Original Article

A Study of Soft Neurological Signs and Its Correlates in Drug-Naive Patients with First Episode Psychosis

Vanishree Gunasekaran, V. Mathan Kumar Venkatesh, T. V. Asokan

ABSTRACT

Background: Soft neurological signs are minor, non localizing, objective abnormalities, thought to reflect damage in cortical and sub-cortical connections or connections within different cortical regions. Regional structural grey matter anomalies have already been observed and correlated with the presence of cognitive deficits and presence of soft neurological signs in schizophrenic patients. **Materials and Methods:** Drug naive patients presenting with first episode of psychosis (FEP)were clinically evaluated for soft neurological signs using the Cambridge Neurological Inventory. The soft neurological signs scores were compared with scores in healthy volunteers. In the patient group, this score was also correlated with demographic and disorder variables. **Results:** Of the 30 patients with FEP, 60% were women. The average age of the participant was 36.2 years. The average duration of illness was 1.55 years. More than 50% of the patients had schizophrenia. 93.3% of patients with FEP had atleast one soft neurological sign compared to 16.6% of controls. The average score on BPRS was 25.86 and on PANSS was 39.29, and BPRS, PANSS scores had a significant correlation with total soft neurological signs score. **Conclusion:** There is a significantly higher incidence of soft neurological signs in patients with FEP, particularly schizophrenia. The presence of soft signs correlated with the severity of psychosis.

Key words: *Cambridge neurological inventory, first episode psychosis, soft neurological signs*

INTRODUCTION

Neurological soft signs (NSS) are subtle neurological abnormalities comprising deficits in sensory integration, motor coordination, and sequencing of complex motor acts.[1] NSS predate the onset of psychosis. Many studies have detected their presence in nonpsychotic first-degree relatives and preschizophrenic children at increased genetic risk. Their presence does not imply a primary tract or nuclear pathology but rather is indicative of a nonspecific impairment either in sensory-motor integration or in cortical-subcortical connections.[2]

Although previously thought to lack in specificity and localizing value, numerous clinical studies to date have concluded that doubts over the validity of NSS simply

Access this article online	
Website: www.ijpm.info	Quick Response Code
DOI: 10.4103/0253-7176.191393	

How to cite this article: Gunasekaran V, Venkatesh VM, Asokan TV. A study of soft neurological signs and its correlates in drug-naive patients with first episode psychosis. Indian J Psychol Med 2016;38:408-13.

Department of Psychiatry, Government Stanley Medical College and Hospital, Chennai, Tamil Nadu, India

Address for correspondence: Dr. Vanishree Gunasekaran
T-2 Parvatham Apartments, 18, West Park Road, Shenoy Nagar, Chennai - 600 030, Tamil Nadu, India. E-mail: vanishreeprithvi@gmail.com

reflects a limitation of our knowledge rather than an unreality in their finding.[1]

Numerous studies have postulated that the presence of NSS is indicative of "psychosis proneness" on a scale of continuum, with schizophrenia being at one end of the spectrum.[3] In fact, many studies have demonstrated that deficits in sensory integration, which significantly correlates with the presence of volume changes in specific brain regions, are the reason for cognitive dysmetria and negative syndrome in schizophrenia. Currently, NSS are one of the well-established biological findings in patients with schizophrenia.[4] Clinical assessment and systematic evaluation of these neurological abnormalities are the next logical step in the interpretation of imaging studies in schizophrenia. Research into their utility as a trait marker/endophenotype is limited partly because of a lack of standardization, affecting both their detection and rating. Further, some of the NSS, especially primitive reflexes, do have a high prevalence in normal population.

Many operational definitions have been used to describe first episode psychosis (FEP), including duration of the episode, use of antipsychotic medication, and first treatment contact. In the present study we simply define FEP patients as subjects presenting for the first time with a clinically evident impairment in functioning resulting from an index episode (first episode) of psychosis, as evident from a prominent delusion, and/or hallucination, and/or disorganised speech, and/or disorganised behavior.

A majority of studies examining the subtle neurological signs have focused on patients with first-episode schizophrenia and their first-degree relatives. Only a handful of studies have attempted to explore the presence of subtle neurological signs in patients with the first episode of mood disorder or brief psychotic disorder.[5]

A neurological examination of all patients presenting with FEP is currently not standardized. Many a time, the evaluation for neurological deficits, aided with imaging studies, results in detection of an insidious lesion that inadvertently shifts the focus of treatment and unrealistically defines psychotic patients as neurologically impaired.[6]

The present study attempts to examine the presence of NSS in patients presenting with FEP.

