Long-term outcome of schizoaffective disorder. Are there any differences with respect to schizophrenia?

Outcome a lungo termine del disturbo schizoaффettivo. Quali differenze rispetto alla schizofrenia?

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SUMMARY. Background. A number of studies suggest that the clinical characteristics and long-term outcome of schizoaffective patients closely resemble those observed in schizophrenia when cases are diagnosed according to DSM criteria. The primary aim was to compare remission and recovery rates in a cohort of chronic schizoaffective and schizophrenic outpatients. Methods. A sample of 102 consecutive outpatients, 46 affected by schizophrenia (45.1%, mean age 44.22±9.97 years) and 66 affected by schizoaffective disorder (54.9%, mean age 43.00±9.07 years) was examined in the study. Personal data and psychiatric history were collected according to AMDP system, premorbid assessment was performed by means of PAS. Axis I and II psychiatric diagnosis was confirmed by means of SCID-I and II. Psychopathological status was evaluated by means of PANSS and CGI-SCH scales; neuropsychological evaluation was performed by means of BACS and MMSE; Functioning, subjective well-being and quality of life were respectively evaluated by means of PSP, SWN and WHOOqol-bref. Results. Schizophrenic and schizoaffective patients investigated were characterized by an overlapping age at onset, mean duration of illness, mean duration of untreated psychosis and common sociodemographic characteristics; subjects’ cross-sectional psychopathological and neurocognitive profiles were remarkably similar. However, schizoaffective patients are more frequently of the female gender, showing a better social premorbid adjustment and a somewhat more complicated clinical course in terms of more frequent hospitalizations and suicidality; outcome measures are substantially better among schizoaffective patients: rates of clinical remission were 43.5% and 54.5% in schizophrenic and schizoaffective patients, respectively; 13% and 25.8% of schizophrenic and schizoaffective patients, respectively, were considered as functionally remitted; recovery was observed in 6.5% and 22.7% of schizophrenic and schizoaffective patients, respectively; the majority of patients, both schizophrenic and schizoaffective, were taking antipsychotics, mainly atypical, although a significantly higher proportion of schizoaffective subjects were on mood stabilizers, antidepressants and benzodiazepines. Conclusion. Compared to schizophrenic patients, DSM-IV-TR schizoaffective patients may be considered as a subgroup of psychotic patients displaying several specific characteristics in terms of clinical course, clinical and functional outcome and treatment.

KEY WORDS: schizoaffective disorder, schizophrenia.
INTRODUCTION

Schizoaffective disorder represents an ongoing challenge for psychiatric nosology, given the uncertainty of its boundaries in relation to schizophrenia and affective disorders. Indeed, the disorder has over the years been considered a variant of schizophrenia in which mood symptoms are more prominent and severe than usual, a severe form of major depressive or bipolar disorder in which episodic-related psychotic symptoms do not remit completely between mood episodes, or a condition reflecting the co-occurrence of two relatively common psychiatric disorders. Moreover, the possibility that schizoaffective disorder may be a distinct form of psychotic disorder, as classified both in DSM-IV-TR and ICD-10, or an intermediate disorder within a spectrum that ranges from schizophrenia and mood disorders should be taken into account. Long-term outcome has represented one of the main parameters evaluated in an attempt to discriminate between schizoaffective disorders and schizophrenia or mood disorders, unfortunately with contradictory results; indeed, several studies reported outcomes which largely resemble those observed in schizophrenia, whilst others described results similar to those found in affective psychoses, and a certain number of papers described outcome findings placed in an intermediate position between schizophrenic and affective psychoses. These contradictory results may be due, at least in part, to the criteria used for diagnosis, as in cases diagnosed according to criteria proposed by DSM, notoriously more stringent than those proposed by ICD, the outcome of schizoaffective disorders closely resembles that of schizophrenia. Starting from these premises, the primary aim of the study was to compare long-term clinical and functional outcome of DSM-IV-TR schizophrenic and schizoaffective outpatients.

METHODS

Sample

In the context of an ongoing prospective follow-up study, all patients with a diagnosis of schizophrenia or schizoaffective disorder according to DSM-IV-TR attending a university community mental health centre between 1 January and 31 December 2010 were enrolled consecutively. Patients with other comorbid mental disorders were included in the study, although those affected by comorbid mental retardation or organic brain diseases were excluded. A sample of 102 consecutive outpatients (71 male, mean age 42.49±7.75 years; 31 female; mean age 44.70±11.76 years) who met the above-mentioned inclusion/exclusion criteria was studied. All patients were submitted to standard care provided in community mental health centres in Italy (pharmacological treatment; clinical monitoring at least on a monthly basis; home care when required; psychosocial and rehabilitation interventions tailored to patient’s needs).

