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Cognitive functioning and insight in schizophrenia and in schizoaffective disorder

Funzionamento cognitivo e insight nella schizofrenia e nel disturbo schizoaffettivo

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SUMMARY. Aim. The aim of this study was to investigate cognitive functioning and insight of illness in two groups of patients during their stable phases, one with schizophrenia and one with schizoaffective disorder. **Methods.** We recruited 104 consecutive outpatients, 64 with schizophrenia, 40 with schizoaffective disorder, in the period between July 2010 and July 2011. They all fulfilled formal Diagnostic and Statistical Manual of Mental disorders (DSM-IV-TR) diagnostic criteria for schizophrenia and schizoaffective disorder. Psychiatric assessment included the Clinical Global Impression Scale-Severity (CGI-S), the Positive and Negative Sindrome Scale (PANSS), the Calgary Depression Scale for Schizophrenia (CDSS) and the Global Assessment of Functioning (GAF). Insight of illness was evaluated using SUMD. Neuropsychological assessment included Winsconsin Card Sorting Test (WCST), California Verbal Learning Test (CVLT), Stroop Test and Trail Making Test (TMT). Differences between the groups were tested using Chi-square test for categorical variables and one-way analysis of variance (ANOVA) for continuous variables. All variables significantly different between the two groups of subjects were subsequently analysed using a logistic regression with a backward stepwise procedure using diagnosis (schizophrenia/schizoaffective disorder) as dependent variable. **Results.** After backward selection of variables, four variables predicted a schizoaffective disorder diagnosis: marital status, a higher number of admission, better attentive functions and awareness of specific signs or symptoms of disease. The prediction model accounted for 55% of the variance of schizoaffective disorder diagnosis. **Discussion.** With replication, our findings would allow higher diagnostic accuracy and have an impact on clinical decision making, in light of an amelioration of vocational functioning.

KEY WORDS: schizophrenia, schizoaffective disorder, cognitive functioning, insight of illness.

RIASSUNTO. Scopo. L'obiettivo del presente studio è stato valutare il funzionamento cognitivo e la consapevolezza di malattia in due gruppi di pazienti in fase stabile, uno con schizofrenia e uno con disturbo schizoaffettivo. **Metodi.** Sono stati reclutati 104 pazienti ambulatoriali consecutivi, 64 con diagnosi di schizofrenia e 40 con diagnosi di disturbo schizoaffettivo, nel periodo compreso tra luglio 2010 e luglio 2011. Tutti i pazienti soddisfacevano i criteri diagnostici previsti dal Diagnostic and Statistical Manual of Mental disorders (DSM-IV-TR). Sono state somministrate la Clinical Global Impression Scale-Severity (CGI-S), la Positive and Negative Sindrome Scale (PANSS), la Calgary Depression Scale for Schizophrenia (CDSS), la Scale to Assess Unawareness of Mental Disorder (SUMD) e la Global Assessment of Functioning (GAF). La valutazione cognitiva comprendeva il Wisconsin Card Sorting Test (WCST), il California Verbal Learning Test (CVLT), lo Stroop Test e il Trail Making Test (TMT). Tutte le variabili risultate significativamente diverse ($p<0,05$) tra i due gruppi al test chi-quadro per le variabili categoriali e all'analisi della varianza (one-way ANOVA) per le variabili continue sono state incluse in un modello di regressione logistica con procedura backward utilizzando la diagnosi (schizofrenia/schizoaffettivo) come variabile dipendente. **Risultati.** Lo stato civile di coniugato, un maggiore numero di ricoveri totali, migliori funzioni attentive e consapevolezza di specifici sintomi o segni di malattia spiegavano il 55% della varianza della diagnosi di disturbo schizoaffettivo. **Discussione.** I risultati di questo studio, se confermati, potrebbero contribuire a una maggiore accuratezza diagnostica, con ricadute sulla pratica clinica, in particolare sul trattamento psicofarmacologico e riabilitativo, migliorando così gli esiti funzionali dei due disturbi.

