Psychological Medicine, 2006, **36**, 1799–1809. © 2006 Cambridge University Press
doi:10.1017/S0033291706008804 First published online 29 August 2006 Printed in the United Kingdom

Bipolar I and bipolar II disorder: cognition and emotion processing

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ABSTRACT

Background. Cognitive impairment may be part of the endophenotype of bipolar disorder (BP), but little is known about patterns and severity of impairment in BP subgroups and their relation to depression. The same applies to deficits in emotion processing known to be present in BP.

Method. To explore the relationship between depression and impairment in cognition and emotion processing and the differences between BP subgroups, we assessed 36 (25 BP I and 11 BP II) patients using a cognitive battery and a facial emotion recognition task.

Results. BP patients were impaired compared to published norms on memory, naming and executive measures (Binomial Single Proportion tests, $p<0{\cdot}05$). Cognitive performance was largely unrelated to depression ratings. Surprise recognition was the only emotion processing impairment in BP patients compared to controls (patients' recognition score 75% *v.* controls' 89%, $p=0{\cdot}024$). Patients with higher depression ratings were more impaired in recognizing expressions of anger ($t_{23}=2{\cdot}21$, $p=0{\cdot}037$). BP II patients were more impaired than BP I patients in IQ, memory and executive measures (Mann–Whitney tests, $p<0{\cdot}05$). Depression severity or exposure to medication or electroconvulsive therapy (ECT) did not explain these differences.

Conclusions. We confirm cognitive impairment and an isolated facial emotion processing deficit in BP patients and suggest that these deficits are largely unrelated to depressive symptoms. Our study also provides evidence that cognitive deficits are more severe and pervasive in BP II patients, suggesting that recurrent depressive episodes, rather than mania, may have a more detrimental and lasting effect on cognition.

INTRODUCTION

Bipolar disorder (BP) is a common and disabling condition; its prevalence is estimated at 1·5–3% of the population (Narrow *et al.* 2002), and 30–50% of those in remission will not achieve premorbid psychosocial functioning (Goodwin & Jameson, 1990). There is evidence that poor outcome is highly associated with cognitive impairment, particularly executive dysfunction (Martinez-Aran *et al.* 2004*a*), and a number of studies have reported that cognitive impairment persists in remission (Ferrier *et al.* 1999; Rubinsztein *et al.* 2000). Deficits in full-scale and performance IQ (Dalby & Williams, 1986), verbal recall (Martinez-Aran *et al.* 2004*b*), visual memory (Coffman *et al.* 1990), conceptual set-shifting (Goldberg *et al.* 1993), planning (Ferrier *et al.* 1999), verbal fluency and abstract reasoning (Coffman *et al.* 1990) and attention (Ali *et al.* 2000) have been reported in BP.

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https://doi.org/10.1017/S0033291706008804 Published online by Cambridge University Press

Table 1. *Bipolar (BP) I and II subgroups: demographic and clinical characteristics*

	Whole BP group mean (range)	BP I ($n=25$)	BP II ($n=11$)	Test statistic for comparison of subgroups
Gender	13 men, 23 women	10 men, 15 women	3 men, 8 women	Fisher's exact $p=0{\cdot}667$
Age (years)	39·0 (21–62)	37·4	42·8	$t_{34}=1{\cdot}61$, $p=0{\cdot}12$
Age at onset (years)	25·3 (11–46)	24·1	28·4	$t_{30}=1{\cdot}4$, $p=0{\cdot}17$
Hospital admissions	3·8 (0–12)	4·4	2·3	$t_{28}=1{\cdot}66$, $p=0{\cdot}107$
Previous depressive episodes	5·1 (0–20)	4·3 (0–10)	7·4 (1–20)	$t_{29}=1{\cdot}86$, $p=0{\cdot}07$
Duration (years)	13·8 (1–32)	13·4	14·9	$t_{30}=0{\cdot}407$, $p=0{\cdot}69$
BDI	10·9 (0–33)	9·9	12·9	$t_{24}=0{\cdot}564$, $p=0{\cdot}587$
NART IQ	113·4 (95–127)	114·3	116·5	$t_{33}=0{\cdot}678$, $p=0{\cdot}502$

BDI, Beck Depression Inventory; NART, National Adult Reading Test.

