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A Comparative Study on Neurological Soft Signs in Patients of Schizophrenia and Their First Degree Relatives

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Abstract :

Background: Neurological soft signs (NSS) are those minute sensory and motor function impairments which have been found to be frequently associated with Schizophrenia patients. NSS have been found to have a familial association. However the pattern of association of NSS with their first degree relatives needs to be evaluated. There is paucity of Indian studies in this area.

Aim and Objectives : We aim to evaluate the pattern of neurological soft signs in patients of schizophrenia and first degree relatives (FDR) of the patients with schizophrenia and to evaluate the association between the patterns of Neurological soft signs in both groups to see whether there is a correlation between the two.

Methodology : Patients who are clinically diagnosed to have Schizophrenia using International Classification of Diseases - 10th revision (ICD-10) research criteria presenting to either Outpatient Unit or Inpatient Unit of Psychiatry Department of the AVBRH hospital will be selected. Only one of the FDRs of each patient will be selected for the study. NSS will be assessed by using Neurological Evaluation Scale (Original version) in both the patient and their FDRs. Later comparison will be made between both the groups using appropriate statistical methods.

Results : The Outcome of this study will help in establishing the association between NSS in patients of schizophrenia and their FDR. This study will help in evaluating the endophenotype status of NSS.

Conclusion : With this study we will be able to recognize the pattern of neurological soft signs in patients with Schizophrenia and the FDRs. It will help us to recognize whether the neurological soft signs are found more frequently in patients or first degree relatives of

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schizophrenia. It will answer whether neurological soft signs can be considered as endophenotypes of schizophrenia.

Keywords :: Neurological Soft Signs (NSS), Schizophrenia, First-degree relatives (FDRs).

INTRODUCTION :

Schizophrenia is a mental disorder which is characterized by disturbances in various domains like thinking, perception, emotions, language, sense of self and behaviour. It is one of the most common of the serious mental disorders. The effect of the illness is found to be severe and long - lasting. Schizophrenia occurs throughout the world. In India, which has a population of about 1.1 billion, the lifetime prevalence of schizophrenia, and other psychotic disorders is 1.3% (1). Many researchers have established that there is an increased prevalence of widespread, minor neuro - anatomical abnormalities in the brain among the patients with schizophrenia (2).

Neurological soft signs (NSS) are the observable, small neurological function impairments - sensory and/ or motor, which are not confined to a specific region of the brain. NSS are not distinctive of any one particular neurological dysfunction or abnormality (3). They are referred to as non - diagnostic abnormalities found during the neurological examination. NSS are said to have corresponded with a wide number of neuro - anatomical dysfunctions and neuro - cognitive dysfunctions. The studies have given a suggestion that the NSS may depict an abnormality in the integration of neural networks (4).

NSS is widely prevalent among different types of psychiatric disorders, most well studied being bipolar mood disorder (BPAD) and, obsessive – compulsive disorder (OCD). But the association of NSS is found to have been more frequently seen with schizophrenia (5,6).

NEUROLOGICAL SOFT SIGNS IN SCHIZOPHRENIA

Neurological soft signs (NSS) have been known to be associated with schizophrenia patients. They have been mainly looked at as endophenotypes (7). Studies in patients who have first episode psychosis (FEP) and those are drug naive and have never been treated with any neuroleptics have shown that NSS are present even before they were given any medications and thus emphasizing NSS may be termed as an inherent feature of schizophrenia as opposed to any adverse effect due to medications (8). The studies have also established that NSS in patients of schizophrenia fulfil three criteria for an endophenotype: (a) Illness association, (b) state-independence (c) also show a pattern of familial association. (9-11).

Rationale : While working in this area, we would be able to establish further relation between neurological soft signs in patients of Schizophrenia and the first degree relatives of patients of Schizophrenia. We plan to administer the psychological tools developed and standardized for Indian Population.

Aim : We aim to evaluate the pattern of neuro-logical soft signs in the patients of

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schizophrenia and the first degree relatives of the patients of schizophrenia.

Objectives :

1. To evaluate the pattern of the neuro-logical soft signs in the patients of Schizophrenia.
2. To evaluate the pattern of the neuro-logical soft signs in the first degree relatives of patients of Schizophrenia.
3. To evaluate the association between the patterns of neuro-logical soft signs in both the groups to see whether there is any correlation between the two.

