Original Research Article

A comparative study of first episode of schizophrenia and first episode of bipolar disorder (mania) patients on measures of neurological soft sign

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Abstract

Background: There is a higher prevalence of Neurological Soft Sign(NSS) in first-episode patients compared with healthy controls. In particular, significantly higher total rates of NSS in patients with first-episode schizophrenia or schizophreniform disorder have been reported. NSS abnormalities have also been reported in other neuropsychiatric disorders, like Schizophreniform disorder and psychosis within the affective spectrum, especially bipolar disorders. However, among the limited studies specifically comparing the NSS abnormalities between Schizophrenia and other neuropsychiatric disorders, the findings had been inconsistent with reference to the specificity of NSS in Schizophrenia.**Method:**A cross sectional hospital based Analytic type of Observational study was carried out between September 2016 and August 2017 on patients of first episode of Schizophrenia and Bipolar Disorder (mania) attending at psychiatric center, department of psychiatry, SMS medical college & hospital, Jaipur. Study included cases of first episode of Schizophrenia and Bipolar Disorder (mania) [diagnosed as per ICD-10 criteria] satisfying inclusion criteria and exclusion (via screening Performa) and healthy controls.**Results:** Thetotal NSS score and four components - Primitive reflexes, motor coordination, sensory integration, and response inhibition were significantly higher in the schizophrenia patients compared to the bipolar patients and controls (P<.001). First Episode Schizophrenia (FES) and First Episode Bipolar Disorder (FEBP) patients were significantly impaired in the performance of NSS items compared to healthy controls, but there are no statistical differences between FES and FEBP groups.**Conclusion:**Present study results concluded that FES and FEBP patients had significantly more NSS on all items compared to the healthy controls. A poorer neurocognitive performance was found amongst FES and FEBP patients as compared to the healthy controls in all the cognitive domains.

Keywords: Neurological Soft Sign, First Episode Schizophrenia, First Episode Bipolar Disorder

Introduction

NSS are defined as those signs that do not in themselves signify to a definite manifest specific neurological response, but taken together may indicate organicity. Hard signs on the other hand refer to impairment in basic motor, sensory, and reflex behaviour. [2] There is still a lack of consensus on the neuro-dysfunctional area underlying NSS; some suggest it to reflect a failure in the integration within or between sensory and motor system,[3] while others view it as deficit in neuronal circuits involving subcortical structures (e.g. basal ganglia, brain stem, limbic system).Although the categorisation of neurological signs as 'soft' (e.g. frontal release and cerebellar signs) and the batteries used to measure them have varied, neurological abnormalities in schizophrenia seem to be localised to three main neurological domains: integrative sensory function; motor coordination; and motor sequencing [4]. Paucity in integrative sensory function (possibly resulting from a parietal dysfunction) are reflected in higher rates of bilateral extinction,impaired audio–visual integration, agraphaesthesia and astereognosis[3,4].Deficits in motor coordination are reported through tests of general coordination, intention tremor, finger–thumb opposition, balance and gait. Finally, poor pursuance in complex motor tasks (possibly resulting from a dysfunction of the frontal–basal ganglial circuitry) has been reported in tests that involve repetitive alternating hand positions, like the fist–edge–palm, the fist-ring and therefore the Ozeretskitests.Studies that evaluated patients with first episode psychosis have reported a high prevalence of NSS, the percentage of patients with NSS varying from 20% [5]to 97.1% [6]. There is a higher prevalence of NSS in first-episode patients compared with healthy controls. In particular, significantly higher total rates of NSS in patients with first-episode schizophrenia or schizophreniform disorder have been reported [7,8].NSS abnormalities have also been reported in other neuropsychiatric disorders, like Schizophreniform disorder and psychosis within the affective spectrum, especially bipolar disorders[9-11]. However, among the limited studies specifically comparing the NSS abnormalities between Schizophrenia and other neuropsychiatric disorders,the findings had been inconsistent with reference to the specificity of NSS in Schizophrenia and Bipolar Disorders. So our specific aim to study neurological soft sign in patients of schizophrenia and bipolar affective disorder (mania) to established the relationship between NSS and Psychotic Disorders

Methodology

Inclusion Criteria

- Age 18–45 years, both sex

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- First episode only
- Meeting the ICD-10 criteria for schizophrenia disorder and bipolar disorder (mania)
- No history of any psychoactive drug.
- Literate enough to understand and perform the questionnaires.
- Willing to participate in the study.

