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ORIGINAL PAPER

Cognitive functioning in severe psychiatric disorders: a general population study

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Abstract In clinical samples, patients with severe psychiatric disorders are found to have cognitive impairments. Less is known whether this applies to samples derived from the general population. We aimed to study cognitive functioning in a population-based sample comprising individuals with schizophrenia, other non-affective psychoses, bipolar disorders, major depressive disorder, and controls derived from the same population. The current analysis was based on 148 persons with severe mental disorders and 66 control subjects, derived from the Psychoses in Finland study. All subjects were interviewed with SCID, and a neuropsychological test battery was administered. Subjects with schizophrenia had a generalized cognitive impairment ($d = 0.43$–1.07), while those with other non-affective psychoses were impaired in verbal memory and processing speed ($d = 0.43$–0.59). Subjects with bipolar disorders were not impaired. Unipolar major depressive disorder associated with slowed processing speed ($d = 0.64$). Our findings on cognitive impairments in subjects with schizophrenia and other non-affective psychoses derived from the general population support previous findings of a generalized cognitive dysfunction in these subjects. However, our results suggest that subjects with bipolar disorders from non-clinical populations may not have significant cognitive impairments. Our results emphasize the importance of using control samples derived from the same population and studied similarly as those with disorders in evaluating cognitive functioning of subjects with severe mental disorders.

Keywords Neuropsychology · Schizophrenia · Bipolar disorder · Psychosis · Major depressive disorder · General population

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Introduction

Numerous studies have confirmed that generalized impairment in cognitive functioning is a core characteristic of schizophrenia [1, 2]. This impairment is present at the onset and enduring after that in a rather unchangeable form [3, 4]. Impairments in cognition have been observed in patients with bipolar disorder, too, [5–8] although they may be less severe and generalized than those in schizophrenia [9], and possibly state dependent at least as regards intensity [10, 11]. Patients suffering from unipolar major depressive disorder have impairments particularly in memory and executive functioning [12–14]. The impairments seem to vary as a function of the

depression severity [15], and the presence of psychotic features may associate with exacerbated impairments in cognitive functioning in affective disorders [16]. A recent population-based study on patients with first-episode psychotic presentation of schizophrenia, bipolar disorder or mania, depressive psychotic disorder, or another psychotic disorder found cognitive impairments characterizing all disorders, being the most severe in schizophrenia and least pervasive in bipolar disorder [17]. There are a number of birth cohort or conscript studies [18, 19] showing that subjects who later develop schizophrenia have early cognitive impairments, while subjects with later bipolar illness may even perform above average level [20]. However, majority of the studies comparing cognitive functioning in severe psychiatric disorders have been conducted in populations derived from clinical settings. It is not well known whether individuals representing the whole population with diagnoses of different major psychiatric disorders have cognitive dysfunctions when compared with unaffected individuals from the same population. In the present study, we set out to explore cognitive functioning among subjects with psychotic and major affective disorders derived from the general population, without a priori knowledge on the diagnosis, phase, or course of their illness.

Methods

Study design

The Psychoses in Finland (PIF) study is a comprehensive general population survey of psychotic disorders. The study design and methodology have been reported in detail previously [21]. The PIF study is an extension of the Health 2000 study, a large general population survey based on a nationally representative two-stage cluster sample of 8,028 persons aged 30 or over [22]. The field work of the Health 2000 study took place between September 2000 and June 2001, and comprised a home interview and a health examination at the local health center, or a condensed interview and health examination of non-respondents at home. The response rate was 93%. Information from health care registers was gathered for the whole sample [22]. Both the original Health 2000 survey and the PIF reassessment were approved by the ethics committees of the National Institute for Health and Welfare (former National Public Health Institute), and the Hospital District of Helsinki and Uusimaa. All subjects signed written informed consents after a detailed description of the respective study.

