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Identifying a cognitive impairment subgroup in adults with mood disorders

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Abstract

Background—We hypothesized that only a minority of patients with mood disorders have measurable cognitive impairment, and this minority drives the small-to-medium effect sizes detected in group studies. Removal of this minority from group statistical analyses will illustrate that the majority appear to have broadly normal cognitive functioning.

Methods—Participants were adults between the ages of 20 and 54, including 659 healthy control subjects, 84 unmedicated outpatients diagnosed with depression, 59 outpatients diagnosed with depression who were on medications at the time of the evaluation, and 43 outpatients with bipolar disorder. All completed the CNS Vital Signs computerized cognitive screening battery.

Results—The prevalence rates of low cognitive test scores were calculated for the healthy control subjects and the patients with mood disorders. Having two scores at or below the 5th percentile occurred in 31.2% of the patients and only 8.2% of the control subjects [$\chi^2(1)=66.67$, $p<.0001$; Odds Ratio=5.1, 95% CI=3.4–7.7]. For the control subjects, this low false positive rate for cognitive impairment was maintained across age groups, sexes, and education levels. A larger proportion of patients with bipolar disorder (41.9%) than patients with depression (27.1–28.6%) met this criterion for cognitive impairment.

Conclusions—This study suggests that cognitive impairment associated with mood disorders is limited to a minority of patients with the majority being broadly cognitively normal. Future research should determine if this identified subgroup has neuroanatomical, neurophysiological, or

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Conflicts of interest

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neuroendocrine abnormalities. Cognitive screening tools of this type might be useful in selecting participants for studies.

Keywords

Computerized testing; Cognitive impairment; Depression; Bipolar disorder

1. Introduction

It is well established that mood disorders are associated with cognitive impairment (Robinson et al., 2006; Zakzanis et al., 1998). The nature and extent to which depression causes objective cognitive impairment, however, is not fully understood. Some studies suggest that cognitive impairment associated with depression is quite limited (Grant et al., 2001; Rohling et al., 2002), difficult to detect, and is more likely to occur in those who are more seriously ill (Fossati et al., 2002; MacQueen et al., 2003; McDermott and Ebmeier, 2009; Tarbuck and Paykel, 1995). There is evidence that neurocognitive functioning improves following treatment (e.g., Bayless et al., 2010; Deuschle et al., 2004; Doraiswamy et al., 2003; Hviid et al., 2010; Neu et al., 2005; O'Connor et al., 2005; Rocca et al., 2005; Vythilingam et al., 2004; Wroolie et al., 2006), although this is not always the case (Frasch et al., 2009; Paelecke-Habermann et al., 2005; Reppermund et al., 2009; Weiland-Fiedler et al., 2004) — especially in older adults (Bhalla et al., 2009; Culang et al., 2009). Indeed, there is some suggestion that cognitive or executive functioning deficits may be a trait risk factor for depression (Douglas and Porter, 2009; Frasch et al., 2009; Micco et al., 2009; Reppermund et al., 2009). Furthermore, worse neuropsychological test performance at baseline is associated with poorer response to treatment (Dunkin et al., 2000; Kampf-Sherf et al., 2004; Mohlman and Gorman, 2005), and cognitive deficits are more pronounced in patients who are unemployed (Baune et al., 2010). It is possible that treatment refractory depression is a subtype characterized in part by cognitive impairment. Likewise, cognitive impairment is pronounced in patients with bipolar disorder and it persists when the patients are euthymic (Langenecker et al., 2007, 2010; Robinson et al., 2006; Torres et al., 2007), with lesser extent and severity of cognitive difficulties relative to schizophrenia (Schretlen et al., 2007). Cognitive impairment is associated with poor treatment adherence in bipolar disorder, but the direction of the relationship is unknown (Martinez-Aran et al., 2009). Mood disorders with psychosis are associated with a large adverse effect on neurocognitive functioning (Bora et al., 2009).

The accurate identification and quantification of neurocognitive impairment are important for research relating to neurobiological underpinnings, treatment, and functional outcome in patients with mood disorders. It is essential, methodologically, that we have accurate methods for identifying those patients who are objectively cognitively impaired and separate them from patients who have the subjective experience of poor thinking skills or thinking that is easily perturbed by negative affect, but perform normally on cognitive testing in controlled conditions. The treatments and outcomes for these two groups may differ markedly, as well as the prognosis. Based on group statistics, in individual studies or in meta-analyses, mood disorders are associated with a small-to-medium adverse effect on cognitive functioning (Robinson et al., 2006; Torres et al., 2007; Zakzanis et al., 1998).

