An exploratory study from eastern India on neurological soft signs and spontaneous movement disorders in schizophrenia spectrum disorders

Shyamanta Das[1], Samrat Singh Bhandari[2], Simanta Talukdar[3], Arunima Dutta[4], Nabanita Barman[5], Dipesh Bhagabati[6]

[1,3]Gauhati Medical College Hospital, Guwahati, Assam, India, [2]Sikkim Manipal Institute of Medical Sciences, Gangtok, Sikkim, India, [4]McLaren Flint, Michigan, USA, [5]Regional College of Nursing, Guwahati, Assam, India, [6]Dispur Hospital, Guwahati, Assam, India

Introduction

The scientific interest in neurological abnormalities in schizophrenia dates to the time of Kraeplin and Bleuler, both of whom had noted neurological and behavioural abnormalities in the early life histories of adult schizophrenic patients. Bender (1947) even asserted that childhood schizophrenia was due to developmental encephalopathies in her monumental study on the condition.[1]

Neurological soft signs (NSS) may represent complex brain function, and are probably because of disrupted neurodevelopment of the brain as a consequence of pre- or perinatal cerebral insult.[2] Neuroimaging studies revealed that NSS was associated with reduced grey or white matter densities in different parts of brain. This pattern of cerebral change associated with NSS support the model of 'cognitive dysmetria' involving disrupted cortico-cerebellar-thalamic-cortical circuit in schizophrenia.[3]

Reports of abnormal involuntary movement date from the first description of the illness; long before the introduction of chlorpromazine in 1952, Kraeplin gave the description of the involuntary movement in patients with schizophrenia. He wrote:

"The spasmodic phenomena in the musculature of the face and of speech which often appear are extremely peculiar disorders. Some of them resemble movements of expression wrinkling of the forehead, distortion with the tongue… but besides we observe specially in the lip muscles, fine lighting-like or rhythmical twitching which in no way bear the stamp of voluntary movements…".[4]

Pooled together, the presence of such obvious signs of neurological dysfunction such as NSS and spontaneous movement disorders (SMD) at various stages of disease inception and progression in schizophrenia spectrum disorders (SSD), may be ample proof of the neurodevelopmental/ neurodegenerative aetiology of SSD and we aim to study the possible neurodevelopmental aetiology of SSD with the help of NSS and SMD.

Hypotheses

1. Most drug naive patients of SSD will have NSS.
2. Most drug naïve patients of SSD will have SMD.

Key questions

What is the prevalence of NSS and SMD in psychotic disorders and what is the possibility of neurodevelopmental or neurodegenerative aetiology?

Materials and methods

Participants' characteristics and study design

It was a cross-sectional observational study done in the Department of Psychiatry, Gauhati Medical College Hospital (GMCH), Guwahati, Assam, India during one year period between 2015 and 2016. Cases were defined as subjects having psychotic symptoms that were either defining factor or associated feature in their diagnosis according to the diagnostic criteria of ICD-10,[5] but have never been treated or never have received any form of psychotropic medications, at least in the preceding six months. Participants included in the study were of either sex, who were 15-50 years of age. Patients who were uncooperative, who had neurological disorder, head injury or who had a history of substance abuse were excluded. The study was approved by the institutional ethics committee of GMCH and written informed consent was taken from the participants.

Tools used for the assessments

a) Socio-demographic proforma standardised in the Department of Psychiatry, GMCH.

b) NSS was assessed by the Heidelberg manual[6] developed by Schroder et al.[7]

c) SMD was assessed by the Modified Abnormal Involuntary Movement Scale (AIMS).[8]

d) Simpson-Angus Rating Scale (SARS) for rating extrapyramidal signs.[9]

e) Barnes Akathisia Rating Scale (BARS) for assessing akathisia.[10]

f) Modified BG Prasad's scale for classification was used to classifv the socioeconomic status (Table 1).[11]

Table 1: Modified BG Prasad's scale for classification of socioeconomic status[23]

Social Class	Original classification of per capita income (Rs./month)	Revised classification for 2016 (Rs./month)
I (Upper Class)	100 and above	6261 and above
II (Upper Middle Class)	50-99	3099-6260
III (Middle Class)	30-49	1835-3098
IV (Lower Middle Class)	15-29	949-1834
V (Lower Class)	<15	<948

Statistical analysis

Descriptive analysis of the data was done. Categorical variables were shown as percentage and continuous variables as mean with standard deviation (SD).