Diagnostic assessment of psychotic disorders in the psychoses in Finland (PIF) study

In the PIF study, we screened subjects with possible psychotic disorder. The screening procedure and the data compilation have been detailed previously [21]. In brief, subjects were screened to participate in the detailed interview whether they reported having been diagnosed with a psychotic disorder, received a diagnosis of possible or definite psychotic disorder from the physician conducting the health examination, or had possible psychotic or manic symptoms in the Composite International Diagnostic Interview (CIDI) [23] conducted as part of the health examination. A register-based screen was also used, including hospital treatment for any psychotic or bipolar disorder, reimbursed antipsychotic medication, disability pension because of psychotic or mood disorder, or mood-stabilizing medication use without a diagnosis of any relevant physical condition. Altogether 746 subjects were screened positive. To obtain population reference data, 150 screen-negative controls were randomly selected for the reinterview from all those who had attended any phase of the Health 2000 study.

The screened subjects and the controls were interviewed using the Research Version of the Structured Clinical Interview for DSM-IV (SCID-I) [24], and a neuropsychological test battery was administered. The reassessment took place from 2002 through 2004.

With the approval of the Finnish Ministry of Social Affairs and Health, we also collected hospital and outpatient case notes from psychiatric and primary care units from all lifetime treatment contacts for all mental health problems of the subjects. The final best-estimate diagnoses using DSM-IV-TR criteria were made by three experienced clinicians, JS, JP, and SIS, based on all available, systematically evaluated information from the interview and case records. Kappa values between the raters ranged from 0.74 to 0.97 for different psychotic disorders [21]. Detailed description of the diagnoses of the whole study group has been published previously [21]. Besides evaluating the diagnoses, the clinicians assessed the average lifetime severity of psychotic and affective symptoms using the Major Symptoms of Schizophrenia Scale (MSSS) [25]. The symptoms in the MSSS were rated as: 1—clearly not present, 2—possibly present but subthreshold, 3—moderate, 4—prominent, and 5—severe.

Subjects

Of the 746 screen-positive subjects, 32 had refused further contact in the baseline Health 2000 assessment and were thus not invited to the reassessment. The remaining 714 screen-positive subjects were invited, and of them, 270 either refused, did not answer, or had other reasons not to attend the interview [21]. Altogether 444 screen-positive individuals and 99 of the 150 randomly selected screen-negative control subjects agreed to participate. They were interviewed, and a neuropsychological test batter was administered.

Table 1 Descriptives of the subjects with schizophrenia (SCH), other non-affective psychotic disorders (ONAP), bipolar disorders (BPD), unipolar major depression (MDD), and control subjects (C)

	SCH	ONAP	BPD	MDD	C
N	23	23	17	85	66
Females/males	12/11	14/9	8/9	49/36	35/31
Age mean (SD)[a]	50.0 (9.0)	51.3 (11.0)	45.6 (9.5)	53.6 (9.2)	50.4 (10.1)
Education					
% Basic	30.4	40.0	33.3	36.0	32.8
% Secondary	34.8	28.0	16.7	36.0	34.3
% High	34.8	32.0	50.0	28.0	32.8
Duration years of illness mean (SD)	21.0 (8.8)	21.2 (11.6)	18.2 (11.3)	13.3 (11.2)	NA
GAF[b,c] mean (SD)	47.8 (14.1)	55.4 (14.1)	71.9 (14.9)	72.4 (12.3)	83.3 (8.9)

[a] Subjects with bipolar disorder are significantly younger than those with MDD ($p = 0.002$) and controls ($p = 0.04$)

[b] Global assessment of functioning

[c] SCH < BPD ($p < 0.001$), MDD ($p < 0.001$), and C ($p < 0.001$)

ONAP < BPD ($p = 0.002$), MDD ($p < 0.001$), and C ($p < 0.001$)

BPD > SCH ($p = 0.002$), BPD < C ($p = 0.02$)

MDD > SCH ($p < 0.001$), ONAP ($p < 0.001$), C ($p < 0.001$)

Of the 444 screen-positive subjects, a final best-estimate diagnosis of severe mental disorder was assigned for 240 subjects, who were included in the present study. From the final analyses of the present study, we excluded all subjects over 70 years of age ($n = 30$), subjects who had a lifetime diagnosis of substance induced psychotic disorder or delirium, current alcohol or other substance use disorder, or dementia or other cognitive disorder ($n = 47$). Further, 15 subjects were excluded as they did not give a valid test performance because of visual problems, neurological disorders, or other problems based on the notes of the interviewer.