However, group statistics can obscure individual and subgroup differences. If present, these individual or subgroup differences in cognition might have important implications for research and clinical practice.

The purpose of this study was to examine cognitive functioning in mood disorders at the level of the individual. We hypothesized, based on our preliminary research, that (a) only a minority of patients with mood disorders have measurable cognitive impairment, (b) this minority is driving the small-to-medium effect sizes detected in group statistics (see also Bora et al., 2009; Burt et al., 1995), and (c) if you remove this minority from the group statistical analyses, the significant effect sizes will virtually disappear. The alternative hypothesis would be that the entire distribution of performance in depressed subjects is shifted about one half standard deviation lower relative to the control group without a bimodal distribution. If our hypotheses are true, the effect sizes reported in the literature seriously under-estimate the degree to which cognitive impairment is associated with mood disorders in a subset of patients. They are diluted by the majority of patients who have no measurable cognitive impairment. Using a large healthy normative sample and archival clinical groups, we will (a) develop and evaluate psychometric criteria for identifying cognitive impairment in adults with mood disorders, and (b) evaluate the above-mentioned hypotheses.

2. Methods

2.1. Participants

A healthy normative sample and three clinical groups were used for this study. Ethical approval for the use of this large, de-identified, archival database was granted by the University of British Columbia. Older adults were excluded. Participants were adults between the ages of 20 and 54, including 659 healthy control subjects, 84 unmedicated outpatients diagnosed with depression, 59 outpatients diagnosed with depression who were on medications at the time of the evaluation, and 43 outpatients with bipolar disorder. Clinicians at the North Carolina Neuropsychiatry Clinics gave a primary diagnosis of depression or bipolar disorder to all patients.

This is a sample of convenience; no formal diagnostic interviewing or symptom rating scales were collected. The clinical characteristics of the patient samples (e.g., age of onset, number of prior episodes, and severity/phase of illness) were not recorded in the database. The authors of this study utilized an archival database; we had no role in data collection or the clinical evaluations of the subjects. The unmedicated outpatients with depression (Iverson et al., 2009a) and the patients with bipolar disorder (Iverson et al., 2009b) were selected from previously published studies. This study is primarily methodological in nature. It was not our intent to characterize or differentiate the nature or pattern of cognitive deficits in depression or bipolar disorder. Heterogeneous samples of outpatients with mood disorders were sufficient to examine the methodological hypotheses and subsequent studies can use carefully characterized clinical information to better understand the causes and mechanisms of cognitive impairment in major depressive disorder and bipolar disorder.

The demographic characteristics of the four samples are described in Table 1. The majority of each sample was women, and the vast majority was Caucasian. Each participant self-reported their total number of years of education. Our experience, when conducting follow-up interviews with research subjects, is that some over-estimate their years of education by counting part-time studies or short-term certificate programs as full years. Thus, the level of education of the four samples might be a slight over-estimate. It is likely, however, that the average education of these samples is clearly greater than high school, with most having some form of technical, college, or university education.

2.2. Measures

CNS Vital Signs is comprised of seven common neuropsychological measures, including verbal and visual memory, finger tapping, symbol digit coding, a Stroop test, a shifting attention test, and a continuous performance test. The battery generates 15 primary scores, which are used to calculate 5 domain scores (Memory, Psychomotor Speed, Reaction Time, Cognitive Flexibility, and Complex Attention). The domain scores are normed, similar to traditional IQ scores, with a mean standard score (SS) of 100 and a standard deviation of 15. As such, low scores in clinical practice or research can be defined in several ways, such as (a) more than 1 standard deviation (SD) below the mean (i.e., <85 SS), (b) below the 10th percentile (i.e., <81 SS), (c) at or below the 5th percentile (i.e., 76 SS), and (d) more than 2 SDs below the mean (i.e., <70 SS). The measures have adequate test-retest reliability, adequate concurrent validity with traditional paper and pencil measures and other computerized tests, and the domain scores have been shown to discriminate between various clinical groups (Brooks et al., 2010; Gualtieri and Johnson, 2005, 2006; Gualtieri et al., 2006; Iverson et al., 2009a,b).

3. Results

Calculations for the base rates of low scores involve simultaneously examining the five domain scores, rather than performance on each domain in isolation. The base rates of low domain scores were calculated by using four cutoff scores that might be routinely used in clinical practice, including: (a) more than 1 standard deviation (SD) below the mean (i.e., <85 SS), (b) below the 10th percentile (i.e., <81 SS), (c) at or below the 5th percentile (i.e., 76 SS), and (d) more than 2 SDs below the mean (i.e., <70 SS).

