Assessment of Enduring Deficit and Negative Symptom Subtypes in Schizophrenia

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Abstract

The clinical importance of subtypes based on enduring deficit or negative symptoms was examined in a group of schizophrenic patients who were assessed twice over a 1-year period. Subgroups of patients with high levels of enduring negative or deficit symptoms, based on the Scale for the Assessment of Negative Symptoms and the Quality of Life Scale, had a poorer prognosis and were consistently worse in social adjustment, quality of life, and thought disorder over the year than were patients with less severe negative symptoms. Subtypes based on Andreasen's negative schizophrenia classification and on enduring thought disorder were only weakly related to other symptoms and social adjustment. Social-skill deficits were weakly related to the enduring negative symptom subtype and Andreasen's negative schizophrenia. The results suggest that enduring negative and deficit symptoms may be associated with a poor outcome in schizophrenia, including more severe positive symptoms, lower levels of social adjustment, and a poorer quality of life.

The deficit syndrome has recently been proposed as a subtype of schizophrenia characterized by enduring negative symptoms (Wagman et al. 1987; Carpenter et al. 1988). Longstanding deficit symptoms are hypothesized to reflect a more meaningful subtype of schizophrenia than more transient negative symptoms, since the latter appear to be more responsive to currently available treatments.

Carpenter et al. (1988) defined the deficit syndrome as the presence of two or more of the following symp-

toms over at least a 1-year period: restricted affect, diminished emotional range, poverty of speech with curbing of interest and decrease in curiosity, diminished sense of purpose, and diminished social drive. In addition, it was specified that these symptoms must not be secondary to positive symptoms, anxiety, depression, mental retardation, or drug side effects. Subsequent to their first study, Carpenter and his colleagues modified the specific symptoms of the deficit syndrome by splitting the poverty of speech symptom into two symptoms: poverty of speech and curbing of interest. This revision resulted in a total of six different deficit symptoms (Kirkpatrick et al. 1989a).

In the first study of the deficit syndrome, Carpenter et al. (1988) obtained ratings from clinicians who were familiar with the patients. Clinicians were given a written description of the deficit syndrome and were engaged in a detailed discussion of the concept. Patients were then classified as either "deficit syndrome." "not deficit." or "unsure." Of 103 schizophrenic or schizoaffective patients, 15 were confidently assigned to the deficit group and 64 to the nondeficit group. A senior clinician agreed with the assignments in 42 out of 44 cases. Patients with the deficit syndrome were found to have more stable anergia/withdrawal subscale scores on the Brief Psychiatric Rating Scale (BPRS; Overall and Gorham 1962) and a worse prognosis than nondeficit patients. The deficit and nondeficit patients did not differ

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in other symptoms or history of the illness, however.

This first step in delineating the construct of the deficit syndrome suggested that clinicians can reliably categorize patients into deficit and nondeficit subgroups based on their general understanding of the concept. Since only global judgments of patients were made, however, it is unknown whether the specific symptoms used to define the construct were actually employed by the judges. In a followup study by the same research group using the Schedule for the Deficit Syndrome (SDS; Kirkpatrick et al. 1989a, 1989b), patients were assigned to deficit- and nondeficit-syndrome subgroups based on a clinical interview with the patient and information available from other sources familiar with the patient, including family members and clinicians. While reliable ratings of symptoms and deficit-syndrome classifications were obtained, the assessment procedure was nevertheless retrospective.

Retrospective research designs have inherent limitations, even when judgments are reliable, because of problems such as memory decay and recency effects, as well as halo effects (Campbell and Stanley 1963; Cook and Campbell 1979). Kay and Opler (1989) have commented that retrospective ratings are not adequate to demonstrate the temporal stability of deficit symptoms, an important characteristic of the deficit syndrome.

The present analysis was conducted to evaluate whether subtypes based on enduring-deficit symptoms, assessed longitudinally using standard psychiatric rating scales administered over a 1-year period, are related to other domains of functioning, such as symptomatology, social adjustment, and quality of life. To compare the validity of subtypes based on enduring deficit symptoms with that of other subtypes, the relationships between three other symptom-based subtypes and domains of functioning were also examined: enduring negative symptoms (based only on the Scale for the Assessment of Negative Symptoms [SANS; Andreasen 1982]), Andreasen and coworkers' (1990) negative-schizophrenia subtype (based on a cross-sectional assessment), and enduring positive symptoms (based on the thought disorder subscale of the BPRS).

A final goal of this study was to ascertain whether enduring negative or deficit symptoms are related to impairments in social skill. Deficits in social skill are prevalent in schizophrenia (Mueser et al., in press) and are correlated with negative but not positive symptoms (Jackson et al. 1989; Bellack et al. 1990b). Both negative symptoms and impairments in social skill are relatively stable over time in the absence of psychosocial interventions (Lewine 1990; Mueser et al., in press). Furthermore, there is an overlap in the definitions of some social skills (e.g., clear communication of affect) and negative symptoms (e.g., blunted affect and alogia). The relationship between social skills and enduring negative symptoms was examined to evaluate whether patients with chronic negative or deficit symptoms are also more likely to have deficits in social skill.

Method

Twenty-six patients were diagnosed as having schizophrenia according to DSM-III-R (American Psychiatric Association 1987); they had been admitted to Eastern Pennsylvania Psychiatric Institute (EPPI) for treatment of an acute symptom exacerbation. EPPI is a community psychiatric hospital with an average length of stay of 21 days. Most patients are referred from community mental health centers in the Philadelphia area and are discharged back to those centers for aftercare. Patients were recruited for the study if they were between the ages of 18 and 55 and had no indication of organic brain syndrome, mental retardation, or alcohol or drug dependence. Diagnoses were made on the basis of either the Structured Clinical Interview for DSM-III-R (SCID; Spitzer et al. 1988) or the Schedule for Affective Disorders and Schizophrenia (SADS; Endicott and Spitzer 1978) as well as a review of hospital records.

The 26 patients were drawn from a larger cohort of 58 schizophrenic patients who were assessed initially. Of the original cohort of 58 patients, 31 (53%) could be contacted and were willing to participate in the followup assessment 1 year later. Five patients were dropped from the current analysis because of missing data, resulting in a final sample size of 26 patients. Only 1 patient had experienced a recent relapse at the followup assessment (i.e., within the past month), this patient was assessed after his symptoms had been stabilized.