Of the 99 controls, we excluded 16 individuals over 70 years of age, and 14 individuals with above-mentioned disorders, or other current Axis I disorders. Those with lifetime mood or anxiety disorder NOS, or with current specific phobia were included. Three more controls with mother tongue other than Finnish were excluded.

The final study sample thus comprised 214 subjects, who were divided into five groups. The first group included 23 subjects with schizophrenia. The second group included 23 individuals with other non-affective psychotic disorders (ONAP) [(schizophreniform disorder ($n = 2$), schizoaffective disorder ($n = 11$), delusional disorder ($n = 3$), brief psychotic disorder ($n = 1$), and psychotic disorder not otherwise specified ($n = 6$)]. The third group included 17 subjects with bipolar disorders [bipolar I disorder ($n = 11$), bipolar II disorder ($n = 3$), bipolar disorder NOS ($n = 2$), cyclothymic disorder ($n = 1$)]. Of the 11 subjects with bipolar I disorder, 4 had psychotic features. The fourth group comprised 85 subjects with major depressive disorders (MDD) (11 with and 74 without psychotic features). The fifth group of the present study included 66 control subjects. The demographic information of the study sample is presented in Table 1.

Examination of non-response

We compared age, sex, and education between participants and non-participants. Similarly to our main analyses, we here excluded subjects who were over 70 years old. No differences in these variables were found among the diagnostic groups or the control subjects.

We further investigated whether persons within the disorder groups who had valid neuropsychological testing available differed from those who were excluded or did not participate using information from the MSSS [25] as well as from some global ratings from the Scale for the Assessment of Positive Symptoms (SAPS) [26] and the Scale for the Assessment of Negative Symptoms (SANS) [27]. These scales had been filled based on the SCID interview and medical records from in- and outpatient treatments, obtained on a lifetime basis [28]. In the examination of non-response, following variables of the MSSS were used: lifetime severity of delusions, hallucinations, positive thought disorder, catatonia, affective deterioration, negative thought disorder, depression, manic symptoms, avolition, anhedonia, bizarre behavior, as well as the course and outcome of the disorder. Differences between participants and non-participants were tested with the Kruskal–Wallis test, as the symptom ratings were ordinal. Significant differences ($p = 0.05$ to <0.001) were observed in the following clinical variables: Non-participants with schizophrenia had less depressive symptoms

than participants, while those with ONAP did not differ from each other in any symptom or outcome measure. Non-participants in the bipolar spectrum group had more severe delusions than participants. Among the MDD group, non-participants differed from participants in having more severe hallucinations, delusions, depression, and avolition.

Neuropsychological test methods

Experienced and trained psychologists or psychiatric nurses administered a neuropsychological test battery to the subjects in a fixed order. The test methods were selected to cover the fundamental cognitive functions: attention, working memory, verbal learning and memory, information processing, executive functioning, and basic ability. Digit Span Forwards and Visual Span Forwards from the Wechsler Memory Scale-Revised (WMS-R) [29] were used to assess auditory and visual attention, respectively. The backward conditions of the Digit Span and Visual Span tests (WMS-R) were used as measures of verbal and visual working memory, respectively. The California Verbal Learning Test (CVLT) [30] was selected for measuring the processes of verbal learning and memory. The analyses included the following variables derived from the CVLT: Total recall in trials 1–5 (verbal learning), semantic clustering (learning strategy), short-delay verbal memory, long-delay verbal memory, and discriminability (recognition memory). Digit Symbol from the Wechsler Adult Intelligence Scale-Revised (WAIS-R) [31] assessed psychomotor and information processing speed. From the Trail Making Test (TMT) [32], we included the difference score calculated subtracting the time to complete part B from the time of completing part A. This index removes the speed element from the test evaluation and leaves a score for executive functioning. WAIS-R Vocabulary subtest was used as the measure of basic verbal ability. The Vocabulary test has been considered as one of the best measures assessing premorbid level of functioning [33].