Ratings

For the purpose of this study, we used baseline data for the cohort enrolled in the above-mentioned prospective follow-up study set up with the aim of evaluating the time course and predictors of remission and recovery in a sample of chronic schizophrenic and schizoaffective outpatients. Personal and social data and clinical history were collected on the basis of a structured interview purpose-developed for the present study. In line with procedures applied in previous papers, these data were integrated with those deriving from the standardized clinical records routinely kept in the University mental health centre in which the study was performed, derived from the Italian version of the Association for Methodology and Documentation in Psychiatry (AMDP). All patients included in the study underwent comprehensive psychiatric evaluation by means of the Structured Clinical Interview for Diagnosis Axis I DSM-IV (SCID-I Research Version) and the Interview Structured Clinical Diagnosis for Axis II of DSM-IV (SCID-II); after having signed an informed consent form. Diagnostic and clinical interviews were conducted by residents in psychiatry trained in the use of the instruments by a specialist; inter-rater reliability, assessed using Cohen’s K before the study, was on the average not lower than 0.80. Premorbid adjustment was evaluated by means of Premorbid Adjustment Scale (PAS), a rating scale designed to evaluate the level of functioning in four major areas (social isolation, peer relationships, ability to function outside the nuclear family and capacity to form intimate sociosexual ties) throughout several periods of the subject’s life (childhood, early and late adolescence, adulthood). Each section of the scale comprises a number of items with a scoring range of 0-6 (0=the hypothetical best adjustment, 6=the worst); the final score at each section is calculated by summing scores obtained at each item and dividing the result by the possible maximum score; an overall score for the entire scale is calculated by averaging the subscale score for all subscales rated for the patient. Severity of symptoms was evaluated by means of PANS (Positive and Negative Syndrome Scale) and Clinical Global Impression-Schizophrenia Scale (CGI-SCH). PANS consists of 30 items grouped into 5 domains: general psychopathology (positive, negative, cognitive, symptoms and depression over the week before the visit on a 7-point scale. Cognitive assessment was performed by means of Brief Assessment of Cognition in Schizophrenia Scale (BACS) and Mini Mental State Examination (MMSE). For the purpose of this study, five of the six subtests provided by BACS, namely list learning (Verbal memory), digit sequencing (Working memory), category instances and controlled oral words association test (Verbal fluency), symbol coding (Attention and Speed of Information Processing) and executive functions (Tower of London) were adopted; a gender/age/education adjusted score was calculated for each subject based upon the correction grids for the Italian population. As an overall measure of cognitive functioning we used the MMSE test; an age/education adjusted score was calculated for each subject based upon the correction grids for the Italian population.

Functioning, Subjective well-being and Quality of life were respectively evaluated by means of PSP (Personal and Social Performance) and Subjective Well-being under Neuroleptics (SWSN); and WHO Quality of Life-Brief questionnaire (WHOQOL-BREF). The PSP scale, developed from SOFAS (Social Occupational Functioning Scale), assesses social functioning of patients...
with schizophrenia in 4 main areas: social activities, personal and social relationships, self-care, and disturbing/aggressive behaviours. PSP should be completed on the basis of data provided by the patient, family or staff-member in charge of the patient. For each area a score ranging from 0 (no disability) to 5 (very severe disability) is attributed according to specific criteria. A comprehensive overall score ranging from 1 (maximum dysfunction) to 100 (maximum functioning) is attributed, based on score obtained at each single area. Total score is usually divided into three levels: 0-30 (functioning so poor that patient needs intensive support and supervision); 31-70 (varying degrees of difficulties); 71 (mild or no functioning difficulties); thus, a total score exceeding 70 indicates a condition of “functional remission”, considering that these scores are related to overall good functioning.

The SWN is a self-administered rating scale developed by Naber in 1995, aimed at evaluating the psychological and physical well-being of patients treated with neuroleptics. For the purpose of the study the short version (20 items, including 5 subscales: mental functions, self-control, physical function, emotional control, social capability), was used. A total score exceeding 80 at SWN indicates a condition of substantial “subjective well-being”.

The WHOQOL is a self-evaluated questionnaire developed by the World Health Organization (WHO QOL Group) to assess subjective quality of life. In the present study, the 26-item short version (WHOQOL-BREF) was used, allowing us to obtain four subscores focusing on the quality of life in 4 areas (physical, psychological, social relationships, environment).

