Psychological Medicine (2010), **40**, 1349–1355. © Cambridge University Press 2009
doi:10.1017/S0033291709991644

ORIGINAL ARTICLE

Gender differences in immediate memory in bipolar disorder

D. Carrus[1], T. Christodoulou[1], M. Hadjulis[1], M. Haldane[1], A. Galea[2], A. Koukopoulos[3], V. Kumari[2] and S. Frangou[1]*

[1] *Section of Neurobiology of Psychosis, Institute of Psychiatry, King's College London, London, UK*
[2] *Department of Psychology, Institute of Psychiatry, King's College London, London, UK*
[3] *Centro Lucio Bini, Rome, Italy*

Background. Gender is known to modulate the clinical course and severity of bipolar disorder (BD). Although cognitive abnormalities are an established feature of BD, there is limited information regarding whether gender also influences the pattern and severity of cognitive impairment.

Method. We evaluated the performance of 86 remitted patients with BD, type 1, (BD-I) (36 male and 50 female) and 46 healthy participants (21 male and 25 female) on tasks of general intellectual ability, memory encoding, recognition and retrieval, response inhibition and executive function (abstraction and perseveration). The impact of illness severity in patients was assessed using the global assessment of functioning (GAF).

Results. We found a gender effect and an interaction between diagnosis and gender on immediate memory, implicating encoding and retrieval processes, both showing male BD-I patients being disadvantaged compared with female patients and healthy controls. Immediate memory correlated with GAF scores and this association was statistically significant for male BD-I patients.

Conclusions. Our findings suggest that gender differences in BD-I are associated with memory function, particularly processes relating to encoding and retrieval, and may contribute to poor functional outcome particularly in men.

Received 11 October 2006; Revised 23 September 2009; Accepted 29 September 2009; First published online 6 November 2009

Key words: Bipolar disorder, encoding, executive function, gender retrieval, memory.

Introduction

Existing literature suggests a significant role of gender in bipolar disorder (BD) (APA, 1994) as it impacts on clinical course and outcome. Although not all studies report gender differences (Kessing, 2004; Baldassano *et al*. 2005; Kawa *et al*. 2005), it generally appears that female BD patients are at increased risk for depression (Curtis, 2005; Suominen *et al*. 2009), rapid cycling and dysphoric or mixed mania (Arnold, 2003; Berk & Dodd, 2004), while the risk of alcohol and substance abuse may be higher for males (Frye *et al*. 2003; Friedman *et al*. 2005; Suominen *et al*. 2009). Some studies report that BD men have an earlier age of onset (Robb *et al*. 1998; Kennedy *et al*. 2005) and worse psychosocial outcome than BD women (Robb *et al*. 1998; Raymont *et al*. 2003; Friedman *et al*. 2005). In contrast, one study investigating clinical features in BD-II patients reported earlier age of onset for women and more Axis I co-morbidity compared with men (Benazzi, 2006).

It is now widely accepted that cognitive abnormalities are a key feature of BD. Most studies have focused on patients with BD, type 1, (BD-I) (APA, 1994) and have reported widespread cognitive impairment during acute episodes of either polarity (Quraishi & Frangou, 2002). Additionally, a number of quantitative meta-analyses (Robinson *et al*. 2006; Torres *et al*. 2007; Arts *et al*. 2008; Bora *et al*. 2009; Stefanopoulou *et al*. 2009) have provided evidence for trait deficits of medium to large effect size in verbal memory and learning, concept formation and perseveration and in response inhibition during inter-episode intervals. To our knowledge only one previous study exists to address directly the issue of gender differences in cognition. Barrett *et al*. (2008) examined letter fluency, spatial working memory, planning and cognitive set shifting in 12 male and 14 female BD out-patients compared with healthy controls. Male patients performed worse than female patients in measures of spatial working memory, indicative of

* Address for correspondence: Dr S. Frangou, Section of Neurobiology of Psychosis (PO66), Institute of Psychiatry, King's College London, De Crespigny Park, London SE5 8AF, UK.
(Email: sophia.frangou@kcl.ac.uk)

https://doi.org/10.1017/S0033291709991644 Published online by Cambridge University Press

poor retention of visuospatial information. However, male patients in this study were both older and more symptomatic than female patients. The potential effect of gender was also explored in the meta-analysis by Arts *et al*. (2008), who reported smaller effect sizes for concept formation and perseveration in studies with higher male:female ratios.

