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COMPARATIVE ANALYSIS OF SOFT NEUROLOGICAL SIGNS IN POSITIVE AND NEGATIVE SUBTYPE OF SCHIZOPHRENIA

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SUMMARY

Background: *The objective of the study was to investigate neurological deficit in schizophrenia and to compare soft neurological signs in positive and negative subtypes of schizophrenia.*

Subjects and methods: *66 patients with schizophrenia were evaluated with the Positive and Negative Syndrome Scale to classify the subtype of schizophrenia: positive subtype (36 patients) and negative subtype (30 patients), all of which were entering into remission. To examine the neurological soft signs we compared scores on the Neurological Evaluation Scale (NES) for positive and negative subtype.*

Results: *The negative subtype of schizophrenia showed significantly higher neurological soft signs in comparison to the positive subtype, with reduced functioning in the sensory integration and motor coordination subscale as well as the other subscale.*

Conclusion: *The main finding in this study indicates that patients with schizophrenia have neurological impairment, and that the negative subtype has significantly higher neurological impairment than the positive subtype. The results further support the significance of the soft neurological signs as a possible marker of different subtypes of schizophrenia.*

Key words: *Schizophrenia - positive/negative subtype - neurological soft signs*

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INTRODUCTION

The relationship between schizophrenia and neurological abnormalities was spotted very early, even from the time of Kraepelin and it has also been the subject of numerous studies over the last 35 years (Rickler 1994). Kraepelin (1919) describes two symptom groups in the diseased, psychical and somatic, and among somatic disorders he refers to: headache, pupils reactivity disorder, reflex disorder, aphasia, convulsions, etc. These studies consistently show a higher frequency of neurological abnormalities among patients with schizophrenia in comparison to other psychiatric and non-psychiatric examinees (Kennard 1960).

Data in the contemporary literature also demonstrate the presence of neurological disorders in schizophrenia. Studies of neurological abnormality are directed to soft neurological signs (SNS), because the diagnostic criteria for schizophrenia exclude cases with focal or classical neurological signs (Woods 1992). Soft neurological signs (SNS) present minor, non-localized, objective abnormalities which reflect a connection disorder among sub-cortical and cortical regions or between cortical regions. Unlike classical signs, SNS are characterized by motor, sensory and integrative functional disorders, which do not reflect localized brain dysfunction (so called no-focal signs of CNS pathology) (Woods et al. 1987). In other words, it has been established that SNS reflect a deficit of sensorial integration (Quitkin et al. 1976) motor co-ordination (Ismail et al. 1998), and sequencing of complex motor acts (Heinrichs & Buchanan 1988). An overall sensor integration deficit is showed in bilateral extinction, audio-visual integration, graphesthesia and stereognosis disorders. The classical motor coordination disorder includes difficulties when performing the "opposition index finger-thumb" test, dysdiadochokinesia, tandem walk and the finger-nose test. Disorders while doing the "fist-

ring", "fist-brink-palm" tests and positive Oseretsky sign reflect difficulties in sequencing of complex motor acts.

A series of studies have been conducted, in an attempt to determine the distinctiveness of these abnormalities in schizophrenia disorders or their relation to special psychopathologic manifestations. It has been found that they are prevalent in 50-65% of patients with schizophrenia (Heinrichs & Buchanan 1988). They are conceptualized as the main characteristics indicating the possibility of the development of psychosis (Tsuang & Faraone 1999). Family studies identified a higher frequency of SNS in the first degree relatives of schizophrenic patients in comparison to the healthy population (Chen et al. 2000, Rossi et al. 1990). The high risk longitudinal studies also demonstrate more frequent SNS in persons at risk of psychotic disorder (Fish 1977, Lawrie et al. 2001). Soft neurological signs described in the studies include deteriorated motor coordination, difficulties in sensorial perception and difficulty in sequencing of complex motor activities. The main goal of this study is to compare the soft neurological signs in patients with schizophrenia with regard to subtype, i.e. positive vs. negative sub-type.