Kruger *et al.* (2003) reported that mild affective symptoms often persist in remission in BP. Many previous studies have not accounted for the impact of affective symptoms, although these can influence cognitive performance variably in different domains (Beats *et al.* 1996; Elliott *et al.* 1996). Thus, impairment of executive function (Ferrier *et al.* 1999; Martinez-Aran *et al.* 2004*a*) has been reported more consistently than impairment of non-verbal recall (Quraishi & Frangou, 2002) in BP patients with residual depressive symptoms.

The pattern of cognitive impairment in BP subgroups also remains to be determined. To our knowledge, one study (Martinez-Aran *et al.* 2004*b*) has compared the cognitive profiles of BP I patients (one or more manic episodes with or without episodes of depression) with those of BP II patients (one or more episodes of both hypomania and depression). That study compared the performance of BP subtypes on eight tests and found BP I patients to be worse at verbal recall. Such interactions between cognitive performance and BP subtype may reflect genetic heterogeneity (MacQueen *et al.* 2005).

Deficits in emotional processing of facial affect, such as facial affect labelling and emotion recognition, have also been reported in BP (George *et al.* 1998; Getz *et al.* 2003). George *et al.* (1998) argued that deficits in facial emotion processing are state dependent. However, these deficits have been documented in remission (Addington & Addington, 1998), although other studies found none (Harmer *et al.* 2002; Venn *et al.* 2004). Two studies found performance on facial emotion processing tasks to be related to cognitive deficits in schizophrenic patients (Kohler *et al.* 2000; Sachs *et al.* 2004). The association between emotion processing and cognitive deficits in BP thus remains to be determined.

Here we present the results of a study of 36 patients with BP I- or BP II-type illness who underwent assessment on an extensive neuropsychological battery that included tests of emotion processing. The aims of the study were to compare the performance of the subgroups across cognitive domains, to determine the role of affective symptoms on cognitive performance and to explore the relationship between emotional processing and performance in several cognitive domains.

METHOD

Subjects

Thirty-six BP patients were included in the study. Patients were recruited from inner-London out-patient psychiatric clinics ($n=25$) and from respondents to an advertisement in the *Journal of the Manic-Depressive Fellowship* ($n=11$). Exclusion criteria were the presence of a co-morbid psychiatric condition, history of neurological or systemic disease, head injury leading to unconsciousness, or alcohol/drug abuse. Twenty-five patients met the criteria for a DSM-IV diagnosis of BP I disorder (10 men, 15 women) and 11 for BP II disorder (three men, eight women), according to the Structured Clinical Interview for DSM-IV (SCID; First *et al.* 1997). Demographics for the whole group and for the bipolar subgroups are described in the Results (Table 1).

Two patients were unmedicated at the time of the study and information on medication was incomplete for four. The rest were receiving

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mood stabilizers (23 lithium, three sodium valproate, four carbamazepine, three lamotrigine) and/or antidepressants (11) and neuroleptics (nine). Three BP I and two BP II patients had received electroconvulsive therapy (ECT). Thirty healthy controls were used to obtain normative data for those tests for which standardized data were not available. The controls were volunteers drawn from non-clinical staff at the National Hospital for Neurology and Neurosurgery and were matched for premorbid IQ with the patient group.

These patients had taken part in a study of structural brain abnormalities using high-resolution magnetic resonance imaging (MRI) and magnetization transfer imaging (MTI) (Bruno *et al*. 2004, 2006).

The study was approved by the relevant ethical committees. Written informed consent was obtained from all participants.

Clinical assessment

All patients were interviewed by a trained psychiatrist (S.B.) using the SCID (First *et al*. 1997) and all met DSM-IV diagnostic criteria for BP. The presence of a current affective episode was assessed using the SCID. Nine patients had a current depressive episode (five BP I, four BP II). The proportion of patients with a current depressive episode did not differ between the BP subgroups ($\chi^2 = 1{\cdot}650$, df = 1, N.S.). None of the patients had a current manic/hypomanic episode. Information about current affective episodes was incomplete for six patients (three BP I, three BP II).