The demographic variables (gender, age, race, marital status, socioeconomic status, years of education) and clinical characteristics (subdiagnosis, age at first symptoms, number of past hospitalizations, prior time in hospital, prognosis) of the patients who were available for the followup assessment and those who were not available were compared using *t*-tests and chi-square tests. None of these tests was significant at the p < 0.05 significance level, indicating that patients who were available for the followup assessment were similar to other schizophrenic patients admitted to the hospital. The characteristics of the patient sample, including both the followed-up patients and the dropouts, are summarized in table 1.

Assessments were conducted to evaluate symptoms, quality of life, social adjustment, and social skill. The first assessment was conducted 2 to 3 weeks after admission to the hospital, when patients' major psychotic symptoms were under pharmacological control, as determined by the inpatient treatment team. The second assessment was conducted 1 year later.

Symptoms were measured by the BPRS and the SANS. Quality of life was measured with the Quality of Life Scale (QLS; Heinrichs et al. 1984). Social adjustment was assessed with the Social Adjustment Scale (SAS; Schooler et al. 1978). The work adjustment subscale of the SAS was not included in the statistical analysis because too few patients worked (n - 8).

One of two interviewers completed the diagnostic interview and the BPRS, and one of three independent

 Table 1. Demographic and historical variables for followed-up patients and dropouts

Variable	Followed-up $(n = 26)$	Dropouts $(n = 27)$
Sex (number)		
Male	14	16
Female	12	11
Race (number)		
Caucasian	14	16
Black	11	11
Other	1	0
Marital status (number)		
Single	21	20
Married/previously married	5	7
Diagnosis subtype (number)		
Paranoid	14	12
Nonparanoid	12	15
Age (mean)	31.77	32.81
Socioeconomic status (Hollingshead and Redlich 1958)	4.81	4.63
Education (years)	11.42	12.44
Age at first psychiatric symptoms	17.83	20.23
Number of prior hospitalizations	6.44	6.62
Prior time in hospital (months)	12.21	7.81
Prognosis (Strauss-Carpenter)	1.71	1.77

interviewers rated the patients on the SANS, QLS, and SAS. Interviewers were not blind to the order of assessment (initial or followup). The same interviewers did not necessarily rate the same patients for both assessments. All interviews were either videotaped or audiotaped and approximately 25 percent of the interviews, drawn randomly over the course of the project, were rated by an independent rater. Reliability was satisfactory on all subscales of the four measures. Intraclass correlation coefficients (ICCs), computed according to the Case 2 formula derived by Shrout and Fleiss (1979), ranged from 0.64 to 0.98. Prognosis was measured using the Strauss-Carpenter Prognostic Scale (Strauss and Carpenter 1974).

Social skills were assessed with a role-play test in which patients were engaged in brief simulated social encounters with a research assistant. The role-play test consisted of 2 practice situations and 12 test situations designed to assess social skill in initiating conversations, negative assertion (e.g., refusing unreasonable requests), and positive assertion (e.g., expressing positive feelings). Role plays were videotaped and four raters rated the appropriateness of four nonverbal skills: gaze, affect, meshing (smoothness of turn-taking and conversational pauses), and length of utterance. Two judges also rated the appropriateness of two verbal skills: praise/appreciation for the positive-assertion scenarios and request/compliance for the negativeassertion scenarios. Finally, overall social skill was rated by two independent raters.

Reliability of the social skill ratings was high, with ICCs (calculated using the same method as the interview measures) ranging from 0.77 to 0.92. All ratings of social skill were made by judges blind to the order of assessment (initial vs. followup), diagnosis, and interview-based ratings of symptoms, social adjustment, and quality of life. Further information on the social skill assessment procedures is contained in Bellack et al. (1990a) and Mueser et al. (1990a). For the statistical analysis of social skill, three measures of social skill were examined: nonverbal skill (sum of z scores for gaze, affect, meshing, and length), verbal skill (sum of z scores for praise/appreciation and request/compliance), and overall social skill.

To determine whether patients who were available for the followup assessment differed from the dropouts in symptomatology, quality of life, social adjustment, or social skill, we performed a series of multivariate analyses of variance (MANOVAs). Separate MANOVAs were performed for each instrument (SANS, BPRS, QLS, SAS, role-play test) with the subscales of the instrument as the dependent variables and followup status (followed up or dropped out) as the independent variable. For the role-play test, the dependent variables were nonverbal skill, verbal skill, and overall social skill. None of these MANOVAs was significant at the p < 0.05 level. These analyses suggest that the patients who were followed up were similar at the initial assessment to the dropouts in the clinical variables studied here.

Deficit Symptoms. Ratings from the SANS and QLS were used to measure deficit symptoms based on their similarity to symptoms of the deficit syndrome described by Carpenter et al. (1988; Kirkpatrick et al. 1989*a*). The SANS is a widely used instrument for the assessment of negative symptoms; it includes several items that closely resemble the Carpenter criteria. The QLS was developed by Carpenter and his colleagues as an instrument to assess deficit symptoms in schizophrenia (Heinrichs et al. 1984). The definitions of deficit symptoms according to the SDS and the corresponding scale items on the SANS and QLS used to measure each symptom in the present study are displayed in table 2.

The terminology used in this article requires brief explanation. We use the term "deficit symptoms" to refer to the specific symptoms from the QLS and SANS listed in table 2 that are similar to the symptoms described by Carpenter et al. for the deficit syndrome (Kirkpatrick et al. 1989a). The term "negative symptoms" is used to refer to symptoms assessed only on the SANS. Therefore, the definitions of deficit symptoms and negative symptoms overlap in the present study. The terms "enduring deficit symptoms" and "enduring negative symptoms" refer to deficit or negative symptoms (as defined above) that were present at the initial and 1-year followup assessments. The term "deficit syndrome" is reserved for discussion of research conducted by the Carpenter group using the SDS. Finally, the term "Andreasen negative schizophrenia" refers to patients subtyped cross-sectionally with the SANS at the initial assessment according to the criteria of Andreasen et al. (1990).