METHODS :

Study design : The study is planned as a cross sectional study done in the hospital-based setting for a period of about 1 year duration (January 2021 to December 2021).

Setting : The research setting is at theInpatient and outpatientdepartmentsof Psychiatry, AcharyaVinobaBhave Rural Hospital (AVBRH), Sawangi (Meghe).

Participants :

INCLUSION CRITERIA :

For the patients :

1. Patients who are clinically diagnosed to have Schizophrenia using the International Classification of Diseases - 10 (ICD-10) research criteria.
2. Patients between the age group of 18 and 60 years, of either sex.
3. Patients should either be remitted or should be having a stable status so that they can co-operate in the study.
4. Patients who wish to give a written informed consent.

For the first degree relatives :

1. One relative of each patient is planned to be incorporated in the study (Parents, siblings or children).
2. Age from 18 to 60 years.
3. They should not have any history of psychiatric illness.
4. Subjects who wish to give the written informed consent.

EXCLUSION CRITERIA for all of the participants :

1. Subjects who do not wish to give written informed consent.
2. Patients who are either acutely ill or are not able to cooperate with the study.
3. Patients who have had any history of developmental delay or any other major organic brain pathology, substance abuse.
4. Patient who have had any past history of head injury.
5. Subjects with any history of medical illness.

ASSESSMENT TOOLS :

1. **Socio-demographic Data and Clinical Data**: It is a semi-structured proforma which is

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designed for this study. It contains the information about socio - demographic details such as age, sex, education, religion, employment status, marital status, place of residence, urban/ rural, socio-economic status, etc. The clinical data sheet also contains variables like age at which the illness started, total duration of the illness, the precipitating factors, any of the treatment history if it is available, duration of the treatment taken, drugs and their doses, any side effects noted, compliance to treatment, current treatment, past medical or psychiatric illness, any family history of psychiatric illness, any medical or surgical history.

2. **Brief Psychiatric Rating Scale** : The scale consists of 18 items. It mainly measures various Psychiatric symptoms which includes the following- Degree of concern over bodily health, anxiety, guilt feelings, any grandiose talks, tension, depressed mood, disorganization with concepts, emotional withdrawal, mannerisms, posturing, motor retardation, hallucinatory or acting out behavior, not being co-operative, odd or strange thought content, suspiciousness, blunt affect, disorientation and excitement. Every symptom is measured from 0 - when the symptom is not assessed, 1 - when the symptom is not present, 2 - for very mild symptom, 3 - for mild symptom, 4 - for moderate symptom, 5 - for moderately severe symptom, 6 - for severe symptom and 7 - for extremely severe symptom(12).
3. **Neurological evaluation scale :** This scale consists of 26 discrete items and has also has few tests for cerebral dominance.Out of the 26 items, 14 of the items are tested bilaterally. The scores can be presented in four sub - items – sensory system integration, complex motor action sequencing, motor system coordination, and the others. Each item is scored using the ratings as follows. 0 score is given for normal, 1 score is given for mild but definite impairment, 2 score is given for marked impairment. A score of 0 or 2 is given for the snout and suck reflexes. Items included in the scale are tandem walking, Romberg's test, Tremors, adventitious overflow, audio-visual integration, stereognosis, graphaesthesia, fist-ring test, fist-edge-palm test, ozeretski test, memory, rhythm tapping test, alternate rapid movements, thumb - finger opposition, mirror movements, extinction, right/left confusion, synkinesis, convergence, gaze impersistence, finger-nose test, glabellar reflex, snout reflex, grasp reflex and suck reflex. (13)

Ethics approval - Ethical clearancefrom the Institutional Ethical Committee will be taken before enrolling patient into the study.