The base rates of low domain scores for healthy adults, stratified by age, sex, race, education, and computer use, are presented in Table 2. As seen in Table 2, it is common for healthy adults to obtain one low score. For example, 41% obtained one or more scores below 1 SD (<16th percentile) and 22.8% obtained one or more scores the 5th percentile. Thus, clinicians and researchers need to be cautious when interpreting a single low CNS VS composite score.

Having two domain scores at or below the 5th percentile seems to be a reasonable psychometric criterion for identifying cognitive impairment, given its low false positive rate. This low false positive rate was maintained across age groups, sexes, and education levels (see Table 2). African Americans (N=49) had higher false positive rates (i.e., 14.3%) than Caucasians (N=570; 7.0%).

The base rates of low domain scores for adults with mood disorders are presented in Table 3. Patients with mood disorders are more likely to obtain low scores than healthy controls subjects. Having two scores at or below the 5th percentile occurred in 31.2% of the patients with mood disorders and only 8.2% of the control subjects [$\chi^2(1)=66.67$, $p<.0001$; Odds Ratio=5.1, 95% CI=3.4–7.7]. A larger proportion of patients with bipolar disorder (41.9%) than patients with depression (27.1–28.6%) had two or more scores in this range.

A minority of each clinical group was identified using this criterion (i.e., 2 or more scores 5th percentile) as having cognitive impairment. The test results for each of these subgroups, compared to healthy controls and patients who did not meet criterion, are presented in Table 4. As seen in Table 4, the means and standard deviations for the clinical groups, after the subgroup is removed, are very similar to the means and standard deviations of the healthy control group.

The percentages of subjects who scored within specific ranges on each domain score were graphed. All showed broadly similar patterns, so three of the five domain scores are illustrated in Figs. 1–3. As seen in these figures, when the subgroup of patients with cognitive impairment is removed, the distributions of scores for the majority of patients with mood disorders look very similar to the distributions of scores for healthy adults.

4. Discussion

The purpose of this study was to examine cognitive functioning in mood disorders at the individual and subgroup levels. As hypothesized (a) only a minority of patients with mood disorders have measurable cognitive impairment, (b) this minority appears to be driving the effect sizes detected in group statistics, and (c) if you remove this substantial minority from the group statistical analyses, the significant effect sizes disappear. Obviously, if you identify a subgroup of patients who perform poorly on cognitive testing, using a cutoff score at or below the 5th percentile on two or more domains, you expect that subgroup, when examined in isolation, to have very low scores across CNS Vital signs (see Table 4). The magnitude of the low scores might be surprising to some readers, however. What is equally interesting is that when the subgroup of patients with obvious cognitive impairment is removed, the remaining majority of each of the three clinical groups has scores that approximate the distributions of healthy adults (see Figs. 1–3). In other words, the majority of patients with mood disorders appear to have broadly normal cognitive functioning, and a minority appear to have frankly impaired cognitive functioning.

This study has several methodological issues and limitations. First, this is not a true sensitivity study and the sensitivity values for cognitive impairment should be interpreted cautiously. This is because we did not have independent criteria for frank cognitive impairment. Future researchers could use independent criteria for cognitive impairment in an attempt to replicate these findings. It is notable that very few previous studies have examined a methodology for identifying cognitive impairment in patients with mood disorders, and the methodology discussed in this study is an important contribution to the literature. The vast majority of studies have simply focused on null hypothesis testing and reporting whether patients differed from control subjects on neuropsychological tests. In

fact, effect sizes have rarely been reported in past studies. Second, the patient groups were samples of convenience. We did not have access, in this archival database, to detailed information regarding their psychiatric history, medication history, comorbid health problems, phase of illness, severity of illness, or severity of their subjective cognitive complaints. Information about these characteristics should be pursued in future studies to clarify the nature and prognosis for this subgroup with cognitive impairment. We also did not have access to more global levels of functioning, such as IQ, and cannot indicate whether these findings are global, or are related to the specific cognitive abilities assessed using the CNS Vital Signs battery. Finally, the patients with mood disorders did not undergo effort testing; thus, we cannot be assured that some of those with very low scores were not providing inadequate effort.

