

COGNITIVE IMPAIRMENT IN PATIENTS AFFECTED BY SCHIZOPHRENIA MEASURED WITH MODA RATING SCALE

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Abstract

Objective: Cognitive impairment in Schizophrenia is the core of the disorder. Several studies suggest the presence of cognitive abnormalities in schizophrenic patients because they perform worse than healthy controls on many neuro-psychological tests. The aim of this study was to assess the cognitive impairment in patients affected by schizophrenia for more than 5 years using *Milan Overall Dementia Assessment* (MODA) test.

Method: The selected patients (N= 67) met DSM IV –TR criteria for schizophrenia and were all treated with antipsychotic drugs. They had had the disease for longer than 5 years, they were in a “stable phase” of schizophrenia and performed a MODA test. The control group was composed of 25 healthy subjects (15 females and 10 males). Subjects older than 65 years old were excluded.

Results: The findings confirmed cognitive impairment among schizophrenic patients, in fact they showed higher rates of Borderline and Dementia at MODA evaluation: MODA Total Score, not influenced by subjects’ age or education, was lower in patients with schizophrenia than in healthy controls. Moreover, schizophrenic patients performed worse on many MODA subtests than healthy controls. Finally, an Odds Ratio= 12 was calculated showing that schizophrenic patients are much more likely to be Borderline or Dementia than healthy subjects.

Conclusions: The results of the current study replicate international findings about cognition in schizophrenia. It is possible to conclude that MODA probably might prove useful in assessing cognitive impairment among schizophrenic patients in routine clinical practice and that other studies are needed to validate the MODA test as a new instrument for assessing cognitive deficits in schizophrenia.

Key Words: cognitive impairment, dementia, moda, schizophrenia

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Background

Several studies suggest the presence of cognitive abnormalities among schizophrenic patients because they perform worse than healthy controls on many neuro-psychological tests (Ganguli et al. 1998). Recently, an impairment in attention, memory, learning and executive functioning has been demonstrated (Saykin et al. 1991, Goldberg et al. 1987, Donohoe et al. 2006). In 1998 Ganguli et al. tested partially remitted community-dwelling patients with schizophrenia using the MMSE (Mini Mental State Examination). They performed approximately 2–3 points below the

population norms at all ages. Patients who did poorly most frequently had difficulty with memory, attention and construction tasks. Contrariwise, Laks et al. (2006) concluded there was no significant cognitive decline in patients with “late-onset schizophrenia” assessed with MMSE, CAMCOG (section B of the Cambridge Examination for Mental Disorder of the Elderly) and ADL (Activities of Daily Living) at baseline and after one year. Similarly, in 1999 Gold et al. studied cognitive functioning in 54 patients with first-episode and recent-onset of schizophrenia at index hospitalization and again after 5 years. This study indicated that cognitive performance does not deteriorate and may improve in

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patients receiving neuroleptics treatment early in their illness. The MMSE was widely used for grading the cognitive state of patients. However Manning et al. (2007), after using the MMSE to examine the cognitive functioning in psychiatric outpatients with schizophrenia, alcohol dependence and dual diagnosis, concluded that the global MMSE score lacks sensitivity for cognitive impairment in these clinical groups.