Statistical methods

The differences in neuropsychological performance between the psychiatric groups and the controls were analyzed with linear regression modeling, separately between each diagnostic group and the control group. Age, sex, and educational level (basic, secondary, or high) were used as covariates in all analyses. As there were some individuals with psychotic type features in the bipolar spectrum group ($n = 4$) and in the MDD group ($n = 11$), the presence of positive psychotic symptoms (delusions or hallucinations, yes/no) was included as a covariate in additional models on these groups. Moreover, we analyzed the effect of the severity of these symptoms (the sum score of lifetime ratings of delusions and hallucinations using the MSSS) on cognitive functions in a combined sample of subjects with schizophrenia, other non-affective psychoses, bipolar spectrum disorders, and major depressive disorders. In additional models separately in each study group, we investigated the association of the current level of functioning, as assessed with the Global Assessment of Functioning (GAF) [34] with neuropsychological test performance. Raw scores of the neuropsychological test data were used in all analyses, except in analyzing the semantic clustering variable, which was log transformed to reach better normality of the distribution. Differences with p-value <0.05 were considered as significant. We also calculated the effect sizes [35] and their 95% confidence intervals between the psychiatric groups and controls. SPSS, version 16.0 [36] was used in analyzing the data.

Results

Table 2 shows the means and standard deviations in the study groups across the scores in neuropsychological test performance. In the linear regression models comparing separately each group with psychiatric disorders and controls, adjusted for age, sex, and educational level (Table 3), subjects with schizophrenia were detected to be impaired in all measured neuropsychological test variables (all p-values < 0.05). Subjects with other non-affective psychotic disorders were found to be impaired in verbal working memory ($p = 0.008$), verbal learning ($p = 0.046$), short-delay verbal memory ($p = 0.011$), long-delay verbal memory ($p = 0.036$), and in psychomotor speed ($p = 0.001$). Persons with bipolar disorders were not impaired in any neuropsychological variables. Persons with major depressive disorder scored significantly lower than controls in verbal ability ($p = 0.036$) and in psychomotor speed ($p = 0.016$).

In additional linear regression models, conducted separately and in each illness group under study, we examined the association of the current level of functioning as assessed by the GAF with neuropsychological test performance (data not shown). Among the subjects with major depressive disorders, the GAF score associated significantly with verbal working memory ($p = 0.02$), information processing speed ($p = 0.01$), and executive functioning ($p = 0.05$), while in the schizophrenia and other non-affective psychosis group only verbal learning ($p = 0.02$ and $p = 0.01$, respectively) associated with the global functioning score. In the bipolar group, no associations were detected.

As there were individuals with a lifetime history of psychosis in the bipolar and MDD groups, we examined the effect of psychosis (yes/no) on cognitive functions

Table 2 Means and standard deviations (SD) of the neuropsychological test variables among subjects with schizophrenia (SCH), other non-affective psychoses (ONAP), bipolar disorders (BPD), unipolar major depression (MDD), and control subjects (C)

	SCH $n = 23$ Mean (SD)	ONAP $n = 23$ Mean (SD)	BPD $n = 17$ Mean (SD)	MDD $N = 85$ Mean (SD)	C $n = 66$ Mean (SD)
Auditory attention[a]	6.1 (1.8)	7.2 (1.9)	7.8 (2.3)	7.3 (2.0)	7.3 (1.8)
Visual attention[b]	7.2 (1.8)	8.0 (1.6)	8.4 (1.7)	7.9 (1.9)	8.0 (1.9)
Verbal working memory[c]	4.7 (2.0)	5.0 (1.7)	6.4 (1.6)	5.6 (1.9)	6.0 (1.7)
Visual working memory[d]	6.9 (2.1)	7.3 (1.6)	7.5 (1.8)	7.7 (1.9)	7.8 (1.7)
Verbal learning[e]	35.6 (14.0)	43.5 (10.8)	49.3 (15.0)	47.1 (11.0)	48.1 (10.8)
Semantic clustering[e]	1.4 (0.8)	1.5 (0.7)	1.9 (0.9)	1.7 (0.8)	1.8 (0.8)
Short-delay recall[e]	8.0 (3.8)	8.7 (3.3)	10.5 (3.7)	10.2 (2.9)	10.5 (3.2)
Long-delay recall[e]	8.0 (4.1)	9.2 (3.4)	11.0 (3.9)	10.6 (2.9)	10.7 (3.4)
Recognition memory[e]	90.0 (7.5)	92.5 (7.7)	94.9 (4.9)	93.1 (6.7)	94.0 (5.9)
Verbal ability[f]	36.3 (14.4)	39.3 (10.8)	44.3 (11.2)	37.8 (10.5)	41.7 (10.5)
Psychomotor speed[g]	37.6 (12.6)	41.3 (14.0)	53.8 (14.8)	43.3 (12.5)	49.3 (14.1)
Executive function[h,i]	92.1 (61.3)	67.6 (43.3)	44.1 (21.7)	67.5 (38.3)	56.1 (41.3)