Exclusion Criteria

- Violent and agitated
- Having a physical disability (e.g. Blind, deaf, speech problems, paralysis, amputation)
- History of significant substance abuse, in last 3 months, except nicotine (ICD-10)
- History of electroconvulsive therapy in the previous six months
- History of neurological disorder/ significant head injury
- Mental retardation
- History of any chronic medical illness

Selection criteria for Controls

Inclusion Criteria

- Age 18–45 years, either sex
- Literate enough to understand and perform the questionnaires.
- Willing to participate in the study.

Exclusion Criteria

- Past history of psychiatric illness
- Having a physical disability (e.g. Blind, deaf, speech problems, paralysis, amputation)
- History of significant substance abuse, in last 3 months, except nicotine (ICD-10)
- History of neurological disorder/ significant head injury
- History of any chronic medical illness

The study setting

The study was conducted at the Psychiatric Centre, SMS medical college, Jaipur, is a government runs tertiary care Centre providing highest level of care and treatment of the state.

Study Design

A cross sectional hospital based Analytic type of Observational study was carried out between September 2016 and August 2017 on patients of first episode of Schizophrenia and Bipolar Disorder (mania) attending at psychiatric center, department of psychiatry, SMS medical college & hospital, Jaipur. Ethical Consideration was taken from research review board & ethical committee of the institution. Study included cases of first episode of Schizophrenia and Bipolar Disorder (mania) [diagnosed as per ICD-10 criteria] satisfying inclusion criteria and exclusion (via screening Performa) and healthy controls. Control group included normal and healthy persons who were taken from hospital staff and bystanders of hospitalized patients (not first degree relatives) and was screened for psychiatric illness by two psychiatrists independently. Prior to participation in the study informed written consent was taken then after applying exclusion and inclusion criteria participants were screened with a specially designed Performa for the study. Those patients who satisfied the screening process were recruited in the study, followed by recording of socio-demographic profile, clinical data.

Instruments of study

1. **Consent form**:This form would be formatted in Hindi language & would be given to patient. The written consent would be taken after screening procedure.
2. **Screening Performa**:The Performa will include all inclusion and exclusion criterions with the Yes / No option before each question.
3. **Socio-demographic profile** :This will include name, age, sex, address, marital status, education, type of family, monthly income, Family H/O of psychiatric illness.& other relevant information of the patient.
4. **Clinical Profile Performa:** This will include detailed history of the psychiatric illness.
5. **Positive and Negative Syndrome Scale Score (PANSS)[25]:** It is a clinician- administered rating scale used to measure severity of psychotic illness, mainly on 3 domains- Positive (7 items), Negative (7 items) and General (16 items).
6. **Young Mania Rating Scale (YMRS) [26]:**The Young Mania Rating Scale (YMRS) is one of the most commonly used rating scales to assess manic symptoms.
7. **Cambridge Neurological Inventory (CNI)[27]:** Cambridge Neurological Inventory has been constructed for standardized neurological assessment of psychiatric patients.Part 2 of the inventory is for Soft sign examinations. There are three groups: The first group of soft sign tests assesses some "primitive reflexes". The second group is concerned with "repetitive sequential motor execution". The third group consists of tests related to "integration of sensory information"