Aim and objectives

The study aims to:

- Estimate and compare the prevalence of NSS in drug-naive patients having FEP, with normal subjects
- Find any difference in the prevalence of soft neurological signs in patients with schizophrenia and patients with other psychoses
- Correlate the presence of NSS with the severity of psychosis, duration of illness, and other demographic variables.

MATERIALS AND METHODS

Participants

Thirty consecutive patients attending the psychiatry outpatient department of Government Stanley Hospital who were drug-naive and presented with an index episode of psychosis were evaluated. Diagnosis was made based on International Classification of Disease (ICD-10). Patients who satisfied the criteria of either schizophrenia or other psychotic disorders, according to ICD-10, were chosen as cases.

Control group included 30 volunteers with no past or present history of mental illness. Subjects who were matched for age and gender with cases were chosen as controls.

Exclusion criteria were the presence of a history of substance dependence, history of antipsychotic drug treatment, and presence of a current or past neurological disorder.

Informed consent was obtained from all patients and participants.

Clinical evaluation

All patients recruited as cases and controls were examined for NSS using the Cambridge Neurological Inventory.[7] It is a bedside neurological evaluation checklist which includes subtle neurological signs in six categories:

- Motor (including casual gait, tandem gait, and Romberg's test)
- Complex motor coordination (including fist–edge–palm, alternating fist palm, diadochokinesis, finger opposition, and rhythm tapping)
- Extraocular movements (visual tracking, gaze persistence)
- Other motor signs (mirror movements, motor persistence, heel shin test, synkinesis, tremors, and choreoathetosis)
- Primitive reflexes (glabellar tap, palmar grasp, palmomental, snout reflexes)
- Sensory integration (stereognosis, graphesthesia, face-hand extinction, right-left disorientation).

Each category has a number of individual neurological tests. The score for each item ranges from 0 to 2. The sum of all individual tests is rated as the total NSS score.

Patients who were diagnosed of psychotic illness by ICD-10 were assessed with rating scales – Positive and Negative Syndrome Scale (PANSS) and Brief Psychiatric Rating Scale (BPRS).

PANSS has three subscales – positive scale (with items P1–7), negative scale (with items N1–7), and general psychopathology scale (with items G1–16). BPRS is an 18-item rating scale and each item is scored from 0 to 7.

Ethical committee approval was obtained. Statistical analysis was done using SPSS software version 10.

RESULTS

Demographic variables among cases and controls

Participants in both the groups – cases and controls – were matched for age and gender. The matching was done to remove any selection bias. The average age of the participants was 36.2 years [Figure 1]. About 60% of the subjects were females [Figure 2].

Duration of psychiatric illness in cases

The duration of illness varied from 5 months (in patients with acute transient psychotic disorder) to 2 years (in patients with schizophrenia). The mean duration of illness was 1.55 years.

Categories of psychiatric diagnosis

Patients with FEP had one of the following diagnoses – schizophrenia, delusional disorder, acute and transient psychotic disorder, psychosis not otherwise specified, bipolar affective disorder, depression [Figure 3]. More than 50% of the patients had a diagnosis of schizophrenia.

Soft neurological signs in cases versus controls

The soft neurological signs were significantly more prevalent in patients with FEP than controls [Table 1].

Twenty-eight out of 30 patients with FEP had NSS. The total score ranged from 1 to as high as 13. Most prevalent was complex motor coordination signs, followed by other motor signs, primitive reflexes, extraocular signs, sensory integration signs, and lastly, motor signs.

Among the controls, 5 out of 30 participants had soft neurological signs. Other motor signs, namely, tremors, motor persistence were seen in three subjects while complex motor coordination signs and extraocular movement signs were each seen in one subject.

The prevalence of soft neurological signs in cases with FEP was higher compared to controls, and the difference was statistically significant.

