

## A Comparative Study of Neurological Soft Signs in Drug Naïve Patients with First Episode of Schizophrenia and Obsessive Compulsive Disorder

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## Abstract

## Original Research Article

**Context:** Neurological soft signs (NSS) are minor neurological signs that reflect dysfunction in areas of motor coordination, sensory function and complex motor tasks, without localization. Schizophrenia and OCD are considered to be neurodevelopmental disorders with structural and functional brain abnormalities. **Aims:** To study the socio-demographic profile of the drug naïve patients with first episode Schizophrenia and OCD and to assess and compare neurological soft signs in them. **Setting and design:** Cross-sectional study includes patients in both in-patient and out-patient setting. **Methods and Material:** A total of 90 patient's i.e. 30 each of drug naïve first episode OCD, Schizophrenia and healthy controls fulfilling the inclusion and exclusion criteria were recruited by non-probability sampling method and subjected to semi-structured Psychiatric Thesis Performa, The Positive and Negative Syndrome Scale (PANSS), Yale Brown Obsessive Compulsive Scale (YBOCS) and Heidelberg Manual for assessment of NSS. **Statistical analysis used:** Statistical analysis was performed using statistical package for social sciences (SPSS 20.0.0) software. The data was analysed using the chi-squared test and Pearson's co-relational analysis. **Results:** On comparison of sociodemographic profile variables, patients of OCD as compared to patients of Schizophrenia were in higher age group ( $p=0.005$ ) and more educated ( $p=0.006$ ). The maximum percentage of NSS was found in schizophrenia (76.7%) followed by OCD (46.7%) and healthy controls (23.3%) and the difference was statistically significant ( $p<0.05$ ). The NSS score significantly correlated with duration of illness of schizophrenia ( $r=0.518$ ) as well as OCD ( $r=0.975$ ). **Conclusions:** NSS are considered as endophenotypes and support the neurodevelopmental basis for both disorders.

**Keywords:** Neurological soft signs, First episode Schizophrenia, Obsessive Compulsive Disorder.

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### INTRODUCTION

Neurological soft signs (NSS) are minor neurological signs that reflect dysfunction in areas of motor coordination, integrative sensory function, and ordering complex motor tasks, but the dysfunctions are not localizable to specific brain structures [1,2]. Schizophrenia and OCD are considered to be neurodevelopmental disorders with structural and functional brain abnormalities in the prefrontal cortex, striatum, and thalamus [3,4]. The limited number of published studies from India has focused on the prevalence of neurological soft signs in drug naïve first episode schizophrenia and OCD. The present study was conducted to assess neurological soft signs in drug naïve first episode schizophrenia and OCD.

### SUBJECTS AND METHODS

Present study was a cross-sectional study in a tertiary care hospital in which socio-demographic profile and neurological soft signs of drug naïve first episode OCD and Schizophrenia were examined among consenting patients. A total of 90 patients i.e. 30 each of drug naïve first episode OCD (group2), Schizophrenia (group3) and healthy controls (group1) were recruited for study by non-probability sampling method. Interview of the patient was conducted with the help of Psychiatric Thesis Performa and Heidelberg manual was employed to assess neurological soft signs. The severity of obsessive and compulsive symptoms was assessed by Y-BOCS scale and the psychopathology in patients of schizophrenia was assessed by PANSS scale. The data thus generated was subjected to appropriate Statistical Analysis to answer the aims and objectives.

## INCLUSION AND EXCLUSION CRITERIA

Patients giving written informed consent and meeting the ICD 10 Criteria for OCD and Schizophrenia were included in the study. However subjects with current or history of neurological illness, Substance dependence, Organic Brain Syndrome, Severe Medical Ailment and mental retardation were excluded from the study.