PAROLE CHIAVE: schizofrenia, disturbo schizoaffettivo, funzioni cognitive, consapevolezza di malattia.

INTRODUCTION

Psychiatric nosology defines and distinguishes schizoaffective disorder from schizophrenia on the basis of a mood disturbance, which may occur in the presence of schizophrenic symptoms and need to be present for a substantial proportion of the total period of illness[1,2].

A review[3] examined demographic, family, biologic, symptomatic, and clinical variables among patients with schizophrenia, schizoaffective disorder, and mood disorders. Regarding each variable, schizoaffective disorder was intermediate between the other disorders, sometimes being more similar to schizophrenia and sometimes being more similar to mood disorders.

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On average, people with schizophrenia have more severe positive and negative symptoms, worse premorbid adjustment, more severe impairment in everyday functioning, and poorer outcome than do people with schizoaffective disorder[3-5].

Validation of the schizoaffective disorder construct as distinct from schizophrenia requires consideration of measurement domains other than the clinical data used to initially define the construct, such as cognitive functions. Currently, as substantial evidence has shown, specific cognitive[6,7] and ToM impairments[8] appear to persist after remission of acute psychotic episode and occur over the entire course of illness. Comparisons of schizoaffective disorder with schizophrenia have yielded varying results.

Many studies have not detected differences between people with schizophrenia and schizoaffective disorder[9-11], but the lack of differences may have sometimes resulted from small sample sizes. Some studies have detected that certain cognitive functions, such as verbal memory and processing speed, are more preserved in schizoaffective disorder than in schizophrenia[12-14].

A review[15] examined cognitive studies of patients who were symptomatic as well as those in which patients had been stabilized. In patients with acute schizoaffective disorder and schizophrenia, few differences were found in neurocognitive performance. However, when stabilized patients were compared, those with schizoaffective disorder tended to have milder deficits than patients with schizophrenia. This difference between state and trait assessments suggests that acute illness impairs cognition more in patients with schizoaffective disorder. In contrast, cognitive deficits in schizophrenia generally seem to change little after stabilization[16]. However, many studies in the review did not differentiate between schizophrenia subtypes, such as paranoid versus disorganized nonparanoid schizophrenia, which may affect cognitive function differently[17].

Lack of insight is a core feature of schizophrenia that impacts negatively on cognitive performance, medication adherence treatment outcome and prognosis[18].

Relationships of insight to diagnosis should be studied in order to add further cues about differences between different psychotic-spectrum conditions. However, studies that have explored systematically this issue are sparse in literature.

Weiler et al.[19] found that insight deficits were more prevalent in schizophrenia, a mixed group of other psychosis and bipolar disorder as compared with major depressive and schizoaffective disorder. Other two studies found that patients with schizophrenia had poorer insight than patients with schizoaffective disorder[20,21].

The purpose of this study was to comparatively assess cognitive functioning and insight in two groups of patients: a group with a diagnosis of schizophrenia and a group with schizoaffective disorder. We administered a battery of neuropsychological tests designed to examine a variety of cognitive abilities (such as attention, memory and executive functions). Insight was measured with the most comprehensive instrument to assess its multidimensional construct, the Scale to assess the Unawareness of Mental Disorder (SUMD)[22]. We hypothesized that patients with schizoaffective disorder would exhibit milder cognitive impairment and better insight than patients with a diagnosis of schizophrenia. We have also investigated the cognitive or clinical factors that could better differentiate the two groups.

MATERIALS AND METHODS

Participants

This study has been conducted at the Department of Neuroscience, University of Turin, Struttura Semplice di Coordinamento a Valenza Dipartimentale (SSCVD), Department of Mental Health ASL TO1, Molinette, Italy, during the period between July 2010 and July 2011.

