Eur Arch Psychiatry Clin Neurosci (2004) 254 : 165–171 DOI 10.1007/s00406-004-0464-7

ORIGINAL PAPER

Victor Peralta · Manuel J. Cuesta

The deficit syndrome of the psychotic illness

A clinical and nosological study

Received: 17 February 2003 / Accepted: 12 September 2003

Abstract The deficit syndrome is thought to be specific to and a subtype of schizophrenia; however, there are scarce or no data on the prevalence and characteristics of this syndrome in non-schizophrenic psychoses. The aim of this study was to explore the prevalence and correlates of different types of negative symptoms (NegS) in a mixed sample of psychotic disorders. Six-hundred and sixty psychotic inpatients were classified according to the presence and type of NegS into the following groups: no NegS, transitory NegS, persistent secondary NeS, persistent doubtful secondary NegS, and persistent primary NegS (i. e., deficit symptoms). Furthermore, the nosological status of this symptom classification such as its clinical and etiological correlates were examined. Depending on the diagnostic criteria used for diagnosing schizophrenia, the prevalence of the deficit syndrome in schizophrenia and in non-schizophrenic psychoses ranged from 14 %–32 % and 2 %–22 %, respectively. Deficit syndromes in both schizophrenic and non-schizophrenic patients shared most of the syndrome-related clinical features. Regarding the associated clinical pattern, the transitory NegS group was closer to the group without NegS than to the groups with enduring NegS. Patient groups with enduring primary and enduring secondary NegS did not show relevant clinical or etiological differences, thus, suggesting that the primary versus secondary issue may be less relevant than previously acknowledged. The deficit syndrome may be diagnosed irrespective of the specific categories of psychotic disorders.

Key words schizophrenia · psychotic illness · deficit syndrome · negative symptoms · validity

V. Peralta (✉) · M. J. Cuesta
Psychiatric Unit
Virgen del Camino Hospital
Irunlarrea 4
31008 Pamplona, Spain
Tel.: +34-848422488
Fax: +34-848429924
E-Mail: victor.peralta.martin@cfnavarra.es

Introduction

The interest in subtyping schizophrenia gained increased attention when Crow (1980) proposed two types of schizophrenia, one of them characterized by negative symptoms (NegS). The negative syndrome was thought to convey poor response to neuroleptics, chronic course, intellectual impairment and structural brain changes. After Crow, many researches have attempted to operationalize the schizophrenic negative syndrome on the basis of different theoretical approaches such as severity and balance between positive and negative symptoms (Andreasen and Olsen 1982; Kay et al. 1986), as an independent dimension of psychopathology (Liddle 1987) or as a psychopathological domain that can be defined irrespective of the presence of psychotic symptoms and takes into account the putative etiology – primary versus secondary – and course – enduring versus transitory – of NegS (Carpenter et al. 1988). Patients with primary and enduring NegS are thought to have the deficit syndrome, which has been recently proposed to be a separate disease within schizophrenia (Kirkpatrick et al. 2001). The concept of the deficit syndrome not only appears to have clinical and neurobiological validity (Galderisi et al. 2002); it has also been empirically verified by means of latent class analysis of symptoms of the psychotic illness (Kendler et al. 1997; Peralta et al. 2002).

Despite the appealing character of the deficit syndrome as currently conceptualized, many questions remain. Among these are the specificity of the deficit syndrome for schizophrenia, and the nature of the transitory **vs** enduring and primary **vs** secondary distinctions of negative symptoms. Taking into account these issues, the general aim of this study was to explore the prevalence and correlates of different types of negative symptoms in a mixed sample of psychotic disorders. Specific aims were: a) to examine the prevalence of the deficit syndrome in schizophrenia (and in other psychotic disorders) using a polydiagnostic approach, b) to comparatively examine the associated features of the

deficit syndrome in schizophrenic and non-schizophrenic psychotic patients, and c) to examine the nosological status and the clinical and etiological correlates of the different types of NegS.

Method

Subjects

Six-hundred and sixty consecutively admitted psychotic inpatients made the study sample. The catchment area from which the sample was derived comprises a population of 250 000. This area is supplied with four psychiatric outpatients clinics, one day hospital, and one inpatient psychiatric facility at the Virgen del Camino Hospital. To be included in the study, patients had to present at least one psychotic symptom as defined by the DSM-III-R criterion A for schizophrenia or severe NegS as defined by the Scale for the Assessment of Negative Symptoms (SANS, Andreasen 1984a). Exclusion criteria were severe drug abuse confounding diagnosis, demonstrable brain disease or mental retardation. The sample included 384 male (58 %) and 276 female having an average education of 9.3 years (s. d. = 3.2). The mean age was 36.0 years (s. d. = 14.0), the mean age at onset was 26.9 years (s. d. = 10.6), and the average number of hospitalizations was 3.4 (s. d. = 4.3). Only patients with high-quality data from several sources including information provided by a close relative were included in the study, and all patients or their legal representatives provided informed consent to participate in the study.