## RESULTS AND OBSERVATIONS

Considering the sociodemographic profile; maximum number of the patients belonged to the age group of 20-30 years in all groups totaling to 54 out of 90 subjects with 25, 14 and 15 in group 1, 2 and 3 respectively. The difference in the distribution of age in the three groups was found to be statistically significant ( $p=0.005$ ). Considering the education of the total sample majority of subjects in group 1 were graduate, 9 out of 30 were studied up to higher secondary in group 2 and 9 out of 30 up to middle school in schizophrenia group. The difference in distribution of education in the 3 groups was statistically significant ( $p=0.006$ ). For rest of the sociodemographic variables although there were differences though marginal in the distribution in three groups but this difference was statistically non-significant with  $p$  value being 0.09, 0.714, 0.350, 0.136, 0.081, 0.182 and 0.192 for gender, religion, residence, family type, occupation, family income and marital status respectively.

Among the patients of group 2 it was seen that majority of the patients, 24(80%) had negative family history while 6(20%) patients had a family history of psychiatric illness. Of these 3 patients i.e. 10% had family history positive of obsessive compulsive disorder, 2(6.7%) were positive for mood disorders and only 1(3.3%) patient had family history of schizophrenia. In Group 3, majority of the patients, 25(83.3%) had negative family history while 5(16.7%) patients had a family history of psychiatric illness. Of these 4 patients i.e. 13.3% had family history positive for schizophrenia, 1 (3.3%) was positive for mood disorder.

In PANSS the mean of positive symptom score was 20.67 and of negative symptom score was 17.67. The mean of General psychopathology was found to be 36.33 and for total PANSS score the mean was 74.67. The maximum correlation was found between positive symptom and NSS total ( $r=0.189$ ), followed by negative symptoms with NSS total ( $r=0.100$ ) and general psychopathology score with NSS total ( $r=0.030$ ). The relationship coefficient ( $r$  value) for PANSS total- NSS total was 0.023. This shows weak correlation in all four categories and it was not statistically significant ( $p>0.05$ ).

Among 30 patients of Obsessive Compulsive Disorder sub group, the mean YBOCS score was 11.37 for obsession subtotal, 11.43 for compulsion subtotal

and 22.8 for the total score. The correlation of symptom severity in OCD patients in terms of YBOCS components (obsession subtotal, compulsion subtotal) as well as YBOCS total score with the total NSS score for which the correlation coefficient was 0.037, 0.020 and 0.008 respectively. This shows weak correlation in all the three categories. Thus no significant correlation was found between symptoms severity and NSS total score;  $p$  value being 0.848, 0.915 and 0.967 respectively i.e. statistically non-significant.

Based on CT findings out of a total 30 patients enrolled for study in group 2 majority of them, 25(83.3%) had CT head within normal limits while 5 of the patients constituting 16.7% of the total had positive findings on CT head. Out of these 2 had diffuse cortical atrophy contributing 6.7% to the total. CT head findings showed basal ganglionic calcification, calcified granuloma and lacunar infarct in 1 patient each constituting 3.3% individually. Out of a total 30 patients enrolled for study in group 3 majority of them, 24(80%) had CT head within normal limits while 6 of the patients constituting 20% of the total had positive findings on CT head. Out of these 4 had diffuse cortical atrophy contributing 13.3% to the total. CT head findings showed basal ganglionic calcification and lipoma in 1 patient each constituting 3.3% individually.

The percentage of patients with  $NSS \geq 1$  as well as the mean of 5 subcomponents of NSS was found to be maximum in schizophrenic patients (76.7%) followed by OCD (46.7%) and minimum in healthy controls (23.3%). Among the 5 subcomponents the maximum impairment was seen in complex motor task followed by motor coordination, spatial orientation, sensory integration and hard signs on that order (Figure 1).

On comparison of neurological soft signs between healthy controls (grp 1) and OCD patients (grp 2) it was found that soft sign scores (total as well as component score) were higher in OCD patients than healthy controls. This difference was statistically significant in total score ( $p$  value= 0.004), motor coordination score ( $p$  value=0.035) and complex motor task ( $p$  value=0.004) (Table 1).

On comparison of neurological soft signs between healthy controls (grp 1) and schizophrenic patients (grp 3) it was found that soft sign scores (total as well as component score) were higher in schizophrenic patients than healthy controls. This difference was highly statistically significant in total score ( $p$  value= 0.000), motor coordination score ( $p$  value=0.000), sensory integration score ( $p$  value=0.001), complex motor task ( $p$  value=0.004) and was statistically significant in spatial orientation score ( $p$  value=0.003) and hard signs score ( $p$  value=0.01) (Table 2).

