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Research Paper

Minor Physical Anomalies, Neurological Soft Signs, and Neurocognitive Dysfunction in Patients with Schizophrenia, Bipolar Disorder and Their Respective Normal Siblings– a Cross-Sectional Case Control Study

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ABSTRACT

Aim : To assess the presence of Minor physical anomalies, Neurological soft signs, and neurocognitive dysfunction in patients with schizophrenia and bipolar disorder and their respective siblings and to assess the difference if any and their clinical relevance. ***Study Design:*** cross-sectional case control study. ***Materials And Methods:*** Socio demographic details as per Performa collected from cases and controls. Complete physical examination including detailed Neurological evaluation done. Afterwards MPA scale, NES scale and neuropsychological tests were applied to both patients and their healthy siblings separately. Likewise 30 subjects were tested in 4 each groups. ***Statistical Design:*** Measures of central tendency and dispersion, tests of significance. ***Results:*** The presence of MPA in schizophrenia patients (63.3%) compared to bipolar illness (50%) was not significantly higher. There is significantly higher presence of NSS between schizophrenia, bipolar patients and their siblings. On Neuroconitive dysfunction, there is a significantly higher prevalence of visual memory impairment, executive dysfunction among schizophrenia patients, bipolar patients compared to their siblings. Verbal memory was impaired in significantly higher proportion in schizophrenia patients compared to other groups. ***Conclusion :*** NSS, MPAs and neurocognitive dysfunction, may help for understanding etiopathogenesis, symptom dimension and treatment response of both illness. This will help in identifying high risk individuals and possible intervention may be imitated early to prevent the occurrence of illness.

Keywords: *Schizophrenia, Bipolar disorder, MPA -Minor physical anomalies, NSS - Neurological soft signs, neurocognitive dysfunction.*

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Schizophrenia is arguably the most puzzling of psychiatric syndromes. Although its phenomenology is fascinating, its pathophysiology and etiology remains unclear.
Is Schizophrenia a neurodevelopment disorder?

The neurodevelopment hypothesis of Schizophrenia states that a proportion of Schizophrenia begins with impaired fetal or neonatal neurodevelopment rather than in young adulthood when psychotic symptoms first becomes manifest. Following are the evidences of neurodevelopmental model.

Craniofacial dysmorphology may provide another clue to the neurodevelopmental process in Schizophrenia. Since cerebral morphogenesis is very closely related to craniofacial morphogenesis, Minor physical anomalies (MPAs) may constitute biological markers of first and early second trimester dysgenesis and have been found to occur in excess in patients with Schizophrenia.

Neurological soft signs (NSS) are present in excess in patients with Schizophrenia. These are Minor neurological abnormalities in sensory and motor performance identified by clinical examination and are thought to reflect a failure in the integration within or between sensory and motor systems.

Neurocognitive dysfunction is one of the core symptom of Schizophrenia and provide important diagnostic information both in the phenotype and prodromal phases. Several studies have demonstrated that a significant proportion of Schizophrenic patients show neuropsychological impairment from early in the course of their illness. Although the range of neurocognitive deficits described is extremely broad, the cognitive functions most frequently compromised are attention, executive function and working memory.

The cause of Bipolar disorder is not entirely known. Genetic, neurochemical and environmental factors probably interact at many levels to play a role in the onset and in the progression of Bipolar disorder. Lohr, Flynn et al., 1993 reported intermediate rates of MPAs in Bipolar disorder [1], Bipolar patients seen to have more neurological dysfunction compared to healthy controls particularly in the areas of complex motor sequencing by Negash et al., 2004 [2]. Ferrier et al., 1999 showed significant cognitive impairment in Bipolar patients both during acute and euthymic periods[3]. The importance of cognition in Bipolar illness lies on its effect on psychological and functional outcome.

SCOPE OF THE STUDY:

There is a need to study MPA, NSS and Neuro cognitive dysfunction and their relationships in patients with schizophrenia and bipolar disorder with their first degree relatives in our native population. Such a study may help in further understanding of schizophrenia and bipolar disorder, preventing expression of illness in those at high risk, and plan for future target of treatment for various dimensions.