In 2008 the NIMH-MATRICES (National Institute of Mental Health – Measurement and Treatment Research to Improve Cognition in Schizophrenia) Psychometric and Standardization Study (PASS) (Green et al. 2008) evaluated 176 patients affected by schizophrenia with two measures of functional capacity (Maryland Assessment of Social Competence, UCDS Performance-Based Skills Assessment) and two interview-based measures of cognition (Schizophrenia Cognition Rating Scale, Clinical Global Impression of Cognition in Schizophrenia). Psychometric properties of all of the measures were considered acceptable. The MATRICES Neurocognition Committee (Nuechterlein et al. 2008) also evaluated more than 90 tests in seven cognitive domains (Verbal and Writing Fluency, Vigilance-Attention, Working Memory, Verbal Learning, Visual Learning, Problem Solving, Social Cognition) to identify the 36 most promising measures and 20 as a beta battery tests. Finally, the consensus cognitive battery developed by NIMH-MATRICES (Kern et al. 2008) included 10 tests (Trail Making Test Part A; Brief assessment of Cognition in Schizophrenia, symbol coding subtest; Hopkins Verbal Learning Test – Revised, immediate recall; Wechsler Memory Scale, 3rd ed., spatial span subtest; Letter-Number Span Test; Neuropsychological assessment Battery, mazes subtest; Brief Visuospatial memory Test- Revised; Category fluency test, animal naming; Mayer-Salovey-Caruso emotional Intelligence Test, managing emotions branch; Continuous Performance Test, Identical Paris Version) that are recommended as the standard battery for clinical trials of cognition-enhancing interventions for schizophrenia and evaluate 8 domains: Speed of processing, Verbal learning, Working memory (nonverbal), Working memory (verbal), Reasoning and problem solving, Visual learning, Social cognition, Attention/vigilance (Nuechterlein et al. 2008). The battery was administered to 300 individuals at five sites in differing geographic regions. For each site, recruitment was stratified by age, gender, and education. Prominent age and education effects were observed across tests.

The development and evaluation of potential co-primary measures is still at an early stage and the current findings offer the initial steps to identify measures in this area. In this study cognitive deficits in schizophrenic patients were assessed using the Italian rating scale MODA (*Milan Overall Dementia Assessment*) (Brazzelli 1994) adjusted for age and educational level of patients. It is already approved for evaluating cognition in the Italian population and it is suitable in the outpatient setting because it allows a thorough cognitive assessment in a short time. Moreover the MODA rating scale explores many cognitive domains and may be considered complete like the MATRICES battery (see **Table 1** in the next paragraph).

Object and Methods

The aim of this study was to assess the cognitive impairment in patients affected by schizophrenia for over 5 years using *Milan Overall Dementia Assessment* (MODA) test (Brazzelli 1994). The authors decided to select patients with more than 5 years of disease according to MRI studies that suggest brain volume changes in schizophrenia during a 5-year period and a gray matter density loss occurs predominantly in left frontal and temporal cortices (van Haren et al. 2007).

The MODA was designed in 1985 on the cognitive model of neuropsychological deficits of Alzheimer's Disease. It was created to describe neuropsychological functions during the clinical examination of patients probably affected by dementia. It has been validated against the MMSE (Mini Mental State Examination) and has a higher sensitivity and specificity in individuals with cognitive deficits than the MMSE. Also, there are a number of limitations to the MMSE (Manning et al. 2007): it is designed as a screening tool for global impairment and is not well suited for the detailed assessment across cognitive domains; it lacks sensitivity in prefrontal brain areas so it is not suitable for assessment of patients affected by schizophrenia.

The MODA is a rating scale composed of three sections: Orientation enquiry, Autonomy scale, Neuropsychological tests. The first section is made up of four different sets of items including temporal orientation, spatial orientation, personal and family orientation. The score range of the entire section is 0-35. The Autonomy Scale considers five aspects of everyday living: walking, dressing, personal hygiene, control of sphincters and eating. The score for each question ranges from 0 (in need of total supervision) to 3 (total autonomy). The overall score range is 0-15. The third section consists of a series of brief neuropsychological tests which assess attention, intelligence, memory, language, space cognition and visual perception. The score range for the whole section is 0-50. The MODA total score ranges from 0 to 100. It is the sum of partial scores and must be adjusted for age and educational level. The cut-off score is 85.5. The examiner can distinguish between *Normal* cognitive functioning (Total score >89.0), *Borderline* cognitive functioning (Total score between 85.5 and 89.0) and *Dementia* (Total score < 85.5).

The MODA subtests explore different cognitive domains (**Table 1**).