Patients were initially evaluated by a clinician-psychiatrist, and if they met Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)[1] criteria for schizophrenia or for schizoaffective disorder, they were seen subsequently by our research team (N.B., I.B.). Subjects were excluded if they had a current disorder other than schizophrenia or schizoaffective disorder on Axis I of the DSM-IV-TR, a current or past codiagnosis of autistic disorder or another pervasive develop mental disorder, a history of severe head injury (coma>48 h).

At the time of study entry, patients had been clinically stable for at least 1 month as judged by the treating psychiatrist, i.e. during this period all patients had to be treated as outpatients, treatment regimen had not been modified, and there was no essential change in psychopathology. In addition to medical records, patients were considered to be in stable phase as assessed from reports from patients themselves, and observations of the psychiatric personnel, relatives and personnel in the psychiatric community.

All patients were submitted to standard care (Standard of Care-SoC), including pharmacological treatment as recommended by the guidelines[23,24], clinical monitoring at least on a monthly basis, home care when required, and psychosocial and rehabilitation interventions tailored to patient's needs.

Patients were evaluated using a semistructured interview to assess demographic features. Data were collected to determine age, gender, education, age at onset of schizophrenia (report of first contact with a psychiatric service), length of illness, and antipsychotic treatment. The diagnosis of schizophrenia and of schizoaffective disorder were confirmed by two expert clinicians (N.B., I.B.) using the Structured Clinical Interview for DSM-IV disorders (SCID)[25]. The two psychiatrists were aware of previous diagnosis and they could also review the previous clinical charts, available for all the patients.

Written informed consent was obtained from all subjects after a complete description of the study. The study was carried out in accordance with Declaration of Helsinki 1995 (as revised in Edinburgh 2000) and was approved positively by the Local Research Ethics Commitee (LREC).

Psychiatric and cognitive assessment

Overall severity of illness was rated using the Clinical Global Impression-Severity scale (CGI-S)[26].

Current levels of psychopathological symptoms were assessed using the Positive and Negative Syndrome Scale (PANSS), which includes Positive Symptoms (PANSS-P), Negative Symptoms (PANSS-N), and General Psychopathology (PANSS-G) subscales[27]. Depressive symptoms were evaluated using the Calgary Depression Scale for Schizophrenia (CDSS)[28].

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To quantify the global functioning of patients, we used the Global Assessment of Functioning scale (GAF)[29]. For the purpose of our study, raters were instructed to use the GAF to measure only psychosocial functioning in the month before rating, as reported in other studies[30-32].

We used the SUMD, to assess insight. For the purpose of this study we used the three central items of the SUMD: awareness of mental illness (SUMDm), awareness of the need for treatment (SUMDf) and awareness of the social consequences of disorder (SUMDs)[22].The scale is composed of two other subscales: awareness of the signs and symptoms (SUMDc) which is the mean of the sums of the scores according to the number of items scored, and attribution of the symptoms (SUMDa), which is the mean of the scores of the symptoms that could be assessed because the patient is aware of them.

In order to index executive functions, we used the number of perseverative errors and the number of completed categories on the Wisconsin Card Sorting Test (WCST)[33]. The California Verbal Learning Test (CVLT) was used in the evaluation of verbal learning and memory[34]. The format of the tests permits assessment of multiple aspects of verbal memory, including overall recall ability, rate of learning over repeated trials, ability to retain learned material over time and subsequent item recognition. Four indices were used: the total number of items correctly recalled over five learning trials, the number of items correctly recalled after 20 minutes, the total number of items correctly recognized and the number of items incorrectly recognized.

The Stroop Test[35] and the Trail Making Test[36] were used to estimate attentional functions and vigilance.

The TMT consists of two parts: Part A measures visual attention and psychomotor speed; Part B measures cognitive flexibility and task switching. The derived score, TMT (B-A),is calculated as the difference in time taken to complete the TMT-A and TMT-B tests and it is also an indicator of prefrontal functioning.

