Cognitive dysfunction among inpatients and outpatients with schizophrenia: relationship to positive and negative symptoms

Tarek Ahmed Okasha[1], Hanan Hussein[1], Eman Shorub[1], Hamed Nagi[1], Ahmed A. Moustafa[2] and Doha El-Serafi[1*]

Abstract

Background: Cognitive impairment is an established feature of schizophrenia and is a strong predictor of eventual social and functional outcome. Few studies have investigated cognitive impairment in hospital long-stay patients with schizophrenia. This study evaluates and compares cognitive function among a sample of patients with schizophrenia in both inpatient and outpatient departments in order to determine the relationship between cognitive impairment and clinical variables.

A cross-sectional comparative study based on a semi-structured interview investigating 100 inpatients with schizophrenia recruited from El-Abassia Mental Health Hospital departments compared to 100 patients with schizophrenia selected from the outpatients' clinic matched with cases. The assessment tools included SCID-I, the Adult Wechsler Intelligence Scale, the computerized version of Wisconsin Card Sorting Test (WCST), Mini-Mental State Examination (MMSE), and Positive and Negative Syndrome Scale (PANSS).

Results: Patients with schizophrenia showed significant deficits on cognitive function with no statistically significant difference between the inpatient and outpatient groups. Executive function was significantly correlated with verbal, non-verbal, and total IQ. Executive function was negatively correlated with the positive and general symptoms of PANSS and not correlated with its negative symptoms. In addition, we did not find any statistically significant relationship between cognitive functions and the duration of illness.

Conclusion: The study provides evidence that institutionalization is not an influential factor on cognitive impairment patients with schizophrenia. However, the psychopathological aspects of the disorder are one of the crucial factors affecting the cognitive function in schizophrenia.

Keywords: Cognition, Schizophrenia, Long-stay hospital, Egyptian sample, Positive and negative symptoms, Inpatient vs. outpatient

Background

Cognitive dysfunction has been viewed as a core feature of schizophrenia since it was first conceptualized. Kraepelin used the term "dementia praecox" to describe the functional and intellectual deterioration as key disease features.

Recent evidence suggests that 50–70% of patients with schizophrenia have neuro-cognitive deficits [1].

Cognitive deficits are reported in high-risk groups prior to the onset of psychotic illness, and deficits are broadly evident at the first episode and remain fairly stable through middle age [2], but there is evidence of exacerbation of deficits in later life, perhaps due to the duration of initially untreated psychosis [3].

* Correspondence: Doha.elserafi@yahoo.com
[1]Psychiatry Institute, Neuro-Psychiatry Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt
Full list of author information is available at the end of the article

Meanwhile, cognitive dysfunctions in schizophrenia have been identified in most cognitive domains, basic sensory and perceptual functions, and higher order cognition, including selective and sustained attention, working memory, episodic memory, processing speed, and problem-solving [4]. These deficits predate the onset of clinical symptoms, represent a decline from previous level of functioning persist over the disease course, and are more closely linked to function than are clinical symptoms of schizophrenia [5, 6].

The association between the severity of cognitive deficits and psychopathologic symptoms is controversial, and many studies showed a significant but modest association between the severity of cognitive deficits and negative symptoms, but no association between cognitive deficits and positive symptoms, such as hallucinations and delusions [6]. In addition, prolonged hospitalization of a patient with schizophrenia was found to impair the cognitive functions to a great extent than that due to schizophrenia alone which is evident by longitudinal follow-up of patients who have been chronically hospitalized most of their adult lives suggesting greater than age-expected cognitive decline and conversion to clinical dementia [5].

Taken together, the evidence above suggests that cognitive deficits in schizophrenia represent a dimensional phenomenon rather than a single complaint. This is also consistent with recent findings of genetic studies, in which multiple genes of small effect individually contribute to illness susceptibility via different pathophysiological processes [7]. Recent evidence suggests that a variant in dysbindin, which slightly elevates risk for schizophrenia, is also associated with the severity of negative symptoms and generalized cognitive deficits [8]. Meanwhile, variants in DISC1 are associated with persecutory delusions and working memory deficits [9].