MATERIALS AND METHODS

Inclusion criteria

- Cases and controls are selected in the age group between 15 and 45 years
- Persons who meet ICD 10 DRC criteria for schizophrenia and bipolar disorder chosen as cases and their first degree relatives who do not meet the ICD 10 DRC criteria chosen as controls
- Patients who are selected as cases should be first episode and drug naïve
- Cases and controls have minimal education of up to 5^{th}std
- Cases and Controls who are willing to participate in the study and who have consented to the study.

Exclusion criteria

- Cases and controls who have current or past medical or neurological illness
- Cases and controls having mental retardation, dementia and substance dependence
- Cases and controls having present or past psychiatry medications or on medication for physical illness.
- Cases who are actually ill, exhibits aggressiveness and violent behavior.
- Controls who have a past history of psychiatric illness.

Tools Used:

1. Proforma: Proforma includes personal demographic details, personal history, past history, family history, physical and Mental status examination and biochemical investigations.

2. Waldrop scale: Waldrop minor physical anomalies scale, a widely used standardized scoring system for the assessment of MPAs, the scale is a simple 5-10min examination for the assessment of 17 anomalies features. Each MPA is given certain weightage ranging from 0-2. The total waldrop score would give an indication as to the number and severity of MPA present in a subject. Six body areas include eyes, ears, mouth, global head, hands and feet.
Green et al., 1998 used the cutoffscore of 3 was chosen because this was the upper limit of normal population in many studies [4]

3. Neurological evaluation scale: Neurological evaluation scale a prevalidated scale developed by Heinrich and Buchanan 1989 [5], used to evaluate the neurological soft signs. It includes 30 items of which 15 items are rated separately for both halves of body. Scoring was done on 3 point scale: 0 absent, 1 mild, 2 marked except for convergence, snout and suck which are scored as either 0 or 2. A total score of 3 and above defines abnormality, 6 or above is significant, Whitty P et al 2002

4. Neuro psychological assessment:

a) Attention:

Digit span:

Digit Span is a measure of attention which is composed of two tasks Digits Forward and Digits Backward. On both tasks, the examiner reads a series of number sequences to the examinee.

b) Memory:

Rey Auditory Verbal Learning test (AVLT):

The test consists of two lists A and B, with 15 different words in each list. It is a measure of auditory memory.

Test of Visuo- constructive Ability

Rey Complex Figure Test

The Visuo Constructive ability was tested using the Rey's Complex Figure Test (Meyers & Meyers, 1995). Rey developed the test in 1941. The test consists of a complex design which is abstract in nature and cannot be named easily.

c) Verbal fluency

Controlled Oral Word Association Test (COWAT): (Benton and Hamsher, 1989)

This test is a measure of phonemic fluency. The subject generates words based on the phonetic similarity of the words. The subjects generates words begins with the letters F,A.S. The subject is asked to generate words for 1 minute in case of each consonant starting with 'ka' going on to 'pa' and 'ma'.

Animal name test (ANT): (LEZAK 1995)

This test is a measure of category fluency which is another form of verbal fluency. In this, it is the content of the words rather than the phonetic similarity of the words that is regulated. Subject is asked to generate the names of as many animals as possible in one minute. The total number of new words generated forms the scores.

d) Executive functions:

Stroop test (Benson and Stuss, 1989)

This test measures the ease with which a perceptual set can be shifted both to conjoin changing demands and by suppress a habitual response in favor of an unusual one. The pre frontal areas are essential for response inhibition.

For all the cards time limit given is 45 seconds within which time the number of words read and the number of errors made is noted. Scoring is done as per manual.

Trail making test

The test measures attention and cognitive flexibility. Has two parts A and B , both parts of the Trail Making Test consist of 25 circles distributed over a sheet of paper.

