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A comparison of cognitive functioning in medicated and unmedicated subjects with bipolar depression

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Abstract

Objective—Neuropsychological studies of bipolar disorder reveal deficits in a variety of domains including affective processing, memory and sustained attention. These findings are difficult to interpret due to the potential confounding effects of mood-stabilizing medications. The present study aims to compare the cognitive performance of medicated and unmedicated subjects with bipolar depression to healthy control subjects.

Method—Unmedicated subjects with bipolar depression (UBD, n=32), subjects with bipolar depression on therapeutic doses of lithium or valproic acid (MBD, n=33), and healthy control subjects (HC, n=52) performed neuropsychological tasks measuring affective processing, visual memory and sustained attention. Performance measures were covaried with age and mood ratings, where applicable.

Results—With regard to affective processing, the MBD group exhibited greater response latency than the UBD and HC groups. For the same task, the MBD group made more omission errors during the happy condition than in the sad condition. On a task of sustained attention, the MBD group made more errors than the HC group. There were no significant group differences on measures of visual memory.

Conclusions—Deficits in affective processing were found in the medicated group, while unmedicated subjects appear to be unaffected. In particular, the MBD group made more errors during happy conditions, indicating a potential attentional bias in subjects with bipolar depression on mood-stabilizing medications. The present study also implicates impairment in sustained attention for medicated subjects with bipolar disorder, particularly those with the type II variety.

Keywords

bipolar disorder; cognition; depression; lithium; valproate

Introduction

Bipolar disorder (BD) is a relatively common, disabling mental illness that affects approximately 1.6% of the U.S. population (1). The disorder is associated with marked impairment in functioning and well-being, even after symptomatic recovery (2-4). There is accumulating evidence that interepisode recovery in BD is not complete (5). Increasingly,

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neuropsychological deficits have been reported in patients with BD. These deficits have been observed during depressed and manic states, with more recent evidence suggesting continuation of deficits during euthymic periods (6).

During depressed states of BD, reported deficits include verbal (7-9), nonverbal (10,11), and episodic memory (12), attention (7), executive function (7), decision-making (11), affective processing (13,14) and verbal learning and fluency (9). Certain impairments may increase with duration and severity of illness and persist during remission (15,16). (See (7,17) for reviews.) During manic states, deficits are widespread and more pronounced (12). Impairment during remission appears to be limited to executive function, memory, or a combination of the two. (See (5) for review.) More recently, attention deficits were observed in medicated euthymic subjects with BD (18). Such deficits were hypothesized to represent a core feature of BD (19). Importantly, subjects with BD, when tested, are generally receiving psychiatric medications that may affect performance on cognitive tests (20).

Affective processing in BD

Deficits in affective processing are central to many theories of depression (21); thus it is important to further evaluate the nature and severity of such deficits. Early research on affective processing focused on patients with major depressive disorder (MDD). This research is relevant to the current study as both MDD and BD involve depressed mood states. Neuropsychological studies of MDD typically reveal a bias towards responding to stimuli with negative emotional tone (21). Depressed patients may be particularly sensitive to negative affective stimuli and may process such stimuli more efficiently (21). An early study reported that individuals with depression required less time to recall unpleasant than pleasant memories, while healthy subjects recalled pleasant experiences more readily than unpleasant ones (22). Hale (1998) found that in subjects with MDD, judgment of negative emotions, but not positive emotions, was related to depression severity and persistence of depressive symptoms (23). In a color-word interference (modified Stroop) task, depressed subjects required more time to name the ink color of negative than positive or neutral words; this effect was not present following symptom remission (24).

In BD, affective bias appears to be mood state dependent. For example, Murphy and colleagues (1999) found that, during an affective go/no-go task, depressed and manic subjects with BD (almost all of whom were medicated) exhibited attentional biases for valenced words congruent with their current mood state. Unlike healthy control subjects, manic subjects took longer to respond to negatively, but not positively valenced words while depressed subjects took longer to respond to positively, but not negatively valenced words (25).