Clinical and diagnostic assessment

The main instrument for assessing symptoms and diagnosis was a modified version (Peralta and Cuesta 1992) of the Manual for the Assessment of Schizophrenia (MAS) (Landmark 1982). This is a semi-structured interview for assessing a broad range of psychosis-related information including sociodemographic and clinical features, current and past symptoms and signs, course of the illness and other illness-related features, all of which are used to diagnose schizophrenia and related disorders from a polydiagnostic point of view. In the modified version of the MAS, 11 additional criteria of schizophrenia were included, and the Diagnostic and Statistical Manual, third version, (DSM-III) criteria were replaced by the DSM-III-R criteria for diagnosing all functional psychotic disorders (APA 1987). To minimize criterion and information variance for final research diagnoses, best estimated DSM-III-R diagnoses were produced on a consensus basis by the authors using all available information. Given that both the DSM-IV (APA 1994) and the tenth edition of the International Classification of Diseases (ICD-10) criteria (WHO 1992) were not available when the study began and that the modified MAS contains the necessary information for diagnosing psychotic disorders according to these systems, patients were re-diagnosed according to DSM-IV and ICD-10 criteria using the best estimated diagnostic procedure. For the present study, we selected 10 diagnostic criteria of schizophrenia in order to examine the influence of diagnostic systems on the prevalence of the deficit syndrome in schizophrenic and non-schizophrenic psychoses, and the DSM-IV breakdown of psychotic disorders to examine the distribution of the different negative symptom groups (see below) across psychotic disorders.

All the patients were assessed by the two authors, with each of them rating approximately half of the patients; inter-rater reliability for clinical features, symptoms and diagnoses was assessed in 33 patients.

Characterization of the different negative symptom groups

We used the Carpenter et al. (1988) criteria for the deficit syndrome to rate the different types of NegS. These criteria were slightly modified to allow for a hierarchichal rating of the different NegS types. First, we omited the necessary criterion of having a DSM diagnosis of schizophrenia for ascertaining the deficit syndrome. Second, we assessed the presence of at least two of the following NegS at the index episode: restricted affect, diminished emotional range, poverty of speech with curbing of interest and decrease in curiosity, diminished sense of purpose, and diminished social drive. Third, in case of the presence of at least two symptoms, their persisting or remitting character over the last year was examined. If NegS were continuously present for one year ore more, they were qualified as enduring. Fourth, in the case of persisting NegS, the relationship with their putative secondary sources (psychotic symptoms leading to social withdrawal or preoccupation with psychotic experiences, depression or anxiety, parkinsonism, and environmental deprivation) was examined. Given that both clinical experience and previous research (Flaum and Andreasen 1995) indicate that the differentiation between primary and secondary NegS is often difficult, we took a probabilistic approach to this question on the basis of the cross-sectional and longitudinal temporal associations between NegS and their potential secondary sources. In this way, persistent NegS were rated as definitely secondary, probably secondary, doubtful secondary, and primary. According to this procedure, patients were initially classified into six groups on the basis of the presence and nature of NegS: [a] no NegS (n = 420, 63.6 %), [b] transitory NegS (n = 68, 10.3 %), [c] persistent NegS definitely secondary (n = 24, 3.6 %), [d] persistent NegS probably secondary (n = 7, 1.1 %), [e] persistent NegS doubtfully secondary (n = 39, 5.9 %), and [f] persistent and primary NegS (i. e., deficit syndrome) (n = 102, 15.5 %). Given the low prevalence rate of persistent NegS rated as definitely secondary or probably secondary, the two groups were subsumed into a single group of "secondary NegS" (n = 31, 4.7 %).

Inter-rater reliability for the NegS classification was as follow: presence vs absence ($\kappa = 0.82$), enduring vs transitory ($\kappa = 0.75$), and primary vs secondary (intraclass correlation coefficient = 0.83). Inter-rater reliability for schizophrenia diagnoses (κ) ranged between 0.64 (Bleuler criteria) and 0.88 (DSM-IV criteria).