Criteria for clinical remission and recovery

To evaluate clinical remission, criteria developed by the Remission of Schizophrenia Working Group24 based on ratings at 8 focal symptoms in positive, negative and general psychopathology subscales of PANSS (P1, P2, P3, N1, N4, N6, G5, G9) were applied. The patient is judged to be in clinical remission when scores obtained at each of these items is ≤3 over a 6-month period. Due to the fact that baseline data from an ongoing, prospective follow-up study were used, severity alone was adopted in evaluating clinical remission, whilst duration was not taken into account, as suggested by the Remission of Schizophrenia Working Group. Given that the criteria published by Andreasen for clinical remission are based on 8 selected items from PANSS, thus excluding all items which significantly contribute towards overall clinical picture and quality of life, such as depressive and other symptoms25, we decided to apply other more restrictive criteria. For the purpose of this study, therefore, clinical remission was defined as fulfillment of other criteria than those established by Andreasen’s et al., namely: 1) achievement of a score ≤3 at each item of the Positive and Negative Scale of PANSS (extended PANSS criterion); 2) obtaining of a score ≤3 at all items of PANSS (overall PANSS criterion).

In view of the lack of consensus in literature as to the definition and criteria of recovery, specific criteria purpose-developed for the present study were adopted. Recovery was primarily defined as the simultaneous fulfilment of Andreasen’s criteria for clinical remission together with the presence of a “functional remission” as evaluated by PSP (score ≤70) and a “subjective remission”, in terms of a full subjective well-being according to SWN scale (score ≤80). Secondary criteria for recovery were defined as: 1) clinical remission plus functional remission; 2) clinical remission plus subjective remission.

RESULTS

Demographic characteristics

A significant difference in gender distribution of cases according to diagnosis was found, with a prevalence of males in schizophrenia (M =48.8%; F=26.7%) and females among schizoaffective disorders (M =51.4%, F=73.3%, p=0.0042). Mean age was 44.22±9.97 and 43.00±9.07 years among schizophrenics and schizoaffective subjects, respectively (t=0.671, df=110, p=0.504); mean years of education were 10.57±4.14 and 11.03±3.68 years, respectively (t=−0.625, df=110, p=0.534). Singles were 89.1% (n=41) among schizophrenics and 84.8% (n=56) among schizoaffective patients; married subjects 10.9% (n=5) and 15.2% (n=10), respectively (χ² square=0.139, df=1, p=0.709); 87% of schizophrenics (n=40) and 78.8% of schizoaffective patients (n=52) had no children (chi square=0.739, df=1, p=0.390); 80.4% of schizophrenics (n=37) and 69.7% of schizoaffective were unemployed or receiving a disability pension (chi square=1.117, df=1, p=0.291); 82.6% of schizophrenics (n=38) and 81.9% (n=54) of schizoaffective subjects were living with their families (chi square=0.066, df=1, p=0.996).

Psychiatric history

A positive family history for mental disorders was found in 69.9% (n=28) and 60.6% (n=40) of schizophrenic and schizoaffective patients, respectively (chi square=0.001, df=1, p=0.978); more specifically, a positive history for schizophrenia was found in 10.9% (n=5) and 10.6% (n=7) of schizophrenics and schizoaffective subjects, respectively (chi square=0.002, df=1, p=0.965); a positive history for bipolar disorders in 2.2% (n=1) and 3% (n=2) of patients, respectively (chi square=0.076, df=1, p=0.782); for major depression in 21.7% (n=10) and 24.2% (n=16) of patients, respectively (chi square=0.095, df=1, p=0.758).

No significant difference in premorbid adjustment was found between schizophrenic and schizoaffective patients, with the sole exception of a significantly better premorbid social adjustment among schizoaffective subjects (SA=2.60±1.52; S=3.33±1.77, t=101, t=2.248, p=0.027). Other data regarding psychiatric history are reported in Table 1. No significant differences were detected between schizophrenic and schizoaffective patients with regard to age at onset, overall duration of illness, duration of untreated psychosis (time between the onset of first clear-cut psychotic symptoms and first antipsychotic treatment), course type of the disorder and distribution based on number of hospital admissions. However, the proportion of schizoaffective patients who had been hospitalized or who had attempted suicide was significantly higher than for schizophrenics, although the number of suicide attempts was similar in schizophrenic and schizoaffective patients. Finally, a similar number of schizoaffective patients had been involved in criminal acts although some differences emerges as regard to types of acts committed; moreover, no difference was found as regard to number of patients admitted to forensic hospitals.