The definition of deficit symptoms employed here differs somewhat from that used by the Carpenter group. Carpenter et al. view deficit symptoms as a specific set of enduring negative symptoms that are not believed to be secondary to other factors, such as psychotic symptoms, anxiety, or depression. Because the data reported here were collected before the concept of the deficit syn-

drome was proposed (1984-87), no attempts were made to distinguish negative symptoms that were primary as opposed to secondary to other symptoms. For this reason, we have chosen to refer to deficit symptoms as those symptoms identified by Carpenter et al. as present in the deficit syndrome and negative symptoms as those symptoms assessed with the SANS. The failure to consider whether deficit or negative symptoms were primary or secondary in the present study may have resulted in subgroups of patients with enduring deficit or negative symptoms that differ from patients with Carpenter's deficit syndrome.

Results

Information on neuroleptic medication dosages was available for the first assessment when patients were receiving inpatient treatment at EPPI, but not for the followup assessment when patients were residing in the community. Since extrapyramidal side effects such as akinesia can resemble negative symptoms (Van Putten and May 1978), we computed Pearson correlations between neuroleptic dosage and deficit and negative symptoms at the first assessment. No correlations were significant at p <0.05, indicating neuroleptic dosage was not related to deficit or negative symptoms.

To examine the interrelationships between deficit and negative symptoms, and to determine their reliability over the 1-year period, Pearson correlations were computed (table 3). All of the deficit and negative symptoms were positively correlated at both assessments, and most of the correlations were statistically significant. The fact that the intercorrelations were not uniform in magnitude

Table 2. Carpenter deficit symptoms and rating-scale items used to measure enduring deficit symptoms

Carpenter deficit symptoms ¹	Rating scale definition
Diminished sense of purpose —The degree to which a person posits goals for his or her life, the extent to which the person falls to initiate or sustain goal- directed activity because of inadequate drive, and the amount of time passed in aimless activity.	Sense of purpose (QLS)—Degree to which the person has realistic, integrated goals for his/her life. Clarity and feasibility of both long- and short-term goals are included.
Curbing of interests —The degree to which the per- son is interested in the world around him or her, both ideas and events. Rating is based on both be- havior and thoughts. Either range or depth may be diminished.	Curiosity (QLS)—Lack of interest in one's surround- ings and failure to pursue understanding and knowl- edge.
Diminished emotional range —An inability to experi- ence pleasure or dysphoria. Rating is based on the intensity and range of a patient's subjective emo- tional experience and should be distinguished from a normal reticence with strangers.	Anhedonia (QLS)—Diminished capacity to experience pleasure that Is not the result of a clear and observ- able depressive syndrome. Apathy and withdrawal in the absence of clear signs of depression may be signs of diminished capacity for pleasure.
Restricted affect —A relatively expressionless face or an unchanging facial expression, reduced expres- sive gestures when emotional material is discussed, diminished vocal inflection.	Global rating of blunting (SANS)—Overall severity of affective flattening or blunting, e.g., unchanging or reduced facial expression, decreased spontaneous movement, lack of expressive gestures, poor eye con- tact, and lack of vocal inflections.
Poverty of speech —Number of words used and amount of information conveyed, including that in- formation which is volunteered that is not abso- lutely required by a literal answer to a question.	Global rating of alogia (SANS)—Impoverished think- ing, i.e., empty or slow thought processes, is inferred from a person's speech. Poverty of content of speech also implies impoverished thinking as do thought blocking and increased latency of response.
Diminished social drive —The degree to which the person seeks or wishes for social interaction. Rating should reflect the person's internal experience, statements, and behaviors. Social success is not considered.	Global rating of anhedonia-asociality (SANS)—Lack of involvement in social relationships, including impair- ment in ability to form and maintain peer relation- ships. Diminished capacity to feel intimacy and close- ness with others. Loss of interest and ability to expe- rience pleasure in social and popsocial activities

Note.-QLS = Quality of Life Scale; SANS = Scale for the Assessment of Negative Symptoms. ¹Definitions adapted from the Schedule for the Deficit Syndrome (Kirkpatrick et al. 1989a).

suggests that the results are not due to rater "halo" effects across the different deficit symptoms. Deficit and negative symptoms were also relatively stable over time, with correlations ranging from 0.19 to 0.55.

Enduring Deficit Symptoms. To classify a subgroup of patients with

enduring deficit symptoms, we examined three different levels of symptom severity for defining the presence of a deficit symptom: mild, moderate, and marked severity. Before we would classify a patient as having enduring deficit symptoms, at least two of the same deficit symptoms had to be present for a 1-year period (Kirkpatrick et al. 1989*a*). According to this classification, 93 percent of the sample had enduring deficit symptoms at the mild severity level, 73 percent had enduring deficit symptoms at the moderate level, and 44 percent had enduring deficit symptoms at the marked level. We chose to classify patients according

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Syr	b	ШО	-	2	ю	4	S	9	7	œ
	-	Sense of Purpose (QLS) ^{1,2}	0.25	0.24	0.19	0.55 ³	0.71 ^{4,5}	0.30	0.26	0.34 ³
	Ś	Curlosity (QLS) ^{1,2}	0.53 ⁶	0.19	0.14	0.45 ³	0.574	0.47°	0.67 ^{4,5}	0.574
	с,	Anhedonia (QLS) ^{1,2}	0.27	0.49 ⁶	0.52 ⁶	0.52 ⁶	0.32 ³	0.634	0.06	0.40 ³
2 eu	4.	Anhedonia-Asociality (SANS) ¹	0.55 ^e	0.66 ^{4.5}	0.68 ^{4.5}	0.37 ³	0.694.5	0.50 ⁶	0.29	0:30
niT	ĿĊ.	Avolition-Apathy (SANS)	0.33 ³	0.29	0.52 ⁶	0.29	0.34 ³	0.42 ³	0.47 ⁶	0.40 ³
	θ.	Blunting (SANS) ¹	0.38 ³	0.13	0.41 ³	0.34 ³	0.48 ⁶	0.50	0.644.5	0.574
	٦.	Alogia (SANS) ¹	0.27	0.11	0.23	0.11	0.43 ³	0.393	0.55	0.634.5
	ω	Attention (SANS)	0.42 ³	0.37 ³	0.33 ³	0.46 ⁶	0.36 ³	0.40 ³	0.45 ⁶	0.470
		QLS = Quality of Life Scale; SANS = Scale ection of scoring for the QLS Items was rev symptoms were used to measure the enduri 35. 301. 58 Bonferroni Bounds correction.	a for the As: lersed to me ing-deficit-ay	sessment of take it consist inptom subg	Negative Symi ent with the S roup.	ANS (i.e., hig	h scoras = w	orse symptom	3).	
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o the marked severity level because his criterion resulted in two groups of patients who were most divergent n their deficit symptoms.