External validity of the different negative symptom groups

Patients classified according to the above mentioned criteria were examined across a number of sociodemographic, clinical, symptomatological and etiological variables which have been shown to be relevant for distinguishing deficit from non-deficit patients (Kirkpatrick et al. 2001). These variables were also used to comparatively examine the associated features of the deficit state in schizophrenic and non-schizophrenic psychoses.

Sociodemographic variables included gender and being married before illness onset. Clinical variables included premorbid adjustment as rated by the Phillips scale (Harris 1975), poor academic achievement, insidious onset, years of illness duration, co-morbid drug abuse, response to treatment at the index episode as rated by the Clinical Global Impressions scale (Guy 1976), and functional deterioration over the past year as rated by the Global Assessment of Functioning (GAF) (APA 1987).

Symptomatological variables included the syndromes of reality-distortion (mean rating of delusions and hallucinations), disorganization (mean rating of positive formal thought disorder, bizarre behavior and inappropriate affect), and negative (mean rating of affective flattening, alogia and avolition), which were rated by means of the SANS (Andreasen 1984a) and the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen 1984b). A depressive syndrome was defined by the mean rating of depressed mood, feelings of guilt and suicidal tendencies as rated by the Manual for the Assessment and Documentation of Psychopathology (Guy and Ban 1982).

Putative etiological variables included summer birth, psychosocial stressors (acute plus chronic) as rated in the DSM-III-R (APA 1987), and a positive family history of schizophrenia in first-degree relatives, which was assessed by means of the Family History-Research Diagnostic Criteria (Andreasen et al. 1977).

Statistics

For univariate analyses χ^2 and Student's t tests were employed for categorical and continuous variables, respectively. In examining the characteristics of the different groups we used χ^2 analysis for categorical variables, which if significant, were followed by pairwise χ^2 analyses. For continuous measures, one-way analyses of variance (with the Tukey Honestly Significance Difference test for multiple comparisons) were used. All statistics were done using the Statistical Package for the Social Sciences (Norusis 1995).

Results

Table 1 shows the prevalence of the deficit syndrome across 10 alternative diagnostic criteria of schizophrenia and their non-schizophrenic psychoses counterparts selected from the expanded MAS. It was evident that the prevalence of the deficit syndrome was highly dependent on the criteria considered, since for schizophrenia it ranged between 14% (Schneider and Cloninger criteria) and 32% (Kraepelin criteria), and for non-schizophrenic psychoses between 2% (Kraepelin criteria) and 22% (Cloninger criteria).

The associated characteristics of the deficit syndrome in schizophrenic and non-schizophrenic psychoses (DSM-IV criteria) are presented in Table 2. The deficit syndrome in the two groups seemed to share most of the associated features, excepting that the deficit syndrome in non-schizophrenic psychoses had a lower rate for insidious onset, less severe disorganization symptoms, and more severe depressive symptoms.

Table 3 presents data on the prevalence of the different negative symptom groups across the DSM-IV breakdown of psychotic disorders. A clear pattern of associations emerged, since while transitory NegS were observed in all forms of psychotic disorders, enduring

Table 1 Prevalence of the deficit syndrome as a function of diagnostic criteria of schizophrenia

Criteria	n of patients meeting the criteria	n (%) of patients with the deficit syndrome
Schneider		
Schizophrenia	447	64 (14.3)
Non-schizophrenic psychosis	213	38 (17.8)
Bleuler		
Schizophrenia	318	86 (27.0)
Non-schizophrenic psychosis	342	16 (4.7)
Kraepelin		
Schizophrenia	296	95 (32.1)
Non-schizophrenic psychosis	364	7 (1.9)
Feighner		
Schizophrenia	257	78 (30.4)
Non-schizophrenic psychosis	403	24 (6.0)
Cloninger		
Schizophrenia	553	78 (14.1)
Non-schizophrenic psychosis	107	24 (22.4)
Guze		
Schizophrenia	190	54 (28.4)
Non-schizophrenic psychosis	470	48 (10.2)
RDC		
Schizophrenia	421	76 (18.1)
Non-schizophrenic psychosis	239	26 (10.9)
ICD-10		
Schizophrenia	419	93 (22.2)
Non-schizophrenic psychosis	241	9 (3.7)
DSM-III-R		
Schizophrenia	354	89 (25.1)
Non-schizophrenic psychosis	306	13 (4.2)
DSM-IV		
Schizophrenia	358	92 (25.7)
Non-schizophrenic psychosis	302	10 (3.3)