Symptomatic status

Mean scores obtained at PANSS and CGI-SCH are reported in Table 2. No differences were found between groups with regard to mean scores at positive, negative, general psy-
chopathology subscales and at total scale of PANSS. When mean scores at each single item of PANSS were taken into consideration, only a few significant differences emerged: a significantly higher score at item N3 (poor relationships) was found among schizophrenics (S=2.04±1.31; SA=1.58±0.946, df=110, t=1.29, p=0.003), while a significantly higher score was found among schizoaffective patients as regard item G3 (ideas of guilt) (SA=1.74±1.20; S=1.26±0.681, df=110, t=2.477, p=0.016) and G6 (Depression) (SA=2.20±1.37; S=1.70±1.03, df=110, t=2.098, p=0.038). No differences were found for CGI positive, negative, depressive, cognitive and total scores.

Neurocognitive status

No significant differences were found between groups with regard to MMSE and at each item of BACS (Table 3).

Functioning and subjective status

No differences were detected in total score and mean score obtained at each subscale of PSP between schizophrenic and schizoaffective subjects; similarly, no differences were found in mean total scores and scores at each subscale of SWB and of WHO-QoL (Table 4).

Outcome

Remission

Data relating to rates of clinical, functional and subjective remission are reported in Table 5. 43.5% (n=20) of schizophrenics and 54.5% (n=36) of schizoaffective patients were deemed to be remitted according to the criteria of Andreasen et al.²⁴, although statistical significance was not reached; when remission was evaluated using all items of positive and negative subscales of PANSS (extended PANSS criterion), 23.9% of schizophrenics (n=11) and 42.4% of schizoaffective subjects (n=28) were seen to be in remission; this difference was statistically significant. On taking into account all items included on the positive, negative and general psychopathology scales of PANSS (overall PANSS criterion), only 15.2% of schizophrenics (n=7) and 28.8% of schizoaffective patients (n=19) were found to be remitted, a difference devoid of statistical significance. Regarding functional remission, 13% of schizophrenics (n=6) and 25.8% of schizoaffective patients were considered remitted, again a difference devoid of statistical significance. Similarly, when subjective well-being was considered, no significant differences emerged as 69.6% of schizophrenic (n=32) and 59.1% (n=30) schizoaffective patients could be considered in a state of “subjective” remission.

Recovery

Recovery rates are reported in Table 6. When evaluation of recovery was based upon rates of remission from both a clinical and functional point of view, 6.5% (n=3) of schizophrenic and 22.7% of schizoaffective patients (n=15) could be considered as “recovered”, a highly significant difference; no statistically significant inter-group difference emerged however when recovery was based upon clinical and subjective remission, as 26.1% of schizophrenics (n=12) and 25.8% of schizoaffective patients (n=17) were considered as “recovered”. Finally, when recovery was evaluated according to clinical, functional and subjective status of well-being, 6.5% patients with schizophrenia (n=3) and 12.1% (n=8) of schizoaffective patients were taken as recovered, a difference lacking statistical significance.

Treatment

In this study, 34.8% (n=16) of schizophrenic and 33.3% (n=22) of schizoaffective patients were prescribed first generation antipsychotics (FGA) (chi square=0.025, df=1, p=0.873);
second generation antipsychotics (SGA) were prescribed in 73.9% (n=34) patients affected by schizophrenia and 78.8% patients affected by schizoaffective disorder (n=52) (chi square=0.042, df=1, p=0.837). Benzodiazepines were more frequently prescribed to schizoaffective (n=43, 65.2%) than to schizophrenic patients (n=21, 45.7%) (chi square=4.209, df=1, p=0.040); similarly, more schizoaffective (n=20, 30.3%) than schizophrenic patients (n=5, p=10.9%) were treated by means of mood stabilizers (chi square=5.904, df=1, p=0.015) or antidepressants, which were prescribed respectively to 36.4% (n=24) and 8.7% (n=4) patients (Chi square=11.067, df=1, p=0.001).