Therefore, existing information regarding gender effects on cognitive function in BD is both incomplete and contradictory. The aim of this study was to expand the available evidence base by examining whether gender influences cognitive function in key domains known to differentiate BD patients from healthy controls. We therefore assessed 86 BD-I patients and compared them in terms of gender on general intellectual ability, memory, concept formation and response inhibition. To minimize potential referral bias and the confounding effect of symptoms, all patients were recruited from a secondary care catchment area-based psychiatric service and were evaluated when in remission.

Methods

Data for the current analysis were drawn from the Maudsley Bipolar Disorder Project cohort (Donaldson *et al*. 2003; Raymont *et al*. 2003; Frangou, 2005; Frangou *et al*. 2005). Details of the sample recruitment and assessment are also outlined below.

Subjects

Patients

Patients were recruited from the out-patient secondary care services of the South London and Maudsley NHS Trust, based on the following inclusion criteria: diagnosis of BD-I according to DSM-IV criteria (APA 1994); aged between 18 and 70 years and meeting DSM-IV criteria for remission in the preceding 6 months; on stable medication (same type and dose) for at least 3 months.

Healthy participants

Healthy individuals, without a personal or family history of psychiatric disorders, were recruited via advertisement in the local newspaper and were matched to patients, on age, gender and education.

Exclusion criteria for both groups included: (*a*) current or lifetime history of substance abuse or dependence as defined in the DSM-IV; (*b*) concomitant medical disorders; (*c*) history of head injury with loss of consciousness.

The study was approved by the Ethics Committee of the Institute of Psychiatry and was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Written informed consent was obtained from all participants after complete description of the protocol.

Assessments

All assessments took place on the same day. The same trained psychiatrist and psychologist conducted the clinical and cognitive assessments respectively of all participants.

Clinical assessment

The diagnosis of BD-I or absence of any diagnosis (in healthy participants) was confirmed using the Structured Clinical Interview for Axis I DSM-IV disorders (First *et al*. 1996). The Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962) was used to assess levels of psychopathology in BD-I patients and healthy participants as it allows for evaluation of non-pathological experiences. Depressive and manic symptoms were rated using the Hamilton Depression Scale (Hamilton, 1960) and Young Mania Rating Scale (YMRS; Young *et al*. 1978) respectively. The general impact of illness severity was assessed with the global assessment of functioning (GAF), where higher scores indicate better function (APA, 1994). Demographic data systematically obtained from all participants included gender, age, years of education, paternal and personal (best ever) socio-economic status, current employment, marital status and ethnicity.

Information about patients' past psychiatric history (hospitalization, polarity of first episode, age at first depressive or manic episode, number of previous episodes), current treatment, duration of illness and age of onset was collected from personal interviews with patients, their carers and medical notes. Age of onset was defined as the age when patients first met full DSM-IV criteria for an affective episode of either polarity. Medication on the day of neuropsychological testing was also recorded.

Cognitive assessment

Although data from the Maudsley Bipolar Project were available on multiple cognitive domains (Donaldson *et al*. 2003; Frangou *et al*. 2005), this analysis focused on performance on cognitive tasks where the largest effect size between BD patients and controls has been noted in meta-analytic studies (Arts *et al*. 2008; Bora *et al*. 2009; Stefanopoulou *et al*. 2009) to maximize the likelihood of detecting a gender effect (if present) and to minimize potential type I errors. Thus, we analysed data from the Wechsler Adult Intelligence Scale, Revised (WAIS-R; Wechsler, 1981),

https://doi.org/10.1017/S0033291709991644 Published online by Cambridge University Press

the Wechsler Memory Scale, 3rd edition (WMS-III; Wechsler, 1998), the Hayling Sentence Completion Task (HSCT; Burgess & Shallice, 1997) and the Wisconsin Card Sorting Test (WCST; Heaton, 1981).

