

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

Outcome a lungo termine del disturbo schizoaffectivo. 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 WHOQoL-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.

RIASSUNTO. Introduzione. Un certo numero di studi indica che le caratteristiche cliniche e gli esiti a lungo termine dei pazienti schizoaffectivi sono molto simili a quelli osservati nella schizofrenia quando i casi sono diagnosticati secondo i criteri del DSM. L'obiettivo principale è stato confrontare tassi di remissione e tassi di "recovery" in una coorte di pazienti ambulatoriali schizoaffectivi e schizofrenici cronici. **Metodi.** È stato esaminato un campione di 102 pazienti ambulatoriali consecutivi, 46 affetti da schizofrenia (45,1%, età media 44,22±9,97 anni) e 66 affetti da disturbo schizoaffectivo (54,9%, età media 43,00±9,07 anni). I dati personali e la storia psichiatrica sono stati raccolti secondo il sistema AMDP; l'adattamento premorbo è stato valutato per mezzo della PAS. La diagnosi psichiatrica è stata confermata mediante SCID-I e II; lo stato psicopatologico è stato valutato per mezzo delle scale PANSS e CGI-SCH; la valutazione neuropsicologica è stata effettuata per mezzo delle scale BACS e MMSE; il funzionamento, il benessere soggettivo e la qualità della vita sono stati rispettivamente valutati per mezzo della PSP, della SWN e della WHOQoL-BREF. **Risultati.** I pazienti schizofrenici e schizoaffectivi esaminati erano caratterizzati da una sovrapponibile età di esordio, durata media di malattia, durata media di psicosi non trattata e caratteristiche socio-demografiche; inoltre, i profili psicopatologici e neurocognitivi trasversali erano molto simili. Tuttavia, i pazienti schizoaffectivi erano più frequentemente donne, mostravano un migliore adattamento sociale premorbo e un decorso clinico più complicato in termini di numero di soggetti con ricoveri e maggiore suicidalità; le misure di outcome erano invece sostanzialmente migliori tra i pazienti schizoaffectivi: i tassi di remissione clinica erano del 43,5% fra gli schizofrenici e del 54,5% fra i pazienti schizoaffectivi; il 13% dei pazienti affetti da schizofrenia e il 25,8% dei pazienti schizoaffectivi erano funzionalmente in remissione; il "recovery" è stato osservato nel 6,5% degli schizofrenici e nel 22,7% degli schizoaffectivi; la maggior parte dei soggetti stava assumendo antipsicotici, per lo più atipici, anche se una percentuale maggiore di soggetti schizoaffectivi era in trattamento con stabilizzatori dell'umore, antidepressivi e benzodiazepine. **Conclusioni.** Rispetto ai pazienti schizofrenici, i pazienti schizoaffectivi secondo il DSM-IV-TR appaiono come un sottogruppo di pazienti psicotici con diverse e specifiche caratteristiche in termini di decorso, esiti clinici e funzionali e trattamento.

PAROLE CHIAVE: disturbo schizoaffectivo, schizofrenia.