Effects of mood-stabilizing medication on cognitive functioning

Medications may play an important role in cognitive deficits in BD (26). Research suggests that treatment with mood-stabilizing medications may result in cognitive side effects. (See (27,28) for reviews.) Indeed, clinicians often have difficulty discerning illness-related deficits from treatment-related deficits (29). Subjects with bipolar disorder, when undergoing neuropsychological testing, are often receiving some combination of mood-stabilizers, antidepressants, anticonvulsants, neuroleptics, benzodiazepines, and antipsychotic medications. These medications may or may not affect performance on cognitive tests (20, 26). Thus, neuropsychological studies of subjects with BD may be confounded by varied medication regimens.

Cognitive side effects of lithium are commonly reported (30,31); however, controversy remains regarding the effect of lithium on cognition. In an early study, Engelsmann and colleagues (1988) found that memory scores remained stable over six years of lithium treatment (32). In

a more recent review, Goodwin and Jamison (1990) reported detrimental effects of lithium to include domains such as memory (long-term and retrieval), associative processing, semantic reasoning, and cognitive and psychomotor speed (30). Similarly, Pachet and Wisniewski (2003) found consistently reported deficits in psychomotor speed and verbal memory in clinical and healthy control populations treated with lithium (28). Cognitive deficits were often present without subjective awareness of the impairment (27).

The effects of anti-epileptic medications used in the treatment of BD (e.g., valproic acid, lamotrigine) on cognition are controversial (33). It has been reported that valproic acid affects cognition less than older anti-epileptic medications (29,34). Aldenkamp and colleagues (2002) studied the effects of valproic acid, lamotrigine, and placebo on cognitive ability in healthy volunteers. Subjects receiving valproic acid were impaired in cognitive activation and alertness (a reaction time measurement) but remained unaffected in other domains (35). Cognitive effects of valproic acid and other anti-epileptic medications appear modest when doses are kept within the therapeutic range and when treatment with multiple medications is avoided (29, 33).

To date, research on cognitive effects of medications in BD is inconsistent (26). For example, researchers from the Maudsley Bipolar Disorder Project concluded that antipsychotic medications were associated with lower general memory scores, but mood-stabilizers were not (26). The inconsistent findings concerning cognition and mood-stabilizing medication are likely attributable to methodological issues (27) and justify further research in this area (28). Additionally, although research supports the presence of deficits in affective processing in subjects with BD, no studies to date have compared affective processing in unmedicated and medicated subjects with BD. The unique design of the present study permits the comparison of medication-free subjects and those receiving mood-stabilizing medications on their performance of an affective processing task.

The goal of the present study was to compare cognitive functioning in subjects with BD on therapeutic doses of either lithium or valproic acid to medication free subjects and healthy subjects. Given that all patients are depressed, we expect to find deficits in affective processing for patients compared to controls. Specifically, we expect that patients with BD will exhibit deficits in processing positively-valenced material. Patients receiving mood-stabilizing medications will exhibit a similar pattern of deficits, although to a greater degree than patients who are medication-free. We predict that as a group, patients with BD will perform worse than healthy control subjects on measures of memory and attention. Patients on mood-stabilizing medications will perform worse than patients who are medication-free.

Method

Participants

Participants were recruited through advertisements placed in the local newspapers of the Washington, D.C. Metropolitan Area. Participants included individuals meeting DSM-IV criteria for bipolar disorder (BD) who were medicated (MBD, $n=33$, 18 female) or unmedicated (UBD, $n=32$, 24 female) at the time of testing and healthy control subjects (HC, $n=52$, 25 female). Patients were excluded for other primary Axis-I diagnoses, major medical conditions, current psychotic features and current substance use. All patients were tested during depressed mood states. Medicated subjects were receiving stable therapeutic doses of either lithium ($n=23$) or valproic acid (sodium valproate; $n=10$) for at least four weeks and all other medications were discontinued for at least four weeks prior to testing. Subjects in the UBD group were free of medications for three to six weeks prior to testing. Serum lithium levels of 0.6-1.2 mEq/L or valproic acid 50-125 mg/ml were kept constant for a minimum of 4 weeks (within this range) before the neuropsychological testing. The UBD group consisted of 7

subjects with a diagnosis of bipolar I disorder and 25 subjects with bipolar II disorder while the MBD consisted of 6 subjects with bipolar I disorder and 27 subjects with bipolar II disorder. Healthy control subjects were free of psychopathology and had no known family history of psychiatric illness.

