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ORIGINAL RESEARCH

Study of Soft Neurological Signs in Schizophrenia Patients

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ABSTRACT

Background:Soft neurological symptoms have been observed in patients with schizophrenia. Several studies have shown neurological abnormalities in schizophrenia patients, but their presence has been complicated by a number of potentially confounding variables such as the duration of the illness, drug doses, and the use of diverse assessment methodologies. Soft neurological symptoms appear to be a characteristic component of schizophrenia as well as a probable biological indication of prognosis. As a result, early detection and action may result in a better prognosis. The assessment of soft neurological symptoms is a straightforward, simple, and low-cost method of determining the severity of brain dysfunction in schizophrenia. The relationship between the presence of schizophrenia and soft neurological symptoms in a patient has not been widely examined in the context of the Indian population. As a result, the purpose of this study is to assess the presence of mild neurological symptoms in individuals with schizophrenia.

Materials and Methods: 80 subjects, 40 patients with schizophrenia and 40 healthy matched controls were evaluated. Tools used were PANSS for evaluation of symptomatology in schizophrenia patients, NES for evaluation of neurological soft signs, MMSE for evaluation of cognitive functions and SESS for evaluation of socio-economic status.

Results: When compared to controls, patients with schizophrenia had significantly higher NES scores. Age, gender, educational position, and disease duration show no link with the existence of soft neurological symptoms in individuals with schizophrenia, according to socio-demographic and clinical characteristics. There are statistically significantpositive associations between the PANSS negative symptom subscale, the Total PANSS score, and the NES scores in patients with schizophrenia. In schizophrenia patients, there is a substantial negative connection between the Total NES score and the Total MMSE score.

Conclusion: Wound infection following previous surgery was the most important risk factor associated with incisional hernia. The other risk factors were obesity and COPD. Polypropylene mesh repair is superior to anatomical repair as it has less recurrence.

Keywords: Schizophrenia, Soft Neurological Signs, Panss Negative Symptom, Nes Scores.

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INTRODUCTION

Schizophrenia, which comprises of variable but profoundly disruptive psychopathology that includes cognition, emotion, perception, and other elements of behaviour, is undoubtedly the most perplexing of the psychiatric diseases. Since its initial description by Kraeplin, the idea of schizophrenia has been through a significant amount of development to become what it is today, which is a disorder. Positive psychotic symptoms, negative symptoms, and disorganizations in thought and behaviour are the three main categories that are used to classify schizophrenia's symptoms. In general, it is accepted that the symptoms of schizophrenia fit into these three distinct categories.[1]The symptomatology and phenomenology of schizophrenia have become increasingly important in the process of diagnosis as time has passed. However, in recent years there has been a significant increase in research into the neurological foundation of schizophrenia, and there has been an effort made to determine the meaning and utility of neurological indications that are associated with schizophrenia.Neurological soft signs are characterised by deficiencies in activities such as sensory integration, motor coordination, and the sequencing of complicated motor acts. These soft signs are considered to be modest neurological disorders. "Soft signals" are neurological indicators that are not readily localizable to specific brain regions, as opposed to "hard signs," which are neurological signs that can be localised to specific brain regions. It is presumed that "soft signs" reflect a widespread malfunction in the brain. Multiple studies have shown, over and over again, that schizophrenia is more likely to exhibit subtle neurological symptoms than other psychiatric disorders do. This is according to the findings of the research' authors. Additionally, research with neuroleptic- naive first-episode patients have shown that soft symptoms are present prior to medication exposure. This lends credence to the idea that soft signs are an inherent component of schizophrenia and bolsters the neuro-developmental etiopathogenesis of the disease.[2-5]

The investigation of the neurological dysfunction associated with schizophrenia entails the utilisation of a wide variety of neuroradiological, neuroanatomical, neuropathological, and neuropsychological examinations.The investigation of neurological soft signals is a procedure that is straightforward, uncomplicated, and very inexpensive for determining the degree of damage. In the event that positive connections are found, they might be useful in a range ofclinical settings, such as the diagnosis or prognosis of schizophrenia.This investigation was carried out with the purpose of studying the presence of soft neurological signs in patients diagnosed with schizophrenia and gaining a better understanding of the relationship between these signs and socio-demographic factors, particular positive and negative syndromes, as well as the level of cognitive impairment associated with schizophrenia.[4-6]

Objectives of the Present Study

To determine the relationship between age, sex, educational level and period of illness and soft neurological signs.