INTRODUCTION

Schizoaffective disorder represents an ongoing challenge for psychiatric nosology, given the uncertainty of its boundaries in relation to schizophrenia and affective disorders¹. 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 disorders². Moreover, the possibility that schizoaffective disorder may be a distinct form of psychotic disorder, as classified both in DSM-IV-TR³ and ICD-10⁴, or an intermediate disorder within a spectrum that ranges from schizophrenia and mood disorders should be taken into account^{5,6}. 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 psychoses². 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 schizophrenia¹. 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 study⁷, 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^{8,9}, 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)¹⁰. All patients included in the study underwent comprehensive psychiatric evaluation by means of the Structured Clinical Interview for Diagnosis for Axis I DSM-IV (SCID-I Research Version)¹¹ and the Interview Structured Clinical Diagnosis for Axis II of DSM-IV (SCID-II)¹², 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)¹³, 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 PANSS (Positive and Negative Syndrome Scale)¹⁴ and Clinical Global Impression-Schizophrenia Scale (CGI-SCH)¹⁵. PANSS consists of 30 items grouped into 3 distinct clusters (positive symptoms, negative symptoms, general psychopathological symptoms); the manual accompanying the scale provides a detailed explanation of individual items and criteria of quantification of symptoms rated on a 7-point scale. CGI-SCH is the adapted version of CGI (Clinical Global Impression Rating Scale)¹⁶, one of the main rating scales currently used in the comprehensive assessment of psychopathology. The CGI scale comprises 3 main scores: severity of illness, global improvement and efficacy index. For the purposes of the present study, the severity score was used: CGI-SCH, as adapted for use in schizophrenia, provides for the assessment of severity and improvement of 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)¹⁷ and Mini Mental State Examination (MMSE)¹⁸. 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 population¹⁹. As an overall measure of cognitive functioning we used the MMSE test¹⁸; an age/education adjusted score was calculated for each subject based upon the correction grids for the Italian population²⁰.

Functioning, Subjective well-being and Quality of life were respectively evaluated by means of PSP (Personal and Social Performance)²¹, Subjective Well-being under Neuroleptics (SWNS)²², and WHO Quality of Life-Brief questionnaire (WHOQOL-BREF)²³. The PSP scale, developed from SOFAS (Social Occupational Functioning Scale), assesses social functioning of patients

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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 fulfilment 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 recovery²⁶, 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 (chi 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 schizoaffectives 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 , $df=101$, $t=2.248$, $p=0.027$). 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 deeds 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 PANNS. 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=1.2.19, p=0.031), 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. With regard to 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 difference 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%

Variable	Schizophrenic pts (n=46)	Schizoaffective pts (n=66)	Statistics	p
Mean age at onset (years)	23.9±10.4	23.1±9.1	t=0.454	0.65
Mean duration of illness (months)	208.52±119.28	186.56±104.36	t= 1.033	0.304
Mean duration of untreated psychosis (months)	33.39±74.01	19.30±41.02	t= 1.289	0.200
Course of illness (n,%)			$\chi^2=1.650$	0.648
Episodic with interepisodic remission	8 (10.9)	13 (19.7)		
Episodic without interepisodic remission	11 (23.9)	13 (19.7)		
Continuous	28 (60.9)	37 (56.1)		
Not defined	2 (4.3)	3 (4.5)		
Pts with hospital admissions (n,%)	26 (56.5)	49 (74.2)	$\chi^2=3.848$	0.05
Hospital admissions (n,%)			$\chi^2=4.196$	0.323
1	7 (26.9)	17 (34.7)		
2-4	17(65.4)	21 (43.9)		
5-7	0 (0.0)	3 (06.1)		
8>	2 (7.7)	8 (16.3)		
Pts with attempted suicides (n,%)	8 (17.4)	25 (37.9)	$\chi^2=5.475$	0.019
Attempted suicides (n,%)			$\chi^2=1.993$	0.369
1	3 (37.5)	13 (52)		
2-3	4 (50.0)	6 (24)		
4>	1 (12.5)	6 (24)		
Pts with criminal acts (N,%)	2 (4.3)	7 (10.6)	$\chi^2=0.715$	0.398
Crimes (n,%)			$\chi^2=9.00$	0.011
Against person	0 (0.0)	1 (14.3)		
Against property	0 (0.0)	6 (85.7)		
Both	2 (100)	0 (0.0)		
Pts with admission in forensic hospitals	1 (2.2)	0 (0.0)	$\chi^2=1.448$	0.229

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);