The WAIS-R yielded an estimate of Full Scale Intelligence Quotient (FSIQ) as a measure of current general intellectual ability.

The WMS-III focuses on immediate, delayed and working memory, tested in two modalities, auditory and visual, and in two task formats, recall and recognition. Five outcome variables from the test were considered: auditory and visual immediate memory, auditory and visual delayed memory and auditory recognition delayed memory.

The HSCT has two sections, in each of which the examiner reads out 15 sentences with the last word missing. In the first section (response initiation) the sentence must be completed with a single word that is contextually predicted (e.g. He posted the letter without a … STAMP). In the second section (response inhibition), the word given has to be totally unconnected (e.g. He posted the letter without a … BANANA). Errors occur when participants fail to suppress the predicted word (category A errors) or supply a semantically connected word (category B errors). The main outcome measures used here were the overall scaled score, total category A error score and total category B error score. The WCST (36 cards computerized version) requires subjects to sort a deck of cards on the basis of a series of unknown categories. Feedback is given after each match to enable identification of the correct matching rule. The card-sorting category changes after a number of correct responses. Number of categories achieved and number of perseverative errors are considered measures of rule discovery and cognitive set shifting respectively.

Statistical analysis

Group comparisons in demographic and clinical variables and FSIQ were undertaken using Student's t test or Pearson's χ^2 as appropriate. Subsequently, three multivariate analyses of variance (MANOVA) were conducted for each neuropsychological test. For the WCST, number of perseverative errors and categories achieved were used as dependent variables, for HSCT the overall score and the number of category A and category B errors and for the WMS-III the scores for auditory immediate and delayed memory, visual immediate and delayed memory and auditory recognition delayed. For all three MANOVA, diagnosis (patient *versus* control) and gender (male *versus* female) were used as using independent factors while FSIQ and total BPRS scores were used as covariates. *Post-hoc* Bonferroni pairwise comparisons were conducted only when the overall model showed a significant effect of diagnosis or a gender by diagnosis interaction. The relationship between clinical variables (number of episodes, age of onset, GAF score) and any significant findings from the above analyses was explored using Pearson's correlation coefficients.

Results

Demographic and clinical features

Data from 86 patients with BD-I (50 female) and 46 healthy controls (25 female) were examined in this study. The mean age of patients was 46.75 (11.19) years and that of healthy participants was 42.65 (11.30). There was no group difference in age [$t = -0.41$, degrees of freedom (df) = 130, $p = 0.66$], gender distribution ($\chi^2 = 0.17$, df = 1, $p = 0.67$) or educational level ($\chi^2 = 0.53$, df = 2, $p = 0.76$). In addition, there was no significant age difference between male and female participants, regardless of diagnostic status ($F = 3.0$, df = 1, 128, $p = 0.83$) nor was there a gender by diagnostic status interaction ($F = 0.39$, df = 1, 128, $p = 0.53$). Clinical and medication details of the patients are shown in Table 1.

The mean BRPS scores of healthy controls was 25.77 (3.30), which just failed to reach statistical significance compared with patients' scores ($t = 1.80$, df = 125, $p = 0.07$). Within the patient group there were no gender differences in age of onset, polarity of first episode, duration of illness, number of episodes or hospitalizations, Hamilton Depression Rating Scale, YMRS and GAF total scores (all p values greater than 0.08) but there were more women with a history of psychosis during mood episodes ($\chi^2 = 6.12$, df = 1, $p = 0.01$). No differences were found in the type of medication prescribed at the time of testing (all $p > 0.33$).