The current study aimed to examine and compare cognitive function among a sample of patients with schizophrenia in both inpatient and outpatient departments and to determine the relationship between cognitive impairment and clinical variables especially for the positive and negative symptoms.

Methods

A cross-sectional, comparative study was conducted at El Abbassia Mental Health hospital among patients diagnosed with schizophrenia recruited from the inpatient wards and outpatient clinic. The patient sampling started from January 2012 till October 2012. The researchers included patients between 30 and 60 years old with no gender preference. They plotted an operational definition for the long-stay hospital patients: those patients with duration of illness of at least 7 years and has been hospitalized for at least the last 5 years consecutively. However, patients whose IQ ≤ 70, receiving

recent course (3 months) of BST (brain synchronizing therapy), were excluded from the current study. Meanwhile, the presence of comorbid neurological or other psychiatric disorders as well as any debilitating disease was considered as exclusion criteria. The recruited outpatient group fulfilled the same inclusion and exclusion criteria except for being hospitalized in the last 3 months. The authors succeeded in collecting 200 patients (100 from the inpatient ward and 100 from the outpatient clinic).

Patients were first interviewed by a trained psychiatrist. The diagnosis of schizophrenia and exclusion of other psychiatric disorders were performed according to DSM-IV by using SCID-I [10], and the IQ was estimated based on the Wechsler intelligence scale for adults [11] to exclude the mentally subnormal cases. They were then evaluated regarding the severity and different symptoms of schizophrenia by using the Positive and Negative Syndrome Scale (PANSS) [12, 13]. Furthermore, the Mini-Mental State Examination (MMSE) was used to screen patients for cognitive impairment, track changes in cognitive functioning over time, and often to assess the effects of therapeutic agents on cognitive function [14], and Wisconsin Card Sorting Test (WCST) allows the clinician to assess different "frontal" lobe functions as strategic planning, priority setting, utilizing environmental feedback to shift cognitive sets, impulsivity control, and directing behavior toward achieving a goal [15].

Data collection regarding socio-demographics and clinical profile was obtained by the researcher according to El Abbassia Hospital admission file. This study has been approved by the Ethics and Research Committee at El Abassia mental hospital. Written informed consent from patients was received prior to data collection.

Statistical analyses

All data were recorded and statistical analysis was done using the Statistical Package for Social Science (SPSS) for Windows (version 17). The results were tabulated, grouped, and statistically analyzed using suitable statistical parameters.

Continuous variables such as age were expressed as mean ± standard deviation, whereas categorical variables such as gender were presented as frequencies. Pearson's chi-square test (χ^2) was used to detect whether there is a significant association between different categorical variables. Furthermore, Spearman's correlation was used to test the association between cognitive functions and different clinical variables. The significance level was set at $p < 0.05$.

Results

Socio-demographic and clinical characteristics across inpatient and outpatient groups

Among the entire sample, the male gender represents nearly 60% of the recruited sample in comparison to

40% female. The mean age was 49.89 ± 7.91 years for the inpatient group and was 43.24 ± 7.76 years for the outpatient group with a highly statistically significant difference ($p = 0.000$). The majority of the outpatient group was from urban places 93%, and only 7% of the outpatient group came from rural places with a highly significant statistical difference ($p = 0.00$) as shown in Table 1. The educational level varies rather in the outpatients as well as the inpatient group showing that 70% of the inpatient group reached a higher level of education in comparison to 46% in the outpatient group with a highly significant statistical difference ($p = 0.001$).

All calculations were performed at 95% confidence limits; the confidence interval is 5%.

Regarding the PANSS, there was no significant statistical difference between both groups ($p = 0.7$). The negative subscale had a mean of 19.18 ± 5.39 in the inpatient group as well as 19.64 ± 5.19 in the outpatient group. The positive subscale had 15.16 ± 5.21 for the inpatient group and 15.74 ± 5.22 for the outpatient group. Meanwhile, the general psychopathology scores were 41.95 ± 12.35 in the inpatients and 42.58 ± 10.66 in the out patients.