[a] Digit Span Forward, WMS-R [29]

[b] Visual Span Forward, WMS-R [29]

[c] Digit Span Backward, WMS-R [29]

[d] Visual Span Backward, WMS-R [29]

[e] California Verbal Learning Test [30]

[f] Vocabulary, WAIS-R [31]

[g] Digit Symbol, WAIS-R [31]

[h] Trail Making Test [32]

[i] Higher score means worse performance

separately in these two groups (data not shown). Among the subjects with bipolar disorder, psychosis had no significant effect on any neuropsychological measure. In the group of subjects with major depressive disorders, the presence of psychosis associated significantly with impaired executive functioning ($p = 0.036$).

We also evaluated the overall contribution of the lifetime severity of positive psychotic symptoms to the neuropsychological test performance. In these analyses, we included subjects with schizophrenia, other non-affective psychotic disorders, bipolar disorders, and major depressive disorders. Age, sex, education, and the sum score of the severity of positive psychotic symptoms were the predictors for the cognitive test data. We found that severity of psychotic symptoms associated significantly with test performance in all except visual attention and visual working memory (p-values between 0.05 and <0.001, data not shown).

Furthermore, we calculated the effect sizes of the cognitive dysfunctions between the groups with psychiatric disorders and controls (Table 4). The effect sizes were generally between medium to large in the schizophrenia group with the highest effect size ($d = -1.07$) in verbal learning. In the group with other non-affective psychoses, we detected medium effect sizes in verbal working memory ($d = -0.59$), short-delay recall ($d = -0.56$), and in psychomotor speed ($d = -0.57$), while only small or zero effects sizes were detected in the groups with mood disorders, except that the MDD group showed a medium effect size in psychomotor speed ($d = -0.64$).

Discussion

To our knowledge, the present study is the first in which a general population-based sample without a priori ascertainment of any particular disorder has been used for comparisons between cognitive functioning among individuals with major psychiatric illnesses and control subjects derived from the same population. The diagnostic procedure was comprehensive, including both personal interview and review of case notes from all lifetime mental health treatment contacts [21].

The present study represents age groups from 30 to 70 years from a representative population-based sample. We further examined whether persons from each diagnostic group from whom we had valid neuropsychological test data were representative of that group. We found no differences between those who participated and non-participants in age, sex, or level of education. Furthermore, the

Table 3 Differences in neuropsychological test scores of subjects with schizophrenia (SCH), other non-affective psychosis (ONAP), bipolar disorders (BPD), unipolar major depression (MDD) from scores of the control group

	SCH versus C			ONAP versus C			BPD versus C			MDD versus C		
	β[i]	T[j]	P[k]	β	t	p	β	t	p	β	t	p
Auditory attention[a]	0.21	3.0	0.004	0.01	0.08	0.934	−0.09	−0.67	0.504	−0.07	−0.61	0.540
Visual attention[b]	0.47	2.1	0.036	−0.02	−0.20	0.821	−0.02	−0.12	0.908	−0.02	−0.22	0.824
Verbal working memory[c]	0.27	3.8	0.001	0.21	2.71	0.008	0.04	0.36	0.723	0.10	1.04	0.301
Visual working memory[d]	0.17	2.3	0.024	0.08	1.70	0.288	0.16	1.36	0.176	−0.01	−0.65	0.948
Verbal learning[e]	2.00	4.7	<0.0001	0.99	2.03	0.046	0.40	0.53	0.597	0.11	0.21	0.836
Semantic clustering[e]	0.07	2.0	0.050	0.05	1.45	0.150	−0.27	−0.48	0.632	0.03	0.07	0.946
Short-delay recall[e]	0.39	3.3	0.001	0.37	2.60	0.011	0.05	1.33	0.187	0.03	0.21	0.836
Long-delay recall[e]	0.49	3.8	<0.0001	0.32	2.13	0.036	0.20	0.90	0.372	−0.01	−0.04	0.969
Recognition memory[e]	0.06	2.5	0.016	0.004	1.40	0.17	0.001	0.42	0.677	0.01	0.31	0.760
Verbal ability[f]	1.01	2.1	0.035	0.53	1.07	0.290	0.07	0.10	0.921	1.15	2.12	0.036
Psychomotor speed[g]	2.31	5.2	<0.0001	1.79	3.37	0.001	0.34	0.45	0.655	1.28	2.43	0.016
Executive function[h]	−6.07	−3.3	0.002	−2.78	−1.43	0.156	1.12	0.45	0.653	−3.53	−1.74	0.084