Cognitive data

Participants' scores on the each of the cognitive tests used are shown in Table 2.

Patients and controls did not differ statistically in FSIQ ($t = 1.55$, df = 125, $p = 0.12$).

We did not find an effect of diagnosis ($F = 2.17$, df = 2, 74, $p = 0.12$) or gender ($F = 0.35$, df = 2, 74, $p = 0.70$) or gender by diagnosis interaction ($F = 0.51$, df = 2, 74, $p = 0.60$) for WCST categories and perseverative errors. There was a significant effect of FSIQ ($F = 8.13$, df = 2, 74, $p = 0.001$) but not of BPRS ($F = 0.19$, df = 2, 74, $p = 0.82$). For HSCT, there was a significant effect of diagnosis ($F = 4.62$, df = 3, 74, $p = 0.005$) but no effect of gender ($F = 1.17$, df = 3, 74, $p = 0.15$) or gender by diagnosis interaction ($F = 0.84$, df = 3, 74, $p = 0.47$). In addition, there was no effect FSIQ ($F = 1.96$, df = 3, 74, $p = 0.12$) nor of BPRS ($F = 0.10$, df = 3, 74, $p = 0.95$).

https://doi.org/10.1017/S0033291709991644 Published online by Cambridge University Press

Table 1. *Demographic and clinical details of patients with bipolar disorder*

	Male bipolar patients ($n=36$)	Female bipolar patients ($n=50$)
Age at assessment	45.4 (12.3)	47.7 (10.3)
Age at onset	24.2 (6.3)	26.3 (9.9)
Duration of illness	19.4 (11.7)	19.3 (10.9)
Number of hospitalizations	4.1 (4.0)	4.4 (3.6)
Age at first depressive episode	27.1 (11.0)	30.4 (12.3)
Age at first manic episode	26.8 (8.8)	31.4 (11.1)
Hamilton Depression Rating Scale	6.1 (7.7)	5.7 (6.2)
Young Mania Rating Scale	1.2 (3.6)	1.5 (2.9)
Brief Psychiatric Rating Scale	26.0 (2.3)	27.6 (4.1)
Global assessment of functioning	74.3 (15.2)	73.1 (14.3)
Total number of episodes	28.7 (38.2)	29.3 (38.3)
Total number of depressive episodes	19.5 (36.3)	21.0 (36.6)
Total number of manic episodes	20.5 (34.9)	20.1 (35.3)
Total number of mixed episodes	0.4 (0.5)	0.8 (0.8)
Polarity of first episode (% depressive)	16 (44.4)	26 (52.0)
No. of subjects with history of psychosis (%)[a]	20 (55.6)	43 (86.0)
No. of subjects on current use of medication (%)	30 (83.3)	46 (92.0)
No. of subjects on antidepressant (%)	12 (33.3)	16 (32.0)
No. of subjects on antipsychotic (%)	13 (36.1)	24 (48.0)
No. of subjects on typical antipsychotic (%)	3 (8.3)	9 (18.0)
No. of subjects on atypical antipsychotic (%)	10 (27.8)	16 (32.0)
No. of subjects on mood stabilizer (%)	27 (75.0)	40 (80.0)

Values are mean (S.D.).

[a] $p=0.01$; all other p values were >0.08.

Table 2. *Cognitive test performance in controls and bipolar disorder (BD) type I patients*

