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Neurological soft signs in schizophrenia: assessment and correlates

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Abstract A German version of the Neurological Evaluation Scale (NES) was administered to 143 schizophrenic patients, 45 of them being severly chronic and disabled. Seventy-eight alcohol-dependent inpatients and 57 healthy volunteers were tested as control groups. Neurological soft signs (NSS) were rated with convincing agreement. Schizophrenic patients are more impaired on all scales than healthy controls. The chronic, severly disabled schizophrenic patients are more impaired compared with the main group of schizophrenic patients and both control groups. A significant difference between the main group of schizophrenic patients and alcohol-dependent patients was only found for the subscale "Motor Coordination". Compared with healthy controls the alcohol-dependent patients show a higher NES total score. The NES total score was related to the relative width of the third ventricle. Total score and subscales were correlated consistently with the level of cognitive functioning as measured by the Raven Standard Progressive Matrices and various neuropsychological tests presumably sensitive to dysfunctions of the prefrontal cortex. The NSS were related to positive as well as to negative symptoms, the correlations with negative symptoms being confined to items of "Cognitive Disorganization". This close association of psychomotor and cognitive dysfunctions may be seen as related to the frequently discussed dysfunctions of the prefrontal cortex or the neurointegrative deficit postulated by Meehl.

Key words Schizophrenia · Alcohol-dependent patients · Neurological soft signs · Neurological Evaluation Scale · Psychomotor impairment · Cognitive impairment

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Introduction

There is growing evidence for neurological abnormalities in schizophrenia. The availability of increasingly sophisticated techniques of structural and functional brain imaging stimulated research on neurological deviance in schizophrenia. On a clinical level neurological soft signs (NSS) have repeatedly been found to be more prevalent in schizophrenic patients than in various control groups (cf. Heinrichs and Buchanan 1988). The NSS are deviant performances on tests identical to or akin to items of a traditional neurological examiniation which do not point to focal neurological impairments and are viewed as indicators of a more generalized brain dysfunction. Meehl (1990) considers them candidates for identifying a genetically determined group of schizophrenics, whereas others (e.g. Shaffer et al. 1983) discuss them as indicators of an increased vulnerability to psychiatric disorders.

Without exception, studies comparing schizophrenic patients with normal controls find a higher prevalence of NSS, as well as of other neurological abnormalities, in schizophrenics (e.g. Buchanan and Heinrichs 1989; Gureje 1988; Quitkin et al. 1976; Rossi et al. 1990). Increased rates of NSS have also been reported for patients with other psychiatric diagnoses, i.e. affective, personality, neurotic and substance abuse disorders (e.g. Bihari et al. 1991; Gureje 1988; Lewis et al. 1986; Manschreck and Ames 1984; Nasrallah et al. 1983; Nickoloff et al. 1991; Quitkin et al. 1976; Walker and Shaye 1982; Woods et al. 1986), but usually schizophrenic patients are found to have the more elevated scores, although the differences may not turn out to be significant.

Besides the consistent finding of a higher prevalence of neurological soft signs in schizophrenia, reports of higher rates of NSS and other neurological abnormalities also in children at risk for schizophrenia and other close relatives of schizophrenic patients stress the possible relevance of NSS for understanding the basis of schizophrenic disorders (Fish et al. 1992; Kinney et al. 1986; Kinney et al. 1991; Marcus et al. 1985; Rossi et al. 1990).

As can be expected, NSS are not distributed evenly among schizophrenic patients. They seem to be most prominent in patients with a history of developmental abnormalities (Crow et al. 1994; Kolakowska et al. 1985), with poor premorbid adjustment (Quitkin et al. 1976; Wegner et al. 1985), with cognitive disturbances (King et al. 1991; Tucker et al. 1975), with a deficit state and a chronic course of the illness (Buchanan et al. 1990; Torrey 1980) and with a poor treatment response (Johnstone et al. 1990; Pollock et al. 1986; Schröder et al. 1992a).

Unfortunately, studies on NSS differ considerably in the selection of items as well as in the instructions to the patients and the clinical raters. The most comprehensive and best-documented scale has been developed by Buchanan and Heinrichs (1989). These authors compiled 26 items from previous studies on soft signs to the Neurological Evaluation Scale (NES). According to conceptual considerations of function and neuroanatomy, the items were grouped into three functional areas of interest: "Sensory Integration", "Motor Coordination" and "Sequencing of Complex Motor Acts". Besides these three, a fourth subscale "Others", and the sum of all items, the NES total score, are recommended as NSS indexes.