Sampling

This is a retrospective naturalistic study. Data were collected reviewing outpatients' medical records in an Italian Mental Health Centre (MHC) between 2003 and 2008. The selected patients [(N= 67; 45 males (67.16 %) and 22 females (32.84 %)] met DSM IV –TR (American Psychiatric Association 2001) criteria for schizophrenia (diagnoses were confirmed by two experienced consultant psychiatrists) and were all treated with antipsychotic drugs. They had more than 5 years of disease, they were in a "stable phase" of schizophrenia (Andreasen et al 2005) and performed a MODA test. Retrospectively patients affected by

Table 1. MODA subtests and cognitive domains explored

MODA subtests	Description	Cognitive domains explored
• Temporal orientation	Perception of time, Recent memory	Orientation, Memory
• Spatial orientation	Ability to maintain body orientation and/or posture in relation to the surrounding environment (physical space) at rest and during motion, Recent memory	
• Personal orientation	Self-actualisation	
• Family orientation	Remote memory	
• Autonomy scale	Considers 5 aspects of everyday living: walking, dressing, personal hygiene, control of sphincters and eating	Social cognition, Problem Solving
• Reversal learning	Feedback processing and reinforcement learning	Verbal Learning, Visual Learning,
• Attention test	Vigilance/ attention	Vigilance-Attention
• Verbal Intelligence	Abstract thinking	Verbal Learning
• Prose memory	Working memory	Working Memory
• Verbal fluency	The ease with which a person can produce words	Verbal Fluency
• Token test	Verbal comprehension of commands of increasing complexity	Verbal learning, Speed of processing
• Finger agnosia	The ability to distinguish the fingers on the hand	Attention, Speed of processing
• Constructional apraxia	Ability to copy 2-dimensional drawings or 3-dimensional assemblies	Visuo-spatial ability, Speed of processing
• Street's completion test	Ability to recognize objects, Awareness of perceptions	Speed of processing

medical conditions that could influence cognitive functioning and patients older than 65 years old were excluded: 13 patients were excluded for comorbidity with medical illness (8 patients were affected by Diabetes, 3 were affected by a neurological disease, 1 was affected by Celiac Disease, 1 patient sustained a traumatic brain injury) and 3 patients were older than 65 years.

The sample finally consisted of 51 patients (34 males and 17 females). The mean age of the overall sample is 45,78 (s.d. 10,63) years: the mean age of male patients is 46,76 (s.d. 10,74); the mean age of females is 43,99 (s.d. 10,50). The mean age of disease was 18,6 years, s.d. 9,07; the mean of years of treatment was 14,03 years s.d. 7,8 (Table 2).

The group of controls was composed of 25 healthy subjects (15 females and 10 males). They were enrolled among mental health operators and their relatives and were clinically evaluated by two experienced consultant psychiatrists to exclude medical and psychiatric

diseases. We excluded subjects older than 65 years old. The mean age of the overall control group is 45,8 (s.d. 10,23) years: the mean age of males is 45,51 (s.d. 10,66); the mean age of females is 45,8 (s.d. 10,23) (Table 2).

Data Analysis

Data were analyzed using 1-way between-subjects ANOVA and Chi-square test. *P-value* <0.05 was considered significant.

Results

MODA divided patients and healthy controls (N= 51 + 25) in three categories: *Normal* cognitive functioning, *Borderline* cognitive functioning and

Table 2. *Schizophrenic Patients and Healthy Controls*

	Schizophrenic Patients			Healthy Controls		
	N	Mean Age	S.D.	N	Mean Age	S.D.
Males	34	46,76	10,74	10	45,51	10,66
Females	17	43,99	10,50	15	45,8	10,23
Total	51	45,78	10,63	25	45,8	10,23

Table 3. *Chi-square test - MODA categories versus Diagnoses*

MODA Categories	Diagnoses		
	Healthy controls	Schizophrenia	Total
Normal	18	9	27
	(8,9)	(18,1)	
Borderline	4	17	21
	(6,9)	(14,1)	
Dementia	3	25	28
	(9,2)	(18,8)	
Total	25	51	76