	Bipolar patients ($n=86$)		Healthy participants ($n=46$)	
Cognitive measure	Male ($n=36$)	Female ($n=50$)	Male ($n=21$)	Female ($n=25$)
Wechsler Memory Scale – III				
Auditory immediate	96.5 (18.4)	97.8 (21.3)	113.2 (18.9)	104.0 (14.6)
Visual immediate	92.2 (20.8)	105.5 (20.2)	110.7 (18.3)	108.0 (12.0)
Immediate memory	93.4 (21.1)	102.4 (23.7)	114.4 (19.8)	107.0 (14.3)
Auditory delayed	92.3 (20.5)	105.8 (19.9)	103.3 (17.6)	98.5 (15.8)
Visual delayed	97.5 (17.4)	101.6 (19.5)	93.6 (14.5)	97.6 (16.1)
Auditory recognition delayed	98.1 (18.4)	102.1 (21.1)	98.5 (17.3)	97.7 (16.4)
Working memory	103.8 (21.5)	99.1 (21.4)	98.6 (15.0)	101.0 (15.4)
General memory	95.2 (20.3)	104.4 (22.8)	105.3 (17.0)	100.9 (15.5)
Wechsler Adult Intelligence Scale – Revised				
Full Scale IQ	112.5 (18.2)	108.5 (20.0)	102.0 (16.2)	102.8 (14.7)
Hayling Sentence Completion Task				
Overall score	4.8 (1.6)	4.7 (2.2)	5.4 (1.8)	5.5 (1.9)
Total category A error score	7.9 (9.3)	9.0 (11.9)	2.8 (4.1)	2.0 (2.6)
Total category B error score	4.4 (4.7)	5.4 (8.0)	1.8 (2.6)	4.1 (6.6)
Wisconsin Card Sorting Test				
Categories achieved	4.1 (2.0)	3.9 (2.1)	4.2 (2.1)	3.6 (2.1)
Perseverative errors	5.1 (4.2)	5.1 (4.6)	6.2 (4.4)	6.2 (3.1)

Values are mean (S.D.).

https://doi.org/10.1017/S0033291709991644 Published online by Cambridge University Press

For the WMS-III, we found a significant effect of diagnosis ($F=4.12$, df $=6,69$, $p=0.001$) and gender ($F=2.81$, df $=6,69$, $p=0.05$) and of their interaction ($F=2.02$, df $=6,69$, $p=0.05$). There was a significant effect of FSIQ (F $=8.39$, df $=6,69$, $p<0.0001$) but not of BPRS ($F=2.0$ df $=6,69$, $p=0.06$).

At the univariate level, the gender by diagnosis interaction was significant for immediate visual and auditory memory and auditory delayed ($p<0.04$) but not for visual delayed memory ($p=0.75$), auditory recognition delayed ($p=0.22$). *Post-hoc* Bonferroni tests revealed that female BD-I patients did not differ from female controls in any WMS-III variables ($p>0.90$ for all tests). In contrast, male BD-I patients performed worse than male controls in auditory ($p=0.002$) and visual ($p=0.002$) immediate memory, while the differences in auditory delayed ($p=0.04$) were at the margins of statistical significance. Male BD-I patients performed worse than female patients in immediate memory ($p=0.05$) and auditory delayed memory ($p=0.04$), but both these findings would not survive Bonferroni correction.

Abnormalities in immediate memory test performance may reflect either encoding or retrieval problems. In order to define more accurately the profile of deficits emerging from the above analysis, we calculated two further WMS-III variables, namely, the subjects' learning slope and the retention score from the verbal paired associates subtest, which are considered measures of encoding. MANOVA with these two measures as independent variables diagnosis (patients *versus* controls) and gender as fixed factors and FSIQ and BPRS as covariates revealed an effect of FSIQ ($F=6.01$, df $=2,73$, $p=0.004$) and diagnosis ($F=2.01$, df $=2,73$, $p=0.05$) but no effect of BPRS ($F=0.51$, df $=2,73$, $p=0.60$) or gender by diagnosis interaction ($F=1.47$, df $=2,73$, $p=0.23$).

To reduce the number of correlations, we only used patients' scores on immediate memory (which is a composite of the visual and auditory immediate memory scores) in examining the effect of age of onset, number of episodes and GAF scores. These analyses were performed separately for male and female patients. A total of six correlations were performed and the threshold for significance was set to $p<0.008$. In men and women, the WMS-III immediate memory score correlated positively with GAF scores (men: $r=0.53$, $p=0.001$; women: $r=0.36$, $p=0.01$) and age of onset, the latter only in men ($r=0.56$, $p=0.001$) and not in women ($r=0.11$, $p=0.44$).