The Stroop Test was used to estimate attentional functions. We employed the traditional version of the Stroop Test based on card presentation, as it permits one to evaluate the ability to inhibit an automatic response while performing a task based on conflicting stimuli.

Neuropsychological tests were administered by one trained psychologist (B.C.), who was unaware of clinical characteristics and results of psychiatric rating scales.

Statistical analyses

The sample of patients has been divided into two groups according to the diagnosis (schizophrenia, schizoaffective disorder). Data are presented as means±standard deviations (SD) or percentages (%), unless stated otherwise. The differences between the two groups were tested using Chi-square test for categorical variables and one-way analysis of variance (ANOVA) for continuous variables.

Clinical and cognitive variables that showed a significant difference in the univariate analysis ($p<0.05$) were subsequently analyzed using a binary logistic regression with a backward stepwise procedure to test their contribution to the diagnosis (schizophrenia/schizoaffective disorder). We also calculated the Nagelkerke R2 for the final models, to estimate the total percentage of variance explained.

Statistical analyses were performed using the software Statistical Package for the Social Sciences, SPSS, version 17 (SPSS Inc., 2008).

RESULTS

One hundred and four consecutive outpatients who met the inclusion criteria were enrolled in the study, 64 (61%) with schizophrenia and 40 (39%) with schizoaffective disorder.

Socio-demographic and clinical characteristics of patients' population are shown in Table 1.

The two groups differed in sex distribution, marital status, age, duration of illness and number of hospitalizations.

Patients with schizophrenia were predominately male and never married. Patients with schizoaffective disorder were older and had a longer duration of illness, and a higher number of hospitalizations; they experienced significantly lower positive, negative and general psychiatric symptom levels than schizophrenia patients. Moreover they showed a better awareness of illness (subscales SUMDm and SUMDc) and a better functioning (GAF).

Because most of the demographic and clinical group differences were considered illness specific, they were not entered as covariates in the main neurocognitive comparisons.

The schizoaffective group performed better than the schizophrenia group at both immediate recall and the total number of items correctly recognized in the CVLT. Significant group differences were found with regard to the ability to shift strategy (TMT b_a) and executive functioning (minor percentage of perservative errors) (Table 2).

The following variables were significantly and independently associated with the schizoaffective disorder diagnosis: being married (OR 0.146; 95% CI 0.038-0.559; p=0.005), a higher number of hospitalizations (OR 1.235; 95% CI 1.076-1.417; p=0.003), the ability to shift strategy (TMTb_a) (OR 0.988; 95% CI 0.978-0.997; p=0.013) and a better awareness of illness (SUMDc) (OR 0.350; 95% CI 0.179-0.683; p=0.002) (R2 Nagelkerke=0.55).

DISCUSSION

The results of the present study have pointed out that some variables such as being married, the number of hospitalizations, the cognitive flexibility and the awareness of illness would differentiate schizophrenia from schizoaffective disorder in a sample of stable patients treated with SOC, representative of the usual setting and modality of care of community mental health centers in Italy.

Our hypothesis that patients with schizoaffective disorder show better cognitive performance as compared to those with schizophrenia was supported by our findings in a set of commonly used neurocognitive measures.

We found that people with schizoaffective disorder have milder impairments in verbal learning and memory and cognitive flexibility than do people with schizophrenia. Our findings, supporting the hypothesis that cognitive performance may distinguish schizophrenia from schizoaffective disorder, are in line with previous studies.