Study size : Sample Size - 130 (65 patients of Schizophrenia and 65 first degree relatives of schizophrenia)

$$n = Z_{\alpha/2}^2 \cdot p \cdot (1-p) \over d^2$$

$Z_{\alpha/2}$ is the level of significance at 5 % i.e. 95% Confidence interval = 1.96

P = prevalence of Schizophrenia = 1.5% = 0.015

D = Desired error of margin = 3% = 0.03

$$N = \frac{1.96^2 \text{x } 0.015 \text{ x } (1-0.015)}{0.03^2}$$

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n = 65

Statistical methods :

Descriptive analysis - For continuous variables, including social variables, demographic variables and clinical variables and for the scores on the scales being used to assess the symptoms or psycho-social variables, analysis will be done using mean, median, range and standard deviation. For categorical variables like social, demographic and clinical variables, it will be computed in terms of percentages and frequency .

Univariate analysis - For identification of any association between different parameters of neurological soft signs in the two groups, univariate analysis will be used. Students't test, or Chi-square test will be used for these comparisons .

Analysis will be done using SPSS version 21 using appropriate statistical methods.

Expected Outcomes/Results :

The Outcome of this study will help in establishing the association between NSS in patients of schizophrenia and their FDR. This study will help in evaluating the endophenotype status of NSS.

DISCUSSION :

In a systemic review and meta analysiscarried out by KishenNeelam et al in 2011, it was found that the NSS shows a pattern of association with family members in patients with schizophrenia which is in accordance with the status of an endophenotype. They also reported of some evidence that some NSS may have a correlation with certain structural abnormalities in the brain which may be specific to certain regions in the brain of patients of schizophrenia. [14].

In a study conducted by Tsuang et alin 1991, and Tsuang and Faraone in 1999, the authors suggested that the NSS are important features of schizophrenia which depicts the possible genetic processes and other non- genetic processes that causes alteration in the growth and development of neurological and behavioral systems (15,16).

In a study conducted by Feng et al in 2016, it was found that NSSs were more predominantly found with patients in schizophrenia and psychotic disorders. . Their association with their first-degree relatives was found to be less than that in the patients of Schizophrenia while in healthy controls, the association was weakest among the three groups. They also suggested that motor co - ordination may be considered as a trait in schizophrenia since the motor co - ordination was found to persist even after the remission of the psychotic symptoms. (17,18).

Chan et al, conducted a meta-analysis in 2010, in which, it was found that the prevalence of NSS in the schizophrenia patients and the first degree relatives of the patients who did not have any history of psychotic illness and the healthy controls showed predominant differences between the groups. These results were also found to be in agreement with the proposal that NSS are inherited and hence are familial and may be considered as

endophenotypes (19).

In a study carried out by Heinreichs and Buchanan et al in 1988, it was studied that NSS is more frequently associated with patients with schizophrenia with the prevalence ranging from 50% - 60%. There was a poor association of NSS with healthy controls on comparison with patients of schizophrenia. They also suggested that abnormalities found during the neurological examination in patients of schizophrenia may be related to different symptom dimensions, any family histroy of psychotic illness and the premorbid risk of developing illness in the individuals (20).

In a study carried out by Chan and Chen et al in 2007 , it was found that NSS prevalence in schizophrenia patients was about 59% in Chinese population, which implies that, across all cultures, there is an association between NSS and Schizophrenia (21).

In a study conducted by Gourion et al in 2004, it was found that parents of patients who were presumed to be carriers had a higher NSS scores than the parents of patients who were presumed to be non-carriers. It shows that a genetic loading may affect NSS scores. The study found that familial factors determine NSS (22).
Although many studies carried out by Bollini et al in in 2007, Compton et al in 2007, and Lawrie et al in 2007, they found no major differences in NSS score when healthy controls and relatives of schizophrenia patients were compared. (23, 24) . Related studies on schizophrenia were reported by Modiet. al. (25) and Patel et. al (26). Few studies on depression and substance abuse were reviewed (27-29).

Limitations :It is a relatively small hospital-based, cross-sectional study. A larger general population-based longitudinal follow up study will help to know more about the comparison of NSS in ppatients of Schizophrenia and the first degree relatives and also the association of NSS with the long term course of the illness.

CONCLUSION:

With the present study we will be able to recognize the pattern of neurological soft signs among patients of Schizophrenia and the FDR of patients with schizophrenia. It will help us to recognize whether the neurological soft signs are found more frequently in patients or first degree relatives of schizophrenia. It will answer whether neurological soft signs can be considered as endophenotypes of schizophrenia.

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