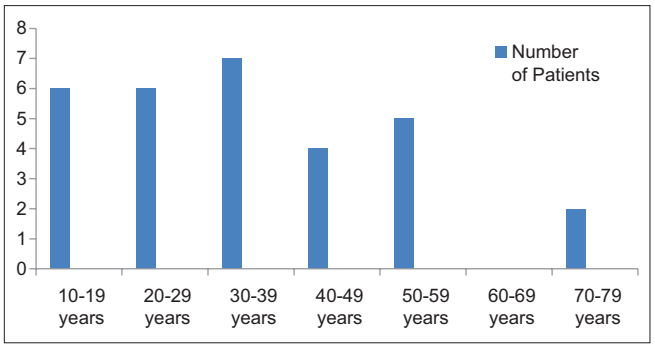

Figure 1: Demographic variable - Age

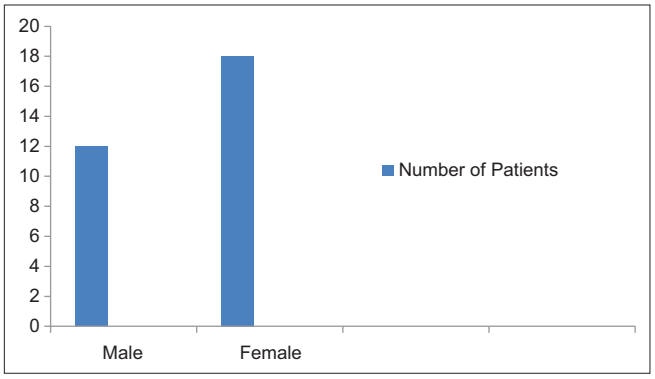

Figure 2: Demographic variable - Gender

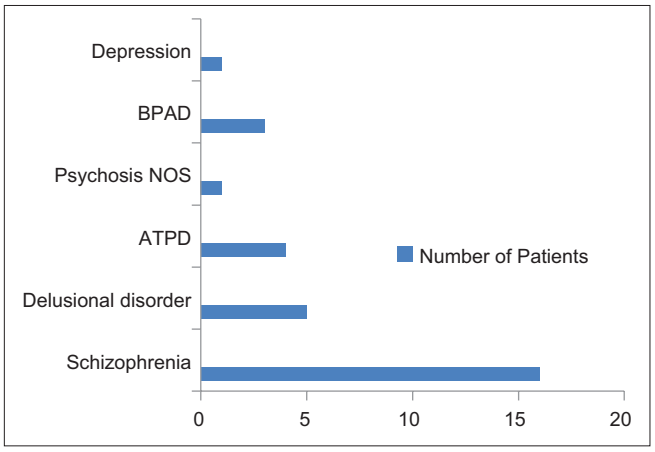

Figure 3: Diagnostic categories in patients

There were no gender differences in the prevalence of soft neurological signs in patients with FEP. This is in contrast to previous studies which observed a higher incidence of soft signs in females.

Soft neurological signs in schizophrenia versus other psychoses

There was a higher prevalence of soft neurological signs in patients with schizophrenia, compared to patients with other kinds of psychoses [Table 2].

All patients with schizophrenia had at least one soft neurological sign. The total NSS score varied from 1 to 13.

In patients with other psychoses, soft neurological signs were seen in 85.7% of subjects. The total NSS score varied from 1 to 8. The difference was statistically significant.

Of all the soft neurological signs, there was a significantly higher incidence of complex motor coordination signs, primitive reflexes, extraocular movement signs, and other motor signs in patients with schizophrenia when compared to patients with other psychoses. There was no difference in the incidence of the sensory integration signs and motor signs between the two groups.

Since soft neurological signs were significantly more prevalent in patients with schizophrenia, we tried to find if there was any difference in the severity of psychosis between the two groups of FEP patients. While comparing BPRS and PANSS scores in patients with schizophrenia and other diagnoses, there were no significant differences [Table 3].

Correlation of total score of soft neurological signs with severity of psychosis

The total soft neurological signs score correlated well with total PANSS score and BPRS scores [Table 4]. The correlation was statistically significant.

A comparison of average scores in rating scales – PANSS and BPRS – in patients with and without soft neurological signs showed no statistically significant difference [Table 5].

Correlation of soft neurological signs with demographic variables

There was no significant correlation between the demographic variables – age, gender or duration of illness with total soft neurological signs score, PANSS, and BPRS scores [Table 6]. The lack of correlation between soft neurological signs and duration of illness signifies the neurodevelopmental origin of the soft signs.

There was also no correlation between the presence of a family history of mental illness and the presence of soft neurological signs.