Information was collected about developmental milestones, education and employment, substance misuse, medical history, duration of illness, medications, and exposure to ECT. Information about hospital admissions and previous affective episodes was obtained from the patients. The number of hospital admissions did not differ between subgroups ($t = 1{\cdot}66$, N.S.). BP II patients reported more depressive episodes than BP I patients (BP I mean 4·26, S.D. = 3·18; BP II mean 7·38, S.D. = 6·12, $t = 1{\cdot}86$, $p = 0{\cdot}07$). Data on depressive episodes were incomplete in five patients.

Depressive symptoms were assessed using the Beck Depression Inventory (BDI; Beck *et al*. 1961). Fifteen patients scored in the normal range (BDI score 0–9), four with current depressive episode, 10 without, one current affective status unknown; 11 scored in the mild to moderate range (BDI score 10–30), two with current depressive episode, nine without; and two scored in the severe range (BDI score above 30), one with current depressive episode, one unknown. Of the eight patients without BDI data, two met SCID criteria for a depressive episode and three did not. Information was incomplete for the remaining three patients.

Neuropsychological assessment

An extensive neuropsychological battery, including tests evaluating both cognition and emotion processing, was administered in the Neuropsychology Department of the National Hospital for Neurology and Neurosurgery.

Cognitive tests

The following cognitive domains were examined:

(1) General intellectual functioning was assessed with the Wechsler Adult Intelligence Scale – Revised (WAIS-R; Wechsler, 1981) and measures of Verbal, Performance and Full-Scale IQ were obtained, pro-rating from four verbal (Vocabulary, Digit Span, Arithmetic, Similarities) and three non-verbal (Picture Completion, Picture Arrangement, Block Design) subtests. Optimal premorbid intellectual functioning was estimated using the National Adult Reading Test (NART; Nelson, 1982). The difference between the NART IQ and the WAIS IQ was considered an index of IQ change. A difference greater than 20 IQ points was taken as evidence of intellectual decline.

(2) Verbal and visual memory were assessed using the Recognition Memory Tests (Warrington, 1984); the Paired Associates Learning Test (PALT; Warrington, 1996); the Rey–Osterreich Complex Figure Test (Rey, 1964) and the Doors and People Test: Shapes subtest (Baddeley *et al*. 1994).

(3) Attention and concentration were measured with the Trail-Making Test A of the Army Individual Test Battery (US Army, 1944).

(4) Naming ability was assessed with the Graded Naming Test (McKenna & Warrington, 1983).

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(5) Executive functions were evaluated with the Modified Wisconsin Card Sorting Test (MCST; Nelson, 1976); the Stroop Colour–Word Test (Trenerry *et al.* 1989); the Controlled Oral Word Association (or Verbal Fluency) Test (Benton, 1968); the Hayling Sentence Completion Task (Burgess & Shallice, 1997); the Spatial Working Memory and the Intra-Dimensional/Extra-Dimensional Set-Shift subtests from the Cambridge Neuropsychological Test Automated Battery (CANTAB) (Sahakian & Owen, 1992); and the Trail-Making Test B of the Army Individual Test Battery (US Army, 1944).

For all tests raw scores were converted into standardized scores, and scores falling at or below the 5th percentile were determined (10th percentile for the Rey–Osterreich Complex Figure Test, the Trail-Making Test parts A and B, and the Controlled Oral Word Association Test as 5th percentile data were not available). Patients were considered to have cognitive impairment in a given task if their scores were at or below the 5th percentile of a normal standard population (or 10th percentile for the tests described above).

Scores on the MCST were calculated according to the number of categories achieved and the percentage of total perseverative errors (Kapur *et al.* 2003). Four or five categories and a score of less than 50% perseverative errors indicated mild impairment. Fewer than four categories and/or a score at or above 50% perseverative errors indicated marked impairment. Patients were considered to have memory impairment or executive impairment if they were impaired on one or more memory or executive tests respectively.