One purpose of the present study was to evaluate a German version of the NES. The study is characterized by the following aspects: (a) the use of a comprehensive instrument for the assessment of neurological soft signs; (b) the assessment of two control groups, one consisting of hospitalized, non-psychotic psychiatric patients and one of healthy volunteers, to address the question of specificity of NSS; and (c) the inclusion of a group of severely disabled, chronic schizophrenic patients to assess the influence of chronicity on NSS. The clinical significance of neurological abnormalities was examined by looking for correlations between NSS and ratings of psychopathology, particularly negative symptoms, neuropsychological test performance and morphological deviances in computed tomography (CT) brain scans.

Subjects and methods

A total of 98 schizophrenic patients (Schiz I) from the inpatient units of two German psychiatric state hospitals[1] participated in the study. They were diagnosed according to DSM-III-R criteria based on the Present State Examination (PSE; Wing et al. 1973). In order to reduce the effects of chronicity and long institutionalization, patients were excluded from the study if they were older than 40 years, if they had been hospitalized for more than 12 months within the past 2 years, if they had not been engaged in some kind of occupational or occupation-like activity during the previous year and/or if they could not name any person with whom they have regular contact. Patients with a diagnosed neurological disorder or with mental retardation were also excluded. The mean age of the schizophrenic patients was 27.4 years (SD 4.5 years); 63% were male. Their average age at first admission was 22.7 years (SD ± 4.5 years) and they had been ill for an average of 4.8 years (SD ± 4.3 years) with a mean duration of previous hospitalizations of 8.2 months (SD ± 11.3 months). At the time of testing all except 2 patients received neuroleptic medication. They average dosage in chlorpromazine equivalence was 474 mg/day (SD = ± 509 mg/day); 30 patients were on clozapine; 10 patients fulfilled criteria for tardive dyskinesia according to criteria of Schooler and Kane (1982). Patients were tested at a time when acute psychotic symptoms had been reduced markedly and when discharge was considered.

The second sample of schizophrenic patients (Schiz II) consisted of 45 severely chronic and disabled inpatients who were referred to a behaviour therapy unit because of treatment resistance (Mohr et al. 1994). The mean age of these patients was 32.4 years (SD = ± 10.0 years); 53% were male. They had an average of 6.0 admissions (SD = ± 4.5), their average age at first admission was 23.0 years (SD = ± 5.3 years) and their mean duration of previous hospitalizations was 22.1 months (SD = ± 20.3 months). All these patients received neuroleptic medication, and about half of them were on clozapine. Only 9 patients (8%) had a total score higher than two on the seven rigidity items of the Simpson-Angus scale (Simpson and Angus 1970), but 13 (29%) of them had tardive dyskinesia according to the criteria of Schooler and Kane (1982). At time of testing the patients were satisfactorily stable with an average BPRS total score (18 items, 7-point scales) of 34.4 (SD = ± 10.8).

A total of 78 male alcoholic patients who met DSM-III-R criteria for alcohol dependence were tested for comparisons. All of them were inpatients of psychiatric state hospitals after a period of withdrawal. The mean age of the patients was 34 years (SD = ± 6.3 years), their average daily alcohol consumption over the previous year had been 250 g (SD = ± 160 g). The period of assured abstinence, time between detoxification and participation in the study was at least 4 weeks. Approximately half of the patients (n = 39) had at least one previous detoxification treatment and 37 of the patients had already been enrolled in an alcohol rehabilitation program before. None of the patients were simultaneously taking any psychoactive drugs.

A total of 57 healthy volunteers were tested as a normal control group. None of them gave evidence of any history of psychiatric disorder. Their mean age was 26.3 years (SD = ± 5.6 years); 48% of them were male.

Procedure

Neurological soft signs and neuroleptic side effects

Neurological soft signs were assessed using a German version of the NES by Buchanan and Heinrichs (1989). A detailed manual was provided for both the examination and the scoring. Following Buchanan and Heinrichs (1989), items were scored on a 3-point scale: 0 no abnormality; 1 mild, but definite abnormality; 2 marked impairment. (In an extended version of the NES four items were added to the subscale "Motor Coordination". The internal consistency of this new scale, "Psychomotor Coordination", was slightly higher (Cronbach Alpha = 0.87), but no increase in concordant validity was seen.) A total of 23 NES items were entered in a principal component analysis.

Neuroleptic side effects were assessed with the Simpson-Angus Scale (Simpson and Angus 1970) and tardive dyskinesia with the Abnormal Involuntary Movement Scale (AIMS; NIMH Research Branch 1975).