Discussion

In this study, gender by diagnosis interactions in BD-I were present in immediate memory, both auditory and visual, but not in general intellectual ability, concept formation and perseveration or response inhibition. Male patients performed worse in immediate memory compared with healthy male participants, while this was not the case for female BD-I patients. Compared with female BD-I patients, males underperformed in immediate memory and auditory delayed memory. Immediate memory correlated with patients' overall level of functioning and this association reached statistical significance for men. This finding underscores the importance of memory function in the outcome of BD and resonates with similar findings already reported (Martinez-Aran *et al*. 2004; Mur *et al*. 2009). However, since male and female patients in our sample did not differ in their overall GAF scores, our data also support existing evidence that cognitive function is not a unique contributing factor to outcome (Mur *et al*. 2009).

In the WMS-III, immediate memory scores are thought to reflect episodic memory encoding and effortful retrieval. Memory encoding refers to the processes involved in transforming the experience of an event into a memory trace that is accessible to conscious recollection. Effortful or explicit retrieval reflects conscious recollection. It is often difficult to differentiate encoding from retrieval abnormalities since successful retrieval depends on the efficacy of encoding. The absence of a significant gender by diagnosis effect on the learning slope and percentage retention indicates that retrieval rather than encoding deficits are greater in BD-I men than women. This is further supported by the finding of gender differences in delayed auditory memory in BD.

Neurocognitive studies are limited when considering the possible neural underpinnings of observed cognitive changes. However, cognitive tasks similar to those employed here have been used in functional imaging studies, making it possible and, we would argue, useful to incorporate neuroimaging findings in discussing our results. The evidence to date suggests that encoding and retrieval engages prefrontal and medial temporal cortices. Functional imaging studies suggest that effective encoding and retrieval are associated with increased activation in the hippocampus and surrounding structures (Kelley *et al*. 1998; Eldridge *et al*. 2005) and in dorsal and ventral prefrontal cortex (Fletcher & Henson, 2001). Frontotemporal dysregulation has been previously noted in remitted BD patients (Deckersbach *et al*. 2006; Robinson *et al*. 2009) and our data suggest that this impairment may also be modulated by gender.

Neither female nor male patients were completely asymptomatic or medication free at the time of assessment. Although the lack of group differences in medication status and level of psychopathology is

https://doi.org/10.1017/S0033291709991644 Published online by Cambridge University Press

encouraging with regard to the validity of our findings, the theoretical possibility that they may contribute to our results cannot be discharged. Both patient groups were comparable in terms of age of onset, duration of illness, number of episodes or hospitalizations and GAF scores. It is therefore unlikely that our findings relate to potential differences in illness severity between men and women with BD-I.

In summary, our results support the notion that gender may modulate the degree of immediate memory dysfunction in BD and its impact on overall level of function.

Acknowledgements

Wellcome Trust (067427/z/02/z) Senior Fellowship in Basic Biomedical Science to V. Kumari.

Declaration of interest

None.

References

APA (1994). *Diagnostic and Statistical Manual of Mental Disorders* (4th edn). American Psychiatric Association: Washington, DC.

Arnold LM (2003). Gender differences in bipolar disorder. *Psychiatric Clinics of North America* **26**, 595–620.

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.

Baldassano CF, Marangell LB, Gyulai L, Nassir, Ghaemi S, Joffe H, Kim DR, Sagduyu K, Truman CJ, Wisniewski SR, Sachs GS, Cohen LS (2005). Gender differences in bipolar disorder: retrospective data from the first 500 STEP-BD participants. *Bipolar Disorders* **7**, 465–470.