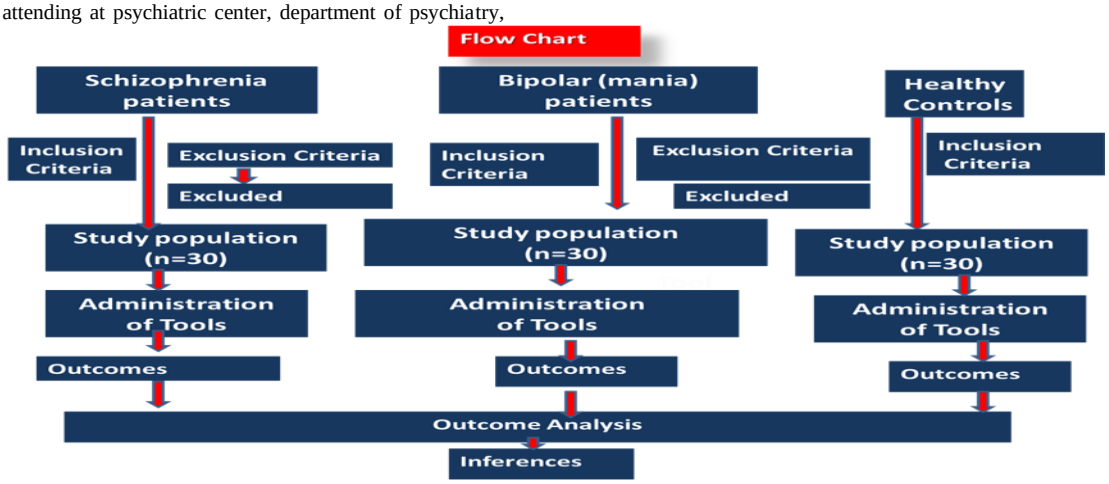

Fig 1:Depiction

Results

Table 1: Comparison of Socio-demographics between groups

Parameter		FES Patients (N=30)Mean(SD)	FEBP Patients(N=30) Mean (SD)	Healthy Controls(N=30) Mean (SD)	P value
AGE		32.56 (7.84)	32.80 (7.29)	32.63 (7.21)	0.815
Gender	Male	24	25	23	0.812
	Female	6	5	7	
Maital status	Married	22	20	21	0.853
	Unmarried	8	10	9	
Education					0.990
Illiterate		6	8	8	
Primary		16	14	14	
Secondary		4	5	4	
Graduate or P.G		4	3	4	
Religion	Hindu	25	22	26	0.39
	Muslim	5	8	4	
Locality	Rural	26	26	22	0.149
	Urban	4	4	8	
Family Type	Nuclear	14	18	19	0.214
	Nuclear Extended	6	2	2	
	Joint	10	10	9	
Socioeconomic Class	Lower	25	22	26	0.39
	Middle	5	8	4	

Table 1 is showing that three groups were comparable to each other according to the socio-demographic data as no statistically significant difference was found among these three groups (P >.05).Majority of the patients were married, Hindu males of rural background belonging to lower socioeconomic class and living in a nuclear family.

Table 2:Comparison of the neurological soft signs among groups A (Schizophrenia patients), B (Bipolar patients) and C (healthy controls)

	Group A(N=30)		Group B(N=30)		Group C(N=30)		P Value
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std. Deviation	
Primitive reflexes							
Snout reflex	.47	.507	.37	.490	0.00	0.000	.000
Grasp reflex	.60	.675	.50	.682	0.00	0.000	.000
Palmomental reflex	.47	.507	.37	.490	0.00	0.000	.000
Motor coordination							
Finger-nose test	.63	.669	.37	.556	.10	.305	.001
Finger-thumb tapping	.73	.691	.50	.731	0.00	0.000	.000
Finger-thumb opposition	1.13	1.332	1.17	1.440	.23	.504	.003
Diadochokinesia	.67	.711	.53	.681	.13	.434	.004
Fist-edge-palm test	1.63	1.542	1.57	1.569	.13	.346	.000
Oseretsky test	2.00	1.531	2.00	1.531	.10	.305	.000
Rhythm tapping test	1.27	.907	1.27	.907	.27	.521	.000
Response Inhibition							
Go/no-go test	.80	.714	.80	.714	0.00	0.00	.000
Sensory integration							
Extinction	.20	.407	.17	.379	0.00	0.00	.040
Finger agnosia	.80	.664	1.00	1.017	.17	.461	.000
Stereognosia	.30	.466	.30	.466	.03	.183	.013
Graphesthesia	1.30	1.088	1.57	1.305	.07	.254	.000
Left-right orientation	.47	.571	.47	.571	.10	.305	.006

