (0.4)	2.9 (0.3)	2.9 (0.3)	n.s.	n.s.	n.s.
	Conflicting instr.	2.8 (0.4)	2.8 (0.4)	3.0 (0.0)	n.s.	n.s.	n.s.
	Inhibitory control	2.7 (0.6)	2.5 (0.8)	2.9 (0.3)	n.s.	n.s.	n.s.

BDI-II = Beck Depression Inventory II; YMRS = Young Mania Rating Scale; GAF; WAT-BA = Word Accentuation Test – Buenos Aires; RAVLT = Rey Auditory Verbal Learning Task; LNST = Letter-Number Sequencing Test; WCST = Wisconsin Card Sorting Test; FAB = Frontal Assessment Examination; Statistical comparison test result *p* values are shown when significance was achieved, in all other cases *n.s.* shows a 'non-significant' difference.

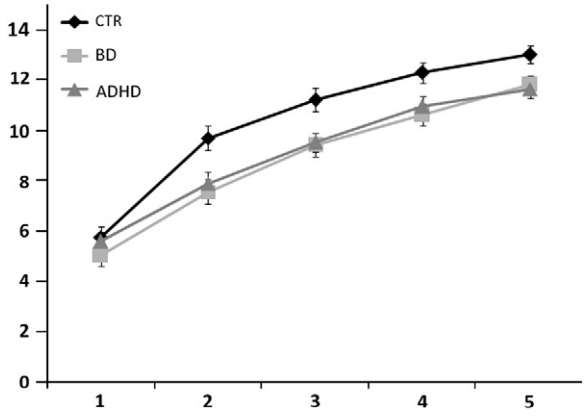

Fig. 1. Mean ± S.E.M. number of words recalled on each trial (1 through 5) during the acquisition phase of the RAVLT. A main effect of trial and a main effect of group are observed, with controls significantly outperforming both ADHD and BD patients.

trial × group interaction ($F_{8,172} = 1.30$, $P = 0.25$). A Bonferroni *post hoc* analysis on group differences showed that controls outperformed ADHD ($P = 0.04$) and BD ($P = 0.01$) patients on the learning phase of the RAVLT, although the patient groups did not differ between each other ($P = 0.99$). While the groups did not differ on performance of the delayed recall phase ($F_{2,43} = 0.50$, $P = 0.61$), a significant difference was observed for the number of words identified during the recognition phase of this task ($F_{2,43} = 6.46$, $P = 0.004$). In particular, BD differed significantly from ADHD ($P = 0.024$) and from controls ($P < 0.01$), but ADHD and controls obtained very similar scores.

On the visual memory task (Table 1), no significant differences were found for the initial phase ($F_{2,43} = 1.47$, $P = 0.24$) or the delayed recall phase ($F_{2,43} = 1.52$, $P = 0.23$). Nonetheless, the groups significantly differed on their ability to recognize the original figure (Fisher's $P < 0.001$), specifically BD from ADHD ($U = 64.0$, $P = 0.027$).

3.3. Executive functions

While the groups did not differ on most tests of executive functioning, including the digit backwards span ($U = 3.36$, $P = 0.19$), the TMT-B ($F_{2,43} = 1.52$, $P = 0.231$), the WCST ($H = 0.07$, d.f. = 2, $p = 0.96$), and the subscales of the FAB, which included motor series programming ($U = 1.16$, $P = 0.561$), conflicting instructions ($U = 3.28$, $P = 0.194$), and inhibitory control ($U = 4.26$, $P = 0.12$), performance on the LNST differed significantly between the groups (Fig. 2, left), with controls scoring significantly better than BD ($P = 0.032$) and ADHD ($P = 0.023$). Scores on the LNST significantly correlated with RAVLT recognition scores ($R = 0.67$, $P < 0.01$; Fig. 2, right).

4. Discussion

This study investigated the potential utility of neuropsychological evaluation in exploring cognitive performance in patients with BD and with adult ADHD from a more comprehensive perspective. This investigation revealed three important findings. First, we found significant differences between both ADHD and BD patients in a test of executive functioning (i.e., the LNST) relative to controls. Second, we found differences between BD patients and controls on the immediate recall phase of the logical memory task and the RAVLT. Finally, the recognition phase of the RAVLT and the Rey Figure were the only measures that reliably differentiated the two clinical groups.