Barrett SL, Kelly C, Bell R, King DJ (2008). Gender influences the detection of spatial working memory deficits in bipolar disorder. *Bipolar Disorders* **10**, 647–654.

Benazzi F (2006). Gender differences in bipolar-II disorder. *European Archives of Psychiatry and Clinical Neuroscience* **256**, 67–71.

Berk M, Dodd S (2004). Review: rapid cycling bipolar disorder associated with female gender and bipolar type II subgroup. *Evidence Based Mental Health* **7**, 91.

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.

Burgess PW, Shallice T (1997). *The Hayling and Brixton Tests*. Bury St Edmunds: Thames Valley Test Company.

Curtis V (2005). Women are not the same as men: specific clinical issues for female patients with bipolar disorder. *Bipolar Disorders* **7** (Suppl. 1), 16–24.

Deckersbach T, Dougherty DD, Savage C, McMurrich S, Fischman AJ, Nierenberg A, Sachs G, Rauch SL (2006). Impaired recruitment of the dorsolateral prefrontal cortex and hippocampus during encoding in bipolar disorder. *Biological Psychiatry* **59**, 138–146.

Donaldson S, Goldstein LH, Landau S, Raymon V, Frangou S (2003). The Maudsley Bipolar Disorder Project: the effect of medication, family history, and duration of illness on IQ and memory in bipolar I disorder. *Journal of Clinical Psychiatry* **64**, 86–93.

Eldridge LL, Engel SA, Zeineh MM, Bookheimer SY, Knowlton BJ (2005). A dissociation of encoding and retrieval processes in the human hippocampus. *Journal of Neuroscience* **25**, 3280–3286.

First M, Spitzer R, Gibbon M, Williams J (1996). *Structured Clinical Interview for DSM-IV Axis 1 Disorders*. New York, NY: New York State Psychiatric Institute, Biometrics Research Department.

Fletcher PC, Henson RN (2001). Frontal lobes and human memory: insights from functional neuroimaging. *Brain* **124**, 849–881.

Frangou S (2005). The Maudsley Bipolar Disorder Project. *Epilepsia*, **46** (Suppl. 4), 19–25.

Frangou S, Donaldson S, Hadjulis M, Landau S, Goldstein LH (2005). The Maudsley Bipolar Disorder Project: executive dysfunction in bipolar disorder I and its clinical correlates. *Biological Psychiatry* **58**, 859–864.

Friedman SH, Shelton MD, Elhaj O, Youngstrom EA, Rapport DJ, Packer KA, Bilali SR, Jackson KS, Sakai HE, Resnick PJ, Findling RL, Calabrese JR (2005). Gender differences in criminality: bipolar disorder with co-occurring substance abuse. *Journal of the American Academy of Psychiatry and the Law* **33**, 188–195.

Frye MA, Altshuler LL, McElroy SL, Suppes T, Keck PE, Denicoff K, Nolen WA, Kupka R, Leverich GS, Pollio C, Grunze H, Walden J, Post RM (2003). Gender differences in prevalence, risk, and clinical correlates of alcoholism comorbidity in bipolar disorder. *American Journal of Psychiatry* **160**, 883–889.

Hamilton M (1960). A rating scale for depression. *Journal of Neurology Neurosurgery and Psychiatry* **23**, 56–62.

Heaton RK (1981). *Wisconsin Card Sorting Test Manual*. Psychological Assessment Resources: Odessa, Florida.

Kawa I, Carter JD, Joyce PR, Doughty CJ, Frampton CM, Wells JE, Walsh AE, Olds RJ, Kennedy N, Boydell J, Kalidindi S, Fearon P, Jones PB, van Os J, Murray RM (2005). Gender differences in incidence and age at onset of mania and bipolar disorder over a 35-year period in Camberwell, England. *American Journal of Psychiatry* **162**, 257–262.