RDC Research Diagnostic Criteria; *ICD* International Classification of Diseases; *DSM* Diagnostic and Statistical Manual

Table 2 Characteristics of the deficit syndrome (n = 102) in DSM-IV schizophrenic and non-schizophrenic psychotic patients*

	Schizophrenia (n = 92)	Other psychoses (n = 10)	t or χ^2 (df = 1)	p
Gender, male, n (%)	56 (60.1)	7 (70.0)	0.31	0.572
Married before illness onset, n (%)	10 (10.9)	1 (10.0)	0.01	1.0**
Premorbid adjustment	7.47 (2.75)	6.70 (2.66)	0.85	0.369
Poor academic achievement, n (%)	45 (48.9)	5 (50.0)	0.00	0.947
Insidious onset, n (%)	50 (54.3)	2 (20.0)	4.25	0.039
Illness duration, years	11.0 (9.8)	17.2 (9.1)	1.90	0.060
Drug abuse, n (%)	25 (27.2)	4 (40.0)	0.73	0.393
Reality-distortion syndrome	2.30 (1.58)	2.00 (1.70)	0.58	0.561
Disorganization syndrome	2.87 (1.12)	2.13 (1.08)	1.99	0.049
Negative syndrome	3.28 (0.97)	3.03(0.90)	0.78	0.439
Depressive syndrome	0.60(1.36)	1.90 (1.91)	2.74	0.007
Response to treatment	2.83 (0.71)	3.00 (0.67)	0.69	0.493
GAF, past year	44.6 (13.3)	46.8 (9.2)	0.49	0.625
Summer birth, n (%)	31 (33.7)	3 (30.0)	0.05	0.813
Pychosocial stressors	2.43 (0.99)	2.20 (0.42)	0.73	0.464
FH of schizophrenia, n (%)	13 (14.1)	1 (10.0)	0.13	1.0**

* Unless that otherwise specified, values are mean (s. d.); ** Fisher exact test
GAF Global Assessment of Functioning; *FH* Family history

Table 3 Distribution of negative symptom type by DSM-IV diagnostic criteria of psychotic disorders

		Type of negative symptoms			
	No negative symptoms	Transitory	Persistent secondary	Persistent doubtful secondary	Persistent primary
	(n = 420, 63.6 %)	(n = 68, 10.3 %)	(n = 31, 4.7 %)	(n = 39, 5.9 %)	(n = 102, 15.5 %)
Schizophrenia (n = 358, 54.2 %)	185 (51.7)	25 (7.0)	22 (6.1)	34 (9.5)	92 (25.7)
Schizophreniform disorder (n = 61, 9.2 %)	48 (78.7)	13 (21.3)	0	0	0
Schizoaffective disorder (n = 37, 5.6 %)	22 (59.5)	7 (18.9)	2 (5.4)	3 (8.1)	3 (8.1)
Mood disorders (n = 88, 13.3 %)	64 (72.7)	14 (15.9)	7 (8.0)	1 (1.1)	2 (2.3)
Delusional disorder (n = 27, 4.1 %)	25 (92.6)	2 (7.4)	0	0	0
Brief psychotic disorder (n = 57 = 8.6 %)	54 (94.7)	3 (5.3)	0	0	0
Psychotic disorder NOS (n = 32, 4.8 %)	22 (68.8)	4 (12.5)	0	1 (3.1)	5 (15.6)

NOS not otherwise specified

NegS were restricted to atypical, affective, schizoaffective, and particularly, schizophrenic disorders. The diagnostic pattern was rather similar for the three groups of enduring NegS.

Table 4 presents data on the external validation of the different NegS groups. Non-discriminating variables included gender, co-morbid drug abuse, summer birth, and a family history of schizophrenia. The associated features for the different NegS groups also showed a relatively characteristic pattern in that transitory NegS differed from enduring NegS on most of the external variables. As a whole, the group with transitory NegS was closer to the group without NegS than to the groups with enduring NegS. On the other hand, the differentiation between enduring primary and enduring secondary NegS was less evident, with the deficit state representing the extreme pole of illness severity.

When the overall severity of psychotic symptoms was examined across groups (the usual procedure to examine levels of positive symptoms in deficit and non-deficit patients), a non-significant difference in the SAPS total score across groups was found ($F = 1.14$, $df = 4$, $p = 0.33$). The same was true when the SAPS total score was compared in patients with a schizophrenic deficit syndrome and those with a non-schizophrenic deficit syndrome ($t = 1.21$, $df = 100$, $p = 0.23$).