The contribution of executive functioning to memory is indisputable, especially when it comes to the manipulating data for memory storage and free recall. Arbitrary sets of information in free recall tests such as the RAVLT imply highly demanding cognitive process that depends on the generation of executive strategies to enhance task performance (Higginson et al., 2003). In contrast, in the recognition phase of the memory tasks included in this study, patients must choose from within a set of stimuli that includes original information learned during the task accompanied by distracting stimuli. Despite the nature of the tasks *per se* – for instance, whether it is verbal or non-verbal –, the recognition phase provides a "multiple choice" scenario that alleviates the demand of memory performance over executive functioning. Thus, a poor performance on the recognition phase of memory tasks might be indicative of problems in information acquisition or storage, rather than problems of a pure executive origin. In our study, while both BD and ADHD patients showed executive deficits, the latter significantly outperformed the BD group on the recognition phase of the RAVLT and Rey Figure. This finding – in combination with immediate recall deficits – suggests that BD patients may actually have difficulties in memory acquisition or storing processes on top of dysexecution. This

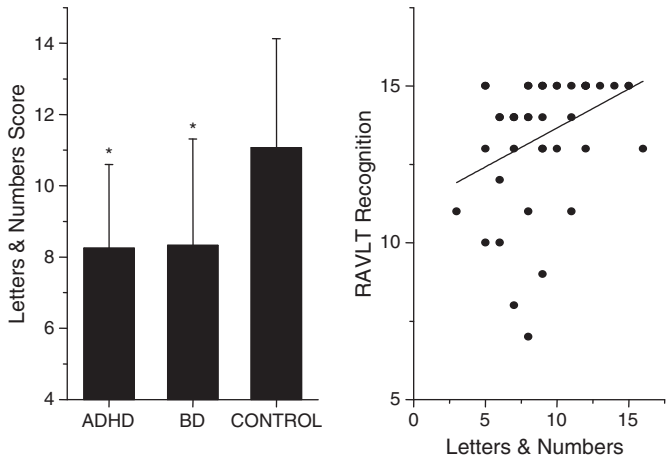

Fig. 2. Performance (Mean ± S.D.) on the letters and numbers test. Both ADHD and BD differed significantly from controls (left panel); the score on this task positively correlated with the number of words identified during the recognition phase of the RAVLT ($p < 0.001$; right panel).

is in contrast with the ADHD patients, who actually benefit from the "executive rescue" of the recognition phase, performing at the level of healthy controls when asked to identify previously learned stimuli. In other words, when the executive demand is minimized, ADHD patients are able to rely on memory storage to identify words previously learned. While it has been speculated that memory deficits in BD euthymic patients could be attributed to a primary executive dysfunction (Robinson et al., 2006), the results of this study argue against that hypothesis. The pattern of deficits found here revealed that while both disorders shared difficulties in the executive domain, performance of the BD group was associated with memory deficits that are independent of executive dysfunction, and should be attributed to impaired learning or storage, which could be associated with hippocampal involvement reported in BD patients (Monks et al., 2004; Javadapour et al., 2010).

The differential role of executive functions in the memory profile of these two disorders may be further supported, in fact, by another finding of the present study. It comes as no surprise that, with executive performance having a potentially pivotal role in memory processing, only the recognition phase of the RAVLT and the Rey Figure, but not the recognition phase of the logical memory task, differentiated BD from ADHD patients. Both logical memory and RAVLT are verbal memory tasks, but it is widely accepted that both tasks depend on executive functions with varying degrees. At least two studies have demonstrated that executive dysfunction is associated with poor performance on unstructured word-list memory tasks but not on logical memory tests (Tremont et al., 2000; Brooks et al., 2006). In fact, both studies used a different definition of "impaired executive functions" and still found convergent results regarding the differential impact of executive functioning on verbal memory. Furthermore, this differential impact of executive functioning has been explored on measures of visual memory, finding both a better performance on this cognitive domain when patients had higher frontal functioning (Simard et al., 2003) and a stronger impact on visual memory performance when the visual tasks required encoding and recall of discrete bits of information, and thus, relied more strongly on proper executive functioning (Temple et al., 2006). Because both the RAVLT and Rey Figure require encoding, processing, and storage of an arbitrary set of information, relative to the logical and cohesive structure underlying the stories of the WMS-R task, our results add further evidence as to how executive performance may be playing a central role in differentiating ADHD from BD patients on said measures. Consistently, the one executive task that demands the most working memory load from the ones included in the present battery, i.e. Letter-Number Sequencing Test, was sensitive enough to distinguish both clinical groups from controls. In this subtest of the WAIS III, letters and numbers are presented orally to the subject in a mixed-up fashion. The subject must rearrange and repeat the list back by saying the numbers in ascending order first, and then the letters in alphabetical order. The mechanisms required for proper completion of this task, resemble – to some extent – those required for memory retrieval.