Composite cognitive scores

To produce the composite cognitive score, cognitive scores were summed across 12 neuropsychological measures for each participant, pro-rating in the case of missing values. In all tests for which standardized normative data were available, a cognitive score was assigned as follows: scores at or above the 50th percentile, 0; 25th–49th percentile, 1; 6th–24th percentile, 2; 0–5th percentile, 3. Thus a patient performing at or below the 5th percentile on all tests would score 36 whereas a patient performing at or above the 50th percentile on all tests would score 0.

Emotion processing task

A variation of the emotional expression multimorph task was administered (Frigerio *et al.* 2002; Coupland *et al.* 2003). This task contains examples of six basic emotional facial expressions (happiness, surprise, fear, sadness, disgust, and anger), taken from the validated Pictures of Facial Affect Series (Ekman & Friesen, 1976). For each basic expression, 18 stimuli were prepared by blending a prototypical expression (100% expression) in varying proportions with a neutral expression (0% expression). The neutral face is gradually morphed through 20 stages in 5% increments into one of the six prototypical expressions. Faces were presented on a computer screen.

Participants viewed each face change rapidly from a neutral to a prototypical expression. They were first asked to state the emotion expressed from a choice of six emotions (happiness, surprise, fear, sadness, disgust, and anger). This provided a measure of their accuracy at recognizing emotion expression. Subsequently, the same face changed slowly from neutral to the emotion previously displayed. Participants were required to state at which stage they recognized the emotion by pressing a key on the computer keypad. This constituted a measure of sensitivity to emotion expression. Following a practice phase consisting of one example of each emotion, the 18 test stimuli were presented in a random order, and this task was performed twice. Thus, each emotion was presented six times.

Scores for sensitivity were derived in accordance with published procedures (Blair *et al.* 2001; Coupland *et al.* 2003). One point was scored for successful recognition of the prototypical expression (stage 20). Twenty points were scored for successfully recognizing a 5% morph (stage 1), as it is 19 stages away from the prototype. Incorrect identification of the emotion expressed scored 0. Additionally, the mean percentage of correct recognition of expression (accuracy) was calculated separately for each expression. The patients' performance was compared with that of a group of 30 healthy controls matched for premorbid IQ

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($t_{63}=1{\cdot}87$, N.S.). Means of accuracy and sensitivity scores were generated for the whole group of patients with BP, for the BP I and BP II subtypes, and for the control group.

To examine the contribution of affective symptomatology to neuropsychological performance, we categorized patients into two groups, according to whether they scored in the normal range on the BDI (0–9) or above that threshold (>9). Fifteen patients scored in the normal range, and 13 scored above the threshold.

Statistical analysis

All data were analysed in SPSS version 11.0 (SPSS Inc., Chicago, IL, USA). The numbers of patients scoring at or below the 5th percentile were determined. Binomial single proportion exact tests were used to test whether these were significantly greater than the number expected if the patients were the same as the healthy standardization sample from whom the published norms were derived. Mann–Whitney tests were used to compare the individual test scores and composite scores across BP subgroups and across groups of patients with and without current depressive episode according to the SCID. Independent samples t tests were used to compare IQ scores across BP subgroups and to compare scores on the facial emotion recognition task between patients and controls and between clinical subtypes and groups with and without depressive symptoms. The proportions of patients in each subgroup taking psychotropic medications, or who had received ECT, were compared using χ^2 tests. McNemar tests were used to compare the numbers of patients impaired across different domains within a group. Pearson's and Spearman's rank-order correlations were used to examine correlations between clinical variables and neuropsychological test scores. Multiple regression analyses were used to determine the significance of subgroup differences in neuropsychological test scores while controlling for the effect of clinical variables.

RESULTS

Demographic statistics for the whole group and for BP I and BP II subgroups are reported in Table 1. There was a trend for BP II patients to be older and to have had an older age of onset; however, the BP I and BP II subgroups were matched for hospital admissions, duration of illness, scores on the BDI and estimated premorbid IQ. The two subgroups did not differ in the proportion of patients who were taking lithium ($\chi^2=0{\cdot}007$, $p=0{\cdot}935$), antidepressants ($\chi^2=1{\cdot}63$, $p=0{\cdot}201$) or neuroleptics ($\chi^2=0{\cdot}285$, $p=0{\cdot}593$), or who had received ECT in the past ($\chi^2=0{\cdot}244$, $p=0{\cdot}621$).