To determine the relationship between positive and negative syndrome of schizophrenia and soft neurological signs.

To determine the relationship between cognitive impairment and soft neurological signs.

Source of Data

This clinical study was conducted in the Department of Psychiatry, RVM Institute of Medical Sciences and research Centre. Patients who attended the Psychiatry Department, either as outpatients or inpatients constituted the population for the investigation. The clinical study wasconducted from the 1st October 2020 to the 31st August 2021.

MATERIALS & METHODS

Method of collection of data

The sample for the study constituted fifty patients diagnosed with schizophrenia who visited the Psychiatry Department, either as inpatients or outpatients and who satisfied the inclusion and exclusion criteria given below.

Inclusion criteria:

Individuals diagnosed with Schizophrenia visiting the Psychiatry Department of RVMIMSas out- patients or admitted on an in-patientbasis.
Age: 20-60 years.
Individuals who are co-operative for testing neurological signs. Individuals who have given written informed consent.

Exclusion criteria:

Individuals with history of head injury, epilepsy, recent high fever. Individuals with altered sensorium, memory deficits, delirium.
History of focal neurological deficits.
History of mental retardation.
Individuals with significant medical illness. Visual or hearing or sensory deficits.
Individuals with substance abuse/ dependence disorder Individuals with a co-morbid psychiatric diagnosis.
Individuals who have received ECT in the last 6 months.

Control:

Controls for the study would be fifty individuals who do not suffer from Schizophrenia and matched with respect to age, sex and socio economic statusattending the other departments atRVM Institute of Medical Sciences and Research Centre.

Inclusion criteria:

Individuals attending other departments of the hospital who are willing to participate in the study and have no history of Schizophrenia.
Age: 20-60 years
Individuals matched for age, sex and socio economic status to the subject sample
Those who have given written informed consent

Exclusion criteria:

Individuals with history of head injury, epilepsy, recent high fever. Individuals with altered sensorium, memory deficits, delirium.
History of focal neurological deficits. History of mental retardation.
Individuals with significant medical illness.
Visual or hearing or sensory deficits.
Individuals with substance abuse/ dependence disorder Individuals with a co-morbid psychiatric diagnosis.
Individuals who have received ECT in the last 6 months.

Procedure

The institutional ethical committee has given their blessing for this study to proceed. Everyone who participated in the study, including those who were assigned to the control

group, gave their informed consent in written form. To determine whether or not the persons in the subjects' (n=40) group and the participants in the control group's (n=40) group satisfied the inclusion and exclusion criteria, a comprehensive physical and mental status examination was performedon each of them. All of the subjects' socio-demographic and clinical information was obtained using a proforma that was specifically prepared for the clinical trial and documented using that proforma. The patients were interviewed in depth to obtain a detailed history that included information on the duration of the illness as well as the symptomatology. The International Classification of Diseases, Diagnostic Criteria for Research (ICD-10 DCR) Guidelines were utilised in order to arrive at the conclusion that the patient suffered from schizophrenia. The Positive and Negative Symptoms Scale was then utilised to determine the extent to which patients were suffering from the symptoms of schizophrenia (PANSS). The Neurological Evaluation Scale (NES) was utilised in order to perform an assessment of non-cognitive neurological symptoms in both the research participants and the healthy controls. Using a tool called the Mini Mental Status Examination, each person in both the experimental and the control groups was tested to determine how well their brains were functioning. The Socio-Economic Status Schedule was used to determine the socioeconomic status of both the test subjects and the control group (SESS- Sodhi and Sharma 1986).

RESULTS

A total of 80 individuals, 40 schizophrenia patients (Cases) and 40 matched individuals (Controls) are included in this study. Patients in the age groups of 25 – 29 years constituted a majority of the cases (30%) followed by patients in the 20 – 24 years age group (28%). Among the controls, a majority is seen in the 20 – 24 years age group (28%) followed by the 25 – 29 years group (22%). There is no significant difference between the ages of cases and controls (p= 0.536> 0.05). Age is not a confounding factor in this statistical assessment.