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Table 2. Symptomatology

Variable	Schizophrenic pts (n=46)	Schizoaffective pts (n=66)	Statistics	p
PANSS mean score				
Positive scale	12.46±5.06	11.14±3.74	t=1.589	0.115
Negative scale	15.61±6.62	13.95±6.10	t= 1.362	0.176
General psychopathology scale	26.74±8.50	27.74±8.14	t=-0.630	0.530
Total scale	54.80 (17.77)	52.83 (15.79)	t=0.617	0.538
CGI-SCH mean score				
Positive scale	2.48±1.36	2.14±1.39	t=1.279	0.204
Negative scale	2.78±1.35	2.43±1.36	t=1.349	0.180
Depression scale	1.85±0.94	2.17±1.27	t=-1.456	0.148
Cognitive scale	2.54±1.17	2.49±1.40	t=0.202	0.840
Overall severity	3.15±0.94	3.14±1.21	t=0.064	0.949

Table 3. Neurocognitive functioning

Variable	Schizophrenic pts (n=46)	Schizoaffective pts (n=66)	Statistics	p
MMSE	25.80±3.42	25.98±4.00	t=-0.249	0.804
BACS				
Verbal memory	9.06±3.98	10.03±5.11	t=-1.028	0.307
Working memory	12.91±5.64	13.04±6.87	t=0.102	0.919
Letter fluency	8.17±4.18	9.59±5.53	t=-1.402	0.164
Semantic fluency	14.28±3.31	15.14±5.59	t=-0.984	0.374
Digit-symbols association	31.12±13.76	30.19±12.65	t=0.347	0.729
Tower of London	10.37±6.80	10.56±5.85	t=-0.152	0.879

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=0.361, df=1, p=0.548); 15.2% of schizophrenics (n=7) and 16.7% schizoaffectives were prescribed both FGAs and SGAs (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 in the light of data reported in the literature, as summarized by Chéniaux et al.⁶ in their review of studies relating to a comparison of schizoaffective disorders with schizophrenia and/or affective disorders.

Table 4. Functioning, well-being and quality of life

Variable	Schizophrenic pts (n=46)	Schizoaffective pts (n=66)	Statistics	p
PSP				
Socially useful activities	2.57±1.36	2.52±1.44	t=0.185	0.853
Personal and social relationships	2.48±1.15	2.41±1.28	t=0.294	0.770
Self-care	0.39±0.74	0.70±1.10	t=-1.630	0.106
Disturbing and aggressive behavior	0.30±0.69	0.33±0.66	t=-0.223	0.824
Total score	57.67±13.48	55.38±16.61	t=0.775	0.440
SWN				
Mental functioning	16.80±3.77	16.09±4.29	t=0.910	0.365
Self-control	17.74±3.99	16.32±4.03	t=1.843	0.068
Physical functioning	18.17±3.84	16.83±3.63	t=1.878	0.063
Emotional control	17.78±4.00	16.14±4.28	t=2.056	0.042
Social competence	17.65±3.43	16.77±3.73	t=1.266	0.208
Total score	88.15±13.62	82.15±15.57	t=2.110	0.037
WHOQOL				
Physical	14.16±2.55	13.42±3.08	t=1.343	0.182
Psychological	12.44±1.38	11.96±1.86	t=1.486	0.140
Social relationships	13.44±3.56	11.80±3.48	t=2.422	0.017
Environment	12.80±2.99	12.10±2.38	t=1.233	0.189
Total score	52.84±10.48	49.28±10.80	t=6.484	0.528

Table 5. Outcome measures

Variable	Schizophrenic pts (n=46)	Schizoaffective pts (n=66)	Statistics	p
Clinical remission				
Andreasen's criteria	20±43.5	36±54.5	χ ² =1.328	0.249
Extended PANSS criteria	11±23.9	28±42.4	χ ² =4.093	0.043
Overall PANSS criteria	7±15.2	19±28.8	χ ² =2.801	0.094
Functional remission	6±13.0	17±25.8	χ ² =2.685	0.101
Subjective remission	32±69.6	39±59.1	χ ² =1.282	0.258
Recovery (clinical*+functional remission)	3±6.5	15±22.7	χ ² =5.278	0.022
Recovery (clinical*+functional+subjective remission)	3±6.5	8±12.1	χ ² =0.960	0.327

*Clinical remission according to Andreasen's criteria.