The total examination, which required approximately 40 min, was videotaped. On the basis of these videotapes, ratings were done by two independent raters. In case of disagreement a consensus score was achieved.

To assess interrater reliability the ratings from 38 videotaped examinations were scored independently by two psychiatric and/or psychological clinicians. In another 30 patients ratings from videotapes were compared with ratings carried out immediately during the examination.

[1] The "Bezirkskrankenhaus Haar", still one of the largest psychiatric hospitals in Germany (1200 beds), is providing psychiatric care for the greater Munich area. The "Psychiatrische Landeskrankenhaus Reichenau" is situated near Konstanz and has a more rural catchment area.

Psychopathology

Negative symptoms were assessed on the basis of semistandardized interviews. Videotapes of these interviews were again rated independently by two trained psychologists and/or psychiatrists on three scales of negative symptoms: SANS (Scale for the Assessment of Negative Symptoms; Andreasen 1982, 1989; Andreasen and Olsen 1983), PANSS (Positive and Negative Syndrome Scale; Kay et al. 1987, 1988) and BPRS (Brief Psychiatric Rating Scale; Lukoff et al. 1986). Consensus scores per item and subject of 98 schizophrenic patients (Schiz I) were entered in a principal component analysis with VARIMAX rotation. This analysis yielded three factors (Schlenker et al. 1995) representing different aspects of negative symptoms: (a) "Diminished Expression" (variance explained by factor 33%); (b) "Social Dysfunction" (18%); and (c) "Cognitive Disorganization" (10%). In addition, five subscales of the SANS, the PANSS negative and positive subscale, and five BPRS subscores (Overall and Gorham 1962) had been subjected to a principal components analysis together with the Strauss-Carpenter prognosis scale (total score of a 5-point, 11-item instrument; Strauss and Carpenter 1974), the Global Assessment of Functioning Scale (GAF), and the summary score of the Disability Assessment Schedule (WHO 1988; German version: Jung et al. 1989), leading to three VARIMAX-rotated factors of general psychopathology: Negative Symptoms (variance explained by factor: 29%), Positive Symptoms (18%) and Social Adjustment (16%).

Neuropsychological tests

Four neuropsychological tests presumably sensitive to frontal lobe dysfunction were applied: the Wisconsin Card-Sorting Test (WCST; Nelson 1976), the Subject Ordered Pointing Task (SOPT; Petrides and Milner 1982), the Weigl Sorting Test (WEIGL; Weigl 1941) and the Tower of London (TOL; Shallice 1982).

Three motor tasks suggested by Luria (1966) to test frontal functioning in brain-damaged patients were compiled to a scale "Set Formation". In these tasks the patient was asked (a) to raise his right hand to one signal and his left hand to another, (b) to show his finger when the examiner shows his fist and his fist when the examiner shows his finger (both times the sequence begins with four alterations and is followed by runs of repetitions) and (c) to draw three different designs composed of alternating components. All three motor tasks test the formation and subsequent overcoming of psychomotor sets. The first and the second task are scored for hesitation and errors, and the third for perseverative mistakes.

The Raven Standard Progressive Matrices Test (Raven 1960) served as a measure of general intelligence and cognitive functioning. In addition, from all subjects we had available the root mean square error scores of smooth-pursuit eye movements following a sinusoidal target under attention-enhancing and attention-distracting conditions (Schlenker et al. 1994).

Computed tomography brain scans

Computed tomography scans of 39 inpatients from the State Hospital Haar were assessed. The CT scans had been taken in clinical routine at 15° cranial to the orbitomeatal line with 8-mm slices on a Siemens Somaton 2N (Siemens, Erlangen, Germany). All CT scans were assessed by the same neurological expert. Brain ratios were calculated for the lateral ventricles, the frontal horns, the third ventricle, the interhemispheric fissure and the sulci laterales. (According to the technique of the ventricular brain ratio these areas were divided by the total area of the brain and multiplied by 100. Area measurement was done with a planimeter.) (Franz et al. 1992).

Results

As far as nothing else is indicated, the following results refer to the main sample of 98 relatively young and not severely disabled schizophrenic patients (Schiz I). Whenever correlations or differences between means are reported to be significant, the null hypothesis had been refused at least on the $P = 0.05$ level.