Table 4 Characteristics of patients by type of negative symptoms*

		Type of negative symptoms						
	No negative symptoms	Transitory	Persistent secondary	Persistent doubtful secondary	Persistent primary	F or χ^2 (df = 4)	p	Post hoc comparisons**
	[1]	[2]	[3]	[4]	[5]			
Gender male, n (%)	246 (58.6)	36 (52.9)	16 (51.6)	23 (59.0)	63 (61.8)	1.89	0.755	–
Married before onset, n (%)	106 (25.2)	15 (22.1)	8 (25.8)	2 (5.1)	11 (10.8)	16.95	0.000	5/3
Premorbid adjustment	4.96 (2.6)	5.71 (3.0)	6.61 (3.4)	7.00 (2.6)	7.40 (2.4)	19.86	0.000	5.4.3/1; 5/2
Poor academic achievement, n (%)	136 (32.4)	22 (32.4)	9 (29.0)	9 (23.1)	50 (49.0)	13.17	0.010	5/3.2.1.4
Insidious onset, n (%)	111 (26.4)	9 (13.2)	12 (38.7)	14 (35.9)	52 (51.0)	34.79	0.000	5/1.2
Illness duration, years	7.9 (9.5)	9.11 (12.9)	11.4 (9.7)	11.8 (10.8)	11.6 (9.9)	4.05	0.003	5/1
Drug abuse, n (%)	161 (38.3)	26 (38.2)	6 (19.4)	16 (41.0)	29 (28.4)	7.82	0.098	–
Reality-distortion syndrome	3.12 (1.3)	2.99 (1.4)	2.72 (1.7)	3.01 (1.4)	2.27 (1.5)	7.52	0.000	5/1.4.2
Disorganization syndrome	1.84 (1.1)	1.84 (1.4)	1.95 (1.1)	2.35 (1.1)	2.80 (1.1)	14.62	0.000	5/3.1.2
Negative syndrome	1.18 (1.0)	3.11 (1.2)	2.87 (1.0)	2.73 (0.8)	3.25 (0.9)	133.75	0.000	5.4.3.2/1
Depressive syndrome	0.86 (1.7)	2.02 (2.6)	2.58 (3.1)	1.31 (1.9)	0.72 (1.5)	11.54	0.000	5.1/2.3; 4/3
Response to treatment	1.73 (0.8)	1.56 (0.7)	2.51 (0.8)	2.26 (0.8)	2.85 (0.7)	44.38	0.000	5.3.4/1.2
GAF, past year	67.2 (15.2)	65.0 (17.7)	48.5 (15.5)	48.9 (12.1)	44.8 (12.9)	59.73	0.000	5.3.4/1.2
Summer birth, n (%)	102 (24.3)	18 (26.5)	7 (22.6)	9 (23.1)	34 (33.3)	3.86	0.424	–
Psychosocial stressors	2.85 (1.2)	2.91 (1.1)	2.67 (1.1)	2.58 (0.9)	2.41 (0.9)	3.52	0.007	5/1
FH of schizophrenia, n (%)	50 (11.9)	4 (5.9)	7 (22.6)	7 (17.9)	14 (13.7)	6.97	0.137	–

* Unless that otherwise specified, values are mean (s. d.); ** Slashes separate significantly different groups
FH Family history; *GAF* Global assessment of functioning

Discussion

Despite previous evidence showing that primary and enduring NegS may be found in psychotic disorders other than schizophrenia (Gerbaldo et al. 1995; Fenning et al. 1996; Edwards et al. 1999; Herbener and Harrow 2001), the deficit syndrome is considered by its developers as both a specific and a separate disease within schizophrenia (Carpenter et al. 1988; Kirpatrick et al. 2001). Our findings show that the deficit syndrome may be found outside the limits of schizophrenia with a prevalence that is highly dependent on the criteria used for diagnosing schizophrenia, or in other words, on the degree to which the definitions of schizophrenia and the deficit syndrome are circular or tautological in terms of chronicity or duration criteria. Longitudinal criteria (i. e., those from Kraepelin) did capture almost all deficit patients, while cross-sectional criteria (i. e., the Schneider, Cloninger or Research Diagnostic Criteria) did allow the deficit syndrome to be found in a relatively substantial proportion of non-schizophrenic psychotic disorders. Even more, in the case of the Cloninger criteria, which are cross-sectional and exclusively based on psychotic symptoms, the rate of the deficit syndrome in non-schizophrenic psychoses was higher than in schizophrenia. This is consistent with the finding that the risk of having a deficit syndrome increases with a longer illness duration (Bottlender et al. 2001).