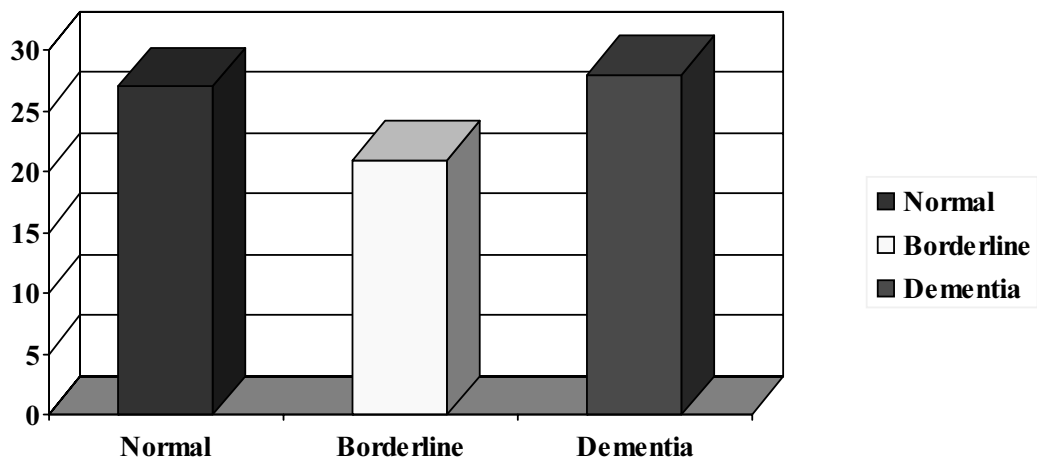


Figure 1. *Schizophrenic Patients and Healthy Controls divided by MODA Categories*

Table 4. 1-way ANOVA Analysis- MODA total Score versus Diagnoses

	N	MODA total Score Mean	S.D.
Healthy Controls	25	90,100	3,768
Schizophrenia	51	83,233	8,080

Table 5. 1-way ANOVA Analysis – MODA subtests Scores Versus Diagnoses

Personal Orientation	N	Mean	S.D.	P value
Healthy Controls	25	10,0	0,0	p=0,0367
Schizophrenia	51	9,7	0,7	
Reversal Learning	N	Mean	S.D.	P value
Healthy Controls	25	4,8	0,6	p=0,0051
Schizophrenia	51	3,7	1,8	
Attention Test	N	Mean	S.D.	P value
Healthy Controls	25	9,7	0,7	p=0,0212
Schizophrenia	51	8,9	1,5	
Verbal Intelligence	N	Mean	S.D.	P value
Healthy Controls	25	4,8	1,1	p<0,0001
Schizophrenia	51	2,9	1,6	
Prose Memory	N	Mean	S.D.	P value
Healthy Controls	25	4,9	1,9	p=0,0237
Schizophrenia	51	3,5	2,6	
Verbal Fluency	N	Mean	S.D.	P value
Healthy Controls	25	4,7	0,7	p<0,0001
Schizophrenia	51	3,4	1,4	
Finger Agnosia	N	Mean	S.D.	P value
Healthy Controls	25	4,6	0,7	p=0,0394
Schizophrenia	51	4,1	1,1	
Street's Completion Test	N	Mean	S.D.	P value
Healthy Controls	25	2,6	0,5	p=0,0224
Schizophrenia	51	2,2	0,7	
Autonomy Scale*	N	Mean	S.D.	P value
Healthy Controls	25	15,0	0,0	p=0,0455*
Schizophrenia	51	14,7	0,8	

* limit value

Dementia. So 27 subjects were defined as *Normal*, 21 subjects as *Borderline* and 28 as affected by *Dementia* (Figure 1).

Borderline and Dementia were more frequent among schizophrenic patients than in healthy controls (Chi-square test: $p < 0,0001$) (Table 3).

Also MODA total scores were compared with Diagnoses obtaining a significant result ($p = 0,0001$). In fact, schizophrenic patients had significantly higher rates of cognitive impairment than healthy controls (Table 4).

Significant differences were also obtained in the comparison of MODA subtests scores with Diagnoses. Schizophrenic patients performed worse than healthy controls in Personal Orientation ($p = 0,0367$), Reversal Learning ($p = 0,0051$), Attention Test ($p = 0,0212$); Verbal Intelligence ($p < 0,0001$), Prose Memory ($p = 0,0237$), Verbal Fluency ($p < 0,0001$), Finger Agnosia ($p = 0,0394$), Street's Completion Test ($p = 0,0224$) (Table 5).

Finally, Odds Ratio (defined as the ratio of the odds of an event occurring in one group and the odds of it occurring in another group) was calculated. An **Odds Ratio = 12** (95% CI: 3,870 to 37,208) was obtained showing that schizophrenic patients are much more likely to be Borderline or Dementia than healthy subjects.