The study was approved by the IRB, and all subjects gave written informed consent before taking part in the study. Patient diagnoses were determined by the Structured Clinical Interview for the Diagnostic and Statistical Manual for Mental Disorders (SCID-I, Patient version(36)). Healthy control status was determined using the SCID-I, Non-patient version. The 10-item, clinician-administered Montgomery Asberg Depression Rating Scale (MADRS; (37)) was administered within 24 hours of cognitive testing to evaluate depression severity. The MADRS was administered by trained clinicians. Among these clinicians, the intra-class correlation coefficient for the MADRS was .81.

Training and reliability for diagnostic interviews

Patient diagnoses were determined by clinicians from the National Institute Mental Health's Mood and Anxiety Disorders Program, each of whom completed a rigorous training program for the SCID-I. Clinicians attended two, three day training workshops and attended a separate six week course during which they watched approximately eleven hours of SCID training videos. In addition, clinicians rated ten videotaped interviews and conducted four live interviews. Clinicians were required to obtain a reliability quotient of at least .75 with the gold standard or consensus ratings. Mandatory “refresher” sessions were held at six month intervals with the goal of preventing rater drift.

Each individual diagnosis from the SCID was used as a separate rating for each rater. A kappa coefficient was calculated for each rater in comparison to a consensus SCID rating. These kappa values were then averaged across raters to obtain an overall kappa. The overall kappa for the entire research group was .88 with a total of 64 raters. In the present study, clinicians were drawn from this pool of reliable raters.

Cognitive testing

Cognitive tasks were presented on a high-resolution touch-screen monitor. Subjects were given standardized instructions for each of the four tasks. The Rapid Visual Information Processing (RVP), Pattern Recognition Memory (PRM) and Spatial Working Memory (SWM) tasks are part of the Cambridge Neuropsychological Test Automated Battery (CANTAB; Cambridge Cognition, Cambridge, United Kingdom). Brief descriptions of the CANTAB tasks can be found below. For more detailed descriptions, please see Sweeney, et al. (12). All subjects were also administered the Wechsler Abbreviated Scale of Intelligence (38) as an estimate of IQ. Cognitive tasks were administered by trained psychologists and research assistants.

Affective processing: Affective Shift (AS). (Murphy et al., 1999)—During the AS task, subjects are instructed to attend to a series of words as they appear on the screen. The words appear one at a time for 300ms, followed by a 900ms response interval. Each trial consists of 9 positively and 9 negatively valenced words. During each of eight trials, subjects must respond (by pressing the space bar on the keyboard) to either negatively (sad) or positively (happy) valenced words. Subjects are initially instructed to respond to happy words (e.g. hopeful, serene) but not sad words (e.g. glum, mistake). After two trials, the instructions change and the subject must respond to sad words. Conditions are alternated in a happy-happy-sad-sad-happy-happy-sad-sad pattern to create shift and non-shift response blocks. A shift block refers to a trial in which the subject must switch from responding to happy words to responding to sad words, or vice versa. A non-shift block refers to a trial in which the subject responds to

the same type of word (happy or sad) as in the previous trial. Performance measures include omission errors (misses), commission errors (false alarms) and reaction time.

Attention: Rapid Visual Information Processing (RVP)—During the RVP, subjects attend to a series of numbers that appear one at a time in the center of the screen for four minutes. They are instructed to press a lever each time they see one of three target sequences of numbers (3-5-7, 2-4-6 or 4-6-8). Performance measures include commission errors (false positives), omission errors (misses) and response latency (reaction time).

