

# Comparison of Neurological Soft Signs between Psychotic and Non Psychotic Patients

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## ABSTRACT

**Introduction:** Neurological Soft Signs (NSS) are a group of non-specific signs manifested in some psychiatric patients. Till date, most studies have focused on NSS in schizophrenic patients.

**Aim:** In the current study, the mean NSS score was compared between psychotic and non psychotic patients.

**Materials and Methods:** This descriptive analytical study was conducted on 96 hospitalized patients having psychotic disorders. The patients were first examined by a psychiatrist and their axis I diagnoses (according to DSM-IV-TR) were made. Accordingly, the patients were divided into three groups of psychotic (schizophrenic and schizoaffective) and bipolar disorder patients with and without psychotic symptoms. Using

a 28-item questionnaire, the patients were neurologically examined and their NSS scores were calculated. The mean scores were compared among the groups.

**Results:** Based on the results, the mean NSS score in psychotic patients (schizophrenic and schizoaffective) was higher as compared to that in non-psychotic patients (bipolar disorder patients without psychotic symptoms) and this difference was statistically significant ( $p < 0.0001$ ).

**Conclusion:** It seems that calculation of NSS score in psychotic patients can help predict the response to pharmaceutical treatment, risk of drug reactions/side effects and prognosis of disease. Drawing a definite conclusion in this regard requires further investigations.

**Keywords:** Disease severity, Mental disorder, Prognosis

## INTRODUCTION

NSS are defined as minor neurological abnormalities that are not usually noticeable and do not indicate a defect in a specific part of the brain. These signs are only detectable via physical examination and are categorized into three groups of sensory integration, motor coordination and consecutive movements [1,2]. On the other hand, part of these signs such as impaired grasp reflex are developmental and are considered normal in a specific age group; while some others such as stereognosis are not considered normal and often occur in dementia patients.

Several studies suggest that there is an association between higher NSS scores with Schizophrenia [3]. This is further supported from the finding that occurrence of some NSS at young age helps predict the occurrence of Schizophrenia in future [4]. Walker EF et al., showed that the mean NSS score was higher in schizophrenic patients than in the general population [5].

Studies with respect to NSS among Schizophrenic patients have been conducted to determine the role of genetics in their development as well as to evaluate their influence on the prognosis, in response to pharmaceutical therapy among such patients [6,7]. It has been reported that the mean score of NSS in schizophrenic siblings was higher than in the general population [8]. Mittal VA et al., demonstrated that the higher the mean score of NSS in schizophrenic patients the slower their response to pharmaceutical therapy and the longer their course of recovery [9].

Since most previous studies have evaluated NSS in schizophrenic patients and less attention has been paid to patients with mood disorders, this study sought to assess NSS in schizophrenic and bipolar patients, and their mean NSS scores were compared.

## MATERIALS AND METHODS

This cross-sectional study was conducted on hospitalized patients in the Psychiatric Department of Imam Hossein Hospital in Tehran, Iran from April 2012 to May 2014. Adult patients (aged: 18-60 years) in both sex who were hospitalized due to psychotic problems were

enrolled in the study. According to previous studies [10,11], sample size in each group was considered to be at least 30.

Subjects with mental retardation, history of substance abuse (except for cigarette smoking), Tourette syndrome, tics and cerebral palsy were excluded. The patients were examined by a psychiatrist and were classified into three groups of schizophrenic and schizoaffective patients, bipolar patients with psychotic symptoms and bipolar patients without psychotic symptoms according to the DSM-IV-TR criteria. The Wechsler test was used to assess the intelligence quotient of patients and Abnormal Involuntary Movement Scale (AIMS) was used to assess the extra pyramidal complications in patients who had used antipsychotics during the six months period prior to their hospitalization.

To assess NSS in patients, a 28-item Neurological Evaluation Scale (NES) questionnaire in Persian language was used. Prior to inclusion of patients, written informed consent was obtained from them. The 28 items included three functional domains of sensory integration, motor coordination and consecutive movements. Each symptom was given a score of zero (problem), one (mild disorder) or two (marked disorder) except for the snout reflex and suck reflex that were given a score of zero (absence of problem) or two (presence of problem). The minimum total acquired score was zero and maximum score was 54. The validity and reliability of NES questionnaire had been previously confirmed by Buchanan RW and Heinrichs DW [12]. The Iranian version of NES questionnaire in Persian language was previously validated by Iranian psychiatrists [13].