etermine which deficit sympistinguished patients with endeficit symptoms and whether ere changes in deficit sympver time, repeated measures of s of variance (ANOVAs) were ed. These analyses are sumin table 4. The results indit patients with enduring defiptoms were significantly n all but one deficit sympogia. Two symptoms—sense ose (QLS) and anhedoniaty (SANS)- distinguished the g deficit symptom group e group without enduring symptoms at the p < 0.05oni Bounds significance level, d for multiple statistical tests. ral, the deficit symptoms were ly stable over the 1-year testeriod. There were no groupinteractions, which indicated nptom patterns were compatween the groups over time.

aphic and Clinical Correlates ring Deficit Symptoms. Parith enduring deficit sympere compared to patients these symptoms on democharacteristics, history of and diagnostic subtype id-nonparanoid) using t-tests -square tests. There was a or patients with enduring defiptoms to have a worse progn the Strauss-Carpenter Progcale (t [23] = 1.73, p <lone of the other clinical or aphic variables were signifilifferent between the groups.

Patients with and without enduring deficit symptoms were compared on other symptoms, social adjustment, quality of life, and social skill

Table 4. Mean deficit symptom ratings at two assessments for enduring deficit-symptom (n = 12) and nondeficit (n = 14) groups

Deficit	Endi dei sym	uring iicit ptom	Nond sym	leficit ptom	Group effect	Time effect	
symptom	Time 1	Time 2	Time 1	Time 2	F statistic ¹	F statistic ¹	
Sense of Purpose (QLS) ²	0.50	0.83	2.50	3.00	40.69 ^{3,4}	1.01	
Curiosity (QLS) ²	0.75	1.67	2.07	3.07	14.66 ³	6.55 ⁵	
Anhedonia (QLS) ²	2.67	2.92	3.43	4.57	4.55 ⁵	4.30 ⁵	
Anhedonia-Asociality (SANS) ⁶	4.09	3.67	2.36	2.07	20.95 ^{3,4}	1.10	
Blunting (SANS) ⁶	2.58	1.83	1.43	0.86	4.15 ⁵	4.12	
Alogia ⁶	1.92	1.50	0.86	0.71	3.47	0.92	

Note.-QLS = Quality of Life Scale; SANS = Scale for the Assessment of Negative Symptoms.

¹Based on repeated measures analyses of variances. No group x time interactions were significant.

²High numbers denote less severe symptomatology.

 $^{3}p < 0.001.$

⁴p < 0.05 Bonferroni Bounds correction.

⁵p < 0.05.

⁶High numbers denote more severe symptomatology.

by performing repeated-measures ANOVAs. Highly significant group effects were found for several measures, indicating that enduring deficit symptom patients were more symptomatic and less socially adjusted than nondeficit patients at both assessments. Deficit symptom patients had worse social adjustment and quality of life on seven of the eight subscales on the SAS and OLS. These patients also had worse thought disorder scores on the BPRS and attention and avolition-apathy scores on the SANS than did the nondeficit patients. Most of these effects were significant at the p <0.05 Bonferroni Bounds corrected significance level. Social-skill impairments were not related to the enduring deficit symptom subtype. In contrast to most of the deficit symptoms (see table 4), nondeficit symptoms and social adjustment tended to improve over the 1-year period. No group-by-time interactions were significant, which suggests that deficit and nondeficit patients improved at similar rates over time. These analyses are summarized in table 5.

Enduring Negative Symptom Subtypes. Subgroups of patients with enduring deficit symptoms were classified according to both the QLS and the SANS. Because the SANS is a widely used instrument for the assessment of negative symptoms and the QLS is not, the question arose as to whether the SANS alone could be used to identify a similar group of patients with enduring negative symptoms. We used the five SANS global ratings (blunting, alogia, anhedonia-asociality, avolitionapathy, and attention) to subtype patients into enduring negative and nonnegative subgroups. When the rule was applied that at least two of the same global SANS symptoms must be present at a marked level of severity for the 1-year period, only

19 percent of the patients were in the enduring negative symptom group. When only one SANS global score had to be elevated over the year to classify a patient as having enduring negative symptoms, 34 percent of the patients were in the enduring negative symptom group. Subsequent analyses were performed using the latter criterion for classifying patients with enduring negative symptoms.

To determine which SANS subscales distinguished the patients with enduring negative symptoms from those without enduring negative symptoms, repeated measures ANOVAs were computed comparing the two groups on each of the subscales. Only one symptom did not differ between the two groups at the p < 0.05 Bonferroni Bounds corrected significance level: alogia (F[1,24] = 3.34, NS). Patients with enduring negative symptoms had consistently more severe ratings on anhedonia-asociality (F = 46.28,

Table 5.	Mean symptom,	social-adjustment	, and social-skill	ratings	at two assessments i	foi
enduring	deficit symptom	(n = 12) and nonc	leficit symptom	(n = 14)) groups	