In summary, the effect sizes reported in the literature under-estimate the adverse effects of mood disorders on cognition because they are diluted by the majority of patients who have no measurable cognitive impairment. This study suggests that cognitive impairment associated with mood disorders is limited to a minority of patients with the majority being broadly cognitively normal. In the future, studies might pursue clinical characteristics that might indicate trait, or trait-by-illness interactions, that result in significant cognitive impairment in this minority. Furthermore, by identifying these individuals with cognitive impairment using very simple computer tests that can be employed in clinics, identification of important research subgroups for further study can be easily pursued. Furthermore, this procedure can lead to early identification of those patients who might need more intense or long-term treatment strategies, in addition to the potential need for vocational rehabilitation and support.

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Fig. 1. Distributions of CNS Vital Signs memory index score in patients with or without impaired cognition. Figure note: Healthy control, N=660. Mood disorder, normal cognition, n=128. Mood disorder, cognitive impairment, n=58. *Normative scores were truncated at 40. Each value represents the percentage of subjects in that score range.

Fig. 2.

Distributions of CNS Vital Signs psychomotor speed index score in patients with or without impaired cognition. Figure note: Healthy control, N=660. Mood disorder, normal cognition, n=128. Mood disorder, cognitive impairment, n=58. *Normative scores were truncated at 40. Each value represents the percentage of subjects in that score range.

Fig. 3.

Distributions of CNS Vital Signs cognitive flexibility index score in patients with or without impaired cognition. Figure note: Healthy control, N=660. Mood disorder, normal cognition, n=128. Mood disorder, cognitive impairment, n=58. *Normative scores were truncated at 40. Each value represents the percentage of subjects in that score range.

Table 1

Demographic characteristics of the samples.

	Healthy Normative sample	Depression unmedicated	Depression medicated	Bipolar disorder
Sample size	659	84	59	43
Mean age (SD)	38.1(10.2)	37.7 (9.9)	40.1 (8.9)	36.6 (9.9)
Age range	20–54	20–54	20–54	21–54
Mean education (SD)	15.8 (2.2)	15.1 (2.2)	14.8 (2.5)	15.1 (2.3)
Education range	7–20	8–20	8–18	8–19
Male/female (%)	36/64	26.2/73.8	27.1/72.9	32.6/67.4
Caucasian/African American/Hispanic (%)	86.5/7.4/2.4	94.9/5.1/0	88.1/10.7/1.2	95.3/2.3/2.3
Computer use sample size	378	80	39	43
Computer use: none/some/frequent (%)	2.1/19.3/78.6	1.3/16.3/82.5	12.8/25.6/61.5	4.7/27.9/67.4

Note: SD = standard deviation. Years of education is based on self-report.

Table 2
Base rates of low domain scores on the CNS Vital Signs in healthy adults (presented as percentiles).