Discussion

The findings confirmed cognitive impairment among schizophrenic patients, and actually showed higher rates of Borderline and Dementia functioning (Odds ratio=12). This is confirmed by Ganguli et al. (1998) that showed patients with schizophrenia perform 2–3 points below the population norms at all ages. MODA Total Score, not influenced by subjects' age and their level of education, was lower in patients affected than in healthy controls. Furthermore, healthy controls in this study performed few points below the sample selected by Brazzelli in 1994 to validate MODA test. His sample was composed of 217 healthy subjects (114 females, 103 males) with a mean age of 60,8 years (s.d.= 18,5; range 20-97). The mean total score was 93,7, corrected by age and level of education. In this study healthy controls' mean total score was 90,1 (s.d.= 3,7), corrected by age [mean age was 45,8 (s.d. 10,23)] and

level of education. Also the comparison between schizophrenic patients and healthy controls (HC2) selected by Brazzelli shows a significant result (Table 6)

According to the findings, Waltz and Gold (2007) showed that impairments in feedback processing and reinforcement learning appear to be prominent aspects of schizophrenia. They administered to 34 patients and 26 controls a modified version of an established probabilistic reversal learning task obtaining that patients showed substantial learning impairments when reinforcement contingencies were reversed, achieving significantly fewer reversals. These results support the idea that ventral Pre-Frontal Cortex dysfunction may contribute to deficits in reinforcement learning exhibited by patients. Wobrock et al. (2008) showed that patients with schizophrenia performed significantly worse in the trail-making test, verbal fluency, verbal learning/memory and the Wisconsin Card Sorting Test (WCST) indicating significant deficits in attention, psychomotor performance such as verbal working memory and cognitive flexibility for schizophrenic patients. The MODA test explores all these domains and in this study deficits in verbal fluency, learning, memory and attention were found among patients. Mo et al. (2008) showed that patients with schizophrenia were impaired in their comprehension of metaphor and irony as compared with healthy controls: performance of 29 schizophrenic patients in remission and 22 healthy controls was compared on metaphor and irony comprehension tasks and first- and second-order theory of mind tasks. Brüne et al. (2005) supposed that ability to interpret such metaphorical speech, typical of many proverbs, crucially depends on schizophrenic patients' ability to infer mental states. As expected, Ojeda N et al. (2008) confirmed that verbal fluency was severely impaired in patients and significantly predicted functional outcome. Moreover, van Beilen et al. (2004) observed that patients obtained lower test results than the controls on verbal fluency test. During the fluency test, they generated fewer words per cluster. Also in the current study deficits in verbal fluency and verbal intelligence were found among the patients. In 2006, Lee et al. (2006) tested 39 schizophrenic patients and 39 healthy controls about prose memory, in terms of recall accuracy, temporal sequence, recognition accuracy and false positives, commission of distortions, and rates of learning, forgetting. The patients with schizophrenia were found to commit more distortions and performed poorer on recall accuracy and temporal

Table 6.

	N	MODA total Score Mean	S.D.
HC2	217	93,7	5,2
Schizophrenia	51	83,233	8,080

sequence accuracy only during the first initial immediate recall.

The findings of the current study confirmed that MODA rating scale allows to evaluate the most important cognitive domains. Moreover a long battery of tests is not needed because it is a short collection of items and may be administered in an outpatient setting during routine medical practice. However some items on MODA may actually be tapping on negative symptoms (eg, blunted affect, psychomotor retardation, extrapyramidal symptoms). Even though there are no data could confirm this hypothesis, probably deficits in verbal fluency, verbal intelligence and autonomy scale in the current study may be influenced by negative symptoms such as psychomotor retardation and blunted affect. A psychopathological assessment might be useful to explain the deficits described by some items.

Conclusion

The results of the current study replicate international findings about cognition in schizophrenia. It is possible to conclude that MODA could well prove useful to assess cognitive impairment among schizophrenic patients in routine clinical practice; also other studies are still needed to validate MODA test as a new instrument for assessing cognitive deficits in schizophrenia.

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