SUBJECTS AND METHODS

The study group consisted of 66 consecutive patients with a diagnosis of schizophrenia (according to ICD 10 criteria). The patients were recruited from the psychiatric inpatient clinic (Institute of Psychiatry, Clinical Centre of Serbia) over a two year period. The inclusion criteria consisted of a diagnosis of schizophrenia that was confirmed by the semi structured psychiatric interview, an age greater than 18 or less than 30, a duration of illness less than one year, a first admission and at minimum, high school level of education. We excluded potential participants if they had associated diagnoses of mental retardation, other psychiatric diagnoses from axis I, neurological disease or damage, alcohol or substance abuse and medical illnesses associated with significant cognitive dysfunction.

All participants gave informed consent for their participation in this study. The evaluation procedure consisted of the measurement of psychopathology and cognitive functioning. Current psychotic symptoms were characterized by using the semi structured psychiatric interview. Information on clinical symptom severity was obtained by using the Positive and Negative Syndrome Scale (PANSS) (Kay et al. 1989). Also, PANSS was administered to classify the subtype of schizophrenia. Considering the results from this scale, we divided participants into two groups: positive subtype (36 patients) and negative subtype (30 patients), all of which were reaching remission. Patients were also assessed for neurological soft signs using the Neurological Evaluation Scale (NES) (Buchanan & Heinrichs 1989).

The Positive and Negative Syndrome Scale (PANSS)

The Positive and Negative Syndrome Scale (PANSS) (Kay et al. 1987) is a measure of positive and negative schizophrenic symptoms and related aspects, such as cognitive, affective, and social functioning. The test has 30 items: (a) 7 items of which represent the positive symptoms; (b) 7 items are related to the negative symptoms; and (c) the remaining 16 items cover related aspects of general psychopathology and functioning. Each item is rated on an interval scale ranging from 1 (absent) to 7 (extreme psychopathology). The total scores may thus range between 30 and 210, with a higher score indicative of a more severe illness.

Neurological Evaluation Scale (NES)

The Neurological Evaluation Scale NES is standardized to assess the neurological impairment in schizophrenia. It consists of 4 subscales (sensory integration, motor coordination, sequencing of complex motor acts and others-consisted of cerebral dominance, short term memory, frontal disinhibition phenomena and abnormal eye movement) with a total of 26 items. Each item is scored from 0 (absent) to 2 (extreme). The intensity of soft neurological signs is operationalized based on the Neurological Evaluation Scale NES (Buchanan & Heinrichs 1989) scores from 0 (zero) to 2 (two): 0 (absent), 1 (mild intensity), 2 (high intensity).

Descriptive statistics were used to summarize the data. The Chi-square test and t-test were used to assess the significance of the observed differences, respectively, for categorical and continuous data. Univariate and multivariate logistic regression analyses were performed to assess the correlation between the observed scales from the positive subtype of schizophrenia. Data analyses were

performed using the Statistical Package for Social Sciences (SPSS) for Windows, version 11 (2003).

RESULTS

The sample consisted of 66 patients (28 female and 38 male), with a diagnosis of a first episode of schizophrenia (ICD 10). Based on the results from PANSS, the participants were divided into two groups: positive subtype (n=36) and negative subtype (n=30), all of which were entering into remission. There was a statistical significant difference in age between positive subtype (mean age = 26.50±3.03) vs. negative subtype (mean age = 22.53±0.517) (t= -1.203; p>0.01). Regarding socio-demographic parameters, statistically significant differences between subtypes were evident in education (Fisher p<0.01); higher educational level was present in the group which consisted of the positive subtype of schizophrenia. There were no differences in the number of male and female patients (p>0.05) (Table 1.).