The associated features of the deficit syndrome in both schizophrenic and non-schizophrenic psychoses were very similar, thus, supporting the validity of the concept irrespective of diagnostic categories of psychosis. It is noteworthy that the associated features of the deficit syndrome in the two psychosis groups were virtually the same as the "ideal deficit syndrome" defined by Kirkpatrick et al. (2001); accordingly, our deficit patients appear to represent well the original concept, which upholds both cross-cultural and procedural validity of the construct. A consistent finding of previous studies is that deficit and non-deficit patients do have similar levels of positive symptoms; however, we found that when positive symptoms were separated into the more valid constructs of reality-distortion and disorganization dimensions a rather different pattern of relationship emerged, in that deficit patients, as compared with non-deficit patients, had higher levels of disorganization symptoms and lower levels of reality-distortion symptoms.

The lack of specificity of the deficit syndrome for schizophrenia needs to be viewed in the context of the poor specificity of other "schizophrenic" symptoms or syndromes (Pope and Lipinsky 1978; Crow 1986; Peralta and Cuesta 1997 and 1999). In this sense, deficit symptoms (like the negative ones) can be conceptualized as a dimension or domain of psychopathology of the psychotic illness. Furthermore, it should be also noted that the deficit state may extend beyond the limits of the psychotic illness since it can be also found in non-psychotic disorders such as schizophrenia simplex, non-psychotic depression or severe personality disorders (i. e., obsessive compulsive disorder, schizotypal disorder or schizoid disorder), all of which raise the question of a non-nosological approach for studying the deficit symptoms (Gerbaldo et al. 1997).

On the basis of the pattern of associations of the different NegS groups, our findings indicate that the distinction between transitory and enduring symptoms is more valid than enduring primary vs enduring secondary distinction. The clinical pattern of the transitory NegS group was closer to that of the group without NegS than to that of the groups with enduring NegS. The different nature of transitory and enduring NegS is in line with previous findings about the different neurobiological basis of these the two types of symptoms (Tandon et al. 2000; Monteleone et al. 2002).

The enduring NegS groups bore similar relationships to external variables with only a few significant differences among groups. These differences had a quantitative rather than qualitative character with the deficit state representing the extreme pole of a severity continuum with the secondary NegS groups. Overall, these findings are in agreement with previous studies on the distinction among types of NegS indicating that while the differentiation between enduring and transitory NegS is relatively easy (and has construct validity), this is not the case for the primary vs secondary distinction. The difficulty in differentiating primary from secondary NegS may be due to a number of factors such as the substantial descriptive overlap between the NegS of schizophrenia and NegS that derive from other sources (Schooler 1994), and the lack of a clear definition of what is primary or secondary (Flaum and Andreasen 1995). For example, it is usually overlooked that extrapyramidal symptoms may be an indigenous feature of schizophrenia (Wolf and O'Driscoll 1999), and that the preexistence of NegS in schizophrenics treated with antipsychotics may favor the presence or exacerbation of extrapyramidal symptoms (McCready et al. 1982). Not considering these facts may conduce to the situation that in those patients with both primary extrapyramidal and NegS, the former may erroneously be judged to be a cause of the latter. Our finding that most external variables did not clearly discriminate among enduring NegS groups might be explained by the fact that the groups with secondary NegS may actually consist of a mixture of both primary and secondary symptoms; an alternative and related explanation would be that the secondary causes operate on a preexisting vulnerability for developing primary enduring NegS. All these findings converge to indicate that the confounding effects of the potential secondary sources of NegS may be less significant than previously considered, and that the primary versus secondary distinction may have been overstated (Möller et al. 1995; McPhillips and Barnes 1997). This was confirmed by our group in a recent study of first-episode schizophrenia spectrum patients, in which it was found that various putative secondary sources (i. e., psychosis,

depression, drug-induced parkinsonism) were no meaningful predictors of NegS (Peralta et al. 2000).