**DISCUSSION**

In view of the fact that the main focus of the study was the comparison of schizoaffective and schizophrenic patients, the findings obtained in the study will initially be discussed by Cheiniau et al. in their review of studies relating to a comparison of schizoaffective disorders with schizophrenia and/or aftec-tive disorders. The sociodemographic characteristics of the schizoaffective patients included in this study closely resemble those observed in schizophrenics in terms of mean age, education, marital and employment status, living conditions; howev-

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**Table 2. Symptomatology**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Schizophrenic pts (n=46)</th>
<th>Schizoaffective pts (n=66)</th>
<th>Statistics</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PANSS mean score</td>
<td></td>
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<tr>
<td>Positive scale</td>
<td>12.46±6.06</td>
<td>11.14±3.74</td>
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<td>Negative scale</td>
<td>15.61±6.62</td>
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<td>General psychopathology scale</td>
<td>26.74±8.50</td>
<td>27.74±8.14</td>
<td>t=0.630</td>
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<td>Total scale</td>
<td>54.80 (17.77)</td>
<td>52.83 (15.79)</td>
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<td>CGI-SCH mean score</td>
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<tr>
<td>Positive scale</td>
<td>2.48±1.36</td>
<td>2.14±1.39</td>
<td>t=1.279</td>
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<td>Negative scale</td>
<td>2.78±1.35</td>
<td>2.43±1.36</td>
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<td>Depressive scale</td>
<td>1.85±0.94</td>
<td>2.17±1.27</td>
<td>t=1.456</td>
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<td>Cognitive scale</td>
<td>2.54±1.17</td>
<td>2.49±1.40</td>
<td>t=0.202</td>
<td>0.840</td>
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<td>Overall severity</td>
<td>3.15±0.94</td>
<td>3.14±1.21</td>
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**Table 3. Neurocognitive functioning**

<table>
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<th>Variable</th>
<th>Schizophrenic pts (n=46)</th>
<th>Schizoaffective pts (n=66)</th>
<th>Statistics</th>
<th>p</th>
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<tr>
<td>MMSE</td>
<td>25.80±3.42</td>
<td>25.98±4.00</td>
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<td>BACS</td>
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<tr>
<td>Verbal memory</td>
<td>9.06±3.98</td>
<td>10.03±5.11</td>
<td>t=-1.028</td>
<td>0.307</td>
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<td>Working memory</td>
<td>12.91±5.64</td>
<td>13.04±6.87</td>
<td>t=-0.102</td>
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<tr>
<td>Letter fluency</td>
<td>8.17±4.18</td>
<td>9.59±5.53</td>
<td>t=-1.042</td>
<td>0.164</td>
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<td>Semantic fluency</td>
<td>14.26±3.31</td>
<td>15.14±5.59</td>
<td>t=-0.984</td>
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<td>Digit-symbols association</td>
<td>31.12±13.76</td>
<td>30.19±12.65</td>
<td>t=0.347</td>
<td>0.729</td>
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<td>Tower of London</td>
<td>10.37±6.80</td>
<td>10.56±5.85</td>
<td>t=0.152</td>
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**Table 4. Functioning, well-being and quality of life**