**Ethical consideration:** The study followed the principles of the declaration of Helsinki and was approved by the Medical Ethics Review Board of Shahid Beheshti University of Medical Sciences, Tehran, Iran. All information about the patients and healthy subjects was kept fully confidential; also all information will be released as a group without participants' name. Study participants did not incur any costs and the study protocol did not have any harm to participants. The written informed consent was obtained from volunteers and details and purpose of the study was disclosed.

## STATISTICAL ANALYSIS

The mean NSS scores in the three groups were analyzed using SPSS version 17.0 (SPSS, Inc., Chicago, IL, USA). To compare the total mean scores among the three groups, One-way ANOVA was applied. Since the difference was found to be significant, Tukey's post-hoc test was used for pairwise comparisons of the groups. The results are expressed as a mean±standard deviation (SD). A p-value less than 0.05 were considered statistically significant.

## RESULTS

A total number of 96 patients including 54 (56.2 %) males and 42 (43.8 %) females with mean age of 34.02±10.14 years old were studied. There were three groups as following; Schizophrenic and schizoaffective patients (n=32), Bipolar disorder patients with psychotic symptoms (n=32), Bipolar disorder patients without psychotic symptoms (n=32).

To assess NSS in patients, 28 items were evaluated. The mean scores for each symptom are shown in [Table/Fig-1].

Of 28 items in the NSS questionnaire, the mean scores of tandem walk, Ozeretski test, glabellar test and grasp reflex were higher in psychotic patients (schizophrenic and schizoaffective) than in non-psychotics (bipolar disorder patients without psychotic symptoms). According to results of ANOVA test, this difference was statistically significant (p<0.001) [Table/Fig-2]. Frequency of NSS in schizophrenic and schizoaffective patients was higher than that in bipolar disorder patients with psychotic symptoms. However, according to Tukey's post-hoc test, this difference did not reach statistical significance (p=0.57).

Neurological Soft Sign	Schizophrenic and schizoaffective patients (N=32) (Mean±SD)	Bipolar disorder patients with psychotic symptoms (N=32) (Mean±SD)	Bipolar disorder patients without psychotic symptoms (N=32) (Mean±SD)
Tandem walk	1.13±0.9	0.56±0.66	0.03±0.17
Romberg test	0.50±0.8	0.16±0.44	0.06±0.24
Adventitious overflow	0.25±0.62	0.13±0.33	0.13±0.33
Tremor	0.25±0.50	0.25±0.50	0.03±0.17
Audio Visual intel	1.03±0.93	1.03±0.93	0.31±0.53
Stereognosis	0.09±0.29	0.13±0.23	0.001±0.0001
Graphesthesia	0.69±0.78	0.87±0.90	0.13±0.33
Fist ring test	1.41±0.61	1.13±0.87	0.72±0.63
Fist-edge- palm test	1.62±0.55	1.81±0.29	0.53±0.67
Ozeretski test	1.13±0.66	0.53±0.67	0.16±0.26
Memory (5 minutes)	1.19±0.82	0.91±0.85	0.24±0.54
Memory (10 minutes)	1.31±0.82	1.41±0.83	0.72±0.72
Rhythm tap (A)	0.69±0.73	0.56±0.66	0.0001±0.001
Rhythm tap (B)	1.16±0.84	1.13±0.87	0.13±0.23
Rapid alternative movement	0.31±0.47	0.16±0.26	0.03±0.17
Finger thumb opposition	1.34±0.70	0.63±0.75	0.13±0.42
Mirror movement	0.25±0.50	0.25±0.44	0.13±0.33
Extinction	0.13±0.23	0.16±0.26	0.0001±0.001
Right-Left Confusion	0.72±0.72	0.84±0.88	0.22±0.49
Synkinesis	1.06±0.75	1.06±0.98	0.28±0.58
Convergence	0.50±0.71	0.16±0.26	0.16±0.26
Gaze Impersistence	0.19±0.39	0.22±0.55	0.09±0.39
Finger to nose test	0.31±0.53	0.31±0.64	0.13±0.33
Glabellar test	1.09±0.77	0.53±0.67	0.13±0.33
Snout reflex	0.47±0.84	0.31±0.73	0.0001±0.001
Grasp reflex	0.78±0.65	0.34±0.48	0.21±0.41
Suck reflex	0.44±0.84	0.50±0.88	0.0001±0.001

[Table/Fig-1]: The mean scores for the NSS in the study groups.