Reliability

Spearman rank correlations between the scores of the two raters were calculated for the NES total score and its four subscales (Table 1). The interrater reliability for the NES total score is rho = 0.99 for ratings from the videotapes and rho = 0.91 between video ratings and ratings during the examination. The corresponding reliabilities for the NES subscales are $0.88 \leq \text{rho} \leq 1.00$ and $0.82 \leq \text{rho} \leq 0.99$, respectively. For all individual items interrater reliability was determinied using Cohen's kappa. For the ratings from the videotapes Cohen's kappa was ≥ 0.80 for 26 items and ≥ 0.50 for all 34 individual items. Comparing ratings from the videotapes with ratings during the examination showed Cohen's kappa being ≥ 0.80 for 14 items and ≥ 0.60 for 29 items, but lower than 0.50 for 5 items. The last five were either rare items, like the rapid alternating movements, or like mirror movements, which have to be scored simultaneously, when the patient is doing the finger–thumb opposition, or may be difficult to assess on videotapes such as in the case of tremor. To allow comparisons with the original study of Buchanan and Heinrichs (1989) the relative frequency of scores ≥ 1 for the individual items, together with their interrater reliability, are presented in Table 1.

The correlations between NES total score and the four subscales range from rho = 0.62 for "Motor Coordination" to rho = 0.79 for "Sequencing of Complex Motor Acts" in the group of schizophrenics (Schiz I). The subscales' intercorrelations range from $0.31 \leq \text{rho} \leq 0.56$, with lower values for "Others" and "Sensory Integration". Among the healthy controls the correlations with the total score are $0.49 \leq \text{rho} \leq 0.79$, the intercorrelations of the subscales $0.11 \leq \text{rho} \leq 0.45$. Consequently, our principal component analysis did not yield a multiple-factor solution. There was a drastic drop in the Eigenvalue after the first factor, which accounted for 20% of the total variance.

The internal consistency (Cronbach alpha) of the total score is $\alpha = 0.81$ for Schiz I as well as for all groups combined ($n = 216$). The internal consistency of the subscales varied from $\alpha = 0.53$ for "Sensory Integration" to $\alpha = 0.80$ for "Sequencing of Complex Motor Acts".

Two years after the first testing, 79 patients could be examined again with two subscales of the NES. The retest reliability was poor for the subscale "Motor Coordination" ($r_{tt} = 0.29$); it was considerably higher for the subscale "Sequencing of Complex Motor Acts" ($r_{tt} = 0.57$). The improvement after 2 years was only marginal for "Motor Coordination" ($z = 1.8$, $p = 0.08$), but significant ($z = 2.3$, $p = 0.02$) for "Sequencing of Complex Motor Acts".

Table 1 Frequencies of positive signs and interrater reliability for Neurological Evaluation Scale (NES) individual items and subscales

	Frequencies of positive signs (% of scores ≥ 1)				Interrater reliability[a]	
	Schizophrenics ($n = 98$)	Alcoholics ($n = 79$)	Healthy controls ($n = 57$)	p (χ^2)	Video × video ($n = 38$)	Video × bedside ($n = 30$)
Sensory integration					1.00	0.99
Audiovisual integration	23.2	15.4	12.3	0.18	1.00	0.88
Stereognosis R	44.0	25.6	28.1	0.02	1.00	1.00
Stereognosis L	47.5	30.8	33.3	0.05	1.00	1.00
Graphesthesia R	46.9	50.6	36.8	0.26	1.00	0.94
Graphesthesia L	35.7	21.5	33.3	0.10	1.00	0.88
Extinction	25.0	8.9	1.8	0.00	1.00	0.65
R/L confusion	33.0	34.2	29.8	0.86	1.00	0.92
Motor coordination					0.88	0.85
Tandem walk	13.0	11.8	3.5	0.10	0.54	0.75
Rapid alternating movements R	12.0	0	0	0.00	1.00	0.47
Rapid alternating movements L	17.0	2.5	0	0.00	0.85	0.54
Finger–thumb opposition R	40.0	27.8	26.3	0.12	0.63	0.66
Finger–thumb opposition L	34.3	29.1	21.1	0.20	0.78	0.80
Finger–nose test R	16.0	10.1	8.8	0.32	0.85	0.65
Finger–nose test L	32.0	20.3	15.8	0.04	0.82	0.65
Sequencing of Complex motor acts					0.98	0.86
Fist–ring R	31.3	19.0	7.0	0.00	0.82	0.60
Fist–ring L	36.7	15.2	10.5	0.00	0.95	0.61
Fist–edge–palm R	40.0	30.4	12.3	0.00	0.86	0.72
Fist–edge–palm L	38.4	32.1	17.5	0.02	0.90	0.91
Ozeretski	40.4	43.0	31.6	0.37	1.00	0.92
Rhythm tapping test B	66.0	43.0	52.6	0.01	0.88	0.90
Others					0.96	0.82
Adventitious overflow R	30.0	15.2	5.5	0.00	0.67	0.48
Adventitious overflow L	37.0	12.7	10.9	0.00	0.57	0.70
Romberg test[b]	3.0	1.3	0	0.24	–	–
Romberg: tremor R	20.0	24.1	10.7	0.13	0.63	0.38
Romberg: tremor L	22.2	21.5	10.7	0.15	0.73	0.46
Memory, 5 min	47.5	29.1	44.6	0.03	0.95	1.00
Memory, 10 min	52.6	28.2	44.6	0.00	1.00	0.94
Rhythm tapping test A	62.0	53.2	43.9	0.09	0.96	0.84
Mirror movements R	13.3	41.8	31.6	0.00	0.94	0.69
Mirror movements L	15.2	49.4	29.8	0.00	0.89	0.46
Synkinesis R	26.0	20.3	29.8	0.42	0.80	0.79
Synkinesis L	20.0	17.7	21.1	0.88	1.00	0.57
Convergence	18.0	24.1	5.4	0.01	0.92	0.51
Gaze impersistence R	26.0	7.7	5.4	0.00	0.70	0.78
Gaze impersistence L	20.0	7.7	3.6	0.00	0.91	0.84