Stip et al.[37] reported significant differences between schizophrenia and schizoaffective patients on computerized measures of visuomotor speed and non-verbal memory. Furthermore, Gruber et al.[38] demonstrated preserved auditory working memory in schizoaffective disorder relative to schiz-

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Table 1. Socio-demographic and clinical characteristics by diagnostic groups

Variable	Schizophrenia	Schizoaffective disorder	$F\chi^2$	p
Gender, M/F	45/19	21/19	3.368	.052
Age, years	37.9±11.5	42.6±10	4.660	.033
Education, years	10.5±0.41	11.7±0.56	3.217	.076
Marital status, married, n (%)	8 (12.5)	15 (37.5)	8.932	.003
Employment, yes n (%)	20 (31.3)	15 (37.5)	0.213	.401
Duration of illness, years	12.1±9.57	19.8±9.58	15.74	.000
PANSS total	74.3±21.6	59.9±20.4	12.07	.001
PANSS positive	15±6.74	13.4±6.15	1.470	.228
PANSS negative	21.6±8.47	18.1±9.08	3.986	.049
PANSS general	38.9±11.5	33.9±13.3	4.043	.047
CDSS	3.98±3.73	5.20±5.06	1.976	.163
CGI-S	4.27±.86	3.83±1.01	5.651	.019
SUMD score				
Awareness of mental disorder	2.49±1.17	1.69±.86	13.95	.000
Awareness of the effects of treatment	2.13±1.10	1.98±.919	.537	.465
Awareness of the social consequences	2.70±1.24	2.38±1.21	1.668	.199
Awareness of the signs and symptoms	3.31±1.15	2.43±1.10	15.07	.000
Attribution of the symptoms	2.63±1.37	2.65±1.18	.008	.928
GAF	53.5±14.5	60.9±12.2	7.19	.009

Data are presented as means±standard deviations (SD) or percentages (%). Statistical analyses: One-way analysis of variance (ANOVA) for continuous and Chi-square test for categorical variables.
PANSS total=Positive and Negative Syndrome Scale, total score; PANSS positive=PANSS Positive Symptom subscale; PANSS negative=PANSS Negative Symptom subscale; PANSS general=PANSS General Psychopathology subscale; CDSS=Calgary Depression Scale for Schizophrenia; CGI-S=Clinical Global Impression-Severity scale; SUMD= Scale for the Assessment of Unawareness of Mental Disorder; GAF=Global Assessment of Functioning.

Table 2. Neuropsychological variables by diagnostic groups

Variable	Schizophrenia	Schizoaffective Disorder	F	p
CVLT 1-5	36.9±11.8	43.2±10.2	7.729	.006
CVLT delayed recall	7.61±3.56	9.07±3.79	3.918	.050
CVLT recognition	13.4±2.38	14.7±1.67	8.712	.005
CVLT false recognition	2.64±2.97	2.93±2.87	.234	.629
CVLT intrusions during learning	1.99±2.77	2.10±2.95	.041	.839
CVLT intrusions during delayed recall	1.04±2.05	.97±1.48	.033	.857
TMT Part a	59.4±25.2	57±32.6	.179	.673
TMT Part b	158.6±86.2	141.6±74.7	1.059	.306
TMT b_a	100±74.5	61.5±56.3	7.855	.006
Stroop world	57.9±14.7	61.6±15.1	1.585	.211
Stroop colour	36.1±8.98	39.1±8.36	2.954	.089
Stroop colour world	20.3±7.91	20.2±5.91	.003	.959
WCST categories	4.93±1.73	5.14±1.65	.379	.539
WCST % total errors	24.9±17.8	26±16.9	.101	.751
WCST % perseverative errors	24.5±19.8	16.7±15.2	4.508	.036

Data are presented as means±standard deviations (SD) or percentages (%).Statistical analyses: One-way analysis of variance (ANOVA) for continuous and Chi-square test for categorical variables.
CVLT 1-5: California Verbal Learning Test; Test TMT: Trail Making Test; Stroop: Stroop Test; WCST: Winsconsin Card Sorting Test.

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ophrenia patients. These results conflict with earlier findings of no group differences on an extensive set of neurocognitive measures[13,39].

Comparisons of schizoaffective disorder with schizophrenia have yielded varying results. This lack of evidence may depend on the sample that is being studied, i.e., the small sample size and the inclusion of patients with mood disorders.