Results

Participants' characteristics

Table 2: Socio-demographic data of the participants

Socio-demographic data	N	%
Sex		
Male	8	50
Female	8	50
Religion		
Hindu	11	69
Muslim	5	31
Occupation		
Unemployed	9	56.3
Homemaker	2	12.5
Teacher	2	12.5
Farmer	1	6.3
Business	1	6.3
Manager	1	6.3
Marital status		
Unmarried	8	50
Married	5	31.3
Separated	2	12.5
Widowed	1	6.3
Education		
Illiterate	3	18.8
Primary education	3	18.8
Secondary education	2	12.5
High school	2	12.5
Higher secondary	4	25
Graduate	2	12.5
Socioeconomic status		
Class I	2	12.5
Class II	6	37.5
Class III	6	37.5
Class IV	2	27.5

The total number of participants was 16 with mean age of 28.7 years with SD 7.7 years. There were equal numbers of male and female participants. The mean duration of illness was 63.2 months with SD 68.8 months (Table 2). 37.5% of the participants were diagnosed with schizophrenia and 12.5% diagnosed with schizoaffective disorder and equally 12.5% of the participants were diagnosed with schizophrenia with tic disorder (Table 3). The mean duration of illness for participants with exclusive diagnosis of schizophrenia was 66 months with SD 81.25 months. Out of the 16 participants, three did not cooperate for assessment of NSS and dyskinesia.

Table 3: Psychiatric diagnosis of the participants

Psychiatric diagnosis	N	%
Schizophrenia	6	37.5
Schizophrenia with tics	2	12.5
Schizoaffective disorder, manic type	2	12.5
Bipolar affective disorder	2	12.5
Severe depressive episode with psychotic symptoms	2	12.5
Mental retardation with psychosis	1	6.3
Unspecified nonorganic psychosis	1	6.3

Table 4: Mean Heidelberg score

Illness	Mean	N	SD
Schizophrenia	6.75	4	3.304
Schizophrenia with tics	9.50	2	4.950
Schizoaffective disorder, manic type	9.00	2	1.414
Bipolar affective disorder	3.00	2	1.414
Severe depressive episode with psychotic symptoms	4.50	2	4.950
Mental retardation with psychosis	26.00	1	-
Total	7.31	13	6.775

NSS assessment findings

The mean Heidelberg score for schizophrenia was 6.75 with SD of 3.304 (Table 4). The motor coordination (MOCO) score for the participants in SSD was relatively stable when compared to score of complex motor task (CMT), right/left and spatial orientation (RLSO), integrative functions (IF), and hard signs (HS) which varied in all the patients (Table 5).

Table 5: Heidelberg score (mean)

Diagnosis	MOCO	IF	CMT	RLSO	HS	Mean Heidelberg score
Schizophrenia	6.25	0.25	0.00	0.25	0.00	6.75
Schizophrenia with tics	4.00	1.50	0.50	2.00	1.50	9.50
Schizoaffective disorder, manic type	4.00	0.00	2.50	1.50	1.00	9.00
Bipolar affective disorder	1.50	0.00	0.00	1.50	0.00	3.00
Severe depressive episode with psychotic symptoms	1.50	0.00	1.00	2.00	0.00	4.50
Mental retardation with psychosis	10.00	2.00	3.00	9.00	2.00	26.00

MOCO=motor coordination, IF=integrative functions, CMT=complex motor task, RLSO=right/left and spatial orientation, HS=hard signs

Findings of SMD assessment

Assessment with AIMS revealed two out of 13 (15%) had dyskinesia. Both of them had the primary diagnosis of schizophrenia and one of them had comorbid tic disorder (Table 6). However, if we only consider SSD (N=ten) then 20% had dyskinesia (N=two).

Table 6: Abnormal Involuntary Movement Scale score

Diagnosis	Facial and oral movements	Extremity movements	Trunk movements	Global judgement
Schizophrenia with tics	Minimal	None	Moderate	Severity, Overall: Moderate Incapacitance: Moderate Awareness: Aware, mild distress
Schizoaffective disorder, manic type	None	Minimal	None	Severity, Overall: Minimal Incapacitance: None Awareness: No awareness

Evaluation of the participants with SARS revealed none of them had mean total score more than 0.3 which is taken as the upper limit of normal range.

Discussion

We found that the motor coordination (MOCO) score of all the participants with SSD was higher when compared to the other scores in NSS assessment. Two out of ten participants with SSD had dyskinesia when assessed with AIMS. Assessment with SARS and BARS did not reveal any significant finding.

This study from the eastern part of India assessed both NSS and SMD in the same participants with SSD and other diagnosis. Earlier from this region, Bhandari and Bhagabati[12] and Sharma and Nath[13,14] had explored SMD and NSS in patients with psychotic disorders respectively.

The mean age of the participants in this study was 28.7 years. Our study showed presence of NSS in both schizophrenia and affective spectrum. MOCO score in our study showed similarity among the participants with SSD which suggest motor discoordination are more common in SSD.

Assessment with AIMS revealed two patients having dyskinesia. If Schooler and Kane's criteria[15] for spontaneous dyskinesia is considered, then only ten per cent (one in ten participants with SSD) can be labelled to have abnormal involuntary movement among SSD patients.