Visual memory: Pattern Recognition Memory (PRM)—During the PRM task, subjects first observe a series of twelve abstract patterns consecutively presented on the screen. Following the presentation of the target patterns, subjects are presented with two patterns (one target and one novel) and are instructed to choose the target pattern. Performance measures include percent of correct responses and response latency (reaction time).

Visuospatial Memory: Spatial Working Memory (SWM)—During the SWM task, several boxes are presented simultaneously in various locations on the screen. On each trial, subjects search for a blue token that has been hidden in one of the boxes. Subjects search by touching boxes one at a time to open them. Once a blue token has been found, the subject places it aside and begins to search for the next token. Only one blue token is hidden at a time, and subjects are instructed that once a blue token has been hidden in a given box, it will never be hidden in the same box again. Performance measures include between errors (subject selects a box where a token has previously been hidden), within errors (subject selects a box where they have already looked during the same trial), and a strategy score (estimate of the subject's ability to adopt an effective strategy while looking for blue tokens). The SWM task increases in difficulty as the task progresses by increasing the number of boxes in which the subject has to search for tokens.

Statistical Analysis

Oneway ANOVAs and χ^2 tests were used to compare demographic variables by group. The Kolmogorov-Smirnov test of normality and Levene's test of homogeneity of variance were used to examine parametric test assumptions for continuous outcome measures. Log and square root transformations were used to handle problems, but such adjustments did not improve the fit to the assumptions. Thus, nonparametric statistics were used.

Spearman's rho correlations were calculated to estimate the magnitude of the linear relationships between age, Montgomery Asberg Depression Rating Scale (MADRS) scores, length of illness, and each outcome measure. Age, MADRS score, or length of illness was included as a covariate in secondary analyses of any measure with a correlation greater than .30. Covariates were handled by regressing out the covariate from the outcome measure in a linear regression and using the unstandardized residuals in Kruskal-Wallis tests as in the primary analysis. All post hoc comparisons were corrected using Hochberg's adjusted Bonferroni procedure.

For all outcome measures where significant group differences were found with the MBD group, Mann-Whitney U tests were run to determine whether differences existed for subjects taking lithium versus valproic acid. Additional tests were run omitting subjects with bipolar I disorder to determine the impact of this smaller patient group on the overall results. One more analysis excluded patients with MADRS scores below 25 to balance the patient depression levels and ensure differences were due to group status instead of depression level. This analysis included 31 patients from the MBD group and 17 patients from the UBD group.

Results

Demographic characteristics

Demographic information is presented in Table 1. Healthy subjects were similar to MBD and UBD subjects on age and full-scale intelligence quotient (FSIQ) scores. The UBD group had a larger percentage of females than the other groups. The MBD group had significantly higher Montgomery Asberg Depression Rating Scale (MADRS) scores than the UBD and HC groups and the UBD group had more depression than the HC group. The MBD and UBD groups were similar in regards to length of illness.

Although the MBD group had significantly higher MADRS scores than the UBD group, none of the outcome measures were moderately related to MADRS scores (r 's $< .30$). Age was correlated with SWM between errors ($r = .37$). Length of illness was correlated with the mean latency for the RVP ($r = .32$) as well as omission errors for the sad, non-shift condition of the affective shift task ($r = -.44$). Each of these significant factors was used as a covariate for the related measure.

Affective Shift task

Mean scores and results for the AS are presented in Figure 1. During the happy shift condition, a significant group difference was noted for omission errors ($p = .001$) that was not significant for the other conditions (sad shift, $p = .93$; happy non-shift, $p = .005$; sad non-shift, $p = .046$). More specifically, the MBD group made more omission errors (misses) than the UBD and HC groups (Figure 1 A). This pattern of performance remained intact when removing BPIs ($p = .01$) or patients with MADRS less than 25 ($p = .007$). Examining the type of medication used in the patient groups was in the direction of indicating more errors in patients on lithium in the happy shift condition ($p = .02$), but this was not significant. Controlling for length of illness did not alter these results.