Whether this neuropsychological pattern is congruent with the neuroanatomical structure and functioning of adult ADHD and BD is a matter of a debate. Hypothetically, the results found in the present study may be accounted by differences in the neurobiological profile of the two disorders. Brain regions relevant to executive tasks such as the dorsolateral prefrontal cortex (DLPFC) and anterior cingulated cortex (ACC) have been previously implicated in both BD and ADHD (Bearden et al., 2001; Seidman et al., 2004; Agarwal et al., 2008). Additionally, brain regions related to the storage of memory – prominently, medial temporal lobes – have been reported specifically in BD (Strakowski et al., 2000; Monks et al., 2004). This anatomical differentiation between the two pathologies matches the distinctive pattern found in the performance of the memory tests. Naturally, the exact neurobiological nature supporting these differences must be further explored, ideally, by combining neuropsychological studies with results from structural and functional neuroimaging data.

Some limitations of this study should be acknowledged. Mainly, and similar to previous studies, the number of patients was restricted, and therefore more subtle differences may have been missed due to a lack of statistical power. However, this is the first empirical study to compare the neuropsychological profile between BD and adult ADHD patients. Also, future studies should also explore the relation between behavioral and neuropsychological measures, for example, by looking at correlations between different subscores on the ADHD Rating Scale and neuropsychological test scores.

Finally, this study has two major clinical implications. First, in the context of high comorbidity and overlapping symptoms between the two disorders, the existence of underlying neurocognitive differences provides empirical support for the discrimination of BD and adult ADHD. Second, it provides further evidence for the use of neuropsychological assessment as a potentially useful source of information for differential diagnosis, complementary to the clinical interview. Extensive use of variables of this caliber requires further exploration, and future research should look at the complex interactions between memory and executive functions in neuropsychiatric conditions like ADHD and BD. Hence, more studies are needed in order to replicate similar findings in larger samples, carrying out longitudinal assessments throughout different mood phases, and including emotional/affective tasks.

Acknowledgement

The present study was funded by a FINECO grant.

References

Agarwal, N., Bellani, M., Perlini, C., Rambaldelli, G., Atzori, M., Cerini, R., Vecchiato, R., Pozzi Mucelli, R., Andreone, N., Balestrieri, M., Tansella, M., Brambilla, P., 2008. Increased fronto-temporal perfusion in bipolar disorder. Journal of Affective Disorders 110, 106–114.

Arts, B., Jabben, N., Krabbendam, L., van Os, J., 2008. Meta-analyses of cognitive functioning in euthymic bipolar patients and their first degree relatives. Psychological Medicine 38, 771–785.

Barkley, R.A., 1997. Behavioral inhibition, sustained attention, and executive functions: constructing a unifying theory of ADHD. Psychological Bulletin 121, 65–94.

Barkley, R.A., Murphy, K.R., 1998. Attention-Deficit Hyperactivity Disorder: A Clinical Workbook, 2nd ed. Guilford Press, New York.

Bearden, C.E., Hoffman, K.M., Cannon, T.D., 2001. The neuropsychology and neuroanatomy of bipolar affective disorder: a critical review. Bipolar Disorder 3, 106–153.

Beck, A.T., Steer, R.A., Brown, G.K., 1996. Manual for the Beck Depression Inventory-II. The Psychological Corporation, San Antonio, TX.