[a] Spearman Rank correlations for subscales, Cohen's Kappas for individual items

[b] In the columns to the right, Cohen's Kappa could not be calculated

Group differences

As shown in Table 2 significant differences were found between the schizophrenic samples and healthy controls (Kruskal-Wallis test; $p \leq 0.001$, Mann-Whitney test $p \leq 0.05$) for the total score and all NES subscales. These differences are not a function of differences between the groups in age, gender and intelligence, because in none of the groups were NSS correlated with age or gender (rho ≤ 0.13), although there were significant correlations of NSS with education (0.20 ≤ rho ≤ 0.32) and intelligence (–0.12 ≤ rho ≤ –0.45). The differences in mean scores between Schiz I and the healthy controls remain significant for the total score and the subscales "Motor Coordination", "Others" and "Motor Sequencing", even when only subgroups of the probands are compared, which are matched for these variables.

On the subscale "Motor Coordination" the main group of schizophrenic patients (Schiz I) performed significantly worse than the alcohol-dependent patients, whose overall performance (total score) was significantly worse than that of healthy controls. The severely disabled schizo-

Table 2 Group differences of NES scores (median and interquartile ranges)

	Schizophrenics I[a] (n= 98) **S**	Schizophrenics II[b] (n = 45) **CS**	Alcoholics (n = 78) **A**	Healthy controls (n = 57) **C**	Kruskal-Wallis $\chi 2$	Mann-Whitney $p < 0.05$[c]
NES subscales						
Sensory integration	3.0 (1.0 – 4.75)	5.0 (3.0 – 7.0)	2.0 (1.0 – 4.0)	1.0 (1.0 – 3.0)	37.8*	CS > S, A, C S > C
Motor coordination	2.0 (1.0 – 3.0)	3.0 (1.0 – 6.0)	1.0 (0.0 – 2.0)	0.0 (0.0 – 2.0)	39.7*	CS > S, A, C S > A, C
Sequencing of complex motor acts	3.0 (1.0 – 6.0)	7.5 (2.0 – 11.0)	2.0 (1.0 – 4.0)	1.0 (0.0 – 2.0)	41.6*	CS > S, A, C S > C
Others	5.0 (3.0 – 7.75)	9.0 (6.0 – 12.0)	4.5 (2.0 – 6.75)	3.0 (2.0 – 5.0)	46.3*	CS > S, A, C S > C
NES total score	12.0 (8.0 – 20.0)	24.0 (15.0 – 33.0)	11.0 (7.0 – 16.0)	6.5 (4.0 – 11.0)	61.1*	CS > S, A, C S > C, A > C

[a] Schizophrenic patients without a severe deficit syndrome
[b] Chronic, severely disabled schizophrenic patients
[c] Bonferroni correction
*$p < 0.001$

Table 3 Spearman rank correlations of NES scores with neuropsychological tests. Schiz I: schizophrenic patients without a severe deficit syndrome (n = 93). WCST Wisconsin Card-Sorting Test; SOPT Subject Ordered Pointing Tast (Petrides); TOL Tower of London; Weigl Weigl Sorting Test

*$p \leq 0.05$
**$p \leq 0.01$
***$p \leq 0.001$
NOTE: Numbers in parentheses are partial correlations (Raven Standard Progressive Matrices partialled out)
[a] From Milner
[b] From Nelson (1976)