DISCUSSION

Numerous studies have looked at the clinical diagnosis, symptom profiles, treatment protocols, and brain changes in patients with FEP.[8] The present study is an attempt to estimate the degree of neurodevelopmental aberration in patients with FEP, by evaluating them for NSS.

The higher prevalence of soft neurological signs in patients with FEP, compared to normal subjects, together with the lack of correlation between the neurological abnormalities score and the duration of illness supports the neurodevelopmental origin of psychosis.

Table 1: Prevalence of soft neurological signs in cases and controls

Soft signs	Motor signs		Complex motor coordination		Extra-ocular movement		Other motor signs		Primitive reflexes		Sensory integration	
	Absent	Present	Absent	Present	Absent	Present	Absent	Present	Absent	Present	Absent	Present
Case	27	3	7	23	18	12	12	18	14	16	25	5
Controls	30	0	29	1	29	1	27	3	30	0	30	0
Chi square	3.158		27.149		11.882		16.484		21.818		5.455	
P value	0.076		0.000**		0.001**		0.000**		0.000**		0.002**	

**Statistically significant

Table 2: Prevalence of soft neurological signs in patients with schizophrenia and other psychoses

	Motor signs		Complex motor coordination		Extra-ocular movement		Other motor signs		Primitive reflexes		Sensory integration	
	Absent	Present	Absent	Present	Absent	Present	Absent	Present	Absent	Present	Absent	Present
Schizophrenia	16	0	4	12	9	7	5	11	6	10	12	4
Delusional disorder	4	1	2	3	4	1	2	3	3	2	4	1
ATPD	3	1	0	4	3	1	2	2	2	2	4	0
Psychosis NOS	1	0	0	1	0	1	0	1	1	0	1	0
BPAD	2	1	1	2	2	1	2	1	2	1	3	0
Depression	1	0	0	1	0	1	1	0	0	1	1	0
Chi square	13.333		29.228		18.051		20.467		26.165		10.255	
P value	0.064		0.006**		0.012**		0.005**		0.000**		0.175	

**Statistically significant. ATPD – Acute and transient psychotic disorder; NOS – Not otherwise specified; BPAD – Bipolar affective disorder

Table 3: Comparison of BPRS and PANSS between patients with schizophrenia and patients with other psychoses

Psychiatric diagnoses	*N*	BPRS	Total PANSS
Schizophrenia	16	23.73	30.33
Others	14	28.00	48.25
P value		0.073	0.360

BPRS – Brief psychiatric rating scale; PANSS – Positive and negative syndrome scale

Table 4: Correlation of total soft neurological signs score with severity of psychosis

Correlation with total NSS score	Pearson	*P* value
BPRS	0.716	0.000**
Total PANSS	0.717	0.000**

**Statistically significant *P* value<0.05. NS – Neurological soft signs

Table 5: Comparison of total scores in BPRS, PANSS among patients with and soft neurological signs

	BPRS	Positive PANSS	Negative PANSS	Gen psych PANSS	Total PANSS
Patients without soft neurological signs	23.5	13	7	28	48
Patients with soft neurological signs	27.04	12.71	10.24	25	47.94
Chi square	1.044	0.091	0.628	0.732	0.007
P value	0.305	0.929	0.539	0.475	0.994

BPRS – Brief psychiatric rating scale; PANSS – Positive and negative syndrome scale

Table 6: Correlation between demographic variables and soft neurological signs score

	Total NSS	BPRS	Total PANSS	Positive PANSS	Negative PANSS	Gen psych PANSS
Age						
Pearson	0.12	0.063	0.03	0.032	0.036	0.024
P value	0.363	0.633	0.839	0.829	0.807	0.87
Gender						
Pearson	0.138	0.078	0.104	0.117	0.102	0.091
P value	0.295	0.556	0.482	0.43	0.490	0.54
Duration of illness						
Pearson	0.173	0.259	0.100	0.192	0.246	0.116
P value	0.351	0.16	0.685	0.432	0.311	0.635

BPRS – Brief psychiatric rating scale; PANSS – Positive and negative syndrome scale

Schizophrenia has long been proven to have functional and structural neurological deficits. In the present study, a higher prevalence of NSS in patients with first-episode schizophrenia, compared to patients with other psychosis, lends further support to this.[9] Does this mean that the presence of a high score of NSS in first-episode schizophrenia has a diagnostic significance? Can the higher prevalence of NSS in patients with FEP, be taken as a predictor of the evolution of this index episode into a schizophrenic type of psychosis later, remains to be explored.