On comparison of neurological soft signs between OCD patients(grp 2) and schizophrenic patients (grp 3) it was found that soft sign scores (total as well as component score) were higher in schizophrenic patients than healthy controls. This difference was not significant statistically (Table 3).

It was found that in group 2 there was strong correlation between Neurological Soft Signs score with duration of illness of OCD( $r=0.975$ ) and it was statistically highly significant ( $p<0.001$ ).In group 3 there was weak correlation between Neurological Soft Signs score with duration of illness of Schizophrenia( $r=0.518$ ) and it was statistically significant ( $p=0.003$ ) (Table 4).

**Table-1: Comparison of neurological soft signs between healthy controls (group 1) and OCD (group 2)**

Variable	Grp 1 Mean (SD)	Grp 2 Mean (SD)	Mean difference	Standard error	p value
Total NSS	0.43(0.86)	3.30(4.43)	-2.867	.879	.004 <sup>S</sup>
Motor coordination	0.20(0.48)	1.07(1.70)	-.867	.343	0.035 <sup>NS</sup>
Sensory integration	0.00(0.00)	0.33(0.84)	-.333	.196	0.210 <sup>NS</sup>
Complex motor task	0.07(0.25)	1.07(1.34)	-1.000*	.304	0.004 <sup>S</sup>
Spatial orientation	0.10(0.40)	0.50(0.90)	-0.400	0.228	0.190 <sup>NS</sup>
Hard signs	0.03(0.18)	0.33(0.71)	-0.300	0.144	0.100 <sup>NS</sup>

NS (Not significant):  $p > 0.05$ ;  $p < 0.05$ , Significant;  $p < 0.001$ , highly significant.

**Table-2: Comparison of neurological soft signs between healthy controls (group 1) schizophrenia (group 2)**

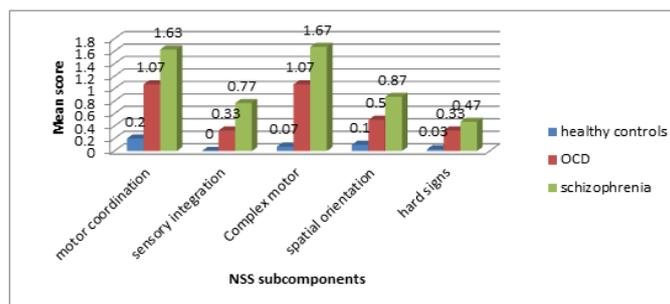
Variable	Grp 1 Mean (SD)	Grp 3 Mean (SD)	Mean difference	Standard error	P value
Total NSS	0.43(0.86)	5.23(3.79)	-4.800	.879	.000 <sup>HS</sup>
Motor coordination	0.20(0.48)	1.63(1.47)	-1.433	.343	.000 <sup>HS</sup>
Sensory integration	0.00(0.00)	0.77(1.01)	-.767	.196	.001 <sup>HS</sup>
Complex motor task	0.07(0.25)	1.67(1.52)	-1.600	.304	.000 <sup>HS</sup>
Spatial orientation	0.10(0.40)	0.87(1.17)	-.767	.228	.003 <sup>S</sup>
Hard signs	0.03(0.18)	0.47(0.63)	-.433	.144	.010 <sup>S</sup>

NS (Not significant):  $p > 0.05$ ;  $p < 0.05$ , Significant;  $p < 0.001$ , highly significant.