	WCST		SOPT (total errors)	TOL (correct solutions)	Weigl (total number)	Set formation (total score)
	Pers. errors[a]	Pers. errors[b]				
NES subscales						
Sensory integration	0.28** (0.19)	0.26* (0.17)	0.34*** (0.23*)	–0.27** (–0.17)	–0.32** (–0.23*)	0.40*** (0.32**)
Motor coordination	0.35*** (0.27**)	0.25* (0.16)	0.05 (–0.12)	–0.17 (–0.07)	–0.26** (–0.17)	0.46*** (0.39***)
Sequencing of complex motor acts	0.44*** (0.33***)	0.49*** (0.41***)	0.23* (0.03)	–0.25* (–0.11)	–0.37*** (–0.24*)	0.69*** (0.63***)
Others	0.31** (0.24*)	0.14 (0.06)	0.06 (–0.09)	–0.17 (–0.13)	–0.21* (–0.14)	0.28** (0.22*)
NES total score	0.49*** (0.42***)	0.37*** (0.29**)	0.20 (0.04)	–0.25* (–0.16)	–0.33** (–0.23*)	0.59*** (0.54***)

phrenic patients (Schiz II) were significantly more impaired on all scales than the other groups.

Correlations

Spearman rank order correlations were calculated between the NSS scores and various anamnestic and clinical variables for schizophrenic patients. No association was found with age, gender, duration of illness and number of previous hospitalizations (rho ≤ 0.13). Furthermore, there were no significant correlations of NSS with extrapyramidal rigidity (Simpson-Angus Scale, seven items) and the AIMS tardive dyskinesia score.

Neuropsychological measurements

All NSS scores are correlated significantly with performance in the Raven Standard Progressive Matrices. For the NES total score the correlation is rho = –0.32, and the NES subscales vary from rho = –0.23 for "Others" to rho = –0.39 for "Sequencing of Complex Motor Acts".

As shown in Table 3 the NES total score and the subscales are correlated consistently with neuropsychological tests supposedly sensitive to prefrontal dysfunctioning such as WCST, SOPT, TOL and the Weigl test. Partialling out performance on the Raven Standard Progressive Matrices reduces the correlations with the SOPT and the TOL to insignificance, but many of correlations with perseverative errors in the WCST and the number of different sortings in the Weigl test remain significant. Our scale "Set Formation" is also significantly correlated with all NSS indexes. Partialling out intelligence, they all stay above the level of significance and are highest with the subscale "Sequencing of Complex Motor Acts" (rho = 0.69), which points to a close relation between the most demanding tasks in the subscale "Sequencing of Complex Motor Acts" and motor tasks which are supposed to be sensitive to frontal lobe damage.

The NES total score shows positive correlations with the root mean square error of smooth-pursuit eye movements both in attention-enhancing (rho = 0.37) and attention-distracting condition (rho = 0.44). In the attention-enhancing conditions the correlations with the NES subscales range from rho = 0.17 for "Sensory Integration" to rho = 0.35 for "Others". For the distracting condition they

Table 4a Correlations of NES scores with factor scores for general psychopathology. Schizophrenic patients (Schiz I) without a severe deficit syndrome ($n = 93$)

	Factor I (negative symptoms)	Factor II (positive symptoms)	Factor III (social adjustment)
NES subscales			
Sensory integration	0.33***	0.11	0.07
Motor coordination	0.07	0.09	0.08
Sequencing of complex motor acts	0.30**	0.27**	0.15
Others	0.13	0.25*	–0.06
NES total score	0.23*	0.28**	0.11

*$p \leq 0.05$
**$p \leq 0.01$
***$p \leq 0.001$

Table 4b Correlations of NES scores with factor scores for negative symptoms. Schizophrenic patients (Schiz I) without a severe deficit syndrome ($n = 93$)

	Factor I (diminished expression)	Factor II (social dysfunction)	Factor III (Cognitive disorganization)
NES subscales			
Sensory integration	0.13 (0.08)	0.15 (0.07)	0.40*** (0.37***)
Motor coordination	–0.04 (–0.12)	–0.01 (–0.07)	0.35*** (0.41***)
Sequencing of complex motor acts	0.09 (0.05)	0.23* (0.17)	0.46*** (0.49***)
Others	0.03 (–0.02)	0.12 (0.14)	0.42*** (0.22*)
NES total score	0.06 (–0.01)	0.12 (0.12)	0.42*** (0.50***)

*$p \leq 0.05$
**$p \leq 0.01$
***$p \leq 0.001$
NOTE: Numbers in parantheses are Simpson-Angus seven-items rigidity score partialled out ($n = 83$)

range from rho = 0.27 for "Sensory Integration" to rho = 0.44 for "Sequencing of Complex Motor Acts" (Schlenker et al. 1994).