Table 1:Data regarding Gender.

Gender	Cases		Controls		Total	
	Count	Percentage	Count	Percentage	Count	Percentage
Males	22	55%	26	65.0%	48	60.0%
Females	18	45.0%	14	35.0%	32	40.0%
Total	40	100.0%	40	100.0%	80	100.0%

In this study, males account for 55% of the study population while females constitute 45% of the population. Among the cases, 65 % are males while 35 % are females whereas among controls 48% are males and 32% are females. There is no significant difference between thegenders of cases and controls (p = 0.536> 0.05). Gender is not a confounding factor in this statistical assessment.

Table 2: Group Statistics.

Group		N	Mean	Std.Deviation	T
Durationofillness	Cases	40	9.87	9.032	
	Controls				
Positive scale	Cases	40	23.87	7.098	Z=16.412
	Controls	40	7.34	4.78	<0.001vhs
Negativescale	Cases	40	20.56	9.41	Z=10.67
	Controls	40	7.32	1.000	<0.001vhs

Generalpsychopatholo gy Cale	Cases	40	33.89	4.521	28.374
	Controls	40	16.32	1.34	<0.001vhs
Total-PANSS	Cases	40	76.98	5.093	56.459
	Controls	40	30.76	1.521	<0.001v hs
Total-NES	Cases	40	11.68	10.410	Z=12.98
	Controls	40	32.67	1.044	<0.001v hs
Total-MIMSE	Cases	40	27.324	2.42	7.655
	Controls	40	29.21	1.230	<0.001v hs
Total-SESS	Cases	40	25.60	4.984	2.515
	Controls	40	27.72	3.774	p=.014sig

The patients have been sick for an average of 9.87 years, with a standard deviation of 9.032 years. The patients that were studied in this sample had a range of sickness durations, with the shortest being two years and the longest being thirty-five years. Scores on the PANSS were compared between the patients and the controls as follows: - On the Positive Scale, the mean score of cases is 23.87 with a standard deviation of 7.98, but the score of controls is 7, suggesting that controls do not exhibit any of the positive symptoms associated with schizophrenia. The results of the comparison of the cases and controls on the Positive Scale show that the p-value is less than 0.001, which indicates a very high level of significance. Importance of the distinction that exists between the groups - On the Negative Scale, the mean score of cases is 20.56 with a standard deviation of 9.41, but the score of controls is 7, indicating that controls do not exhibit any of the negative symptoms associated with schizophrenia. - The finding that the p-value for the comparison of the scores on the Negative Scale between the patients and the controls is less than 0.001 indicates that the difference between the groups is highly significantly different. The mean score on the General Psychopathology Scale, which was given to cases, was 33.89, and the standard deviation was 4.52, whereas the mean score for controls was 16.34, and the standard deviation was 1.34. This demonstrates the existence of traits suggestive of general psychopathology among both groups, with cases exhibiting a substantially higher score as compared to controls. This is because the presence of these features is present in both groups.

The fact that the p value for the comparison of the scores on the General Psychopathology Scale between the cases and the controls is less than 0.001 indicates that the difference between the groups is extremely significantly different from one another. The total mean score on the PANSS among the patients is 76.96, with a standard deviation of whereas the mean score forcontrols is 32.96 with a standard deviation of 1.044 and the mean score for cases has a standard deviation of 5.093.The fact that the p value for the comparison of the overall PANSS scores between the cases and the controls was less than 0.001 indicates that there is a difference that is extremely significant between the two groups.In this particular study, there was a prevalence rate of 60 percent for soft neurological symptoms among schizophrenia patients. The study involved a total of 80 patients, and 24 of those individuals scored on the NES.In terms of the overall score on the NES, the cases have a mean score of 11.58 and a standard deviation of 10.40, whereas the controls have a mean score of 0.44 and a standard deviation of 1.053.The finding that the p value for the comparison of the NES scores between the cases and the controls is less than 0.001 indicates that there is a very highly significant difference between the two groups.The mean total MMSE score for patients with the condition is 27.44, with a standard deviation of 2.417, while the mean score for healthy controls is 29.22, with a standard deviation of 1.130.When comparing the MMSE scores of the two groups, there is a significant gap between them.Relevant in light of the fact that the p value was determined to be less than 0.001. The mean score on the SESS for cases

is 25.70, while the mean score for controls is 27.72, with a standard deviation of 3.774. The standard deviation of the cases' scores is 4.244, while the standard deviation of the controls' scores is 3.774.
A comparison of the SESS scores of the two groups reveals that p = 0.014, indicating that there is a significant difference between the cases and the controls.