In conclusion, our data show that the deficit state is neither specific nor a clearly defined subtype of schizophrenia, and that the transitory/enduring distinction of NegS seems to be more valid than the primary/secondary distinction. A major implication of our findings is that recognizing the deficit syndrome outside the limits of schizophrenia has a direct relevance for clinical practice since the diagnosis of this disabling condition in disorders other than schizophrenia represents the first step for its adequate treatment. The transnosological character of the deficit syndrome allows it to be studied regardless of the traditional diagnostic categories. In this respect, the relatively well-established neurobiological correlates of the schizophrenic deficit syndrome (Kirkpatrick et al. 2001) and the promising therapeutical approaches to treat it (Möller 2001) need to be further explored in deficit patients with other diagnoses. A further caveat regarding the definition of the deficit syndrome is whether it should be defined as a categorical or as a dimensional construct. While the deficit syndrome has been traditionally conceptualized as a categorical construct, a number of reports suggest that deficit symptoms varies along a continuum of severity (Mueser et al. 1991; Mayerhoff et al. 994; Edwards et al. 1999; Herbener and Harrow 2001). Future studies should examine the comparative validity of the dimensional and categorical definitions of deficit symptoms.

The results of this study need to be considered in the context of several potential limitations. First, the assessment of NegS was, in part, retrospective and the validation of the different NegS types requires fully prospective longitudinal assessments across multiple time points. Second, the primary vs secondary distinction was not applied to transitory negative symptoms. It is therefore possible that the primary/secondary distinction is more valid for transitory than for enduring NegS. Finally, the grouping of patients according types of NegS and the external validation study were not made under entirely blind conditions.

References

1. American Psychiatric Association (1987) Diagnostic and Statistical Manual for Mental Disorders, 3rd edn revised. APA, Washington DC
2. American Psychiatric Association (1994) Diagnostic and Statistical Manual for Mental Disorders, 4th edn. APA, Washington DC
3. Andreasen NC, Endicott J, Spitzer RL, Winokur G (1977) The family history method using diagnostic criteria: reliability and validity. Arch Gen Psychiatry 34:1229–1235
4. Andreasen NC, Olsen S (1982) Negative v. positive schizophrenia: definition and validation. Arch Gen Psychiatry 39:789–794
5. Andreasen NC (1984a) The Scale for the Assessment of Negative Symptoms (SANS). University of Iowa: Iowa, IA
6. Andreasen NC (1984b) The Scale for the Assessment of Positive Symptoms (SAPS). University of Iowa: Iowa, IA
7. Bottlender R, Jäger M, Groll C, Strauss A, Möller HJ (2001) Deficit states in schizophrenia and their association with the length of illness and gender. Eur Arch Psychiatry Clin Neurosci 251: 272–278
8. Carpenter WT, Heinrichs DW, Wagman AMI (1988) Deficit and nondeficit forms of schizophrenia. Am J Psychiatry 145:578–583
9. Crow TJ (1980) Molecular pathology of schizophrenia: more than one disease process? Br Med J 280:66–68
10. Crow TJ (1986) The continuum of psychosis and its implications for the structure of the gene. Br J Psychiatry 149:419–429
11. Edwards J, McGorry PD, Waddell F, Harrigan SM (1999) Enduring negative symptoms in first-episode psychosis: comparison of six methods using follow-up data. Schizophr Res 40:147–158
12. Fenning S, Bromet E, Galambos N, Putnam K (1996) Diagnosis and six-month stability of negative symptoms in psychotic disorders. Eur Arch Psychiatry Clin Neurosci 246:63–70
13. Flaum M, Andreasen NC (1995) The reliability of distinguishing primary versus secondary negative symptoms. Compr Psychiat 36:421–427
14. Galderisi S, Maj M, Mucci A, Cassano GB, Invernizzi G, Rossi A, Vita A, Dell'Osso L, Daneluzzo E, Pini S (2002) Historical, psychopathological, neurological and neuropsychological aspects of deficit schizophrenia: a multicenter study. Am J Psychiatry 159:983–990
15. Gerbaldo H, Fickinger MP, Wetzel H, Helisch A, Philipp M, Benkert O (1995) Primary enduring negative symptoms in schizophrenia and in major depression. J Psychiatr Res 29:297–302
16. Gerbaldo H, Georgi K, Pieschl D (1997) The deficit syndrome in first-admission patients with psychotic and non-psychotic disorders. Eur Psychiatry 12:53–57
17. Guy W (1976) ECDEU Assessment Manual for Psychopharmacology: Publication ADM 76–338. US Department of Health, Education and Welfare: Washington, DC
18. Guy W, Ban T (1982) The AMDP System: Manual for the Assessment and Documentation in Psychopathology. Springer, Berlin
19. Harris JG (1975) An abbreviated form of the Phillips rating scale of premorbid adjustment in schizophrenia. J Abnorm Psychol 84:129–137
20. Herbener ES, Harrow M (2001) Longitudinal assessment of negative symptoms in schizophrenia/schizoaffective patients, other psychotic patients, and depressed patients. Schizophrenia Bulletin 27:527–537
21. Kay SR, Opler LA, Lindenmayer JP (1986) Significance of positive and negative syndromes in chronic schizophrenia. Br J Psychiatry 149:439–448
22. Kendler KS, Karkowski-Shuman, O'Neill A, Straub RE, MacLean CH, Walsh D (1997) Resemblance of psychotic symptoms and syndromes in affected sibling pairs from the Irish study of high-density families: evidence for possible genetic heterogeneity. Am J Psychiatry 154:191–198
23. Kirkpatrick B, Buchanan R, Ross DE, Carpenter WT (2001) A separate disease within the syndrome of schizophrenia. Arch Gen Psychiatry 58:165–171
24. Landmark J (1982) A manual for the assessment of schizophrenia. Acta Psychiat Scand 65 (suppl. 298):1–88
25. Liddle PF (1987) The symptoms of chronic schizophrenia: a re-examination of the positive-negative dichotomy. Br J Psychiatry 151:141–151
26. Mayerhoff DI, Loebel AD, Alvir JMJ, Szymanski SR, Geisler SH, Borenstein M, Lieberman JA (1994) The deficit state in first-episode schizophrenia. Am J Psychiatry 151:1417–1422
27. McCreadie RG, Barron ET, Winslow GS (1982) The Nithsdale schizophrenia survey: II. Abnormal movements. Br J Psychiatry 140:587–590
28. McPhillips MA, Barnes TRE (1997) Negative symptoms. Curr Op Psychiatry 10:30–35
29. Möller HJ, Müller H, Borison RL, Schooler NR, Chouinard G (1995) A path-analytical approach to differentiate between direct and indirect drug effects on negative symptoms in schizophrenic patients. Eur Arch Psychiatry Clin Neurosci 245:45–49
30. Möller HJ (2001) Amisulpiride: efficacy in the management of chronic patients with predominant negative symptoms of schizophrenia. Eur Arch Psychiatry Clin Neurosci 251:217–224
31. Monteleone P, Di Lieto A, Martiadis V, Bartoli L, Maj M (2002) Correlations between negative symptoms and peripheral G protein levels in mononuclear leukocytes of deficit and nondeficit schizophrenics. Eur Arch Psychiatry Clin Neurosci 252:214–218