For reaction time, there were significant group differences for all conditions (happy shift; $p < .001$, sad shift, $p < .001$; happy non-shift, $p < .001$; sad non-shift, $p = .0023$). In each case, the MBD group required more time to respond than the UBD group and the HC group (Figure C). After excluding BPIs, the initial group differences remained significant (happy shift, $p < .001$; sad shift, $p < .001$; happy non-shift, $p = .002$; sad non-shift, $p = .008$). Similarly, after excluding those with less severe depression, there were no changes in the results (happy shift, $p < .001$; sad shift, $p = .003$; happy non-shift, $p = .004$; sad non-shift, $p = .015$). No significant reaction time differences were found between medicated patients on lithium versus valproic acid (p 's $> .58$).

For commission errors, there were no group differences (happy shift, $p = .79$; sad shift, $p = .06$; happy non-shift, $p = .41$; sad non-shift, $p = .22$). Excluding BPIs (p 's $> .04$) or less severely depressed patients (p 's $> .23$) did not alter these results. Patients on lithium made more, but not significantly more, commission errors than those on VPA in the happy shift ($p = .02$) and sad shift conditions ($p = .02$).

CANTAB tasks

The mean scores and statistics for the CANTAB outcome measures are presented in Table 2. Significant group differences were present on the RVP. The MBD group made significantly more omission errors (misses) than the HC group. The MBD group had longer response latencies than the HC and UBD groups. Removing BPIs eliminated the omission errors effect ($p = .01$), and the latency effect ($p = .10$). Removing less depressed patients from the analysis also eliminated the significance of the omission errors ($p = .18$) and latencies ($p = .06$). Covarying for length of illness did not alter the significance of the results. There were no group differences with commission errors.

On the two memory measures (SWM and PRM), no significant differences were found. Covarying for age, removing the BPIs, and examining only patients with MADRS scores above 24 did not change these results.

When comparing patients taking lithium or VPA, the VPA group tended to make more between errors on the SWM than the lithium group, though this did not reach significance ($p=.02$). No other lithium versus VPA comparisons were significant.

Discussion

The present study reports affective processing and attention deficits for subjects with BD on lithium or valproic acid, but did not find such deficits for unmedicated subjects. In particular, the MBD group made more errors during happy conditions of the Affective Shift task, indicating a relative attentional bias in subjects with bipolar depression while on mood-stabilizing medications. Visual memory measures were similar for the subjects with bipolar depression, regardless of medication status, and the healthy subjects. Although the medicated patients had significantly higher MADRS scores than the unmedicated patients, examining only patients with more severe levels of depression did not affect the results. This suggests that depression severity did not significantly contribute to the reported deficits. It is also notable that MADRS scores were not at least moderately correlated with any outcome measures. Further, covarying for age or length of illness for relevant variables made little change in the results, suggesting that differences detected represent true group differences, irrespective of these characteristics. Similarly, examining only patients with bipolar II disorder made little change in the results. It should be emphasized that most patients in this study had bipolar II disorder, and the degree to which these findings can be generalized to all patients with BD is uncertain.

Affective processing

Medicated subjects with BD displayed an attentional neglect of positively valenced material not demonstrated by unmedicated BD or healthy subjects. The selective deficit in processing positively valenced material for medicated subjects is an important clinically relevant finding. Interestingly, a study including medicated subjects with MDD and healthy controls found a trend such that depressed subjects responded more slowly than healthy controls to positive words on the AS task (21). Similarly, in a study including primarily medicated subjects with BD, patients were slower than controls to respond to happy targets (25). We believe that the present study reveals a similar effect; however this neglect for positive words is reflected in error rates with medicated BD subjects making more errors when responding to happy words. It is noteworthy that in a study with adolescents with recent first episode major depression, almost all of whom were not receiving medication, a selective deficit in accurately processing positively valenced material was also found (39).