Table 3: NES scores according to ICD – 10 Diagnosis.

Group	N	Mean	Std.Deviation	Minimum	Maximum
F20.0	29	9.32	8.427	0	22
F20.3	3	15.00	11.231	0	25
F20.5	11	16.00	13.282	0	24

Out of 40 patients studied, 29 are diagnosed with Schizophrenia: Paranoid type, 3 with Schizophrenia: Undifferentiated type and 11 with Schizophrenia: Residual type.
In this study, the mean NES score of the patients in the Schizophrenia: Paranoid group is 9.302with a standard deviation of 8.427 whereas the patients in the Schizophrenia: Undifferentiated group patients have a mean NES score of 15 with a standard deviation of 11.231 and those in the Schizophrenia: Residual group have a mean score of 16 with a standard deviation of 13.282. Analysis between the three groups does not show any statistically significant difference in the mean NES scores (p = 0.212 > 0.05).

DISCUSSION

This investigation is carried out on fifty schizophrenia patients and fifty individuals without schizophrenia who attended the outpatient and inpatient departments, of the Department of Psychiatry, RVM Institute of Medical Sciences and Research centre. By and large, patients coming to this hospital belong to the middle and lower socioeconomic class. The hospital has three psychiatry units with a bed strength of 120 in the Psychiatry Department. The average number of patients attending the\ psychiatry outpatient department is about 40. The present study is conducted from 1st October 2020 to the 31st of August 2021.
The duration of illness among the schizophrenia patients in this study varied between 2 years to 35 years with a mean of 10.32 years. On the PANSS positive and negative scales, the patients scored a mean of 24.60 and 21.56 respectively while controls scored 7 points (which is the baseline score) on both the subscales. This confirmed the presence of positive and negative symptoms only among patients of schizophrenia. Analysis of the two groups shows that the difference between them was found to be very highly significant. On the general psychopathology subscale of the PANSS, both cases and controls scored higher than the baseline. However, the mean score of the schizophrenia patients group is much higher than that of the control group and the difference between the two groups is also found to be very highly significant. This suggests that features of general psychopathology such as somaticconcern, anxiety, guilt feelings, tension, mannerisms and posturing, depression, motor retardation, uncooperativeness, unusual thought content, disorientation, poor attention, lack of judgment and insight, disturbance of volition, poor impulse control, preoccupation and active social avoidance may be seen in individuals without schizophrenia. However, they certainly present to a higher degree in schizophrenia patients. The total PANSS score among cases and controls also shows a very highly significant difference between the two groups.In this study, the prevalence of neurological soft signs is estimated to be 62%.
Previous studies have reported specific prevalence rates ranging from 29% to 80% 20, 21, 37, 39 53, 56. Tucker et al in 1975 have reported a prevalence rate of 57.8% for mild to moderate neurological impairment among patients with schizophrenia.[6]

Ninety-two per cent prevalence has been reported by Manschrek et al,[7] schizophrenia patients as compared to 52% in affective disorders and 5% in normal individuals. In their review, Heinrichs and Buchanan have estimated the prevalence of soft neurological signs in schizophrenia patients to be between 50% - 65% as compared to 5% observed in controls.40 Also the study by Nizamie et al have reported a similar prevalence of neurological soft signs among Indian patients with schizophrenia.[8]A meta-analysis of all the studies done from 1966 to January 2008 has shown that on an average a substantial majority of patients i.e. 73% perform outside the range of healthy control subjects on aggregate Neurological soft sign measures.[9] Thus, it appears that the prevalence of soft neurological signs among the patients in this study is similar to the rates reported previously in the literature.