5. Socioeconomic scale (S.E.Gupat and B.P.Sethi1978, Kuppusamy 1961)

Socioeconomic scale consists of scores based on three variables namely education, occupation, and income. On the basis of ten point scale. It consists of ten categories are grouped with 5 social class namely very high, high, upper middle, lower middle and very low.

Operational design:

The study was approved by institutional ethical committee.

The sample was chosen from psychiatry outpatient department, patients diagnosed as schizophrenia and bipolar as per ICD10 DRC are chosen as cases and their healthy siblings were chosen as controls. All the patients and their siblings were screened depending on the

inclusion and exclusion criteria, discussed with senior psychiatrist and on his advice were included in the study.

The subjects were explained about the nature of the study and obtained informed consent. Socio demographic details as per proforma collected from cases and controls. Complete physical examination including detailed Neurological evaluation done. Biochemical and laboratory investigations were done. Afterwards MPA scale, NES scale and neuropsychological tests were applied to both patients and their healthy siblings separately. Likewise 30 subjects were tested in 4 each groups. The socioeconomic status was assessed using SES scale. The testing has been done in two sessions on consecutive days.

Statistical design:

Statistical design was formulated using the data collected as above, for each of the scales and sociodemographic variables the central values and dispersion were calculated. In comparison of the data's for categorical variables chi-square and for numerical variables student t test were used.

RESULTS AND INTERPRETATION

Table 1, Table showing comparison of socio demographic profile between schizophrenia patients and bipolar patients.

Sl.No	Variables	Schizophrenia (N=30) n	Bipolar (N=30) n	P value
1	Age			
	18-30	23	18	0.267
	31-45	7	12	
2	Gender			
	M	20	23	0.567
	F	10	7	
3	Education			
	<10yrs	18	14	0.438
	>10yrs	12	16	
4	Marital			
	Unmarried	16	14	0.796
	Married	14	16	
5	Domicile			
	Rural	21	23	0.770
	Urban	9	7	
6	Occupation			
	UE	26	12	<0.001**
	Employed	4	18	
7	SES			
	Low	29	26	0.350
	Mid	1	4	
	High	0	0	

*p<0.005 , ** p<0.001

Table 1 shows on comparison of schizophrenia and bipolar patients, schizophrenia patients were younger than bipolar. Both groups predominantly belong to male gender, from rural background and from low socioeconomic status. Majority of schizophrenia patients were unemployed (86.7%) compared to bipolar patients who were predominantly employed (60%) which show statistically significant difference.

Table 2, Table showing comparison of presence of MPA and NSS between schizophrenia patients and their siblings.

Sl. No	Variable	Schizophrenia (N=30) n	Siblings (N=30) n	P value
1	MPA			
	Present	19	15	0.434
	Absent	11	15	
2	NSS			
	Present	28	19	0.012*
	Absent	2	11	

MPA- Minor Physical Anomalies , NSS- Neurological Soft Signs.

Table 2 shows majority of patients among schizophrenia individuals (63.3%) had minor physical anomalies compared to 50% of sibling had MPAs, and on comparison no difference could be made out... Among schizophrenic patients twenty eight (93.3%) had neurological soft signs compared to nineteen siblings (63.3%) had neurological soft sings and the difference is significant

Table 3, Table showing comparison of presence of MPA and NSS between bipolar patients and their siblings

SL.No	Variable	Bipolar (N=30) n	Sibling (N=30) n	P value
1	MPA			
	Present	15	11	0.434
	Absent	15	19	
2	NSS			
	Present	22	11	0.009*
	Absent	8	19	

MPA- Minor Physical Anomalies , NSS- Neurological Soft Signs.

Table 3 shows among bipolar patients fifteen had (50%) MPAs and among siblings eleven (36.7%) had MPAs, and on comparison no difference could be made out. Majority of bipolar patients had neurological soft signs (73.3%) and eleven (36.7%) siblings had neurological soft signs, the difference is significant.

Table 4, Table showing comparison of presence of MPA and NSS between schizophrenia patients and bipolar patients.