Attention

Our study verifies previous research (7,18,19) reporting attention deficits in medicated BD subjects. We found that subjects with BD, while on lithium or valproic acid, had difficulty with the RVP task, a measure of sustained attention. Additionally, the MBD group took longer to respond to stimuli on the Affective Shift task regardless of the emotional valence of stimuli. Although not significant, the MBD group was also slower to respond than the other two groups on the PRM task. Our interpretation of these collective findings is that the MBD group experienced psychomotor slowing while the other two groups did not.

Memory

Previous studies report deficits in memory in subjects with BD (10,12,42,43). We did not find impairments in visual memory in our sample. Memory problems are cited as common side effects of lithium treatment in particular (30); however, in the present study, neither medicated nor unmedicated subjects with BD exhibited such deficits. It is particularly surprising that the patients did not perform worse than controls in light of the severity of their symptoms. It is possible that, had we applied a test of verbal memory or perhaps a more sensitive measure of visual memory, we might have detected deficits similar to those found in previous studies.

Lithium versus valproic acid

When differences were noted in the MBD group's performance relative to the unmedicated group, post-hoc tests were performed to investigate differences between those receiving lithium and valproic acid. For commission errors in the AS task, results indicated a trend in the direction for more errors in patients on lithium in the happy shift condition, but this was not significant. It is therefore possible that the deficit in affective processing found in the MBD group may be driven by the lithium and not the valproic acid group. A larger sample size is needed to further address this question.

Clinical implications

Goodwin and Jamison (1990) discuss the importance of “lessened enthusiasms” as a side effect of medication treatment for BD (30). Likewise patients with BD note “dulling of the senses” as a side effect of mood-stabilizing medications. The potential contribution of medication to these symptoms may go unnoticed by clinicians who consider them to be manifestations of the illness itself (30). This study found that patients with BD on mood-stabilizing medications made significantly more errors when responding to positively valenced material than their unmedicated counterparts, suggesting a deficit in processing positive material. The AS task appears to be a sensitive measure of affective processing and may detect affective blunting experienced by patients receiving mood-stabilizing medications. Given that unmedicated patients performed similarly to healthy controls and these results do not seem to be due to differences in levels of depression, this research suggests that clinicians should be vigilant in looking for signs of affective blunting during treatment with mood-stabilizers. Patients who experience blunting of affect may require adjunctive psychological treatment.

Harmer and colleagues (2002) suggest that sustained attention deficits may partially explain the impairment in social and occupational functioning that persists during euthymia for subjects with BD (19). The present findings suggest that such attentional impairment may be specifically related to treatment with mood-stabilizing medications. These deficits, which are often presumed to be related to the illness itself, may in fact be an effect of medication or a combination of the two. If further research confirms that impaired attention is indeed a side effect of a specific medication or mood-stabilizing medications in general, this should be considered in determining the best treatment for patients.

Limitations

The brief nature of the current neuropsychological battery was necessary within the context of a larger treatment protocol. To fully assess the affects of mood-stabilizing medications on cognitive functioning in BD, a more comprehensive battery of tests should be employed. Martinez-Aran and colleagues (2004) observed deficits in verbal memory and executive function in euthymic subjects with BD (the majority of whom were receiving medications). These deficits are argued to be trait- rather than state-dependent deficits (43). The present study did not include measures of verbal memory or traditional measures of executive functioning. Further research including such measures would greatly strengthen our understanding of the

effects of mood-stabilizing medications on cognition in BD. Additionally, the RVP may have too high a memory load to be considered a true continuous performance task. Future research using a more traditional measure of sustained attention would be helpful in elucidating the effects of medication on attention in BD. Robinson and colleagues (2006) report evidence that cognitive impairment is a vulnerability factor for bipolar disorder that worsens as the illness progresses (44). Further research aimed at disentangling illness from medication-related deficits would also greatly advance our understanding of cognitive functioning in BD.