Psychopathology

Correlations with ratings of psychopathology were carried out on two levels:

1. General Psychopathology. A principal component analysis of the subscales from BPRS, SANS and PANSS together with the overall scores from the Strauss-Carpenter Prognosis Scale, the Global Assessment of Functioning Scale (DSM-III-R) and the Disability Assessment Schedule had resulted in three VARIMAX-rotated factors, two of which showed correlations with NES scores. The NES total score correlated with "Negative Symptoms" (rho = 0.23) and with "Positive Symptoms" (rho = 0.28), but not with "Social Adjustment" (rho = 0.11). The correlation with "Negative Symptoms" is based primarily on correlations with the subscales "Sensory Integration" and "Sequencing of Complex Motor Acts", and the correlations with "Positive Symptoms" on correlations with "Sequencing of Complex Motor Acts" and "Others".

2. Negative Symptoms. A separate principal component analysis had been based on the individual items from the SANS, PANSS and BPRS covering negative symptoms. This analysis also had resulted in three VARIMAX-rotated factors, which can be considered independent aspects of the general component "Negative Symptoms" from the above analysis. Surprisingly, neither of the two main components of negative symptoms, "Diminished Expression" and "Social Dysfunction", was found to correlate significantly with any of the NSS scores ($-0.04 \leq \text{rho} \leq 0.15$). The exception is a correlation between "Sequencing of Complex Motor Acts" and "Social Dysfunction" (rho = 0.23). Correlations are confined to the third component of negative symptoms, "Cognitive Disorganization", which is defined mainly by loadings on "Impaired Abstract Thinking" (PANSS), and the three SANS items "Inattention During Testing", "Social Inattentiveness", and "Reduced Content of Speech". This third component of negative symptoms correlates quite highly (rho = 0.42) with the NES total score and with the NES subscales "Sensory Integration", "Motor Coordination" and "Sequencing of Complex Motor Acts" ($0.40 \leq \text{rho} \leq 0.46$).

Computed Tomography brain scans

Correlations between NSS scores and measurements of external and internal cerebral fluid spaces were calculated for 39 schizophrenic patients, 17 of which belonged to the severely chronic and disabled group (Schiz II). The NES total score was consistently related to the relative width of the third ventricle (rho = 0.58, $p \leq 0.001$), of the interhemispheric fissure (rho = 0.39, $p \leq 0.05$) and of the sulci laterales on slices I (rho = 0.35, $p \leq 0.05$) and II (rho = 0.61, $p \leq 0.001$). The correlations remained significant after partialling out age and duration of hospitalization, which were correlated positively with brain abnormality.

Discussion

Neurological soft signs can be assessed with high reliability. Our indexes of interrater reliability for total score and subscales of the NES scale are concordant with the findings of Buchanan and Heinrichs (1989) who reported high intraclass correlations for the total score and the NES subscales (rho ≥ 0.70). According to both studies most items can be scored reliably by different raters. These results are also in agreement with studies by Quitkin et al. (1976) and Rossi et al. (1990). Internal consistency had been examined by Schröder et al. (1992a) for a 17-item NSS scale.

Their internal consistency of $\alpha = 0.85$ for schizophrenic patients and of $\alpha = 0.89$ for healthy controls is quite comparable to our findings of a Cronbach alpha for the NES total score of $\alpha = 0.81$ for schizophrenic patients and $\alpha = 0.78$ for healthy controls.

There is some controversy in the literature as to what extent NSS can be considered unspecific with respect to the localization of putative CNS dysfunctions (Quitkin et al. 1976; Shaffer et al. 1983), or whether they can be grouped reasonably according to areas of functioning (Buchanan and Heinrichs 1989) and/or the cerebral lobes (Cox and Ludwig 1979; Merriam et al. 1990). The highly significant correlations among all the NES subscales found in this study suggest that most of their common variance reflects only an unspecific factor of functional impairment. This conclusion is supported by the fact that a principal component analysis of NES items showed a drastic drop in the Eigenvalue after the first factor, which accounted for 20% of the total variance. This result is somewhat at variance with Buchanan and Heinrichs (1989) who reported intercorrelations of their three functionally defined subscales lower than what we had found. There is no reason to assume a greater variance in the general level of functioning on our core group of schizophrenic patients on which these correlations had been determined. Subjecting their scale, which consisted of 17 items, to a principal component analysis, Schröder et al. (1992a) reported six factors to emerge. However, these factors were so difficult to interpret that they only refer to the total score in later studies (Schröder et al. 1992b, 1993).