Number of domain scores below cutoffs	Age groups				Sex		Race		Education groups				Computer use	
	Total sample	20-29	30-39	40-49	50-54	M	F	Cauc	A-A	12	13-15	16+	Some	Frequent
	N = 659	N = 155	N = 177	N = 238	N = 89	N = 236	N = 420	N = 570	N = 49	N = 27	N = 94	N = 226	N = 73	N = 297
<i><16th percentile (1 SD)</i>														
Zero domain scores below cutoff	59.0	62.6	55.4	59.2	59.6	61.4	57.4	60.5	49.0	55.6	51.1	60.6	50.7	61.3
1 or more domains below cutoff	41.0	37.4	44.6	40.8	40.4	38.6	42.6	39.5	51.0	44.4	48.9	39.4	49.3	38.7
2 or more domains below cutoff	18.2	20.0	17.5	19.7	12.4	12.3	21.7	17.0	22.4	14.8	21.3	19.0	26.0	17.2
3 or more domains below cutoff	7.7	8.4	7.9	7.6	6.7	5.1	9.3	7.2	8.2	3.7	11.7	6.6	11.0	7.4
4 or more domains below cutoff	2.1	2.6	2.3	1.3	3.4	0.8	2.9	1.8	4.1	-	3.2	2.2	5.5	1.7
5 domains below cutoff	0.6	0.6	1.1	0.4	-	0.4	0.7	0.5	2.0	-	3.2	0.4	4.1	0.3
<i><10th percentile</i>														
Zero domain scores below cutoff	68.0	73.5	61.6	68.5	69.7	69.5	66.9	69.6	59.2	66.7	60.6	67.3	57.5	69.7
1 or more domains below cutoff	32.0	26.5	38.4	31.5	30.3	30.5	33.1	30.4	40.8	33.3	39.4	32.7	42.5	30.3
2 or more domains below cutoff	12.0	13.5	11.9	11.8	10.1	9.3	13.6	10.5	20.4	11.1	14.9	13.3	17.8	11.8
3 or more domains below cutoff	4.1	4.5	2.8	3.8	6.7	2.1	5.2	4.0	4.1	3.7	4.3	4.0	6.8	3.4
4 or more domains below cutoff	0.9	0.6	1.1	0.8	1.1	0.4	1.2	0.7	2.0	-	1.1	1.3	4.1	0.3
<i>5th percentile</i>														
Zero domain scores below cutoff	77.2	80.0	74.0	77.3	78.7	79.2	76.0	78.9	63.3	77.8	73.4	76.1	69.9	78.8
1 or more domains below cutoff	22.8	20.0	26.0	22.7	21.3	20.8	24.0	21.1	36.7	22.2	26.6	23.9	30.1	21.2
2 or more domains below cutoff	8.2	9.7	7.3	7.6	9.0	6.8	9.0	7.0	14.3	7.4	8.5	9.7	12.3	7.7
3 or more domains below cutoff	1.8	1.9	1.1	1.3	4.5	0.8	2.4	1.6	2.0	-	2.1	2.7	4.1	1.7
4 or more domains below cutoff	0.3	-	-	0.4	1.1	-	0.5	0.2	-	-	-	0.4	-	0.3
<i>2nd percentile (2 SDs)</i>														
Zero domain scores below cutoff	89.5	92.9	89.8	88.2	86.5	90.3	89.0	90.5	83.7	88.9	89.4	85.8	83.6	88.9
1 or more domains below cutoff	10.5	7.1	10.2	11.8	13.5	9.7	11.0	9.5	16.3	11.1	10.6	14.2	16.4	11.1
2 or more domains below cutoff	2.7	1.9	1.7	3.4	4.5	3.0	2.6	2.1	2.0	-	2.1	4.0	6.8	2.4
3 or more domains below cutoff	0.3	0.6	--	-	1.1	0.4	0.2	0.2	-	-	1.1	0.4	1.4	0.3

Note: Based on the following five domain scores: Memory, Psychomotor Speed, Reaction Time, Complex Attention, and Cognitive Flexibility. M = Male, F = Female; Cauc = Caucasian and A-A = African American. Computer use is self-report as 'some' or 'frequent'. Demographic variables were missing for some subjects. Data are presented as percentiles [e.g., 85.5% of the total healthy sample have no domain scores less than or equal to the 2nd percentile (2 SDs), and 10.5% have one or more low domain scores in this range]. First Definition of Cognitive Impairment: 4 scores below 1 SD, OR 3 scores below 10th percentile, OR 2 scores below 5th percentile: False positives in total sample: 8.6%. Using this Boolean algorithm, 32.8% of the adult clinical sample is impaired. Second Definition of Cognitive Impairment: 2 scores below 5th percentile: False positives in total sample: 8.2% (see Table 2, total sample column). Using this criterion, 31.2% of the adult clinical sample is impaired (Table 3, total clinical sample column). The information presented in Table 2 is ready for use by clinicians and researchers. It allows a more sophisticated and evidence-based approach to the interpretation of cognitive test performance.

Table 3

Base rates of low domain scores on the CNS Vital Signs in adults with mood disorders (presented as percentiles).

Number of domain scores below cutoffs	Total clinical sample	Unmedicated depression	Heterogeneous depression	Bipolar disorder
	N= 186	N = 84	N = 59	N = 43
<i><16th percentile (1 SD)</i>				
Zero domain scores below cutoff	36.6	38.1	39.0	30.2
1 or more domains below cutoff	63.4	61.9	61.0	69.8
2 or more domains below cutoff	44.1	44.0	35.6	55.8
3 or more domains below cutoff	26.9	27.4	22.0	32.6
4 or more domains below cutoff	17.7	17.9	13.6	23.3
5 domains below cutoff	9.1	9.5	8.5	9.3
<i><10th percentile</i>				
Zero domain scores below cutoff	43.0	42.9	47.5	37.2
1 or more domains below cutoff	57.0	57.1	52.5	62.8
2 or more domains below cutoff	38.2	36.9	33.9	46.5
3 or more domains below cutoff	23.7	23.8	16.9	32.6
4 or more domains below cutoff	15.6	14.3	13.6	20.9
5 domains below cutoff	7.5	8.3	5.1	9.3
<i>5th percentile</i>				
Zero domain scores below cutoff	48.9	51.2	50.8	41.9
1 or more domains below cutoff	51.1	48.8	49.2	58.1
2 or more domains below cutoff	31.2	28.6	27.1	41.9
3 or more domains below cutoff	19.4	17.9	15.3	27.9
4 or more domains below cutoff	12.9	11.9	10.2	18.6
5 domains below cutoff	6.5	7.1	3.4	9.3
<i>2nd percentile (2 SDs)</i>				
Zero domain scores below cutoff	60.8	64.3	61.0	53.5
1 or more domains below cutoff	39.2	35.7	39.0	46.5
2 or more domains below cutoff	24.2	22.6	20.3	32.6
3 or more domains below cutoff	15.1	15.6	11.9	18.6
4 or more domains below cutoff	8.6	8.3	6.8	11.6
5 domains below cutoff	4.8	4.8	3.4	7.0