Linear regression model with age, sex, and education as the covariates

[a] Digit Span Forward, WMS-R [29]

[b] Visual Span Forward, WMS-R [29]

[c] Digit Span Backward, WMS-R [29]

[d] Visual Span Backward, WMS-R [29]

[e] California Verbal Learning Test [30]

[f] Vocabulary, WAIS-R [31]

[g] Digit Symbol, WAIS-R [31]

[h] Trail Making Test [32], score reversed

[i] Standardized regression coefficient

[j] t-value for the standardized β coefficient

[k] Two-tailed p-value for t

analysis of non-response concerning symptoms, course, and outcome indicated that there was little or no selection bias among persons with schizophrenia or other non-affective psychoses. Responders with bipolar spectrum disorders had less delusions, and those with major depressive disorder had less severe symptoms and more favorable course than non-responders, suggesting some selection bias toward less severe disorder in the affective disorder groups.

We found that subjects with schizophrenia scored consistently worst in all used neuropsychological tests, thus showing a generalized impairment across cognitive functions. In our study, this was detected in comparing the subjects with schizophrenia with a group of representative population controls. Our results from this non-clinical sample accords with the well-established observation of cognitive impairments being among the core features of schizophrenia [1, 2], being present already in patients with their first episode of the illness [37]. The effect sizes varied between moderate to large, the effect size of verbal learning being the largest. This result is in line with a previous meta-analysis [38], and a review [39], in which global verbal memory impairments showed the highest effect sizes among several neuropsychological test variables. However, as Cirillo and Seidman [39] pointed out, it is important to relate this impairment with the observed generalized cognitive dysfunction. Low scores on tests assessing verbal learning and memory may be explained by cognitive impairments in attention, working memory, and other information processing measures [40].

Verbal learning and memory, as measured with the CVLT [30], has been included as one of the standard measures of cognition in the multisite collaboration project COGS (The Consortium on the Genetics of Schizophrenia), searching for quantitative endophenotypes related to schizophrenia [41]. Our results provide further evidence for this test method as a valid measure in schizophrenia research.

Patients with other non-affective psychotic disorders, including mostly subjects with schizoaffective disorder, showed impairments in several measures of verbal learning and memory, and in psychomotor speed, albeit these

Table 4 Effect sizes (d30) and 95% Confidence Intervals (CI) of the neuropsychological impairments among subjects with schizophrenia (SCH), other non-affective psychoses (ONAP), bipolar disorders (BPD), and unipolar depressive disorders (MDD)