The neurological soft signs in this study were evaluated using the Neurological Evaluation Scale and the mean NES score among patients was found to be 11.68. This scale has been used in most of the published studies in this area. In an earlier study by Venkatasubramanian et al (2001), the mean NES total score was 16.9 with a standard deviation of 6.973. Also, the previous studies have had a sample size of 25 patients and 32 patients with schizophrenia respectively and an equal number of healthy controls. The comparison of the mean NES scores among cases and controls in this study reveals a very highly significant difference between the two groups studied. This suggests that neurological soft signs are highly prevalent among patients with schizophrenia.

Relationship of soft Neurological signs with ICD – 10 diagnoses:

This study found that the mean NES score of the patients in the Schizophrenia: Paranoid group is lower than that of the patients in the Schizophrenia: Undifferentiated group and those in the Schizophrenia: Residual group. This suggested a relationship between Soft Neurological Signs and the subtypes of schizophrenia other than the paranoid subtype. However, an analysis between the three groups did not show any statistically significant difference in the mean NES scores according to the ICD – 10 diagnoses of the patients.

This is consistent with findings reported previously that no differences were noted between the subtypes of schizophrenia in terms of neurological signs.[10,11] The findings of this studyprobably reinforce the view that soft neurological signs are not specific to schizophrenia subtypes.[10]

Relationship of soft neurological signs with positive and negative syndrome of schizophrenia:

In this study, a negative correlation is noted between the Total NES scores and the Positive symptom subscale of the PANSS. However, this correlation is not found to be statistically significant in the analysis. A positive correlation is observed between the Total NES scores and the negative subscale of PANSS among the patients in this study. A statistical analysis of the significance of this co-relation revealed that in this study, the relationship between the negative subscale and Total NES scores is highly significant. A positive correlation is observed between the Total NES scores and the general psychopathology subscale of PANSS. However, an analysis of the correlation did not reveal any statistically significant relationship between the two. A positive correlation is observed between the Total NES scores and the Total PANSS score among the patients in this study and this co-relation is found to be highly significant.

Previous studies have examined specifically the relationship between the positive and negative syndrome in patients of schizophrenia and the presence of soft neurological signs. Neurological abnormalities have been correlated with the total number of psychiatric symptoms by Tucker and Silberfarb.[12] Browne et al,[13] described a correlation between

neurological soft signs and total symptom severity and positive symptoms whereas Sanders et al reported no correlations with global measures of psychopathology and soft signs and Flykt et al showed no correlation of soft signs with positive and negative dimensions of schizophrenia.[14,15]

Several other studies have demonstrated the positive relationship between soft neurological signs with negative symptoms (Schroeder et al, Wong et al).[16,17] Mohr et al reported a positive relationship with both positive and negative syndromes.[18]

However, there are also several studies refuting any relationship of soft neurological signs with both positive and negative symptoms (Kolakowskaet al).[19]

The results of this study appear to be consistent with previous studies which have demonstrated a significant relationship between soft neurological signs with negative symptoms in schizophrenia.

Relationship of soft neurological signs cognitive functions:

The individuals in this study had a negative correlation between their Total NES and Total MMSE scores. An examination of the significance of this correlation indicated a statistically significant relationship between the Total NES scores and the Total MMSE scores, implyingthat patients with more neurological soft symptoms have more cognitive impairment. This is consistent with prior research that has found cognitive abnormalities in schizophrenia patients with neurological soft symptoms. Several investigations have found a link between soft neurological symptoms and cognition abnormalities (Mosher et al).[20] According to studies, more evidence of neurological soft symptoms is connected with more severe impairment of cognitive functioning.

CONCLUSION

The current research concludes that adult patients with schizophrenia might exhibit soft neurological indications, and the presence of these signs is connected with the negative syndrome of schizophrenia. The non-urgent neurological symptoms that were observed in patients who suffer from schizophrenia are also associated with the manifestation of cognitive impairment.