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; however,

er, a significant difference in distribution of cases was observed, with a higher proportion of females among schizoaffective patients and of males among schizophrenic subjects. These results are only partly in agreement with Cheniaux et al.⁶ 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 prevailed among schizophrenics. As far as family morbidity was concerned, no significant difference was detected in terms of presence of schizophrenia, bipolar disorders or major depression in family members of the schizophrenic and schizoaffective patients included in the study. This result is only partially in line with the above cited review⁶, which reported how the majority of studies published had found a familial risk of schizophrenia 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 regard 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 literature⁶, 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 generally 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 pronounced in schizophrenia, while positive symptoms and cognitive deficits are reported as being more severe in schizophrenia 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 schizophrenia⁶. With regard to cognitive deficits, a recent meta-analytic study focusing on cognitive functioning²⁷ reported how in 6 of 12 cognitive domains people with schizophrenia performed worse than those with schizoaffective or affective psychosis; 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 patients with a very similar overall mean duration of illness (approx. 15 years), using as outcome measures both clinical and functional remission, and recovery, evaluated according to standardized criteria. The findings of the study demonstrate that the proportion of schizoaffective patients meeting criteria for clinical remission was at least ten percentage points higher than that observed among schizophrenic patients, irrespective 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 schizophrenics, a highly significant difference; in relation to recovery 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 control 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 patients. The above mentioned results are partly consistent with data reported in the review published by Cheniaux et al.⁶, demonstrating a more favourable clinical evolution for schizoaffective patients in 24 studies when compared to schizophrenic 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.²⁸, reported how in the very long-term patients with schizoaffective disorders featured a significantly better outcome than those with schizophrenia, but a significantly poorer outcome than subjects with affective disorders and surgical conditions (control group); Jager et al.²⁹, using ICD diagnostic criteria, found a substantially similar prognosis in schizoaffective and affective patients, while Lay et al.³⁰, adopting similar criteria, demonstrated that outcome of schizoaffective adolescents increasingly resembled that observed in schizophrenic rather than affective psychotic patients; Grossman et al.³¹, using RDC criteria, reported how schizoaffective patients featured a somewhat better post-hospital functioning than patients with schizophrenia, a poorer functioning than bipolar manic patients and significantly poorer functioning than patients with unipolar depression. Several years later, on the basis of a longer follow up study, the same group³² found that a better outcome in schizoaffective than in schizophrenic patients, although poorer than the outcome observed in subjects suffering from psychotic affective disorder, with significant negative prognostic implications for mood-incongruent psychotic symptoms; Williams and McGlashan³³, adopting DSMIII criteria, reported no significant differences between schizoaffective and schizophrenic patients at virtually all outcome measures, while Pope et al.³⁴, using similar criteria, found no difference between patients with manic and schizoaffective disorders, but significant differences between these disorders and schizophrenia. Further, Marneros et al.³⁵, using slightly modified DSMIII criteria for diagnosis, found that in the long-term schizoaffective disorders occupied a position situated halfway between affective and schizophrenic disorders when taking into account all aspects of outcome, although displaying greater similarities with affective than schizophrenic disorders. Finally, Tsuang and Coryell³⁶ adopting DSMIII-R criteria, found that baseline diagnosis was a powerful predictor of long-term outcome, with patients affected by schizoaffective disorders featuring a comparable prognosis to that of schizophrenics, and a markedly worse prognosis compared to

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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^{37,38}, 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 view¹. 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 paliperidon, a second generation antipsychotic, was recently approved specifically for use in schizoaffective patients⁴². The need for an individualized treatment plan for patients affected by schizoaffective disorder, including both pharmacotherapy 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 antidepressants in schizoaffective-depressive type patients⁴³. 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 tranquillizers).

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 da-

ta 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 emphasized⁴⁴, 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 collocation 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 revised⁴⁷, 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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