Our study failed to find any parkinsonian features among the participants. Two of the participants with the diagnosis of schizophrenia reported nonspecific sense of inner restlessness, but none had qualified to be tagged as having akathisia.

Higher NSS score has been found to be associated with reduced gray matter at the precentral gyrus, the inferior frontal gyrus, the cerebellum, and the thalamus as well as was found to be associated with reduced white matter at the temporal lobe, the cerebellum, and the inferior frontal gyrus.[16] Smaller volume of thalamus has also been found to correlate with both the total score and motor subscale scores of NSS scale. As thalamus is known as the relay centre which screen and relay selected information between peripheral, cortical, and subcortical structures, the changes in this may possibly explain inefficiency in the communication between widespread brain region and result in abnormal behavioural expression of NSS.[16] The changes in different structures may suggest neurodegeneration, but the absence of gliosis poses a question on this hypothesis. It has been suggested that schizophrenia is the result of ongoing neurodevelopmental process and a neurodegenerative or neuroprogressive process [17]. The neuroprogressive process is developmentally determined decrease in the connections between cortical synapses.[18] NSS and SMD represent domains generally considered sharing neurobiological mechanisms of neurodevelopmental or neurodegenerative origin of schizophrenia and related psychiatric disorders, and exploring this may give answer to many unanswered questions related to the disorder.

Though our study has its limitations like a small sample size, lack of any biological correlate, but we have tried assessing both NSS and SMD in the same group of participants.

Conclusion

As psychiatry is evolving and the diagnosis is moving towards more biological basis, NSS and SMD may be considered relevant points to be included in the diagnostic criteria provided the assessment is done in uniform by all.

References

1. Weinberger DR, Marenco S. Schizophrenia as a neurodevelopmental disorder. In: Hirsch SR, Weinberger DR, editors. Schizophrenia. 2nd ed. London: Blackwell; 2003:326-48.
2. Danielyan A, Nasrallah HA. Neurological disorders in schizophrenia. Psychiatr Clin N Am. 2009;32:719-57.
3. Thomann PA, Wüstenberg T, Santos VD, Bachmann S, Essig M, Schröder J. Neurological soft signs and brain morphology in first-episode schizophrenia. Psychol Med. 2009;39:371-9.
4. Kirkpatrick B, Tek C. Schizophrenia: clinical feature and psychopathology concepts. In: Sadock BJ, Sadock VA, editors. Kaplan & Sadock's comprehensive textbook of psychiatry. 8th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:1416-35.
5. World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: World Health Organization; 1992.
6. Pridmore S. Download of psychiatry [Internet]. University of Tasmania; 2006 [cited 2017 Aug 24]. Available from: http://eprints.utas.edu.au/287/
7. Schröder J, Niethammer R, Geider FJ, Reitz C, Binkert M, Jauss M, et al. Neurological soft signs in schizophrenia. Schizophr Res. 1991;6:25-30.
8. Guy WA. Abnormal Involuntary Movement Scale (AIMS). In: ECDEU assessment manual for psychopharmacology. Washington, DC: U.S. Department of Health Education and Welfare; 1976:534–7.
9. Simpson GM, Angus JW. A rating scale for extrapyramidal side effects. Acta Psychiatr Scand Suppl. 1970;212:11-9.
10. Barnes TR. A rating scale for drug-induces akhathisia. Br J Psychiatry. 1989;154:672-6.
11. Khairnar MR, Wadgave U, Shimpi PV. Updated BG Prasad socioeconomic classification for 2016. J Indian Assoc Public Health Dent. 2016;14:469-70.
12. Bhandari SS, Bhagabati D. Prevalence of spontaneous dyskinesia in first episode, drug naïve schizophrenia and its relation to the positive and negative symptoms of schizophrenia. Open J Psychiatry Allied Sci. 2017;8:113-23.
13. Sharma P, Nath K. Neurological soft signs in psychoses. I: a comparative study of prevalence amongst drug naive first episode patients. Open J Psychiatry Allied Sci. 2016;7:15-22.
14. Sharma P, Nath K. Neurological soft signs in psychoses. II: an explorative study of structural involvement amongst drug naive first episode patients. Open J Psychiatry Allied Sci. 2016;7:23-30.
15. Schooler NR, Kane JM. Research diagnoses for tardive dyskinesia. Arch Gen Psychiatry. 1982;39:486-7.
16. Zhao Q, Li Z, Huang J, Yan C, Dazzan P, Pantelis C, et al. Neurological soft signs are not "soft" in brain structure and functional networks: evidence from ALE meta-analysis. Schizophr Bull. 2014;40:626-41.
17. Lieberman JA. Pathophysiologic mechanisms in the pathogenesis and clinical course of schizophrenia. J Clin Psychiatry. 1999;60 Suppl 12:9-12.
18. McGlashan TH, Hoffman RE. Schizophrenia as a disorder of developmentally reduced synaptic connectivity. Arch Gen Psychiatry. 2000;57:637-48.

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