Comparison of neurocognitive function subtests across inpatient and outpatient groups

As shown in Table 2, there was no statistically significant difference regarding the intellectual function (that was assessed by both WAIS and MMSE) among both groups ($p > 0.05$). Meanwhile, there was no statistically significant difference between the inpatients and outpatients among the frontal lobe cognitive functions (that were assessed by WCST) ($p > 0.05$).

Correlation between the executive function and the general intellectual abilities

Table 3 showed a significant positive correlation between the category completed and the total, verbal, and performance IQ denoting higher overall executive performance with higher total and subtype IQ. However, the total percentage of errors was inversely correlated to the total, verbal, and performance IQ indicating lower concentration abilities with higher intellectual abilities.

Correlation between the executive function and schizophrenia symptom severity

Table 4 showed a significant inverse correlation between the category completed and both the positive symptoms and the general psychopathology scores which implies the higher overall executive functions with less severe positive symptoms ($p = 0.001$, $r = -0.226$). In contrast, the authors found no significant correlation between the negative symptoms and frontal lobe functions.

Discussion

Cognitive impairment is a crucial factor related to treatment outcome, and neurocognitive deficits appear to

Table 1 Sociodemographic and clinical characteristics across inpatient and outpatient groups

Variables	Inpatient group ($n = 100$)	Outpatient group ($n = 100$)	P value*
Age	**49.89 ± 7.91**	**43.24 ± 7.76**	**0.000**
Sex			**0.885**
Male	61 (61%)	60 (60%)	
Female	39 (39%)	40 (40%)	
Marital status			**0.670**
Single	69 (69%)	61 (61%)	
Married	22 (22%)	26 (26%)	
Divorced	7 (7%)	10 (10%)	
Widow	2 (2%)	3 (3%)	
Residency			**0.000**
Urban	73 (73%)	93 (93%)	
Rural	27 (27%)	7 (7%)	
Educational level			**0.001**
Read and write to primary	30 (30%)	54 (54%)	
Higher than primary education	70 (70%)	46 (46%)	
PANSS			
Positive symptoms	15.6 ± 5.21	15.74 ± 5.22	0.539
Negative symptoms	19.18 ± 5.39	19.64 ± 5.19	0.432
General psychopathology	41.95 ± 12.35	42.58 ± 10.66	0.7

*Independent *t* test

Table 2 Comparison of neuro-cognitive function subtests across inpatient and outpatient groups

Variables	Inpatient group (*n* = 100) Mean ± SD	Outpatient group (*n* = 100) Mean ± SD	*P* value*
WAIS			
WAIS—total	89.41 ± 10.46	86.99 ± 10.72	0.108
WAIS—verbal	95.61 ± 13.22	92.33 ± 11.50	0.063
WAIS—performance	87.00 ± 12.34	85.74 ± 13.51	0.492
MMSE	21.05 ± 454	21.85 ± 4.57	0.215
WCST			
Category completed	2.21 ± 179	2.75 ± 2.07	0.05
Total errors	67.35 ± 20.12	61.97 ± 23.65	0.085
Preservative errors	21.00 ± 15.74	12.54 ± 0.099	0.0921
Non-preservative errors	46.60 ± 29.67	28.98 ± 1.41	0.160
Time to complete 1st category	20.21 ± 21.39	20.44 ± 0.585	0.559
PANSS			
Positive symptoms	15.6 ± 5.21	15.74 ± 5.22	0.539
Negative symptoms	19.18 ± 5.39	19.64 ± 5.19	0.432
General psychopathology	41.95 ± 12.35	42.58 ± 10.66	0.7

WAIS Wechsler Adult Intelligence Scale, *MMSE* Mini-Mental State Examination, *WCST* Wisconsin Card Sorting Test, *PANSS* Positive and Negative Syndrome Scale
*Independent *t* test

contribute independently to lower quality of life [16, 17] and also interfere with social function in patients with schizophrenia [18, 19]. Schizophrenia is considered the most common chronic variety of psychosis in Egypt and represents the major bulk of inpatients in our mental hospitals [20]. The aim of this study was to assess and compare the cognitive function pattern among a sample of subjects with schizophrenia in both inpatient and outpatient departments and to determine the relationship between cognitive impairment and clinical variables.