32. Mueser KT, Douglas MS, Bellak AS, Morrison RL (1991) Assessment of enduring negative symptoms subtypes in schizophrenia. Schizophr Bull 17:565–582
33. Norusis MJ (1995) Statistical Package for the Social Sciences. Version 6.1. SPSS Inc, Chicago IL
34. Peralta V, Cuesta MJ (1992) A polydiagnostic approach to self-perceived cognitive disorders in schizophrenia. Psychopathology 25:232–238
35. Peralta V, Cuesta MJ, Farre V (1997) Factor structure of symptoms in functional psychosis. Biol Psychiatry 42:806–815
36. Peralta V, Cuesta MJ (1999) Diagnostic significance of Schneider's first-rank symptoms in schizophrenia. Comparative study between schizophrenic and non-schizophrenic psychotic disorders. Br J Psychiatry 174:243–248
37. Peralta V, Cuesta MJ, Martinez-Larrea A, Serrano JF (2000) Differentiating primary from secondary negative symptoms in schizophrenia: a study of neuroleptic-naive patients before and after treatment. Am J Psychiatry 157:1461–1466
38. Peralta V, Cuesta MJ, Giraldo C, Cardenas A, Gonzalez F (2002) Classifying psychotic disorders: issues regarding categorical vs. dimensional approaches and time frame to assess symptoms. Eur Arch Psychiatry Clin Neurosci 252:12–18
39. Pope HG, Lipinski JF (1978) Diagnosis in schizophrenia and manic-depressive illness. Arch Gen Psychiatry 35:811–828
40. Schooler NR (1994) Deficit symptoms in schizophrenia: negative symptoms versus neuroleptic-induced deficits. Acta Psychiatr Scand 89 (suppl 380):21–26
41. Tandon R, DeQuardo JR, Taylor SF (2000) Phasic and enduring negative symptoms in schizophrenia: biological markers and relationship to outcome. Schizophr Res 45:191–201
42. Wolf A-S, O'Driscoll GA (1999) Motor deficits in schizophrenia: the evidence from neuroleptic-naïve patients and populations at risk. J Psychiatry Neurosci 24:304–314
43. World Health Organization (1992) The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. WHO, Geneve