Note: Based on the following five domain scores: Memory, Psychomotor Speed, Reaction Time, Complex Attention, and Cognitive Flexibility. Data are presented as percentiles [(e.g., 48.9% of the total healthy samples have no domain scores less than or equal to the 5th percentile (2 SDs), and 31.2% have two or more low domain scores in this range)].

Table 4

Performance on CNS Vital Signs in patients with and without cognitive impairment.

	N	CNS Vital Signs domain scores				
		Memory	Psychomotor speed	Reaction time	Complex attention	Cognitive flexibility
Healthy controls	660	100.0 (14.8)	100.2 (15.1)	100.2 (14.8)	100.1 (15.1)	100.1 (15.0)
All patients with mood disorders	186	91.1 (21.1)	90.8 (21.8)	90.6 (23.2)	84.3 (31.9)	88.4 (26.7)
Normal cognition	128	97.3 (16.6)	98.0 (15.7)	99.3 (14.1)	100.6 (15.4)	102.0 (13.2)
Impaired cognition	58	77.5 (23.4)	74.8 (24.6)	71.5 (27.6)	48.2 (29.0)	58.5 (24.5)
Depression, no medication	84	90.3 (22.3)	90.7 (22.8)	91.0 (24.4)	86.5 (31.4)	90.1 (27.1)
Normal cognition	60	95.6 (16.6)	99.1 (15.1)	100.4 (13.3)	101.0 (15.4)	102.6 (13.9)
Impaired cognition	24	77.0 (28.7)	69.9 (25.8)	67.3 (29.5)	50.1 (32.0)	58.6 (26.6)
Depression, medication	59	92.6 (19.8)	91.7 (20.3)	93.6 (19.2)	83.0 (33.3)	88.2 (24.3)
Normal cognition	43	98.7 (16.9)	96.7 (15.5)	98.4 (14.6)	98.9 (17.8)	99.1 (12.0)
Impaired cognition	16	76.3 (18.0)	78.1 (25.4)	80.7 (24.1)	40.1 (26.8)	59.1 (25.4)
Bipolar disorder	43	90.9 (20.7)	89.6 (22.0)	85.9 (25.5)	81.7 (31.2)	85.5 (29.4)
Normal cognition	25	99.3 (16.2)	97.8 (18.0)	98.1 (15.3)	102.6 (11.0)	105.4 (13.1)
Impaired cognition	18	79.2 (20.9)	78.3 (22.5)	68.9 (27.5)	52.8 (26.7)	57.7 (22.1)
Effect sizes (Cohen's d)						
Controls vs. MD/Normal		0.18	0.14	0.06	0.03	0.13
Controls vs. MD/Impaired		1.45	1.60	1.81	3.20	2.64
MD/Normal vs. MD/Impaired		1.06	1.26	1.52	2.67	2.60

Note: Values are mean scores with standard deviations in parentheses. Effect sizes (Cohen's d) are presented for comparisons between healthy controls, all patients with a diagnosed mood disorder and normal cognition (MD/Normal), and all patients with a diagnosed mood disorder and impaired cognition (MD/Impaired). The Complex Attention and Cognitive Flexibility domains had the largest effect sizes. The Complex Attention domain is generated by adding the number of errors committed in the Continuous Performance Test, the Shifting Attention Test, and the commission errors on the Stroop Test. For Cognitive Flexibility, the number of correct responses on the Shifting Attention Test, minus the number of errors on the Shifting Attention Test and commission errors on the Stroop Test, is used to create a domain score. These scores have medium to high correlations in the healthy control sample ($r=.77$) and the mood disorders sample ($r=.89$).