Neuropsychological performance of the whole BP group

Neuropsychological test scores and numbers of patients impaired in each test are shown in Table 2. When the number of patients scoring below the 5th percentile was significantly larger than expected in the normative population, this is indicated in the table. This was the case for the following cognitive domains: visual and verbal recall (Shapes Test, Rey recall, PALT1) and recognition memory (Recognition Memory for Faces and Recognition Memory for Words), naming (Graded Naming Test) and selected measures of frontal executive function – in particular, response initiation and suppression (Hayling Sentence Completion Task), set-shifting (CANTAB: ID/ED Set-Shift) and spatial working memory (CANTAB Spatial Working Memory).

Fig. 1 depicts numbers of patients presenting with specific cognitive impairments. The most common impairment was a selective executive dysfunction and the next commonest was impairment in executive function and memory. Selective impairments in memory or naming were much less frequent. There was a trend for more patients to be impaired in executive function than in memory (McNemar's exact test, $p=0{\cdot}077$) and impairment in memory was commoner than in naming (McNemar's exact test, $p=0{\cdot}035$). Other patterns of cognitive impairment were far less common (Fig. 1).

Comparison between BP I and BP II subgroups

The BP I subgroup was only impaired with respect to the normative data in verbal recognition and spatial working memory. The BP II subgroup was also impaired in these measures and additionally in four memory measures

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Table 2. *Standardized neuropsychological test scores for the whole bipolar group*

Standardized neuropsychological tests	Mean (S.D.)	Range	Number impaired[a]	*n*	Binomial single proportion test (*p*)
General intelligence					
WAIS-R Full IQ	110·56 (16·91)	82–143	0	36	0·158
WAIS-R Verbal IQ	114·36 (15·95)	86–149	0		0·158
WAIS-R Performance IQ	105·25 (17·25)	74–139	1	35	0·457
IQ change[b]					
Full IQ change	3·58 (12·91)	−30 to 24	2		N.A.
Verbal IQ change	−2·29 (11·79)	−30 to 14	0		
Performance IQ change	8·03 (14·90)	−22 to 34	9		
Memory					
Recognition Memory: Words	43·97 (5·80)	25–50	6*	36	0·016
Recognition Memory: Faces	40·69 (5·07)	29–50	7**	35	0·004
Paired Associate Learning: Trial 1	17·67 (4·74)	6–24	6*	36	0·016
Paired Associate Learning: Trial 2	22·61 (2·32)	13–24	2		0·543
Rey Recall[c]	20·38 (7·34)	10·5–34	10***	30	<0·001
Doors and People Visual Recall (Shapes)	30·69 (5·53)	19–36	8***	36	<0·001
Language					
Graded Naming Test	20·5 (6·37)	4–28	6*	36	0·016
Executive functions					
Phonemic Fluency (FAS[c])	51·89 (16·13)	19–103	1	36	0·226
Hayling Task	16·84 (3·72)	5–22	5*	33	0·046
Stroop Test	101·22 (12·68)	68–112	2	36	0·528
Trail-Making B[c]	75·68 (26·08)	32–142	4	34	0·892
ID/ED Set-Shift errors	24·67 (20·85)	7–66	5*	32	0·04
SWM: Errors	34·83 (23·39)	0–82	6**	30	0·006
SWM: Strategy	35·93 (5·58)	20–45	10***		<0·001
MCST[d]					
Categories	5·61(0·90)	3–6			
Errors	9·79 (14·64)	0–77	7	36	N.A.
Perseverative errors	4·06 (6·00)	0–31			
Attention					
Trail-Making A[c]	33·5 (10·54)	17–69	0	34	0·056

ID/ED Set-Shift, Intra-Dimensional/Extra-Dimensional Set-Shift; SWM, Spatial Working Memory; MCST, Modified Wisconsin Card Sorting Test; WAIS, Wechsler Adult Intelligence Scale; NART, National Adult Reading Test.

[a] Number impaired refers to number of patients scoring at or below the 5th percentile according to standardized norms.

[b] IQ change = NART IQ – WAIS-R IQ. For IQ change, criterion for impairment is decline greater than or equal to 20 IQ points.