<table>
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<tr>
<th>Variable</th>
<th>Schizophrenic pts (n=46)</th>
<th>Schizoaffective pts (n=66)</th>
<th>Statistics</th>
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<tr>
<td>PSP</td>
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<tr>
<td>Socially useful activities</td>
<td>2.57±1.36</td>
<td>2.52±1.44</td>
<td>t=0.185</td>
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<td>Personal and social relationships</td>
<td>2.48±1.15</td>
<td>2.41±1.28</td>
<td>t=0.294</td>
<td>0.770</td>
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<td>Self-care</td>
<td>0.39±0.74</td>
<td>0.70±1.10</td>
<td>t=1.630</td>
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<td>Disturbing and aggressive behavior</td>
<td>0.30±0.69</td>
<td>0.33±0.66</td>
<td>t=-0.223</td>
<td>0.824</td>
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<tr>
<td>Total score</td>
<td>57.67±13.48</td>
<td>55.38±16.61</td>
<td>t=0.775</td>
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<td>SWN</td>
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<tr>
<td>Mental functioning</td>
<td>16.80±3.77</td>
<td>16.09±4.29</td>
<td>t=0.910</td>
<td>0.365</td>
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<td>Self-control</td>
<td>17.74±3.99</td>
<td>16.32±4.03</td>
<td>t=1.843</td>
<td>0.068</td>
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<td>Physical functioning</td>
<td>18.17±3.84</td>
<td>16.83±3.63</td>
<td>t=1.878</td>
<td>0.063</td>
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<td>Emotional control</td>
<td>17.78±4.00</td>
<td>16.14±4.28</td>
<td>t=2.056</td>
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<td>Social competence</td>
<td>17.65±3.43</td>
<td>16.77±3.73</td>
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<tr>
<td>Total score</td>
<td>88.15±13.62</td>
<td>82.15±15.57</td>
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<td>WHOQOL</td>
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<tr>
<td>Physical</td>
<td>14.16±2.55</td>
<td>13.42±3.08</td>
<td>t=1.343</td>
<td>0.182</td>
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<td>Psychological</td>
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<td>11.96±1.36</td>
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<td>Social relationships</td>
<td>13.44±3.56</td>
<td>11.80±3.48</td>
<td>t=2.422</td>
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<td>Environment</td>
<td>12.80±2.99</td>
<td>12.10±2.38</td>
<td>t=1.233</td>
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<tr>
<td>Total score</td>
<td>52.84±10.48</td>
<td>49.28±10.80</td>
<td>t=0.648</td>
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**Table 5. Outcome measures**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Schizophrenic pts (n=46)</th>
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<td>Clinical remission</td>
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<tr>
<td>Andreasen’s criteria</td>
<td>20±43.5</td>
<td>26±45.2</td>
<td>χ²=1.328</td>
<td>0.249</td>
</tr>
<tr>
<td>Extended PANSS criteria</td>
<td>18±23.9</td>
<td>28±24.2</td>
<td>χ²=4.093</td>
<td>0.043</td>
</tr>
<tr>
<td>Overall PANSS criteria</td>
<td>22±5.59</td>
<td>19±28.8</td>
<td>χ²=2.801</td>
<td>0.094</td>
</tr>
<tr>
<td>Functional remission</td>
<td>6±13.0</td>
<td>17±25.8</td>
<td>χ²=2.685</td>
<td>0.101</td>
</tr>
<tr>
<td>Subjective remission</td>
<td>32±69.6</td>
<td>39±59.1</td>
<td>χ²=1.282</td>
<td>0.258</td>
</tr>
<tr>
<td>Recovery (clinical*+functional remission)</td>
<td>3±6.5</td>
<td>15±22.7</td>
<td>χ²=5.278</td>
<td>0.022</td>
</tr>
<tr>
<td>Recovery (clinical*+subjective remission)</td>
<td>3±6.5</td>
<td>8±12.1</td>
<td>χ²=0.960</td>
<td>0.327</td>
</tr>
</tbody>
</table>

*Clinical remission according to Andreasen’s criteria.

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er, a significant difference in distribution of cases was ob-
served, with a higher proportion of females among schizoa-
ffective patients and of males among schizophrenic subjects.
These results are only partly in agreement with Chenaux et al. who reported in schizoaffective patients prevalence rates of females and married subjects that were higher than or equal to those found in schizophrenia, while unemployment prev-
vailed among schizophrenics. As far as family morbidity was
concerned, no significant difference was detected in terms of
presence of schizophrenia, bipolar disorders or major depres-
sion in family members of the schizophrenic and schizoaffect-
ive patients included in the study. This result is only partially
in line with the above cited review, which reported how the
majority of studies published had found a familial risk of schiz-
ophrenia in probands affected by schizophrenia which was
higher than or similar to that observed among schizoaffective
patients, while the familial risk for major depression among
schizoaffective patients was reported as being higher than or
similar to that found among schizophrenic subjects. With re-
gard to psychiatric history, several significant differences were
revealed, demonstrating in schizoaffective subjects a better
premorbid adjustment, higher proportion of patients who had
been admitted to hospital and had attempted suicide. These
findings concur at least in part with those reported in the liter-
ature, where age at onset of schizophrenia is lower than or
similar to that observed in schizoaffective disorder, whilst the
total number of hospitalizations and suicidal behaviour is gen-
erally similar or higher among schizoaffective patients, who
generally display a better premorbid adjustment. When taking
into account symptomatology, no significant differences could
be detected in scores obtained at positive, negative, affective
and cognitive scales, although more severe, specific depressive
symptoms were found in schizoaffective patients, and negative
symptoms in schizophrenic patients. These results are partly
convergent with those found in literature, where only negative
symptoms are consistently reported as being more pro-
nounced in schizophrenia, while positive symptoms and cogni-
tive deficits are reported as being more severe in schizophre-
nia or similar to those manifested in schizoaffective patients,
while affective symptoms are reported as being more severe in
schizoaffective patients or similar to those found in schizo-
phrenia. With regard to cognitive deficits, a recent meta-analy-
cal study focusing on cognitive functioning reported how in
6 of 12 cognitive domains people with schizophrenia per-
formed worse than those with schizoaffective or affective psy-
chosis; however, inter-group differences were slight and the
distribution of effect sizes showed a substantial heterogeneity,
leading the authors to conclude that neuropsychological data
do not provide evidence for categorical differences between
schizophrenia and other groups.