	Endurin symp	g deficit itoms	Nond symp	leficit otoms	Group	Time effect
Rating scale	Time 1	Time 2	Time 1	Time 2	F statistic ¹	F statistic ¹
Brief Psychiatric Rating Scale ²						
Anxiety/Depression	3.98	4.94	3.86	4.37	0.07	0.17
Hostility	8.41	6.25	7.57	5.93	0.36	8.53 ³
Activation	7.54	6.00	6.00	5.00	2.59	4.48 ⁴
Thought Disorder	15.17	13.00	9.64	7.64	13.76 ^{5,6}	3.33
Anergia	9.44	7.33	7.43	7.07	0.98	1.99
Schedule for Assessment of Negative Symptoms ^{2,7}						
Attention	2.50	1.58	1.07	0.21	16.91 ^{5,6}	10.90 ³
Avolition-Apathy	3.50	2.58	2.00	1.29	14.15 ^{5,6}	6.23 ⁴
Quality of Life Scale ^{7,8}						
Interpersonal Relations	9.39	15.75	19.75	29.73	18.13 ^{5,6}	18.78 ^{5,6}
Role Functioning	1.67	2.67	3.86	6.14	5.11 ⁴	3.03
Intrapsychic Foundations	12.91	18.75	22.24	28.67	26.57 ^{5,8}	15.50 ^{5,6}
Commonplace Objects/Activities	5.00	5.67	6.36	7.64	6.324	8.55 ³
Social Adjustment Scale ²						
Household	5.78	3.89	5.00	3.46	4.954	52.75 ^{6,6}
Social/Leisure	6.58	6.00	5.71	4.43	18.24 ^{5,6}	19.41 ^{5,8}
External Family	6.29	4.71	4.75	3.83	8.62 ³	14.10 ^{5,6}
General	6.50	5.08	5.64	3.86	19.56 ^{5,6}	60.25 ^{5,6}
Role-play test ⁸						
Overall social skill	2.30	2.56	2.60	2.88	1.59	2.76
Nonverbal social skill	- 1.06	- 0.24	1.13	0.47	2.21	0.01
Verbal social skill	0.17	- 0.06	0.03	0.06	0.00	0.05

¹Based on repeated measures ANOVAs; no group x time interactions were significant.

²High numbers denote worse symptoms and social adjustment.

⁴p <0.05.

⁵p <0.001.

⁶p < 0.05 Bonferroni Bounds correction.

⁷Individual items used in the enduring deficit symptom criteria were not included in these analyses.

⁸High numbers denote better quality of life and social skill.

p < 0.001), avolition-apathy (F = 13.04, p = 0.001), attention (F = 12.76, p = 0.002), and blunting (F = 8.59, p = 0.007). Thus, patients in the enduring negative symptoms group differed markedly from other patients on most of the SANS subscales.

There was a significant overlap between the enduring negative symptom subtype and the enduring deficit symptom subtype (table 6). The enduring negative symptom subtype was slightly more restrictive than the enduring deficit symptom subtype, with all of the patients classified in the former group also classified in the latter group. Repeated measures ANOVAs comparing the symptoms, quality of life, social adjustment, and social skill of patients with and without enduring negative symptoms yielded results similar to analyses of the enduring deficit symptoms

 $^{^{3}}p < 0.01.$

Table 6. Chi-square tests between enduring deficit symptom subtypes, enduring negative symptom subtypes, Andreasen subtypes, and positive-symptom subtypes



Table 6. Chi-square tests between enduring deficit symptom subtypes, enduring negative symptom subtypes, Andreasen subtypes, and positive-symptom subtypes—Continued



Note.--NS = not significant.

¹p < 0.05 Bonferroni Bounds correction.

subtype, with prominent differences in social adjustment, quality of life, and thought disorder on the BPRS (table 7). Patients with enduring negative symptoms, however, scored worse on overall social skill and nonverbal skill than did nonnegative patients (table 7), whereas skills did not differ between patients with and without enduring deficit symptoms (table 5). Subtypes of patients based on the presence of two enduring negative symptoms at a moderate level of severity yielded similar results to subtypes based on one enduring negative symptom at a marked level of severity.

Differences between patients with and without enduring negative symptoms in clinical or demographic variables were explored by computing *t*-tests and chi-square tests. Like the patients with enduring deficit symptoms, patients with enduring negative symptoms had a worse prognosis on the Strauss-Carpenter Prognostic Scale (t[23] = 3.39, p = 0.003) but did not differ on any other variables.

Andreasen Negative Symptom Subtypes. The clinical use of subtypes based on enduring deficit or negative symptoms was compared with a cross-sectional subtyping method, Andreasen's criteria for the assessment of negative schizophrenia. We first examined the distribution of patients with negative, mixed, and positive schizophrenia according to the criteria of Andreasen and Olsen (1982). These criteria specify that negative schizophrenia requires the presence of at least two SANS ratings of at least marked severity and the absence of any positive symptoms at the same severity level. Positive schizophrenia requires the presence of at least one positive symptom of at least marked severity, in the absence of any negative symptoms at the same level of severity. Schizophrenic patients who fail to meet criteria for either negative or positive schizophrenia are classified as mixed.

According to these criteria, the majority of patients were classified as having mixed schizophrenia, with relatively few patients classified as having either negative or positive schizophrenia. Similarly, Andreasen et al. (1990) reported that 76 percent of a sample of 110 patients were classified as having mixed schizo-

Table 7. Mean symptom, social adjustment, and social skill ratings at two assessments for enduring negative symptom (n = 9) and nonnegative symptom (n = 17) groups

	End	uring ative	Nonne	egative	Group	
Rating scale	Time 1	Time 2	Time 1	Time 2	F statistic ¹	
Brief Psychiatric Rating Scale ²						
Anxiety/Depression	8.67	11.78	10.53	9.53	0.02	
Hostility	8.44	6.89	7.71	5.65	0.96	
Activation	8.06	6.22	6.00	5.06	3.98	
Thought Disorder	15.33	13.56	10.53	8.29	9.52 ³	
Anergia	9.48	7.00	7.77	7.29	0.34	
Quality of Life Scale ⁴						
Interpersonal Relations	6.30	12.56	19.56	29.12	32.99 ^{5,8}	
Role Functioning	0.89	3.22	3.88	5.24	3.42	
Intrapsychic Foundations	11.67	17.89	21.26	27.37	21.30 ^{5,6}	
Commonplace Objects/Activities	4.89	5.44	6.18	7.41	5.30 ⁷	
Social Adjustment Scale ²						
Household	6.00	4.14	5.00	3.40	11.86 ³	
Social/Leisure	6.78	6.00	5.77	4.71	13.01 ^{5,6}	
External Family	6.40	5.00	4.93	3.86	8.30 ³	
General	6.67	5.22	5.71	4.00	19.55 ^{5,6}	
Role-play test ³						
Overall social skill	2.07	2.47	2.66	2.87	4.17 ⁷	
Nonverbal social skill	- 2.14	- 0.50	1.28	0.47	5.22 ⁷	
Verbal social skill	- 0.05	- 0.44	0.16	0.23	0.64	

¹Based on repeated measures ANOVAs. No group x time interactions were significant. See table 5 for time effects.