As for the awareness of illness, our data confirmed the hypothesis of a better awareness of illness in patients with schizoaffective disorder, replicating findings of the few previous studies[20-22].

Despite a poor awareness of illness is one of the most typical symptoms of schizophrenia, few studies have examined specifically the clinical value of this parameter.

We found a better awareness of illness in the sample of patients with schizoaffective disorder using a high sensitivity scale in the assessment of level of insight.

Cognitive impairments are the most consistent determinant of deficits in everyday functioning in schizophrenia, as demonstrated by the results of two large-scale meta-analyses[40,41].

Studies exploring the impact of insight on functioning have focused on different components. While some investigated functional outcome in the classical sense (general level of functioning), others concentrated on more specific aspects, such as work behavior or social functioning, suggesting a relationship between insight and functional outcome[42].

Recent studies showed a small, albeit statistically significant, positive relationship between insight and general cognitive functioning[43].

Evidence that, a schizoaffective diagnosis is associated with a better prognosis and better social integration[3,44], on the functional level, may be related to milder cognitive and insight impairment.

On the basis of these findings, we hypothesized that the better social functioning in the sample of patients with schizoaffective disorder could be attributable to improved cognitive performance and to a greater awareness of illness, but further studies are required with larger samples to confirm this hypothesis.

In our sample schizophrenia and schizoaffective disorder can be distinguishable based on other two factors, marital status and number of hospitalizations.

The greater proportion of married subjects in the sample of patients with schizoaffective disorder, in line with previous findings, could indicate a better social outcome. Social outcome has often been evaluated by using sociodemographic indices (e.g. married/not married, occupied/unemployed, independent/not independent living) or measures including both clinical and social aspects (GAF), which are biased by patients' clinical conditions. Our finding is in agreement with previous studies and may be related to the later age of onset and the better premorbid adjustment[3,45].

Schizoaffective disorder was related to a higher number of hospitalization than schizophrenia probably because it constitutes a more episodic disorder[3,46].

However, a number of factors limit the conclusions that may be drawn from this study. First, the data presented are cross-sectional and are unable to address such questions as the evolution of differences between the two groups over time, considering the poor stability of the schizoaffective disorder diagnosis[47-49]. Second, our sample was small and the small number of patients with schizoaffective disorder could limit the statistical power to identify differences between schizophrenia and schizoaffective disorder.

Despite these limitations, this study has some strengths that should be noted. First this study was conducted in a sample of stable patients treated with SOC representative of the usual setting and modality of care of community mental health centers in Italy. Second, we evaluated how a pattern of signs and symptoms not pathognomonic of the illness may distinguish schizoaffective disorder from schizophrenia. The neurocognitive assessment was conducted using a large battery of neuropsychological tests and the awareness of the disease was investigated with a multi-dimensional scale.

With replication, along with more research with broader samples, including longitudinal designs, these findings could have important implications for clinical practice. A better diagnostic definition of schizoaffective disorder could require consideration of measurement domains, such as neurocognitive performance, and could aid to develop an individualized treatment plan[50-52]. Furthermore, patients with schizoaffective disorder more cognitively equipped and exhibiting less severe psychopathology could participate in rehabilitation or remediation program to maximize their independence and improve their functional outcomes.

Our finding of a better awareness of illness in the schizoaffective disorder adds to a very sparse research literature on this topic; this replication and more detailed examination of diagnostic group differences in insight has clinical, theoretical, and nosological value. Future studies could examine whether in patients with schizoaffective disorder insight is associated with cognitive performance and social functioning. A better ability in cognitive flexibility and set shifting could improve everyday functioning and social integration.

In conclusion our findings suggest that in the differential diagnosis between schizophrenia and schizoaffective disorder, the clinician should take into account a number of not pathognomonic signs and symptoms because the symptoms do not seem to have a crucial role in differentiating the two disorders.

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