The presence of soft neurological signs in patients with other psychosis supports the hypothesis that neurological abnormalities are not specific to any particular kind of psychosis.[10,11] The present study also made a similar observation. However, we could not observe any specific soft neurological sign that was significantly more prevalent in patients with other psychosis.

As already established,[12,13] the total NSS score correlated significantly with BPRS and PANSS scores, proving the presence of a relationship between the degree of neurological anomaly and the severity of mental illness. Many studies have found a correlation between the presence of soft neurological signs and the presence of negative symptoms.[14] In the present study, there were no correlations between soft neurological signs and negative scale of PANSS. The presence of such a correlation will help in identifying a subgroup of patients with schizophrenia, with worse prognosis.

In the present study, we found no gender differences in the prevalence of soft neurological signs. In a previous study, motor coordination signs were observed to be less common in male than female patients with psychosis.[15] Interestingly, in another study, soft neurological signs were more common in female.[16]

CONCLUSION

NSS in patients with FEP have a possible diagnostic and prognostic significance.

Limitations

The sample size used in the study was 30 cases and 30 controls. A larger sample could have given more information about the correlation between specific categories of soft neurological signs and the various first episode psychoses.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Heinrichs DW, Buchanan RW. Significance and meaning of neurological signs in schizophrenia. Am J Psychiatry 1988;145:11-8.
2. Alexander GE, DeLong MR, Strick PL. Parallel organization of functionally segregated circuits linking basal ganglia and cortex. Annu Rev Neurosci 1986;9:357-81.
3. Barkus E, Stirling J, Hopkins R, Lewis S. The presence

of neurological soft signs along the psychosis proneness continuum. Schizophr Bull 2006;32:573-7.
4. Chan RC, Gottesman II. Neurological soft signs as candidate endophenotypes for schizophrenia: A shooting star or a Northern star? Neurosci Biobehav Rev 2008;32:957-71.
5. Baldwin R, Jeffries S, Jackson A, Sutcliffe C, Thacker N, Scott M, *et al*. Neurological findings in late onset depressive disorder: Comparison of individuals with and without depression. Br J Psychiatry 2005;186:308-13.
6. Picchioni MM, Dazzan P. Clinical significance of neurological abnormalities in psychosis. Adv Psychiat Treat 2009;15:419-27.
7. Chen EY, Shapleske J, Luque R, McKenna PJ, Hodges JR, Calloway SP, *et al.* The Cambridge neurological inventory: A clinical instrument for assessment of soft neurological signs in psychiatric patients. Psychiatry Res 1995;56:183-204.
8. Dazzan P, Murray RM. Neurological soft signs in first-episode psychosis: A systematic review. Br J Psychiatry Suppl 2002;43:50-7.
9. Bombin I, Arango C, Buchanan RW. Significance and meaning of neurological signs in schizophrenia: Two decades later. Schizophr Bull 2005;31:962-77.
10. 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 4 years of illness. Schizophr Res 2006;86:110-7.
11. Goswami U, Sharma A, Khastigir U, Ferrier IN, Young AH, Gallagher P, *et al.* Neuropsychological dysfunction, soft neurological signs and social disability in euthymic patients with bipolar disorder. Br J Psychiatry 2006;188:366-73.
12. Tosato S, Dazzan P. The psychopathology of schizophrenia and the presence of neurological soft signs: A review. Curr Opin Psychiatry 2005;18:285-8.
13. Prikryl R, Ceskova E, Kasparek T, Kucerova H. Neurological soft signs, clinical symptoms and treatment reactivity in patients suffering from first episode schizophrenia. J Psychiatr Res 2006;40:141-6.
14. Galderisi S, Maj M, Mucci A, Cassano GB, Invernizzi G, Rossi A, *et al.* Historical, psychopathological, neurological, and neuropsychological aspects of deficit schizophrenia: A multicenter study. Am J Psychiatry 2002;159:983-90.
15. Dazzan P, Lloyd T, Morgan KD, Zanelli J, Morgan C, Orr K, *et al.* Neurological abnormalities and cognitive ability in first-episode psychosis. Br J Psychiatry 2008;193:197-202.
16. Gourion D, Goldberger C, Olie JP, Lôo H, Krebs MO. Neurological and morphological anomalies and the genetic liability to schizophrenia: A composite phenotype. Schizophr Res 2004;67:23-31.