Table 1. Sociodemographic and clinical variables in the positive and negative subtype of schizophrenic patients

	positive (n=36)	negative (n=30)	p
Gender, male n (%)	14 (46.7)	24 (66.7)	0.102
Age (mean ± SD)	26.50±3.03	22.53±0.517	0.000
Education, years (mean ± SD)	14.13±2.03	12.50±1.14	0.000
Onset of illness (age) (mean ± SD)	22.45±5.21	18.93±32	0.000

The total PANSS mean scores (110±5 and 114±4, respectively) and general psychopathology subscale scores (53±6 and 56±5, respectively) were not found to be significantly different between the subtypes.

Overall, statistically significant differences where found between subtypes in almost all the subtests of the NES scale. The total score of the Neurological Evaluation Scale was significantly higher in the negative subtype group, indicating higher neurological impairment in the patients with negative symptoms (Table 2).

Table 2. The Neurological Evaluation Scale (NES) scores of the positive and negative subtype of schizophrenic patients

	positive (n=36)	negative (n=30)	p
Sensory Integration	1.83±1.79	3.47±0.50	0.000
Motor Coordination	1.17±1.36	2.07±1.01	0.004
Sequencing of Complex Motor Acts	1.83±1.08	2.47±0.50	0.003
Others	5.67±2.53	10.93±1.01	0.000
Total	10.50±3.69	18.94±3.76	0.000

DISSCUSION

The main finding in this study indicates that patients with schizophrenia have neurological impairment, and that patients with the negative subtype have significantly higher neurological impairment than those with the positive subtype. Tiryaki et al. (2003) found that patients with the negative subtype show a significant defect on all subscales of the NES. We observed that different subgroups of neurological soft signs occur more frequently in patients PANSS negative symptoms, for example, „sequencing of complex motor acts“ and „sensory integration.“ Twelve studies of the negative subtype of schizophrenia showed that these patients have significantly more problems on the NES scale, subscale of sensory integration. These findings are in accordance with our results that the score on the Sensory Integration subscale was the most discriminating variable between the groups. These signs are putatively associated with frontal-prefrontal and parietal brain areas. (Heinrichs & Buchanan 2005). Also, many studies report the connection between negative symptoms and frontal and/or prefrontal signs which can be related to the Neurological Evaluation Scale total score (Flyckt 1999, Varambally 2006).

However, relationships between neurological signs and different clinical symptoms are not a consistent finding. For example, Tiryaki et al. (2003) found that the subscore of sequencing of complex motor acts is a significant predictor of deficit state, which is the negative subtype of schizophrenia. However, results of our study showed that the scores on Sequencing of Complex Motor Acts subscales, although highly signi-

ficantly different, were not the highest among the subscales.

We also assessed a potential influence of sociodemographic variables upon SNS prevalence in positive and negative subtypes of schizophrenia. Our results showed that there are no gender differences in the presence and severity of SNS between the study groups. On the other hand, we find statistically significant differences in the age and educational level between the positive and negative subtypes of schizophrenia. Recent studies also showed a positive correlation between older age and more SNS and an inverse correlation between education and neurological impairment in patients with first episode schizophrenia (Mohr et al. 2003, Cuesta et al. 1996). A tendency of an earlier onset of illness in the negative subtype patients was again confirmed in our study, therefore indicating a deeper neurological impairment. Poorer premorbid adjustment was found in our study, based on the years of education as reported in previous studies (Buchanan et al. 1989).

CONCLUSION

The significance of neurological soft signs which are connected with schizophrenia have not yet been fully examined and explained, in part because of the unresolved methodological questions and problems. In comparison to all other psychiatric disorders schizophrenia causes more fear, brings greater destructiveness and chaos into family life, and requires more frequent hospitalizations. Because of all the aforementioned issues, a deeper insight and a better understanding of the disease is needed. Examination of neurological soft signs as a possible marker of schizophrenia can be beneficial in early recognition and prevention. Further research in this field is needed to achieve better understanding of the illness.

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