In this study, patients with schizophrenia (both inpatient and outpatient groups) showed an overall cognitive impairment on various neuropsychological tests that is consistent with many studies that revealed clinical cognitive impairment in 50–85% of patients with schizophrenia [21–26]. These deficits are not specific to one

brain region or one neuropsychological process and may reflect both multifocal and diffuse brain diseases suggesting that structural damage, mainly consisting of white matter micro-ischemic lesions, may be responsible for the development of cognitive impairment in patients with schizophrenia [27, 28].

There was no statistically significant difference in the cognitive functions between the long-stay inpatient and outpatient groups of patients with schizophrenia. Similar to our results, Harvey and colleagues [29] concluded that there is minimal evidence that hospitalization, long or short, leads to cognitive and functional changes, but rather that the reason for these hospitalizations may underlie cognitive and functional declines. At the same time, Mosiołek, et.al; 2016 [30] found that most cognitive functions show a slight connection to the age and

Table 3 Correlation between IQ and executive functions

Variables	Verbal IQ		Performance IQ		Total IQ	
	r	*P* value*	*r*	*P* value*	*r*	*P* value*
WCST						
Category completed	0.485	0.000	0.442	0.000	0.596	0.000
Total errors	− 0.461	0.000	− 0.445	0.000	− 0.573	0.000
Preservative errors	0.101	0.155	0.123	0.084	0.125	0.077
Non-preservative errors	− 0.396	0.000	− 0.391	0.000	− 0.488	0.000
Times to complete 1st category	0.179	0.011	0.058	0.412	0.130	0.067

WCST Wisconsin Card Sorting Test, *IQ* intellectual quotient
*Independent *t* test

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Table 4 Correlation between executive functions and schizophrenia symptom severity

Variables	Positive symptoms		Negative symptoms		General psychopathology	
	r	*p* value	*r*	*p* value	*r*	*p* value
WCST						
Category completed	− 0.226	0.001	− 0.142	0.000	− 0.223	0.002
Total errors	0.220	0.002	0.122	0.000	0.224	0.001
Preservative errors	− 0.186	0.008	− 0.079	0.267	− 0.157	0.027
Non-preservative errors	0.260	0.000	0.133	0.060	0.237	0.001
Times to complete 1st category	− 0.043	0.547	− 0.056	0.429	0.025	0.725

Spearman correlation
WCST Wisconsin Card Sorting Test

the time of disease onset whereas perseverative errors (cognitive rigidity) seem to be associated with the difference between the time when the disease begun and the number of years since the first hospitalization. The longer the period of time spent without hospitalization the greater the cognitive rigidity shown in their study which could be connected with fixed deficits caused by a long period when patients were not treated, at least in some cases. Also, Davidson's study it 2000 suggested that cognitive impairment is responsible for long-term hospitalization, rather than supporting the notion that cognitive impairment is a secondary result of long-term institutionalization [31]. In contrast to the current study, Ojeda in 2007 reviews 30 studies published in patients with schizophrenia both first and multiple psychotic episodes. However, the results suggest that significant cognitive symptoms are present at the onset of the disease and these remain stable in the subsequent period between 2 and 5 years. Their deterioration increases with the course of the disease, especially in institutionalized patients [32]. The difference between these studies may be related to different clinical criteria in addition to the evaluation methods used.