Biederman, J., Faraone, S.V., Spencer, T., Wilens, T., Norman, D., Lapey, K.A., Mick, E., Lehman, B.K., Doyle, A., 1993. Patterns of psychiatric comorbidity, cognition, and psychosocial functioning in adults with attention deficit hyperactivity disorder. The American Journal of Psychiatry 150, 1792–1798.

Bora, E., Yucel, M., Pantelis, C., 2009. Cognitive endophenotypes of bipolar disorder: a meta-analysis of neuropsychological deficits in euthymic patients and their first-degree relatives. Journal of Affective Disorders 113, 1–20.

Brassett-Harknett, A., Butler, N., 2007. Attention-deficit/hyperactivity disorder: an overview of the etiology and a review of the literature relating to the correlates and life course outcomes for men and women. Clinical Psychology Review 27, 188–210.

Brooks, B.L., Weaver, L.E., Scialfa, C.T., 2006. Does impaired executive functioning differentially impact verbal memory measures in older adults with suspected dementia? The Clinical Neuropsychologist 20, 230–242.

Burin, D.I., Jorge, R.E., Arizaga, R.A., Paulsen, J.S., 2000. Estimation of premorbid intelligence: the word accentuation test — Buenos Aires version. Journal of Clinical and Experimental Neuropsychology 22, 677–685.

Carlson, G.A., 1998. Mania and ADHD: comorbidity or confusion. Journal of Affective Disorders 51, 177–187.

Davidson, M.A., 2008. ADHD in adults: a review of the literature. Journal of Attention Disorders 11, 628–641.

Dubois, B., Slachevsky, A., Litvan, I., Pillon, B., 2000. The FAB: Frontal Assessment Battery at bedside. Neurology 55, 1621–1626.

Ferrier, I.N., Stanton, B.R., Kelly, T.P., Scott, J., 1999. Neuropsychological function in euthymic patients with bipolar disorder. The British Journal of Psychiatry 175, 246–251.

Fleck, D.E., Shear, P.K., Zimmerman, M.E., Getz, G.E., Corey, K.B., Jak, A., Lebowitz, B.K., Strakowski, S.M., 2003. Verbal memory in mania: effects of clinical state and task requirements. Bipolar Disorders 5, 375–380.