²High numbers denote worse symptoms and social adjustment.

⁴High numbers denote better quality of life and social skill.

⁶p < 0.001.

^ep < 0.05 Bonferroni Bounds correction.

⁷ρ < 0.05.

phrenia according to the criteria of Andreasen and Olsen (1982).

Andreasen et al. (1990) proposed alternative criteria for the classification of negative schizophrenia. These criteria specify that at least two negative symptoms on the SANS must be present to at least a marked degree irrespective of the presence of positive symptoms. When we classified our subjects according to these more recent criteria of Andreasen et al. (1990), 38 percent met criteria for negative schizophrenia. Statistical analyses were performed on the subtypes based on the more recent criteria.

The negative schizophrenia subtype was significantly related to the enduring negative symptom subtype but not to the enduring deficit symptom subtype, although the trend was in the expected direction (table 6). To compare the negative and nonnegative schizophrenia groups on the clinical measures, repeated-measures ANOVAs were performed as described above. These analyses are summarized in table 8. This table reveals that the group effects, which compare negative and nonnegative groups, are fewer and weaker than the group effects for either the enduring deficit symptom (table 5) or enduring negative symptom (table 7) subgroup analyses. In addition, none of these group effects was significant at the Bonferroni Bounds correction level for multiple statistical tests. The significant group-by-time interactions reflect marked differences at the first assessment between the negative and nonnegative groups that were no longer present at the 1-year followup.

³*p* < 0.01.

Table 8. Mean symptom, social adjustment, and social skill ratings at two assessments for
Andreasen negative symptom (n = 10) and nonnegative symptom (n = 16) groupsTop
Top
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	Andreasen negative		Nonne	gative	Group	Group × time	
Rating scale	Time 1	Time 2	Time 1	Time 2	F statistic ^{1,2}	F statistic ^{1,2}	
Brief Psychlatric Rating Scale ³							
Anxiety/Depression	7.70	9.60	11.25	10.75	3.05	1.33	
Hostility	7.80	5.80	8.06	6.08	0.12	0.02	
Activation	7.05	5.70	6.50	5.31	0.31	0.02	
Thought Disorder	12.00	9.80	12.31	10.31	0.05	0.01	
Anergia	11.03	7.30	6.69	7.13	4.16	7.61⁴	
Social Adjustment Scale ³						1	
Household	6.00	3.63	4.93	3.64	3.39	6.45 ⁴	
Social/Leisure	6.60	5.40	5.81	5.00	2.59	0.74	
Work	7.00	5.50	5.75	4.33	4.05	0.26	
Extended Family	6.33	4.17	4.85	4.15	2.33	6.43 ⁴	
General	6.60	4.60	5.69	4.31	3.97	2.24	
Quality of Life Scale⁵							
Interpersonal Relations	9.71	20.74	18.25	25.04	3.03	1.14	
Role Functioning	0.60	4.70	4.25	4.44	1.52	4.354	
Intrapsychic Foundations	11.20	21.53	22.15	25.69	10.70 ⁸	5.24 ⁴	
Commonplace Objects/Activities	4.50	6.00	6.50	7.19	5.324	1.36	
Role-play test ⁵							
Overall social skill	1.89	2.44	2.81	2.91	10.99 ⁶	1.89	
Nonverbal social skill	- 2.26	1.09	- 0.69	0.32	4.51 ⁴	2.81	
Verbal social skill	- 0.59	0.28	0.34	0.09	0.56	1.92	

¹Based on repeated measures ANOVAs; see table 5 for time effects.

²No differences were significant at Bonferroni Bounds correction ($\rho < 0.05$).

³High numbers denote worse symptoms and social adjustment.

⁴ρ < 0.05.

⁵High numbers denote better quality of life and social skill. ${}^{6}p < 0.01$.

p < 0.01.

Enduring Positive Symptom Subtypes. The subgroups of patients with enduring deficit and negative symptoms both had significantly higher levels of thought disorder on that BPRS subscale. To evaluate whether stable positive symptoms are related to negative symptoms, other symptoms, and social adjustment, a subgroup of patients with enduring positive symptoms was formed through a method similar to that used to derive the enduring negative symptom subgroup. The four symptoms on the BPRS that comprise the thought disorder subscale were used to derive an enduring positive symptom subgroup: hallucinations, delusions, grandiosity, and conceptual disorganization. When we used the criterion that at least one positive symptom must be present at a severity level of at least moderate at both assessments, we found that 66 percent of the patients had enduring positive symptoms.

Repeated-measures ANOVAs were performed on the clinical variables contrasting the enduring positive and nonpositive subgroups (table 9). Patients with enduring positive symptoms had worse anxiety-depression and hostility scores on the BPRS but did not differ on any negative symptoms, measures of quality of life, or social skill from patients without enduring positive symptoms.

There were significant group-bytime interactions on the interpersonal R relations and intrapsychic foundations subscales of the QLS; both of these interactions indicated that patients with enduring positive symptoms improved at a slower rate than did patients without these symptoms.

Table 9. Mean symptom, social adjustment, and social skill ratings at two assessments for enduring positive symptom (n = 14) and nonpositive symptom (n = 12) groups