[c] Criterion of impairment is a score at or below the 10th percentile.

[d] Impairment according to criteria of Kapur *et al.* (2003).

* $p<0·05$, ** $p<0·01$, *** $p<0·001$.

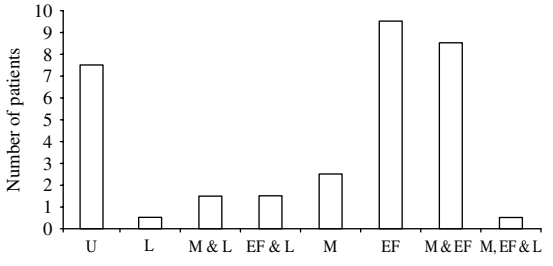


FIG. 1. Numbers of patients impaired (below the 5th percentile), shown according to cognitive domain. U, Unimpaired; EF, executive function; L, language; M, memory.

(Recognition Memory for Faces, the Shapes Test, Rey Complex Figure Recall and PAL 1) and three additional executive measures (Hayling Sentence Completion Task, the Stroop Test and ID/ED Set-Shift).

Comparisons of neuropsychological performance in the BP I and BP II subgroups are shown in Table 3. The main finding was that BP II patients scored significantly lower than BP I on the measures described above (except verbal recognition) and additionally on Full-Scale IQ change, Spatial Working Memory and Trail-Making part B.

Composite cognitive scores

The BP II subgroup had a significantly higher composite cognitive score (denoting greater impairment) than the BP I subgroup ($U=78·0$, $p=0·041$).

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Table 3. *Numbers of patients impaired and score comparisons for bipolar subgroups I and II*

Standardized neuropsychological tests	Bipolar I				Bipolar II				Score comparisons Mann–Whitney *U* (*p*)
	Mean (S.D.)	Range	Number impaired[a]	*n*	Mean (S.D.)	Range	Number impaired	*n*	
General intelligence									
Full IQ change[b]	−0·50 (12·67)	−30 to 18	0	24	12·82 (8·93)	−7 to 24	2	11	52·5 (0·004)
Memory									
RMF	42·00 (5·02)	29–50	3	24	37·82 (4·05)	31–43	4	11	68 (0·023)
PALT1	18·68 (4·72)	6–24	3	25	15·36 (4·11)	9–20	3	11	70 (0·020)
Rey Recall[c]	21·93 (5·99)	12·5–34	3	20	17·30 (9·04)	10·5–34	7	10	52·5 (0·035)
DPVR: Shapes	31·92 (4·61)	21–36	3	25	27·91 (6·61)	19–36	5	11	87·5 (0·086)
Executive functions									
TMTB[c]	69·08 (23·29)	32–142	2	24	91·50 (26·73)	56–135	2	10	62·5 (0·028)
SWM errors	27·95 (22·73)	0–70	3	21	50·89 (25·10)	10–82	3	9	46·00 (0·028)
SWM strategy	34·71 (6·16)	20–45	4		38·78 (2·22)	34–41	5		50·0 (0·045)

RMF, Recognition Memory for Faces; PALT1, Paired Associates Learning Test 1; TMTB, Trail-Making Test part B; SWM, CANTAB Spatial Working Memory subtest; WAIS, Wechsler Adult Intelligence Scale; NART, National Adult Reading Test.

[a] Number impaired refers to number of patients scoring at or below the 5th percentile according to standardized norms.

[b] Full IQ change = NART IQ – WAIS-R IQ; number impaired is number with decline greater than or equal to 20 IQ points.

[c] Number impaired refers to number of patients scoring at or below the 10th percentile according to standardized norms.