First, M., Spitzer, R., Gibbon, M., Williams, J., 1996. Structured clinical interview for DSM-IV Axis I Disorders-Clinical Version (SCID-CV). American Psychiatry Press, Washington, DC.
Galanter, C.A., Leibenluft, E., 2008. Frontiers between attention deficit hyperactivity disorder and bipolar disorder. Child and Adolescent Psychiatric Clinics of North America 17, 325–346.
Galanter, C., Pagar, D., Davies, M., Li, W., Carlson, G., Abikoff, H., Eugene Arnold, L., Bukstein, O., Pelham, W., Elliott, G., Hinshaw, S., Epstein, J., Wells, K., Hechtman, L.H., Newcorn, J., Greenhill, L., Wigal, T., Swanson, J., Jensen, P., 2005. ADHD and manic symptoms: diagnostic and treatment implications. Clinical Neuroscience Research 5, 283–294.
Hamilton, A., 1960. A rating scale for depression. Journal of Neurology, Neurosurgery and Psychiatry 23, 56–62.
Hantouche, E.G., Akiskal, H.S., Lancrenon, S., Allilaire, J.F., Sechter, D., Azorin, J.M., Bourgeois, M., Fraud, J.P., Chatenet-Duchene, L., 1998. Systematic clinical methodology for validating bipolar-II disorder: data in mid-stream from a French national multi-site study (EPIDEP). Journal of Affective Disorders 50, 163–173.
Hervey, A.S., Epstein, J.N., Curry, J.F., 2004. Neuropsychology of adults with attention-deficit/hyperactivity disorder: a meta-analytic review. Neuropsychology 18, 485–503.
Higginson, C.I., King, D.S., Levine, D., Wheelock, V.L., Khamphay, N.O., Sigvardt, K.A., 2003. The relationship between executive function and verbal memory in Parkinson's disease. Brain and Cognition 52, 343–352.
Huxley, N., Baldessarini, R.J., 2007. Disability and its treatment in bipolar disorder patients. Bipolar Disorders 9, 183–196.
Javadapour, A., Malhi, G.S., Ivanovski, B., Chen, X., Wen, W., Sachdev, P., 2010. Hippocampal volumes in adults with bipolar disorder. The Journal of Neuropsychiatry and Clinical Neurosciences 22, 55–62.
Joffe, R.T., MacDonald, C., Kutcher, S.P., 1988. Lack of differential cognitive effects of lithium and carbamazepine in bipolar affective disorder. Journal of Clinical Psychopharmacology 8, 425–428.
Judd, L.L., Akiskal, H.S., Schettler, P.J., Coryell, W., Endicott, J., Maser, J.D., Solomon, D.A., Leon, A.C., Keller, M.B., 2003. A prospective investigation of the natural history of the long-term weekly symptomatic status of bipolar II disorder. Archives of General Psychiatry 60, 261–269.
Kent, L., Craddock, N., 2003. Is there a relationship between attention deficit hyperactivity disorder and bipolar disorder? Journal of Affective Disorders 73, 211–221.
Kessler, R.C., Adler, L., Barkley, R., Biederman, J., Conners, C.K., Demler, O., Faraone, S.V., Greenhill, L.L., Howes, M.J., Secnik, K., Spencer, T., Ustun, T.B., Walters, E.E., Zaslavsky, A.M., 2006. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. The American Journal of Psychiatry 163, 716–723.
Kolur, U.S., Reddy, Y.C., John, J.P., Kandavel, T., Jain, S., 2006. Sustained attention and executive functions in euthymic young people with bipolar disorder. The British Journal of Psychiatry 189, 453–458.
Kurtz, M.M., Gerraty, R.T., 2009. A meta-analytic investigation of neurocognitive deficits in bipolar illness: profile and effects of clinical state. Neuropsychology 23 (5), 551–562.
Martinez-Aran, A., Vieta, E., Reinares, M., Colom, F., Torrent, C., Sanchez-Moreno, J., Benabarre, A., Goikolea, J.M., Comes, M., Salamero, M., 2004. Cognitive function across manic or hypomanic, depressed, and euthymic states in bipolar disorder. The American Journal of Psychiatry 161, 262–270.
Milberger, S., Biederman, J., Faraone, S.V., Murphy, J., Tsuang, M.T., 1995. Attention deficit hyperactivity disorder and comorbid disorders: issues of overlapping symptoms. The American Journal of Psychiatry 152, 1793–1799.
Monks, P.J., Thompson, J.M., Bullmore, E.T., Suckling, J., Brammer, M.J., Williams, S.C., Simmons, A., Giles, N., Lloyd, A.J., Harrison, C.L., Seal, M., Murray, R.M., Ferrier, I.N., Young, A.H., Curtis, V.A., 2004. A functional MRI study of working memory task in euthymic bipolar disorder: evidence for task-specific dysfunction. Bipolar Disorders 6, 550–564.
Najt, P., Perez, J., Sanches, M., Peluso, M.A., Glahn, D., Soares, J.C., 2007. Impulsivity and bipolar disorder. European Neuropsychopharmacology 17, 313–320.
Nelson, H.E., 1976. A modified card sorting test sensitive to frontal lobe deficits. Cortex 12, 313–324.