REFERENCES

1. Zec, R. F. (1995). Neuropsychology of schizophrenia according to Kraepelin: disorders of volition and executive functioning. European Archives of Psychiatry and Clinical Neuroscience, 245(4), 216-223.
2. Moskowitz, A., & Heim, G. (2011). Eugen Bleuler's Dementia praecox or the group of schizophrenias (1911): a centenary appreciation and reconsideration. Schizophrenia bulletin, 37(3), 471-479.
3. Tiwari, A. K., Zai, C. C., Müller, D. J., & Kennedy, J. L. (2022). Genetics in schizophrenia: where are we and what next?. Dialogues in clinical neuroscience.
4. Alaghband-Rad J., Mc. Kenna K., Gordon C. T., Albus K. E., Hamberger S. D., Rumsey J. M., Frazier J. A., Lenane M. C., Rapoport J. L. Childhood- Onset Schizophrenia: The Severity of Premorbid Course. Journal of the American Academy of Child & Adolescent Psychiatry 1995; 34(10): 1273- 1283.
5. Done D. J., Crow T. J., Johnstone E. C., Sacker A. Childhood antecedents of schizophrenia and affective illness: Social adjustments at ages 7 and 11. British Medical Journal 1994; 309: 699-703.
6. Tucker C. J., Campion E. W. Sensorimotor functions and cognitivedisturbance in psychiatric patients. American Journal of Psychiatry 1975; 132 (1): 17-21.

7. Manschreck T. C., Ames D. Neurological features and psychopathology. Biological Psychiatry 1984; 19: 703-719.
8. Nizamie S. H., Nizamie A., Sangma M. W., Sharma P. L. Soft neurological signs and minor physical anomalies in schizophrenia. Indian J. Psychiat. 1989; 31 (3): 230-237.
9. Chan R. C. K., Xu T., Heinrichs R. W., Yu Y., Wang Y. Neurological soft signs in schizophrenia: A meta-analysis. Schizophrenia Bulletin.2010; 36(6): 1089-1104.
10. Nasrallah H. A., Tippin J., McCalley-Whitters M. Neurological soft signs in manic patients: A comparison with schizophrenic and control groups. Journal of Affective Disorders 1983; 5 (1): 45-50.
11. Manschreck T. C., Ames D. Neurological features and psychopathology. Biological Psychiatry 1984; 19: 703-719.
12. Tucker G. J., Silverfarb P. M. neurological dysfunction in schizophrenia: Significance for diagnostic practice. In Psychiatric Diagnosis: Exploration of Biological Predictors. Edited by Akiskal H., Webb W. New York: Spectrum; 1978: 453-462.
13. Browne S., Clarke M., Gervin M., Lane A., Waddington J. L., et al. Determinants of neurological dysfunction in first-episode schizophrenia. Psychol Med 2000; 30: 1433-1441.
14. Sanders R. D., Keshavan M. S., Schooler N. R. Neurological examination abnormalities in neuroleptic naive patients with first break schizophrenia: Preliminary results. American Journal of Psychiatry 1994; 151: 1231-1233.
15. Flykt L., Sydow O., Bjerkenstedt L. Neurological signs and psychomotor performance in patients with schizophrenia, their relatives and healthy controls. Psychiatry Research 1999; 86: 113-129.
16. Schroeder J., Buchsbaum M. S., Siegel B. V. Structural and functional correlates of subsyndromes in chronic schizophrenia. Psychopathology 1995; 28 (1): 38-45.
17. Wong A. H., Voruganti L. N., Heselgrove R. J. Neurocognitive deficits and neurological signs in schizophrenia. Schizophrenia research 1997; 23 (2): 139- 146.
18. Mohr F., Hubmann W., Cohen R., Bender W., Haslacher C., Honicke S., Schlenker R., Wahlheim Ch., Werther R. Neurological soft signs in schizophrenia: assessment and correlates. Eur Arch Psychiatry ClinNeurosci (1996) 246 : 240-248.
19. KolakowskaT.,Williams A. O., Jambor K., ArdernM. Schizophrenia with good and poor outcomes. III: Neurological 'soft' signs, cognitive impairment andtheir clinical significance. British Journal of Psychiatry 1985; 146: 348-357.
20. Mosher L. R., Pollin W., Stabeneau J. R. Identical twins discordant for schizophrenia: Neurologic findings. Archives of General Psychiatry 1971; 24: 422-430.