	SCH versus C		ONAP versus C		BPD versus C		MDD versus C	
	d	95% CI	*d*	95% CI	*d*	95% CI	*d*	95% CI
Auditory attention[a]	−0.67	−1.15 to −0.18	−0.05	−0.53 to 0.42	0.26	−0.22 to 0.73	0.00	−0.47 to 0.47
Visual attention[b]	−0.43	−0.90 to 0.06	0.00	−0.47 to 0.47	0.22	−0.26 to 0.69	−0.05	−0.53 to 0.42
Verbal working memory[c]	−0.73	−1.21 to −0.24	−0.59	−1.07 to −0.10	0.24	−0.24 to 0.71	−0.23	−0.70 to 0.25
Visual working memory[d]	−0.50	−0.97 to 0.01	−0.30	−0.77 to 0.18	−0.17	−0.65 to 0.30	−0.06	−0.53 to 0.42
Verbal learning[e]	−1.07	−1.56 to −0.56	−0.43	−0.90 to 0.06	0.10	−0.38 to 0.57	−0.09	−0.57 to 0.38
Semantic clustering[e]	−0.50	−0.98 to −0.02	−0.39	−0.86 to 0.09	0.12	−0.35 to 0.59	−0.13	−0.60 to 0.35
Short-delay recall[e]	−0.74	−1.22 to −0.25	−0.56	−1.03 to −0.07	0.00	−0.47 to 0.47	−0.10	−0.57to 0.38
Long-delay recall[e]	−0.75	−1.23 to −0.26	−0.44	−0.92 to 0.04	0.08	−0.39 to 0.56	−0.03	−0.50 to 0.44
Recognition memory[e]	−0.63	−1.11 to −0.14	−0.23	−0.71 to 0.24	0.16	−0.32 to 0.63	−0.15	−0.62 to 0.33
Verbal ability[f]	−0.47	−0.94 to 0.02	−0.23	−0.70 to 0.25	0.24	−0.23 to 0.72	−0.37	−0.85 to 0.11
Psychomotor speed[g]	−0.85	−1.33 to −0.35	−0.57	−1.05 to −0.08	0.32	−0.16 to 0.79	−0.64	−0.97 to −0.31
Executive function[h]	0.69	0.27 to 1.24	0.28	−0.20 to 0.75	−0.32	−0.80 to 0.16	0.28	−0.20 to 0.75

[a] Digit Span Forward, WMS-R [29]

[b] Visual Span Forward, WMS-R [29]

[c] Digit Span Backward, WMS-R [29]

[d] Visual Span Backward, WMS-R [29]

[e] California Verbal Learning Test [30]

[f] Vocabulary, WAIS-R [31]

[g] Digit Symbol, WAIS-R [31]

[h] Trail Making Test [32], score reversed

impairments were not as severe as those among individuals with schizophrenia. The effect sizes in auditory and visual attention were smaller in this group than in the schizophrenia group, with a medium effect size in auditory, and close to medium effect size in visual attention. A polydiagnostic study on cognitive impairment in non-affective psychosis found that particularly patients with core schizophrenia and deteriorating course, excluding those with schizoaffective disorder, show cognitive deficits [42]. This was found in another study [43], too, in which schizoaffective patients were cognitively closer to patients with non-psychotic mood disorder than those with schizophrenia. Several studies on cognitive deficits in schizophrenia have included patients with schizoaffective disorder into the schizophrenia group, but it may be that these disorders should be analyzed separately.

Subjects with bipolar disorder scored better than those with non-affective psychoses or unipolar major depressive disorder, and even better than the controls in some test measures, albeit statistically insignificantly. Bipolar subjects also scored highest of all subjects in verbal ability, assessed with the Vocabulary subtest from the WAIS-R [31] that is among the best single estimates of general premorbid ability [33]. In several studies on bipolar disorder, particularly functions related to executive functioning have been found impaired [7, 44–46], being so also among patients in their first episode [17] and among young patients at age 7–17 with very early onset [47]. In our study, executive functioning was assessed only using the Trail Making Test, which may not have been tapping those aspects of this function that have been found most impaired in bipolar disorder, i.e., planning and response inhibition [7, 45]. Including measures assessing these aspects of executive functioning could have revealed impairments among the subjects with bipolar disorder under study, too.

Mean age of the bipolar group was the lowest of all groups, and although we took age into account in all analyses, it may be that aging with subsequent increase in the number of episodes may bring out cognitive impairments in this group [48]. Partly in line with our results, a recent study on patients with a first-affective episode with psychotic symptoms and a positive history of mania found only selective deficits in cognition against a generally preserved cognitive function [49]. In our study, according to the SCID interview, administered at the day of testing, about 90% did not have acute symptoms of depression or mania, thus being euthymic at the time of testing. Although similar results to ours have been published recently [50], impairments emerging in the subjects of the present study

in acute illness phases cannot be excluded. The analysis on non-responders showed that subjects with more delusions did not participate in the neuropsychological testing. Although psychosis does not necessarily correlate with cognitive impairments in bipolar disorder [12], it may be that subjects with a more severe form of the disorder were among non-participants. Moreover, we excluded persons with any current comorbid substance use disorders, which may have affected the results, too. This population-based but small bipolar sample may also be limited with possible type II error consequences.