The primary aim of our study was to compare long-term
outcome of a cohort of schizophrenic and schizoaffective pa-
tients with a very similar overall mean duration of illness (ap-
prox. 15 years), using as outcome measures both clinical and
functional remission, and recovery, evaluated according to stan-
dardized criteria. The findings of the study demonstrate
that the proportion of schizoaffective patients meeting crite-
rria for clinical remission was at least ten percentage points
higher than that observed among schizophrenic patients, irre-
spective of the remission criteria adopted. However, when
adopting only one of the extended criteria for remission, i.e.
the evaluation of scoring at all items of positive and negative
subscales of PANSS, the latter differences achieved statistical
significance. With regard to functioning, the proportion of
schizoaffective patients found to be remitted was approx. 13
percentage points higher than that detected among schizo-
phrenics, a highly significant difference; in relation to recov-
ery rates, likewise a highly significant difference (more than
16 percentage points) emerged between schizoaffective and
schizophrenic patients when recovery was considered in
terms of clinical plus functional remission. These results seem
to indicate that long-term outcome of chronic schizoaffective
patients is somewhat better than in schizophrenic patients,
both in clinical and functional terms; unfortunately, no con-
trol group made up of patients with affective psychoses was
set up, thus preventing us from predicting whether long-term
outcome of schizoaffective patients is worse than or similar to
that observed in psychotic major depressed or bipolar pa-
tients. The above mentioned results are partly consistent with
data reported in the review published by Chenaux et al.,
demonstrating a more favourable clinical evolution for
schizoaffective patients in 24 studies when compared to schiz-
ophrenic subjects and further reporting a similar outcome in
an additional 15 studies. When taking into account long-term
prospective studies, the prognosis of schizoaffective disorders
appears to differ markedly between studies. Indeed using the
criteria of Feighner et al. for diagnosis, Tsuang et al., reported
how in the very long-term patients with schizoaffective dis-
orders featured a significantly better outcome than those with
schizophrenia, but a significantly poorer outcome than sub-
jects with affective disorders and surgical conditions (control
group); Jager et al., using ICD diagnostic criteria, found a
substantially similar prognosis in schizoaffective and affective
patients, while Lay et al., adopting similar criteria, demon-
strated that outcome of schizoaffective adolescents increas-
ingly resembled that observed in schizophrenic rather than
affective psychotics; Grossman et al., using RDC cri-
teria, reported how schizoaffective patients featured a some-
what better post-hospital functioning than patients with
schizophrenia, a poorer functioning than bipolar manic pa-
tients and significantly poorer functioning than patients with
unipolar depression. Several years later, on the basis of a
longer follow up study the same group reported that a better
outcome in schizoaffective than in schizophrenic patients,
although poorer than the outcome observed in subjects suffer-
ing from psychotic affective disorder, with significant nega-
tive prognostic implications for mood-incongruent psychotic
symptoms; Williams and McGlashan, adopting DSMIII cri-
teria, reported no significant differences between schizoaffect-
tive and schizophrenic patients at virtually all outcome mea-
ures, while Pope et al., using similar criteria, found no dif-
terence between patients with manic and schizoaffective dis-
orders, but significant differences between these disorders
and schizophrenia. Further, Marneros et al., using slightly
modified DSMIII criteria for diagnosis, found that in the
long-term schizoaffective disorders occupied a position situ-
ated halfway between affective and schizophrenic disorders
when taking into account all aspects of outcome, although dis-
playing greater similarities with affective than schizophrenic
disorders. Finally, Tsuang and Coryell adopting DSMIII-R
criteria, found that baseline diagnosis was a powerful predic-
tor of long-term outcome, with patients affected by schizoaffect-
tive disorders featuring a comparable prognosis to that of
schizophrenics, and a markedly worse prognosis compared to
Long-term outcome of schizoaffective disorder

psychotic depressed patients. Although prospective studies are the best equipped to evaluate outcome, the findings emerging from the studies cited above are somewhat puzzling, reporting how the outcome of schizoaffective disorder may to some degree resemble the outcome observed in affective disorders or schizophrenia, largely due to methodological differences, i.e. diagnostic criteria adopted, characteristics of the cohort enrolled (first onset, chronic or mixed samples), duration of follow-up, etc. Moreover, the lack of diagnostic stability and reliability, particularly evident in the case of schizoaffective disorders\(^7\),\(^8\), constitutes a serious challenge to the validity of comparative follow-up studies.