Nierenberg, A.A., Miyahara, S., Spencer, T., Wisniewski, S.R., Otto, M.W., Simon, N., Pollack, M.H., Ostacher, M.J., Yan, L., Siegel, R., Sachs, G.S., S.T.E.P.-B.D. Investigators, 2005. Clinical and diagnostic implications of lifetime attention-deficit/hyperactivity disorder comorbidity in adults with bipolar disorder: data from the first 1000 STEP-BD participants. Biological Psychiatry 57, 1467–1473.
Partington, J.E., Leiter, R.G., 1949. Partington's pathway test. The Psychological Center Bulletin 1, 9–20.
Peluso, M.A., Hatch, J.P., Glahn, D.C., Monkul, E.S., Sanches, M., Najt, P., Bowdena, C.L., Barrattg, E.S., Soaresahi, J.C., 2007. Trait impulsivity in patients with mood disorders. Journal of Affective Disorders 100, 227–231.
Reichenberg, A., Weiser, M., Rabinowitz, J., Caspi, A., Schmeidler, J., Mark, M., Kaplan, Z., Davidson, M., 2002. A population-based cohort study of premorbid intellectual, language, and behavioral functioning in patients with schizophrenia, schizoaffective disorder, and nonpsychotic bipolar disorder. The American Journal of Psychiatry 159, 2027–2035.
Rey, A., 1941. L'examen physiologique dans le cas d'encephalopathie traumatique. Archives de Psychologie 28, 286–340.
Robinson, L.J., Thompson, J.M., Gallagher, P., Goswami, U., Young, A.H., Ferrier, I.N., Moore, P.B., 2006. A meta-analysis of cognitive deficits in euthymic patients with bipolar disorder. Journal of Affective Disorders 93, 105–115.
Seidman, L., Valera, E., Bush, G., 2004. Brain function and structure in adults with attention-deficit hyperactivity disorder. The Psychiatric Clinics of North America 27, 323–347.
Simard, S., Rouleau, I., Brosseau, J., Laframboise, M., Bojanowsky, M., 2003. Impact of executive dysfunctions on episodic memory abilities in patients with ruptured aneurysm of the anterior communicating artery. Brain and Cognition 53, 354–358.
Strakowski, S.M., DelBello, M.P., Adler, C., Cecil, D.M., Sax, K.W., 2000. Neuroimaging in bipolar disorder. Bipolar Disorder 2, 148–164.
Tamam, L., Tuglu, C., Karatas, G., Ozcan, S., 2006. Adult attention-deficit hyperactivity disorder in patients with bipolar I disorder in remission: preliminary study. Psychiatry and Clinical Neurosciences 60, 480–485.
Tamam, L., Karakus, G., Ozpoyraz, N., 2008. Comorbidity of adult attention-deficit hyperactivity disorder and bipolar disorder: prevalence and clinical correlates. European Archives of Psychiatry and Clinical Neuroscience 258, 385–393.
Temple, R.O., Duncan Davis, J., Silverman, I., Tremont, G., 2006. Differential impact of executive function on visual memory tasks. The Clinical Neuropsychologist 20, 480–490.
Thompson, J.M., Gray, J.M., Crawford, J.R., Hughes, J.H., Young, A.H., Ferrier, I.N., 2009. Differential deficit in executive control in euthymic bipolar disorder. Journal of Abnormal Psychology 118, 146–160.
Tremont, G., Halpert, S., Javorsky, D.J., Stern, R.A., 2000. Differential impact of executive dysfunction on verbal list learning and recall. The Clinical Neuropsychologist 14, 295–302.
Wechsler, D., Stone, C.P., 1987. Wechsler memory scale-revised (WMS-R). The Psychological Corporation, San Antonio, TX.
Wechsler, D., 1997. Wechsler Adult Intelligent Scale III [Manual], 3rd. Ed. The Psychological Corporation, San Antonio, TX.
Wender, P.H., Wolf, L.E., Wasserstein, J., 2001. Adults with ADHD. An overview. Annals of the New York Academy of Sciences 931, 1–16.
Wilens, T.E., Biederman, J., Wozniak, J., et al., 2003. Can adults with attention-deficit/hyperactivity disorder be distinguished from those with comorbid bipolar disorder? Findings from a sample of clinically referred adults. Biological Psychiatry 54, 1–8.
Wingo, A.P., Ghaemi, S.N., 2007. A systematic review of rates and diagnostic validity of comorbid adult attention-deficit/hyperactivity disorder and bipolar disorder. The Journal of Clinical Psychiatry 68, 1776–1784.
Young, R., Biggs, J., Ziegler, V., Meyer, D., 1978. A rating scale for mania: reliability, validity, and sensitivity. The British Journal of Psychiatry 133, 429–435.
Youngstrom, E.A., Birmaher, B., Findling, R.L., 2008. Pediatric bipolar disorder: validity, phenomenology, and recommendations for diagnosis. Bipolar Disorders 10, 194–214.
Zametkin, A.J., 1995. Attention deficit disorder: born to be hyperactive? JAMA 273, 1871–1874.