Regarding the schizophrenia profiles, the current study confirmed the impact of positive and general symptoms of schizophrenia on cognitive functions; this is in agreement with prior reports of significant correlations of positive symptoms with working memory [33], source monitoring [34], and auditory distractibility [35] as the overall trend is for general neuro-cognitive impairment not to be correlated with positive symptoms. This low correlation across various patient samples suggests that positive symptoms are largely not the sole cause of the cognitive impairment found in patients with schizophrenia. On the other hand, it was found that negative symptoms had a non-significant correlation with cognitive functions. In contrast to the current study, Davidson revealed significant correlations between cognitive impairment and negative symptoms, and their magnitude did not change throughout the entire lifespan. These

associations prove the hypothesis that the two symptoms share a common biological substrate [36].

In line with the current study, the total, verbal, and performance IQ were positively correlated with the executive function. Previous studies notified that schizophrenia is associated with global intellectual impairment and deficits in executive functioning, memory, and attention [37], and the performance of patients with schizophrenia differs from controls by approximately one to two standard deviation which has a greater impact on cognitive functions and associated with worse psychosocial functioning [22, 38, 39, 40].

Finally, the authors did not find any evidence for a relationship between the duration of illness and the cognitive deficits among the sample of schizophrenia. Although some researchers implied that those psychotic episodes may be neurotoxic, with increasing length of illness especially without treatments associated with a poor prognosis, no study has yet yielded direct evidence that this has occurred. Most studies of cognitive function evaluation in schizophrenia have revealed that cognitive deficits are present during the early years of illness and remain stable throughout the course of the disorder [32, 41] supporting the model of cognitive deficits as primary domain related to schizophrenia, although there was no relation found between duration of illness and cognitive impairment [42].

The current work is one of the scarce Egyptian studies evaluating the cognitive function among long-stay inpatients with schizophrenia and its relation to clinical variables. This study design has several strengths and weaknesses. First, the use of selected cognitive tests to measure the cognitive functions may prevent a global understanding of the different cognitive domains. In addition, the authors cannot rule out the effect that neuroleptic medications had a direct effect on cognitive functions even though analyses did not reveal significant correlations. Further, the small sample size may be a factor that reduced statistical power, so, potentially heightens the occurrence of type II errors.

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Conclusion

To conclude, the authors found that long institutionalization was not the influential cause for cognitive deterioration in patients with schizophrenia; however, other causes such as the presence of psychopathology and positive and negative symptoms are the cornerstone in the level of cognitive deterioration especially the executive functions. Cognitive deficits in long-stay inpatients with schizophrenia need to come into focus as regards investigation and treatment, and it is important to throw the highlights on the preventable factors that may contribute to its development. This may improve the outcome and prognosis of those patients to sustain high work productivity and offer better quality of life.

The results of the current study could not be generalized due to several limitations in the study design as the number of recruited sample which could be increased in further studies with multicentered selection of cases. Also, some data are collected from the patient's files retrospectively and could be affected by documentation bias.

Abbreviations
SCID: Structured Clinical Interview for DSM; WCST: Wisconsin Card Sorting Test; MMSE: Mini-Mental State Examination; PANSS: Positive and Negative Syndrome Scale; IQ: Intelligence quotient; BST: Brain synchronizing therapy; WAIS: Wechsler Adult Intelligence Scale

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Authors' contributions
TO was a major contributor in guiding, revising, analyzing, and interpreting the collected data and the manuscript. DS analyzed and interpreted the patients' data concerning the results of the tests done and was a major contributor in writing the manuscript. ES was a major contributor in writing and data collection for updated references. HN was a major contributor in collecting the sample and performing the test. All authors read and approved the final manuscript.

Availability of data and materials
All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate
Approval of Ain Shams University, Faculty of Medicine ethical committee was obtained before starting the research. Informed written consent was obtained from the participants and their caregivers. Participation in the study was clarified to be free and voluntary and would not imply a direct benefit for patients. Withdrawal from the study is guaranteed at any point without consequences. Confidentiality is preserved. Results could be used for scientific publication.

Consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests

Author details
[1]Psychiatry Institute, Neuro-Psychiatry Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt. [2]School of Social Sciences and Psychology, & Marcs Institute for Brain and Behavior, Western Sydney University, Sydney, New South Wales, Australia.

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