In good agreement with previous studies (Buchanan and Heinrichs 1989; Gureje 1988; Quitkin et al. 1976; Rossi et al. 1990; Schröder et al. 1992a; Woods et al. 1986) schizophrenics show considerably more NSS than healthy controls. Schizophrenics show significantly more signs in "Motor Coordination" than alcohol-dependent inpatients, which were found to have a significantly higher NES total score than healthy controls. This corresponds to Woods et al. (1986) who found patients with alcohol and/or other drug dependencies to have NSS somewhat intermediately between schizophrenic patients and healthy controls. In line with the studies of Buchanan et al. (1990) and Torrey (1980) our sample of severly chronic and disabled schizophrenics showed more NSS than our main group of schizophrenic patients, who had been selected as not severely alienated from the demands of everyday life. Chronicity, if seen as a heading for a less favourable course and the overall severity of the illness, is related to more neurological abnormalities in schizophrenic patients.

In a subsample of our schizophrenic patients, we found an association between NES total score and CT parameters, most clearly with the relative width of the third ventricle and sulci laterales. These relations were independent of age and duration of previous hospitalization. Schröder et al. (1991) also reported a correlation between the width of the third ventricle and their NSS index, but not – similar to this study – between the ventricle brain ratio (VBR) and soft signs. This negative finding is in line with previous studies by King et al. (1991) and Kolakowska et al. (1985), but in discordance with the study by Weinberger and Wyatt (1982).

In this study, similar to Buchanan and Heinrichs (1989), age and gender were not correlated significantly with the NES total or any of its subscales. According to Heinrichs and Buchanan's (1988) overview, previous studies have provided conflicting results on the effect of age, whereas NSS have been seen more frequently in male than female patients. In line with previous reports (King et al. 1991; Kolakowska et al. 1985; Rossi et al. 1990) the NES total score and the NES subscales were not found to correlate with dosage of neuroleptic medication or with extrapyramidal side effects. Apparently, NSS in schizophrenics is not primarily a sequelae of neuroleptic medication. In our study, similar to Kolakowska et al. (1985), NSS and tardive dyskinesia were not correlated, as found by King et al. (1991) and Wegener et al. (1985).

Neurological soft signs were found to be related consistently with the level of cognitive functioning as measured by the Raven Standard Progressive Matrices and by various neuropsychological tests presumably sensitive to dysfunctions of the prefrontal cortex. This finding corresponds to previous reports by King et al. (1991), Kolakowska et al. (1985) and Quitkin et al. (1975). These results fit into the pattern of findings indicating a more severe impairment in the severely disabled schizophrenics particularly in tests considered to be related closely to the activation of the prefrontal cortex (cf. Andreasen et al. 1992; Weinberger et al. 1986, 1988). Interestingly, this association is seen most clearly for the subscale "Sequencing of Complex Motor Acts", which in turn is correlated with poor performance in smooth-pursuit eye movements, often discussed as a marker for schizophrenic vulnerability.

Neurological soft signs were found to be correlated both with positive and negative symptoms, but not with the general level of "Social Adjustment" as assessed by various rating scales. This finding is in line with previous results from Mosher et al. (1971) and King et al. (1991). Apparently, it is not the generalized deficit, but more specifically, the severity of schizophrenic psychopathology, whether predominantly "positive" or "negative" in nature, that is related to the number of NSS.

The correlations between NSS and the factor scores from the more specific principal component analysis of the individual items for negative symptoms indicate that such a conclusion can easily be misleading. Neurological soft signs are not correlated with the two main aspects of negative symptoms, "Diminished Expression" and "Social Dysfunction". They are correlated only with the third component of negative symptom items "Cognitive Disorganization". This correlation of NSS with "Cognitive Disorganization" in particular can be interpreted in two ways: Firstly, it might only reflect the trivial fact that patients with symptoms of cognitive disorganization have problems to understand and follow instructions during the examination of NSS. However, it is unlikely that this can explain much of this common variance, because the psychologists who carried out the examinations ascertained in each case and for each task through a number of trials

that the patient had understood the instruction and was motivated to cooperate.

Secondly, it might indicate an aetiologically important association of psychomotor and cognitive deficiencies as proposed in Meehl's (1990) model of schizotaxia, the genetically determined neurointegrative defect in schizophrenic disorders, which he explicitly sees related to both "soft neurological signs" and "cognitive slippage".

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