Effect of depressive symptomatology on neuropsychological performance

There were no significant differences in test performance between the 15 patients with normal BDI scores (0–9) and the 13 who had residual depressive symptoms in any neuropsychological tests. The group with normal BDI scores was impaired with respect to the normative sample on five measures, in the domains of memory and executive function; the group with residual depressive symptoms was also impaired on four measures in the same domains. When the BP group was considered as a whole, the scores of only two of the 10 cognitive measures in which they were impaired correlated with BDI score [Shapes Test score ($r = -0{\cdot}401$, $p = 0{\cdot}034$) and spatial working memory error score ($r = 0{\cdot}431$, $p = 0{\cdot}040$)]. Poorer performance of BP II patients with respect to BP I patients was related to BDI score only in the Shapes Test. BP II patients performed worse than BP I patients in another six tests, but in multiple regression analyses none of these differences were related to BDI scores. Apart from a trend for slower Stroop performance in depressed patients ($t = 2{\cdot}07$, $p = 0{\cdot}07$), there were no differences in neuropsychological scores between patients with and without a current depressive episode according to the SCID. The number of previous depressive episodes was negatively correlated with performance on the spatial working memory test ($\rho = 0{\cdot}337$, $p = 0{\cdot}085$) and positively correlated with composite cognitive score ($\rho = 0{\cdot}326$, $p = 0{\cdot}07$).

Emotion processing task

Patients underperformed with respect to controls in accuracy on the expression of surprise ($t_{80} = 2{\cdot}327$, $p = 0{\cdot}024$). Sensitivity scores did not differ between patients and controls. The BP I subgroup scored above the controls for accuracy in identifying disgust ($t_{52} = 1{\cdot}96$, $p = 0{\cdot}055$). There were no significant differences in either accuracy or sensitivity scores between BP I and BP II subgroups. Scores on recognition of surprise were correlated with scores on visual recognition memory (Spearman's $\rho = 0{\cdot}361$, $p = 0{\cdot}039$). Disgust recognition scores did not correlate with any cognitive variables.

Patients with elevated BDI scores underperformed with respect to controls on sensitivity to happiness ($t_{37} = 1{\cdot}93$, $p = 0{\cdot}062$). These patients also underperformed with respect to euthymic patients on sensitivity to anger ($t_{25} = 2{\cdot}21$, $p = 0{\cdot}037$).

Sensitivity to happiness and anger was correlated with performance on verbal recall (happiness and PALT1 $\rho = -0{\cdot}417$, $p = 0{\cdot}014$; PALT2 $\rho = -0{\cdot}469$, $p = 0{\cdot}005$ anger and PALT2 $\rho = -0{\cdot}575$, $p < 0{\cdot}001$). Differences in verbal recall performance accounted for underperformance on anger sensitivity in patients with elevated

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BDI scores with respect to those with normal BDI (difference in mean anger sensitivity score, controlling for the effect of verbal recall performance, 2·094, $p = 0·126$).

DISCUSSION

This study documents the cognitive and emotion processing of BP patients. Moreover, it is one of the few studies to investigate formally the neuropsychological differences between BP I and BP II patients. Our study provides further evidence that BP patients are impaired with respect to the normative population on measures of recall and recognition memory and aspects of executive function, namely response generation and suppression, attentional set-shift and spatial working memory. Our findings suggest that abnormalities in emotion processing (recognition of surprise) are also present in BP patients.

Temporal lobe abnormalities, a substrate for memory deficits, have been described in imaging studies of BP patients (Chang *et al.* 2005) and we have found a correlation between IQ decline and temporal lobe abnormalities (Bruno *et al.* 2004) in our patients. The executive deficits observed in our patients are in keeping with our earlier findings of structural abnormalities in the dorsolateral prefrontal areas in the same group of subjects (Bruno *et al.* 2004). In addition, structural and functional imaging abnormalities (Lennox *et al.* 2004) in the subgenual anterior cingulate in BP patients (Bruno *et al.* 2004) and in patients with major depressive disorder (Cotter *et al.* 2002) are likely to be related to the emotion processing deficit reported here.