Kelley WM, Miezin FM, McDermott KB, Buckner RL, Raichle ME, Cohen NJ, Ollinger JM, Akbudak E, Conturo TE, Snyder AZ, Petersen SE (1998). Hemispheric specialization in human dorsal frontal cortex and medial temporal lobe for verbal and non-verbal memory encoding. *Neuron* **20**, 927–936.

Kennedy N, Boydell J, Kalidindi S, Fearon P, Jones PB, van Os J, Murray RM (2005). Gender differences in incidence and age at onset of mania and bipolar disorder over a 35-year period in Camberwell, England. *American Journal of Psychiatry* **162**, 257–262.

https://doi.org/10.1017/S0033291709991644 Published online by Cambridge University Press

Kessing LV (2004). Gender differences in the phenomenology of bipolar disorder. *Bipolar Disorders* **6**, 421–425.

Martinez-Aran A, Vieta E, Colom F, Torrent C, Sanchez-Moreno J, Reinares M, Benabarre A, Goikolea JM, Brugue E, Daban C, Salamero M (2004). Cognitive impairment in euthymic bipolar patients: implications for clinical and functional outcome. *Bipolar Disorders* **6**, 224–232.

Mur M, Portella MJ, Martinez-Aran A, Pifarre J, Vieta E (2009). Influence of clinical and neuropsychological variables on the psychosocial and occupational outcome of remitted bipolar patients. *Psychopathology* **42**, 148–156.

Overall JE, Gorham DR (1962). The Brief Psychiatric Rating Scale. *Psychological Reports* **10**, 790–812.

Quraishi S, Frangou S (2002). Neuropsychology of bipolar disorder: a review. *Journal of Affective Disorders* **72**, 209–226.

Raymont V, Bettany D, Frangou S (2003). The Maudsley bipolar disorder project. Clinical characteristics of bipolar disorder I in a Catchment area treatment sample. *European Psychiatry* **18**, 13–17.

Robb JC, Young LT, Cooke RG, Joffe RT (1998). Gender differences in patients with bipolar disorder influence outcome in the medical outcomes survey (SF-20) subscale scores. *Journal of Affective Disorders* **49**, 189–193.

Robinson JL, Bearden CE, Monkul ES, Tordesillas-Gutiérrez D, Velligan DI, Frangou S, Glahn DC (2009). Fronto-temporal dysregulation in remitted bipolar patients: an fMRI delayed-non-match-to-sample (DNMS) study. *Bipolar Disorders* **11**, 351–360.

Robinson LJ, Thompson JM, Gallagher P, Goswami U, Young AH, Ferrier IN, Moore PB (2006). A meta-analysis of cognitive deficits in euthymic patients with bipolar disorder. *Journal of Affective Disorders* **93**, 105–115.

Stefanopoulou E, Manoharan A, Landau S, Geddes J, Goodwin G, Frangou S (2009). Cognitive functioning in patients with affective disorders and schizophrenia: a meta-analysis. *International Reviews of Psychiatry* **21**, 1–21.

Suominen K, Mantere O, Valtonen H, Arvilommi P, Leppämäki S, Isometsä E (2009). Gender differences in bipolar disorder type I and II. *Acta Psychiatrica Scandinavica*. Published online: 20 May 2009. doi:10.1111/j.1600–0447.2009.01407.x.

Torres IJ, Boudreau VG, Yatham LN (2007). Neuropsychological functioning in euthymic bipolar disorder: a meta-analysis. *Acta Psychiatrica Scandinavica* (Suppl.) **434**, 17–26.

Young R, Biggs J, Zieglar V, Meyer D (1978). A rating scale for mania: reliability, validity sensitivity. *British Journal of Psychiatry* **133**, 429–435.

Wechsler D (1981). *Wechsler Adult Intelligence Scale – Revised (WAIS-R) Manual*. Psychological Corporation, New York.

Wechsler D (1998). *Wechsler Memory Scale, 3rd edn: Administration and Scoring Manual*. London: Psychological Corporation.

https://doi.org/10.1017/S0033291709991644 Published online by Cambridge University Press