Table 3:Comparison of the neurological soft signs among groups A (Schizophrenia patients), B (Bipolar patients) and C (healthy controls)

	Group A		Group B		Group C		P value
	Mean	SD	Mean	SD	Mean	SD	
Primitive reflexes	1.53	1.63	1.07	1.20	0.00	0.00	<0.001
Motor coordination	8.07	5.19	7.40	5.58	0.97	1.00	<0.001
Response Inhibition	.80	.71	.80	.71	0.00	0.000	<0.001
Sensory integration	3.03	2.24	3.50	2.73	0.37	0.56	<0.001

Total score	13.47	7.651	10.80	5.792	1.33	1.213	0.000

Table no 2 and 3 showing that total NSS score and four components - Primitive reflexes, motor coordination, sensory integration, and response inhibition were significantly higher in the schizophrenia patients compared to the bipolar patients and controls (P<.001). FES and FEBP patients were meaningful impaired in the performance of NSS items compared to healthy controls, but there are no statistical differences between FES and FEBP groups.

Table 4:Inter group comparison of the Neurological soft signs among groups A (Schizophrenia patients), B (Bipolar patients) and C (healthy controls)

Neurological soft signs	Group AVS B		Group AVS C		Group B VS C	
	Mean diff	P Value	Mean diff	P Value	Mean diff	P Value
Primitive reflex						
Snout reflex	0.1	0.61	0.467	0.001	-0.367	0.002
Grasp reflex	0.1	0.765	0.6	0.001	-0.5	0.002
Palmomental reflex	0.1	0.61	0.467	0.001	-0.367	0.002
Motor coordination						
Finger-nose test	.267	.133	.133	.001	-.267	.133
Finger-thumb tapping	.233	.271	.733	.001	-.500	.004
Finger-thumb opposition	-.033	.993	.900	.010	-.933	.007
Diadochokinesia	.133	.685	.533	.004	-.400	.038
Fist-edge-palm test	.067	.978	1.500	.001	-1.433	.001
Oseretsky test	0.000	1.000	1.900	.001	-1.900	.001
Rhythm tapping test	0.000	1.000	1.000	.001	-1.000	.001
Response Inhibition						
Go/no-go test	0.000	1.000	.800	.001	-.800	.001
Sensory integration						
Extinction	.033	.915	.200	.047	-.167	.116
Finger agnosia	-.200	.559	.633	.004	-.833	.001
Stereognosia	0.000	1.000	.267	.028	-.267	.028
Graphesthesia	-.267	.553	1.233	.001	-1.500	.001
Left-right orientation	0.000	1.000	.367	.015	-.367	.015

Table 5: Inter group comparison of the Neurological soft signs among groups A (Schizophrenia patients), B (Bipolar patients) and C (healthy controls)

	Group AVS B		Group AVS C		Group B VS C	
	Mean diff	P Value	Mean diff	P Value	Mean diff	P Value
Primitive reflex	.467	.276	1.533	.000	1.067	.002
Motor coordination	.667	.830	7.100	.000	6.433	.000
Response inhibition	0.000	1.000	.800	.000	.800	.000
Sensory integration	-.466	.662	2.668	.000	3.133	.000

Table 4 and 5 shows that FES and FEBP patients were consequential impaired in the performance of NSS items compared to healthy controls, but there are no statistical differences between FES and FEBP groups.