NSS	Mean difference	Standard error	p-value
<b>Tandem walk</b>			
schizophrenic and schizoaffective patients-bipolar with psychotic symptoms	0.55	0.169	p<0.001
schizophrenic and schizoaffective patients -bipolar without psychotic symptoms	1.17	0.169	
Bipolar disorder with and without psychotic symptoms	0.62	0.169	
<b>Ozeretski test</b>			
schizophrenic and schizoaffective patients-bipolar with psychotic symptoms	0.55	0.153	p<0.001
schizophrenic and schizoaffective patients -bipolar without psychotic symptoms	0.97	0.153	
Bipolar disorder with and without psychotic symptoms	0.41	0.153	
<b>Glabellar test</b>			
schizophrenic and schizoaffective patients-bipolar with psychotic symptoms	0.48	0.161	p<0.001
schizophrenic and schizoaffective patients -bipolar without psychotic symptoms	0.97	0.161	
Bipolar disorder with and without psychotic symptoms	0.48	0.161	
<b>Grasp reflex</b>			
schizophrenic and schizoaffective patients-bipolar with psychotic symptoms	0.41	0.136	p<0.001
schizophrenic and schizoaffective patients -bipolar without psychotic symptoms	0.55	0.136	
Bipolar disorder with and without psychotic symptoms	0.14	0.136	

[Table/Fig-2]: ANOVA for the tandem walk, ozeretski test, glabellar test, grasp reflex among the three groups.

## DISCUSSION

The current study revealed that the frequency of NSS in psychotic patients was significantly higher than in non-psychotic patients (bipolar disorder patients without psychotic symptoms). Also, the frequency of these symptoms in psychotic patients (schizophrenic and schizoaffective) was higher (but not significantly) than in bipolar disorder patients with psychotic symptoms.

Most previous studies [2, 14, 15] have shown that NSS are only seen in schizophrenic patients; whereas, our study showed that these symptoms were also detectable in mood disorder (bipolar) patients; however, the mean score of the latter group was lower than that acquired by the psychotic patients.

Our findings in this regard are somehow similar to the findings of a study by Zhao Q et al., in China in 2012 [11]. However, in the aforementioned study, patients with major depressive disorder were also included, which were not evaluated in our study. The mean NSS score in patients with major depressive disorder in the study by Zhao Q et al., was different from that in bipolar patients and was closer to the value acquired by the general population.

Another study on obsessive compulsive disorder patients [16] indicated that the mean NSS score in these patients with psychotic symptoms was higher than the score acquired by patients with obsessive compulsive disorder alone. The mean NSS score in the aforementioned two groups was higher than that in general population. Part of these findings is in line with our results.

In our study, NSS were noted in bipolar disorder patients without psychotic symptoms. Although the mean scores acquired by these patients were significantly lower than those acquired by psychotic

patients, they could not be compared with the value in a healthy population since a healthy control group was not included in our study, which was a limitation of our study. In a study by Irandoost P et al., on an Iranian population [10], it was reported that the mean NSS score in bipolar disorder patients without psychotic symptoms was different from that in a healthy population.

There is a question whether examination of NSS alone can help make a decision regarding the type of disorder and its psychotic or non-psychotic nature. However, we did not focus on answering this question since it was not among the objectives of the current study. But, a study conducted in 2006 in Ireland [17] evaluated 242 patients presenting with the first episode of psychosis according to DSM-IV criteria and revealed that psychotic or non psychotic nature of a disease cannot be determined merely based on the presence of NSS and the acquired scores.

## LIMITATION

The main limitation in the present study is the lack of healthy control group, who could well have different characteristics. Future studies are needed to assess NSS score in psychotic patients to predict the response to pharmaceutical treatment, risk of drug reactions/side effects and prognosis of disease.