Conversely to schizophrenia and affective disorders, to date only a small number of naturalistic studies included the treatment of schizoaffective disorder from a systematic point of view\(^1\). In a recent review of 33 studies, all of which were undertaken using standardized diagnostic criteria and including 14 randomized controlled trials, Jäger et al.\(^39\) reported how the studies reviewed did not allow them to provide consistent recommendations as to whether schizoaffective disorder should be treated primarily with antipsychotics, mood stabilizers or a combination of these drugs, mostly due to the limited comparability of the studies examined, a conclusion substantially shared by other authors\(^40\),\(^41\). Moreover, few randomized controlled trials have been conducted regarding specifically schizoaffective disorder, and only paliperidone, a second generation antipsychotic, was recently approved specifically for use in schizoaffective patients\(^8\).

The need for an individualized treatment plan for patients affected by schizoaffective disorder, including both pharmaco-therapy and psychoeducation, has recently been emphasized, suggesting the preferential use of atypical antipsychotics plus mood stabilizers, or of atypical antipsychotics alone in schizoaffective-bipolar type patients, and a combination of an atypical antipsychotic in association with anti-depressants in schizoaffective-depressive type patients\(^8\). This suggestion seems to be reflected by the findings of the present study. Indeed, our cross sectional survey demonstrates clearcut differences in the routine treatment of chronic schizoaffective patients compared to schizophrenic patients, considering that antipsychotics (mainly first generation antipsychotics) are the most frequently prescribed treatment in both schizophrenic and schizoaffective patients; however, frequency of use of mood stabilizers, antidepressants and benzodiazepines is quite significantly higher among schizoaffective patients. This evidence tends to support the finding that, irrespective of whether or not schizoaffective disorder is present as an autonomous disorder, in common clinical practice treatment of the disorder varies considerably with respect to the treatment generally prescribed in other psychoses such as schizophrenia, particularly due to the need to address the phase-dependent, affective component of this disorder with specific treatments (mood stabilizers, antidepressants, minor tranquilizers).

CONCLUSIONS

Before drawing any conclusions, a number of limitations of the present study should be underlined, in particular the retrospective nature of the data collected, a limitation which is at least in part counterbalanced by the good quality of data obtained from clinical records, stored by means of a structured data recording system. Secondly, the limited number of cases examined should be taken into account, although the diagnosis of these cases was ascertained by means of structured diagnostic interviews. Moreover, due to the limited number of subjects included, no subtyping of cases, in particular of schizoaffective patients, was envisaged. Another limitation is constituted by the above-mentioned lack of a control group made up of patients suffering from affective psychoses. Finally, it should be taken into account that the study focused on a selected cohort of patients, namely those who were still in contact with the centre, thus excluding others who had died, moved away, refused to stay in treatment for a series of reasons, including scarce insight and/or marked severity of illness or having no further need for continuing care. However, even bearing in mind these limitations, a number of interesting findings bearing relevant practical implications emerge from the study. First, based on the consideration that the study relates to a naturalistic sample of chronic psychotic outpatients in charge of an Italian community mental health centre, the relevant frequency of schizoaffective disorder, similar to or even higher than that observed for schizophrenia should be emphasized\(^44\), thus confirming the epidemiological relevance of these patients in outpatient services. Although schizoaffective patients share with schizophrenics a certain number of sociodemographic and cross-sectional symptomatologic characteristics, the data obtained in this study underline several marked differences. Indeed, schizoaffective patients are most frequently females, show a better social premorbid adjustment and a somewhat more complicated clinical course in terms of more frequent hospitalizations, and suicidality; more importantly, the long-term outcomes observed in these patients, at least in terms of clinical and functional remission and recovery rates, are somewhat better than those found in schizophrenia. Finally, the treatment of these patients, at least from a pharmacological point of view, varies quite considerably from the treatment of schizophrenia. Based on the above-mentioned methodological limitations, it did not prove possible to draw any conclusions from this study with regard to the nosological status of schizoaffective disorder, nor could suggestions be given regarding the possible future directions of the nosographic localization of the disorder. Given the complexity and uncertainty of data present in the literature it is hardly surprising that some authors claim that the disorder should be omitted from the future versions of ICD and DSM\(^45\),\(^46\), while others suggest that the diagnostic criteria should be revised\(^47\), or that a dimensional approach would be more useful in describing these cases\(^48\),\(^49\). The data obtained in the present study however support the hypothesis of the existence of a specific subset of patients, substantially distinct from pure schizophrenic patients and usually described under the label of schizoaffective disorder, and that, irrespective of their diagnostic labelling, the therapeutic needs of these patients may differ markedly from those of schizophrenic subjects.

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