Discussion

Major focus of the this present study was to assess the Neurological soft Signs (NSS) in first episode of Schizophrenia and first episode of Bipolar Disorder (Mania) patients and compared the findings with healthy control group. Socio-demographic profile:Table 1 is showing that three groups were comparable to each other according to the socio-demographic data as no statistically significant difference was found among these three groups. Majority of the patients were married, Hindu males of rural background belonging to lower socioeconomic class and living in a nuclear family. Neurological Soft Signs (NSS) in Schizophrenia and Bipolar patients In present study, the total NSS score was significantly higher in the schizophrenic patients compared to the bipolar patients and controls (P=.000). While assessing NSS, it was divided into four components of Primitive reflexes, motor coordination, sensory integration, and response inhibition and the mean scores in the FES patient group were 1.53±1.63, 8.07±5.19, 3.03±2.24 and 0.80±0.71 respectively. Whereas the mean scores in the FEBP were 1.07.±1.20, 7.40±5.58, 3.50±2.73 and 0.80±0.71 and mean in healthy controls were 0.00.±0.00, 0.97±1.00, 0.37±0.56 and 0.00±0.00 in the same order. Our study also showed that FES and FEBP patients were significantly impaired in the performance of NSS items compared to healthy controls, but there are no statistical differences between FES and FEBP groups. These findings of present study consistent with Nasrallah et al[16], in which chronic schizophrenia, bipolar I disorder patients and healthy controls compared on NSS, no significant difference between the two diagnostic groups was

found but both schizophrenic and bipolar I patients performed worse on NSS scale compared to controls.This present study showed that neither the total NSS nor subscale scores distinguished patients of FES from FEBP. Our findings are consistent with those of Whitty et al.'s [13] results in that patients with schizophrenia and manic depression were indistinguishable supported NSS measurement alone. Discordant findings reported by previous study [12]were due to differences in the sample characteristic of patients with mood disorders, which consisted of both patients with major depression and bipolar disorder. Findings of this present studyin accordance with high score of NSS being demonstrated in drug-naive first-episode psychosis patients[17]. Some studies had suggested that NSS expression during the remission phase of illness could also be a far better indicator of real trait-like features of schizophrenia[15].In fact NSS are considered to be the consequence of an integration failure between the motor and there for the sensory systems and in sub-cortical systems[17]. Impaired motor coordination would be the result of a dysfunction in the striato¬-thalamo-frontal and fronto-cerebellar circuits, involved in both schizophrenia and mood disorders[12]. The excess of sensory integration abnormalities, found in other studies[11,18], is correlated with the reduced volumes of the left medial frontal area and right superior lateral parietal cortex in first-episode psychosis patients. In accordance with other studies[11,19], the subscore of motor integration was significantly higher in FEBP than in comparison groups. This might associated with a dysfunction with in the fronto-subcortical circuit, involved with in the genesis of cognitive impairment which is common in BP and in their healthy relatives [1,19,20].Our results also suggest that patients with schizophrenia and bipolar affective disorder appear to be biologically more almost like oneanother. This notion is supported by evidence at several levels. Genetic studies have shown that schizophrenia and bipolar affective disorder share an identical genetic architecture[21]); while neurobiological studies have shown that patients with schizophrenia and bipolar affective disorder share an similar reduction in densities of reelin[22]. Reelin and GABA are well-known to be involved in neurodevelopment, like neuronal migration, synaptogenesis; and therefor the disturbance of GABA and reelin systems could also be associated with the pathophysiology of schizophrenia [23]. Indeed, Murray, et al.[24] had proposed a model that positioned schizophrenia and bipolar affective disorder on similar genetic background,and attributed their differences in clinical manifestation to environmental factors. Our results have provided further evidence supporting this.

Conclusion

According to the socio-demographic data no significant difference was found among the three study groups.Thetotal NSS score and four components - Primitive reflexes, motor coordination, sensory integration, and response inhibition were significantly higher in the schizophrenia patients compared to the bipolar patients and controls. FES and FEBP patients were significantly impaired with in the performance of NSS items compared to healthy controls, but there are not any statistical differences between FES and FEBP groups.Extending the assessment with follow-up observation of neurological evaluations, in FES and FEBP of patients, would be of great clinical interest, in order to assess that they are also present or absent in chronic patients of schizophrenia and bipolar patients.

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