In the present study, the subjects with major depressive disorder represent a severe form of the disorder, because they were selected to participate in the study either because they had disability pension for MDD, free outpatient antipsychotic and antidepressive medication, which requires evidence of psychotic symptoms, or they reported symptoms suggestive of a psychotic disorder in the CIDI interview or health examination. However, the analysis of non-response showed that non-responders with MDD had more severe symptoms than responders, suggesting an even graver neuropsychological impairment associated with severe MDD than reported here. The responders, too, scored lower than controls in all neuropsychological tests, being significantly impaired in verbal ability and in psychomotor speed, measured using the timed WAIS-R [31] Digit Symbol subtest. This test demands apart from motor performance also visual working memory and general information processing speed and is considered a measure of integrating distributed brain networks [51]. Our results are in line with the study by Rund et al. [52], who found that patients with recurrent non-psychotic depression had mild cognitive deficits, mainly in measures of processing speed and working memory. In the present study, processing speed was impaired in all other illness groups except bipolar spectrum disorders.

Presence of lifetime psychosis associated with executive functioning as measured with the Trail Making Test among the individuals with MDD, which is partly in line with the results of Hill et al. [53], who found a different neuropsychological profile among patients with psychotic depression from that of the non-psychotic mode. Our group of subjects with a psychotic form of MDD was, however, too small for an analysis of a detailed neuropsychological profile. Of the subjects with MDD, 70% had used treatment services during the past 12 months, and the lower GAF score associated with worse performance functions related to information processing, working memory, and executive functioning, suggesting that the level of cognitive functioning in MDD may be related to current symptoms.

We further analyzed the effect of the severity of psychotic symptoms on cognitive functions among a combined group of subjects with schizophrenia, other non-affective psychoses, bipolar spectrum disorders, and major depressive illnesses. All other functions except visual attention and visual working memory associated with severity of these symptoms of the disorder. Visual attention and visual working memory were impaired only among subjects with schizophrenia, and it may be that these dysfunctions are trait markers, or endophenotypes [54] of this disorder rather than a general indicator of psychosis [40, 55, 56].

In many studies, the study samples have been recruited via psychiatric clinics fulfilling the diagnoses a priori. We did not ascertain our subjects for any specific diagnosis, but selected individuals screened positive for any signs of psychotic or manic symptomatology, and assigned the diagnoses based on all available data on their health and symptoms [21]. While this representativeness is a strength of the present study, it may have added heterogeneity within the groups used in the analyses.

The control group in the present study was randomly selected from the same population as the subjects with psychiatric disorders, and the same diagnostic evaluation was applied to all groups. The control group that took part in the interview and neuropsychological testing was representative and did not differ from those who did not participate. The individuals that ended up in the final control group did not suffer from current psychiatric disorders, albeit we allowed presence of lifetime diagnoses of minor depressive disorders or current specific phobias that are common in the general population. In the present study, the effect sizes in the comparisons between subjects with schizophrenia and controls tended to be smaller than those reported e.g., in the meta-analysis by Dickinson et al. [1], probably reflecting the use of this genuine population-based control group. The same phenomenon may have diminished the effect sizes and other differences in all comparisons.

In conclusion, our study on this epidemiological sample of subjects with psychiatric disorders and controls, while being in line with previous results on the generalized cognitive dysfunction among individuals with schizophrenia, revealed a discrepancy between our results and those from several previous studies on cognitive functioning of subjects with bipolar disorder. Current symptoms and global functioning associated with neuropsychological test performance particularly in major depressive disorder. Our results also emphasize the importance of using a representative control sample derived from the same population as the subjects with psychiatric disorders when investigating possible neuropsychological deficits associated with these disorders.

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Conflicts of interest The authors declare that they have no conflict of interest.

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