**Table-3: Comparison of neurological soft signs between schizophrenia (group3) and OCD (group 2)**

Variable	Grp 2 Mean (SD)	Grp 3 Mean (SD)	Mean difference	Standard error	p value
Total NSS score	3.30(4.43)	5.23(3.79)	-1.933	.879	.077 <sup>NS</sup>
Motor coordination	1.07(1.70)	1.63(1.47)	-.567	.343	.230 <sup>NS</sup>
Sensory integration	0.33(0.84)	0.77(1.01)	-.433	.196	.075 <sup>NS</sup>
Complex motor task	1.07(1.34)	1.67(1.52)	-.600	.304	.124 <sup>NS</sup>
Spatial orientation	0.50(0.90)	0.87(1.17)	-.367	.228	.247 <sup>NS</sup>
Hard signs	0.33(0.71)	0.47(0.63)	-.133	.144	.626 <sup>NS</sup>

NS (Not significant):  $p > 0.05$ ;  $p < 0.05$ , Significant;  $p < 0.001$ , highly significant



**Fig-1: Comparison of mean of NSS subcomponents in 3 groups**

**Table-4: Correlation of NSS score with duration of illness**

Variable-NSS score with duration of illness	Correlation coefficient(r value)	p value
Group 2(OCD)	0.975	0.000 <sup>HS</sup>
Group 3 (Schizophrenia)	0.518	0.003 <sup>S</sup>

NS (Not significant):  $p > 0.05$ ;  $p < 0.05$ , Significant;  $p < 0.001$ , highly significant

## DISCUSSION

The Present study was carried out in a tertiary care hospital to assess the sociodemographic profile of drug naive patients with first episode of Obsessive Compulsive Disorder and schizophrenia and healthy controls; to assess neurological soft signs in drug naive patients with first episode of Obsessive Compulsive Disorder and schizophrenia and to compare it with healthy controls.

In our study, taking into account the sociodemographic variables of the three groups, it was seen that maximum number of the patients belonged to the age group of 20-30 years in all groups. The mean age of first episode OCD group was  $25.63 \pm 9.38$  while for first episode schizophrenia group it was  $24.07 \pm 6.24$  and in healthy controls the mean age was  $26.67 \pm 4.78$ . In line with our study, Bachmann *et al.* [5] conducted a similar study and found that mean age was  $27 \pm 7.7$  in first episode schizophrenia and  $28 \pm 3.8$  in healthy controls while Guz *et al.* [6] found that mean age of the OCD group was  $36.3 \pm 8.8$  years which was higher in comparison to our study. Maximum patients were males in all the 3 groups in our study with 19 out of 30 in OCD group, 24 out of 30 in schizophrenia group and 15 out of 30 in healthy controls. Sevincock *et al.* [7] also found that the no of males were 11 out 15 in OC schizophrenia group, 22 out of 38 in non OC schizophrenia group and 13 out of 24 in healthy controls. Majority of the patients belonged to sikh religion i.e. 22 out of 30 in OCD group and 23 out of 30 in schizophrenia group and 22 out of 30 in healthy controls. Hembram *et al.* [8] conducted a study in Indian setting and found majority of patients belonged to hindu religion with 23 out 30 being hindus in schizophrenia without first rank symptoms group and 24 out of 30 in schizophrenia with first rank symptoms group. This difference can be attributed to difference in distribution of religion in various parts of India. Comparing the marital status 18 out of 30 were married in control group while majority were single in OCD (16/30) and schizophrenia group (19/30). Mhalla *et al.* [9] found that in first episode psychosis group 46 out of 61 were single.

Considering the family history of psychiatric illness it was seen that family history was positive for psychiatric illness in 16.7% of patients in OCD group and 20% of the patients of schizophrenia group. In a study conducted by Thomas *et al.* [10] family history was positive in 24% of the patients of schizophrenia.

The neurological soft signs were seen in 76.7 % of schizophrenic patients, 46.7% of patients with Obsessive Compulsive Disorder and in only 23.3% of

healthy controls. In conjunction with our study, the prevalence of NSS in first episode psychosis was found to be 68% in study by Emsley *et al.* [11] and 78% in study by Flyct *et al.* [12]. However Gupta *et al.* [1] in a study comparing NSS in schizophrenia and healthy controls found that NSS were present in 48% of schizophrenia group and 0% of healthy controls. Bolton *et al.* [13] also found that NSS were higher in schizophrenia in comparison to Obsessive Compulsive Disorder which in turn was higher in comparison to normal healthy controls.