## CONCLUSION

Regarding the significant higher mean NSS score in psychotic patients (schizophrenic and schizoaffective) in comparison to non-psychotic patients (bipolar disorder patients without psychotic symptoms), calculation of NSS score in psychotic patients might predict the response to pharmaceutical treatment, risk of drug reactions/side effects and prognosis of disease.

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## REFERENCES

- [1] Tucker GJ, Campion EW, Silberfarb PM. Sensorimotor functions and cognitive disturbance in psychiatric hospitals. *The American journal of psychiatry*. 1975;132:17-21.
- [2] Heinrichs D, Buchanan R, Am J Psychiatry - The significance and meaning of neurological soft signs in Schizophrenia. *The American Journal of Psychiatry*. 1988;145:11-18.
- [3] Woods B. Utility of neurological soft sign and hard signs in psychiatric research. *Psychiatric Annals*. 2003;33:181-89.
- [4] Fellick J, Thomson A, Sills J, Hart C. Neurological soft signs in mainstream pupils. *Archives Disease Child*. 2001;85(5):371-74.
- [5] Walker EF. Neuro developmental precursors of Schizophrenia: The neuropsychology of Schizophrenia. Hillsdale NJ Erlbaum. 1994:119-29.
- [6] Boks MP, Liddle PF, Russo S, Kneegtering R, van den Bosch R-J. Influence of antipsychotic agents on neurological soft signs and dyskinesia in first episode psychosis. *Psychiatry research*. 2003;119(1):167-70.
- [7] Bombin I, Arango C, Buchanan RW. Significance and meaning of neurological signs in schizophrenia: Two decades later. *Schizophrenia Bulletin*. 2005;31(4):962-77.
- [8] Ismail BT, Cantor-Graae E, Cardenal S, McNeil TF. Neurological abnormalities in schizophrenia: Clinical, aetiological and demographic correlates. *Schizophrenia research*. 1998;30(3):229-38.
- [9] Mittal VA, Hasenkamp W, Sanfilippo M, Wieland S, Angrist B, Rotrosen J, et al. Relation of neurological soft signs to psychiatric symptoms in schizophrenia. *Schizophrenia research*. 2007;94(1):37-44.
- [10] Irandoost P, Faridhosseini F, Amini H, Noroozian M, Saghale T. Neurological soft signs: A further step in the diagnosis of bipolar-I disorder? *Iranian Journal of Psychiatry*. 2009;4(1):7-12.
- [11] Zhao Q, Ma Y-t, Lui SS, Liu W-h, Xu T, Yu X, et al. Neurological soft signs discriminate schizophrenia from major depression but not bipolar disorder. *Progress in Neuro Psychopharmacology and Biological Psychiatry*. 2013;43:72-78.
- [12] Buchanan RW, Heinrichs DW. The Neurological Evaluation Scale (NES): A structured instrument for the assessment of neurological signs in schizophrenia. *Psychiatry research*. 1989;27(3):335-50.
- [13] Amini H, Rahimi- Nejad F, Noroozian M, Sharifi V, Shakiba M. Neurological soft signs in patients with first episode psychosis, their first-degree relatives and healthy controls. *Iranian Journal of Psychiatry and Clinical Psychology*. 2007;13(2):89-96.
- [14] Cox SM, Ludwig AM. Neurological Soft Signs and Psychopathology I. Findings in Schizophrenia. *The Journal of nervous and mental disease*. 1979;167(3):161-65.
- [15] Rossi A, De Cataldo S, Di Michele V, Manna V, Ceccoli S, Stratta P, et al. Neurological soft signs in schizophrenia. *The British Journal of Psychiatry*. 1990;157(5):735-39.
- [16] Peng Z-w, Xu T, Miao G-d, He Q-h, Zhao Q, Dazzan P, et al. Neurological soft signs in obsessive-compulsive disorder: The effect of co-morbid psychosis and evidence for familiarity. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*. 2012;39(1):200-05.
- [17] Whitty P, Clarke M, McTigue O, Browne S, Gervin M, Kamali M, et al. Diagnostic specificity and predictors of neurological soft signs in schizophrenia, bipolar disorder and other psychoses over the first four years of illness. *Schizophrenia research*. 2006;86(1):110-17.

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