	positive symptoms		Nonpo symp	ositive toms	Group effect	Group × time
Rating scale	Time 1	Time 2	Time 1	Time 2	F statistic ^{1,2}	F statistic ^{1,2}
Brief Psychiatric Rating Scale ³						
Anxiety/Depression	10.50	12.57	9.17	7.67	6.63 ⁴	3.33
Hostility	9.00	7.36	6.75	4.58	8.90 ⁵	0.16
Activation	7.18	6.43	6.17	4.33	4.094	0.83
Anergia	7.74	6.71	9.08	7.75	1.08	0.03
Schedule for Assessment of Negative Symptoms ³						
Blunting	1.71	1.14	2.25	1.50	0.64	0.08
Alogia	1.14	1.21	1.58	0.92	0.02	1.70
Anhedonia-Asociality	3.21	3.21	3.08	2.33	1.09	1.32
Avolition-Apathy	2.93	2.43	2.42	1.25	3.76	1.06
Attention	1.57	1.00	1.92	0.67	0.00	1.63
Quality of Life Scale ⁶						
Interpersonal Relations	14.84	19.00	15.12	28.50	1.76	6.924
Role Functioning	3.14	3.71	2.50	5.50	0.17	1.59
Intrapsychic Foundations	17.64	21.00	18.28	27.69	1.98	4.214
Commonplace Objects/Activities	5.36	6.36	6.17	7.17	1.24	0.00
Social Adjustment Scale ³						
Household	5.42	4.08	5.20	3.10	5.054	2.97
Social/Leisure	6.14	5.57	6.08	4.67	1.74	4.21 ⁴
External Family	5.60	4.50	5.00	3.78	2.06	0.04
General	6.14	4.93	5.92	3.83	5.29 ⁴	5.03 ⁴
Role-play test ⁶						
Overall social skill	2.63	2.71	2.23	2.76	0.49	2.06
Nonverbal social skill	0.92	0.05	- 0.99	0.24	0.72	2.84
Verbal social skill	0.25	- 0.52	- 0.13	0.67	0.58	3.80

¹Based on repeated measures ANOVAs; see tables 4 and 5 for time effects.

²No differences were significant at Bonferronl Bounds correction ($\rho < 0.05$).

³High numbers denote worse symptoms and social adjustment.

⁶High numbers denote better quality of life and social skill.

Neither of these interactions was significant at the Bonferroni Bounds significance level, however. Chisquare tests indicated that the enduring positive symptom subtype was marginally related to the enduring deficit symptom subtype, but not to the other subtypes (table 6). Subtypes of patients based on the presence of two enduring positive symptoms at a mild level of severity yielded similar results to subtypes based on one enduring positive symptom at a moderate level of severity.

It may appear puzzling that

subtypes based on enduring deficit or negative symptoms had worse thought disorder scores, but the subtype based on enduring positive symptoms did not have worse negative or deficit symptoms. This finding may reflect the fact that positive symptoms were less stable over the

⁴ρ < 0.05. ⁵ρ < 0.01.

1-year period than were deficit or negative symptoms; the correlations for positive symptoms between initial and followup assessments were significant for grandiosity (r = 0.46, p< 0.008) and hallucinations (r =0.50, p < 0.004) but not for conceptual disorganization (r = -0.01, NS) and delusions (r = 0.18, NS). These correlations are generally lower than the correlations over time for the deficit or negative symptoms (table 3).

Discussion

The present investigation was conducted to examine whether subtypes of schizophrenia based on enduring deficit or negative symptoms over a 1-year period distinguished clinically meaningful domains of functioning, social adjustment, quality of life, and social skill. This research was stimulated by Carpenter et al. (1988), who proposed the concept of the "deficit syndrome" as a subtype of schizophrenia based on the presence of enduring negative symptoms that are not secondary to positive symptoms, negative affective states, or medication side effects. Previous research on the deficit syndrome has classified patients into deficit syndrome and nondeficit groups according to retrospective clinical judgments, which are subject to rater bias and memory decay. The use of two independent assessments conducted over a 1-year period provides a more objective measure of the presence of deficit or negative symptoms at both time points, although fluctuations in these symptoms between the assessments are nevertheless possible (as are any such fluctuations between any two time points). The enduring deficit and negative symptom subtypes derived here should not be interpreted

as equivalent to the deficit syndrome defined by Carpenter et al. for two reasons. First, the items from the SANS and QLS we chose to use were similar, but not identical, to the symptoms specified on the SDS. Second, no attempt was made to judge whether negative or deficit symptoms were secondary to positive symptoms or mood. Our investigation, however, represents a step toward further understanding of the clinical validity of subtypes based on enduring deficit or negative symptoms in schizophrenia.

The most striking finding was that patients with enduring deficit symptoms (based on the SANS and QLS) over the 1-year assessment period tended to have much worse social adjustment, guality of life, and thought disorder scores than did patients without enduring deficit symptoms (table 5). When the SANS alone was used to classify patients with enduring negative symptoms, a similar pattern of results was obtained in which patients with enduring negative symptoms were more impaired in a range of domains of functioning (table 7). Furthermore, most of the group differences based on subtypes of enduring deficit or negative symptoms were significant at the Bonferroni Bounds significance level of p < 0.05 corrected for multiple statistical tests, suggesting that these effects are quite robust. In contrast to subtypes based on enduring deficit or negative symptoms, subtypes based on a single assessment of negative symptoms according to Andreasen and co-workers' (1990) criteria for negative schizophrenia were not related to different domains of functioning at the Bonferroni Bounds corrected level (table 8), nor were subtypes based on enduring positive symptoms (table 9). The results suggest that approaches

to assessing negative or deficit concepts that use a longitudinal repeated-measures evaluation result in more powerful markers for a clinically valid syndrome than does a single cross-sectional evaluation.

There was an overlap between subtypes of negative schizophrenia based on Andreasen's criteria and subtypes of patients with enduring deficit or negative symptoms, although the overlap achieved statistical significance for only the negative schizophrenia and enduring negative symptom subtypes (see table 6). The weak relationship between Andreasen's subtype and the enduring deficit and enduring negative subtypes suggests that patients with high but transient levels of negative symptoms may have been included in the Andreasen negative schizophrenia group, and that these patients subsequently improved. This conjecture is supported by the fact that patients in Andreasen's negative symptom subgroup tended to improve more than did the nonnegative patients in several areas of functioning, as indicated by the significant group-by-time interactions (table 8).

Negative symptoms measured with the SANS and "deficit" symptoms selected from the QLS and SANS based on their similarities to symptoms described by Carpenter et al. for the deficit syndrome (Kirkpatrick et al. 1989a) were all positively intercorrelated at both assessments and showed relatively high reliabilities over the 1-year assessment period, although not all the correlations were statistically significant (table 3). These symptoms appear to reflect a single dimension of negative symptoms, which is related to the severity of impairment in other areas of functioning. Different criteria for subtyping patients according to enduring negative or deficit symptoms resulted

2022

in different subgroups of patients, but the subtypes bore similar relationships to other clinical variables. These data suggest that the severity of enduring negative symptoms varies along a continuum and may not reflect a distinct subtype.