It is notable that the MBD group as a whole was more severely depressed than the UBD group. Although efforts were made to ensure that the effects noted were due to medication status alone, future research including groups more closely matched on depression severity would be helpful. Research involving euthymic patients and patients in (hypo)manic episodes would also help disentangle mood- from medication-related effects. In the current study, two-thirds of the MBD group was taking lithium. Future research should include greater numbers of patients taking valproic acid, and the effects of other medications on cognition should also be examined.

More generally, the present study has a relatively small sample size. Samples of 32 per group have only 50% power to detect a moderate level difference ($d=.50$) between groups. While the degree of clinically important difference has not been determined for the tasks included here, it is notable that significant differences were found with relatively small groups. Future studies would benefit from larger sample sizes.

Conclusion

Impairments in affective processing and attention were found in medicated but not unmedicated subjects. Specifically, subjects with BD on mood-stabilizing medications were impaired in processing positively valenced material. This finding supports the notion that affective blunting may occur as a result of treatment with mood-stabilizing medications. Further research implementing a more comprehensive neuropsychological battery including a complex assessment of executive functioning, verbal memory and the measurement of other aspects of emotional processing is warranted. Similarly, longitudinal research focusing on the relationship between cognitive functioning and other symptomatic changes in patients with BD treated with mood-stabilizing medications would be valuable. The current study suggests that medication status may contribute to cognitive deficits reported in previous studies.

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Figure 1.

Results for the Affective Shift Task. (A) During the happy shift condition only, the MBD group made significantly more omission errors than the UBD and HC groups. (B) No group difference were present for commission errors. (C) Increased reaction time by the medicated bipolar group compared to unmedicated bipolar and healthy control groups was present for all conditions.

Table 1

Demographic characteristics of the sample. UBD, unmedicated bipolar disorder; MBD, medicated bipolar disorder; HC, healthy control; MADRS, Montgomery Asberg Depression Rating Scale.

	UBD (N=32)	Mean (SD) Range	MBD (N=33)	HC (N=52)	p
Age	35.3 (8.7) 21-54		41.1 (10.9) 21-58	37.0 (10.1) 21-59	.06
Sex (% Female)	75%		55%	48%	.05 UBD>MBD,HC
IQ	115.9 (12.1) 90-136		114.7 (11.8) 89-138	118.3 (10.7) 95-139	.35
MADRS	25.7 (8.3) 14-41		32.1 (5.8) 14-44	0.2 (0.6) 0-3	<.001 (MBD>UBD>HC)
Illness duration (months)	236.6 (127.7) 36-468		262.4 (117.3) 60-516		.40

Note: MADRS scores range from 0 to 60, with 0-8 indicating normal mood, 9-17 indicating mild depression, 18-34 indicating moderate depression, and 35 or greater indicating severe depression.

Table 2

Mean scores and results for CANTAB outcome measures. SWM, Spatial Working Memory; PRM, Pattern Recognition Memory; RVP, Rapid Visual Information Processing.

	Mean (SD)			p
	UBD (N= 33)	MBD (N= 32)	HC (N= 52)	
SWM between errors	28.1 (22.4)	24.9 (16.8)	18.9 (18.7)	.07
SWM within errors	3.0 (5.5)	1.9 (3.4)	2.0 (3.3)	.49
SWM strategy	33.5 (7.0)	32.0 (6.3)	31.0 (5.5)	.23
PRM percent correct	91.5 (8.4)	91.4 (8.8)	92.3 (6.9)	.99
PRM latency	1904.7 (600.1)	2205.5 (473.0)	1998.2 (682.0)	.004
RVP omission errors	8.9 (5.4)	11.1 (4.8)	6.7 (4.2)	.001 [*] MBD > HC
RVP commission errors	1.0 (1.3)	0.7 (1.1)	0.8 (1.3)	.43
RVP latency	454.3 (66.3)	509.0 (90.4)	469.4 (97.9)	.03

* Significant after Hochberg's adjusted Bonferroni Correction.