On comparison of neurological soft signs between healthy controls (grp 1) and schizophrenic patients (grp 3) it was found that soft sign scores (total as well as component score) were higher in schizophrenic patients than healthy controls. This difference was highly statistically significant in total score ( $p$  value= 0.000), motor coordination score ( $p$  value=0.000), sensory integration score ( $p$  value=0.001), complex motor task ( $p$  value=0.004), spatial orientation score ( $p$  value=0.003) and was statistically significant in hard signs score ( $p$  value=0.01). Arango *et al.* [2] conducted a similar study on NSS in schizophrenia using neurological evaluation scale and found that on comparing means the difference was highly significant for total score, sensory integration and others ( $p < 0.001$ ) and significant for motor coordination ( $p=0.008$ ) and complex motor task ( $p=0.001$ ).

On comparison of neurological soft signs between healthy controls (grp 1) and OCD patients (grp 2) it was found that soft sign scores (total as well as component score) was higher in OCD patients than healthy controls. This difference was statistically significant in total score ( $p$  value= 0.004), motor coordination score ( $p$  value=0.035) and complex motor task ( $p$  value=0.004). Karadag *et al.* [14] found that on comparing OCD patients with healthy controls, the difference was statistically highly significant for all the sub components ( $p < 0.001$ ). Bolton *et al.* [15] found that difference was highly significant for motor coordination and sensory integration ( $p < 0.001$ ) and non-significant for hard signs ( $p=0.119$ ). Our findings were also in conjunction with study conducted by Tripathi *et al.* [16] where maximum score was found in the sub component of motor coordination in all the three groups. NSS in study conducted by Dhuri *et al.* [17], OCD patients were significantly higher in all the subscales of motor coordination, sensory integration, complex motor tests, right/left and spatial orientation, and hard signs.

Among patients of group 2 i.e. OCD, in terms of YBOCS score the mean score was 11.37 for obsession subtotal, 11.34 for compulsion subtotal and

22.8 for total score. No significant correlation was found between symptoms severity and NSS total score; p value being 0.848, 0.915 and 0.967 respectively. Jaafari *et al.* [18] also found similar results in that mean score was 10.8 for obsession subtotal, 11.5 for compulsion subtotal and 22.2 in total YBOCS score which was comparable to the results in our study. Thomas *et al.* [10] also found similar results that scores on the NSS (total or subscales) did not correlate significantly with Y-BOCS total score or subscale scores for obsessions or compulsions.

In the group of schizophrenia, the mean score on PANSS scale was 20.67 for positive symptom scale, 17.67 for negative symptom scale, 36.33 for general psychopathology and 74.67 on total score of PANSS. This shows weak correlation in all four categories and it was not statistically significant ( $p > 0.05$ ). However Chen *et al.* [19] found that correlation of total NSS was maximum with negative symptoms ( $r = 0.346$ ) followed by total PANSS score ( $r = 0.327$ ) and positive symptoms ( $r = 0.192$ ) which was different from our study. Braun *et al.* [20], similar to our results did not find any correlation of positive or negative symptoms with neurological soft sign score.

On studying the correlation of Neurological Soft Signs score with duration of illness, it was found that there was strong correlation between Neurological Soft Signs score with duration of illness of OCD ( $r = 0.975$ ) ( $p < 0.001$ ) and Schizophrenia ( $r = 0.518$ ) ( $p = 0.003$ ). Dutta *et al.* [21] found similar results i.e. increase in the total NSS score was also observed with the increase in the duration of illness, with the maximum score being in subjects with illness duration of more than 15 years. The difference was found to be statistically significant ( $p = 0.000$ ).

## CONCLUSIONS

All these findings support the neurodevelopmental basis of both schizophrenia and Obsessive Compulsive Disorder. Thus neurological soft signs are considered as endophenotypes for both the disorders and early recognition of these can play a pivotal role in improving the prognosis of such disorders.

### Limitations

- First, the sample size remained relatively small, despite being larger than in previous studies, and we cannot exclude a lack of power to detect differences, especially when sub grouping the patients with regard to their age at onset. Also, we were not able to analyze separately the patients with tics, although they appear to have specific neurological features.
- Effect of medication on the total score of neurological soft signs warrants another study.

### Conflicts of interest

The authors declare that there are no conflicts of interest regarding publication of literature.

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