Patients with enduring deficit or negative symptoms differed most strongly from others in anhedoniaasociality on the SANS and anhedonia on the QLS, which were strongly correlated with each other at both assessments. Kirkpatrick and Buchanan (1990) recently reported that deficit-syndrome patients had significantly higher scores on social and physical anhedonia on the Chapman scales (Chapman et al. 1976). A large body of research has implicated anhedonia, "hypohedonia," and asociality as important prognostic indicators in schizophrenia. Meehl (1962, 1989) has hypothesized that anhedonia or hypohedonia increases the likelihood that a genetically vulnerable person (i.e., a person with the "schizotype") will develop schizophrenia. Premorbid asociality is predictive of the course of schizophrenia (Zigler and Glick 1986), and it is correlated with the severity of negative symptoms (Dupue and Dubicki 1974; Andreasen and Olsen 1982; Pogue-Geile and Harrow 1984; Mueser et al. 1990b). Furthermore, anhedonia and asociality in schizophrenia are also correlated with current functioning and are predictive of outcome (Harrow et al. 1977; Strauss and Carpenter 1977). These studies suggest that severe enduring negative symptoms in schizophrenia may be preceded by poor premorbid social adjustment and anhedonia, which reflect a basic neural integrative defect (Meehl 1989) that is associated with the severity of the illness.

An intriguing relationship was found between enduring negative

symptoms and positive symptoms. Subgroups of patients with enduring deficit or negative symptoms had worse thought disorder scores on the BPRS, suggesting that some deficit or negative symptoms may have been secondary to positive symptoms. Subgroups of patients with enduring positive symptoms (based on the symptoms in the thought disorder subscale), however, did not have worse negative symptoms than did patients without enduring positive symptoms. This may be due, in part, to the greater reliability of negative symptoms compared with that of positive symptoms over time. Thus, chronic negative symptoms were predictive of positive symptoms, but chronic positive symptoms were not predictive of negative symptoms.

The asymmetrical relationship between negative and positive symptoms raises the question of whether negative symptoms could precede or cause positive symptoms. This possibility is compatible with Weinberger's (1987) neurodevelopmental model of schizophrenia. According to this model, early lesions of the prefrontal cortex, particularly the dorsolateral prefrontal cortex (DLPFC), may result in subtle cognitive, motivational, and social impairments like those present in persons with premorbid asociality. Diminished dopamine activity in the mesocortical system, which projects from the midbrain to the prefrontal cortex, may decrease inhibitory control over subcortical areas, resulting in dopamine hyperactivity in the mesolimbic system. This hyperactivity, secondary to a lesion in the DLPFC, could lead to the development of psychotic symptoms.

Chronically suboptimal physiological activation of the DLPFC, indicated in some patients by decreased cerebral blood flow to this area during mental testing (Berman et al. 1986; Weinberger et al. 1986), would be associated with enduring negative symptoms and an increased vulnerability to positive symptoms as well. Additional longitudinal research employing path analysis or structural equation modeling on larger sample sizes is needed to test the hypothesis that negative symptoms can worsen positive symptoms. We are currently conducting such a study.

The present study did not find differences between patients with enduring deficit symptoms and those with nondeficit symptoms in subdiagnosis or history of illness, a result similar to Carpenter and associates' (1988) finding of patients with the deficit syndrome. In addition, we found that enduring deficit or negative symptoms were associated with worse scores on the Strauss-Carpenter Prognostic Scale, which is also similar to Carpenter and associates' finding with the deficit syndrome. On the other hand, Carpenter et al. found that patients with the deficit syndrome were more likely to be male and to have higher levels of anergia on the BPRS, but did not have higher levels of thought disorder, in contrast to the patients with enduring deficit or negative symptoms studied here. We were surprised to find that anergia was not higher in the enduring deficit or negative symptom patients. The failure of Carpenter et al. to find greater thought disorder among deficitsyndrome patients may reflect their attempts to include only patients with primary-deficit symptoms. This and the other differences between the two studies cannot be explained without additional research, since the two studies used different rating instruments and procedures for assessing their patients.

A consistent pattern of impairment in social skill was not evident in the different subtypes of schizophrenia examined. Overall social skill and nonverbal skill tended to be worse in patients with enduring negative symptoms and Andreasen's negative schizophrenia, but not in patients with enduring deficit symptoms or enduring positive symptoms. In no case was social skill related to any of the subtypes at the Bonferroni Bounds corrected p < 0.05 significance level. Some relationship between social skill and negative symptoms was expected because of the overlap in the constructs. It appears, however, that patients with enduring negative or deficit symptoms do not necessarily have worse social skills than other schizophrenic patients. The findings suggest that the impoverished social functioning of patients with enduring deficit or negative symptoms is not solely attributable to impairments in social skill. Whether social-skills training can improve the social functioning of patients with enduring deficit or negative symptoms remains to be determined.

In summary, the present study suggests that subtypes of schizophrenia based on enduring negative or deficit symptoms yield clinically valid differences in other domains of functioning. In comparison, subtypes based on a cross-sectional assessment of negative symptoms or on enduring positive symptoms may not yield clinically meaningful results. While the sample size studied here was not large, a pattern of results emerged that supported the importance of enduring negative symptoms and raised testable hypotheses for future research.

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Announcement

Nominations are being solicited for the Seventh Annual Arthur P. Noyes Award in Schizophrenia under the auspices of the Pennsylvania Office of Mental Health and the Commonwealth of Pennsylvania.

The award includes an honorarium of \$3,000 that will be presented at the Seventh Annual Conference on Schizophrenia in Philadelphia, Pennsylvania, March 12–13, 1992. The recipient will be asked to make a presentation relevant to his or her contributions to the understanding and treatment of schizophrenia.

Eligibility is unrestricted with respect to age, gender, discipline, and geographic location. Nominations should be accompanied by a letter detailing the reasons for recommending the nominee, and one sample of the nominee's published work.

Nominations should be sent to Paul J. Fink, M.D., Medical Director, Philadelphia Psychiatric Center, 4200 Monument Road, Philadelphia, Pennsylvania 19131. The deadline for nominations is December 3, 1991.

For further information about the award, please contact:

Edward Volkman, M.D. Coordinator for the Noyes Award Philadelphia Psychiatric Center 4200 Monument Road Philadelphia, PA 19131 Telephone: 215-456-8925