Contrary to previous reports we did not find a significant correlation between the severity of depressive symptoms and cognitive performance (Scott *et al.* 2000; Kruger *et al.* 2003). This may be because most of our patients were euthymic or had only mild to moderate symptoms of depression. However, patients with residual depression were less sensitive to expressions of happiness and anger than euthymic subjects. Although an 'affective bias' (reduced response to positive emotional stimuli) has been reported in unipolar depression (Murphy & Sahakian, 2001), this was not observed in bipolar depression (Rubinsztein *et al.* 2006). Moreover, in our depressed group of patients, there was also reduced sensitivity to negative emotional stimuli (anger). Harmer *et al.* (2004) reported that treatment with selective serotonin or serotonin–norepinephrine reuptake inhibitors (SSRIs or SNRIs) reduced responsiveness to negative emotional expressions. However, as the majority of our patients using antidepressants were in the euthymic group (who scored better on the emotion expression task) and not the depressed group, antidepressant usage would not account for the effect we detected. Thus it is more likely that poor emotion processing in these patients is due to depression-related cognitive deficits. This explanation is further supported by the correlations found between emotion processing and cognitive measures. Such correlations have previously been detected in schizophrenia but not in BP (Addington & Addington, 1998). However our data suggest there may be a stronger connection between emotion processing and cognition in BP patients than was previously thought.

Turning now to discuss differences between BP I and BP II, it is noteworthy that neuropsychological comparisons across BP subtypes have been investigated previously in only one paper. Martinez-Aran *et al.* (2004*b*) reported poorer verbal recall in BP I than in BP II patients in a sample that included euthymic as well as depressed and manic patients. In our study BP II patients performed significantly worse than BP I patients across a large range of memory and executive functions, whereas the BP I group differed from the normative population only on tests of verbal recognition and spatial working memory. While there may appear to be a discrepancy between our results and those of Martinez-Aran *et al.* (2004*b*), it should be emphasized that the underperformance of their BP I patients was limited to a single cognitive test (with no subgroup differences found on the remaining seven tests). Manic symptoms in their BP I subgroup may have accounted for their limited underperformance. By contrast, our patients did not have elevated mood, and as the mean BDI scores did not differ across subgroups, differences in cognitive impairment could not be attributed to more severe depressive symptoms in the BP II group.

The mechanism leading to cognitive deficits in BP is yet to be determined. Van Gorp *et al.* (1998) found that the number of affective episodes negatively correlated with cognitive scores, and in our study previous depressive episodes

https://doi.org/10.1017/S0033291706008804 Published online by Cambridge University Press

correlated with poor spatial working memory and poor overall cognitive score. Nonetheless, some patients with BP of recent onset performed poorly in this study, as did family members of BP patients in another study (Ferrier *et al.* 2004), suggesting that cognitive deficits may precede or be a risk factor for the disorder.

Our results lend support to the view that cognitive impairment in BP is a trait and is likely to be part of the endophenotype (MacQueen *et al.* 2005). The cognitive differences between BP I and BP II described here may help to distinguish between these two BP subgroups in a way that may prove useful in genetic studies. Glutamatergic neurotoxicity, caused by dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis (Cotter *et al.* 2001*b*), predominantly affecting the hippocampus (Sherwood Brown *et al.* 1999) and prefrontal cortex (Cotter *et al.* 2001*a*), could be a possible explanation for the cognitive changes and structural abnormalities described in BP.

Our sample size, although comparable to that of other studies (Ferrier *et al.* 1999; Rubinsztein *et al.* 2000; Clark *et al.* 2002), may not have been large enough to reveal differences between the two subgroups in emotion processing and may also have been too small to detect neuroanatomical differences that could be responsible for the cognitive contrasts we observed. The effect of medication on cognitive performance needs to be considered. In our study the effects of mood stabilizers, and lithium in particular, may have contributed to deficits on tests heavily weighted on psychomotor speed (Performance IQ) (Koscis *et al.* 1993; Azorin, 2003) and possibly to memory impairment (Pachet & Wisniewski, 2003). Adverse effects of neuroleptics (Mishara & Goldberg, 2004) and ECT (Little *et al.* 2003) on cognition and a possible protective effect of SSRIs (Amado-Boccara *et al.* 1994) have been reported, but medication effects are unlikely to have substantially influenced subgroup differences in our study, as the proportion of patients on lithium or neuroleptics or having received ECT did not differ across the subgroups.

ACKNOWLEDGEMENTS

We thank Dr Daniel Altmann for statistical advice and Dr James Blair for making the emotion processing task available to us. We also thank all the subjects who took part in the study. Dr Stefania Bruno was supported by a grant from the Brain Research Trust.

DECLARATION OF INTEREST

None.

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