SL.No	Variable	Schizophrenia (N=30) n	Bipolar (N=30) n	P value
1	MPA			
	Present	19	15	0.434
	Absent	11	15	
2	NSS			
	Present	28	22	0.083
	Absent	2	8	

MPA- Minor Physical Anomalies , NSS- Neurological Soft Signs.

Table 4 shows nineteen schizophrenia patient (63.3%) had MPAs and fifteen (50%) of bipolar patients had MPAs. Among schizophrenia patients twenty (93.3%) had NSS and twenty two (73.3%) bipolar patients had NSS? On comparison of two variables there is no statistical difference.

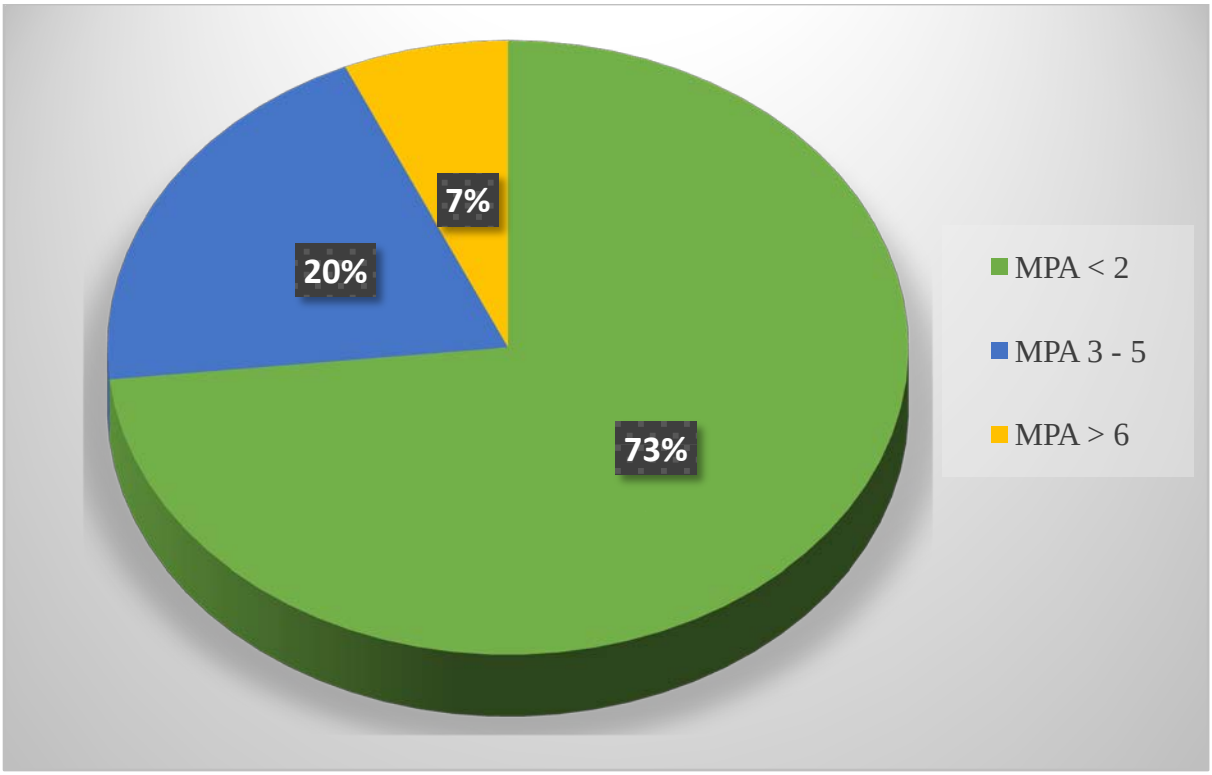
Table 5, Table showing comparison of MPA –T and NSS score between schizophrenia patients and their siblings.

Sl.No	Variable	Schizophrenia (N=30) n	Siblings (N=30) n	P value
1	MPA			
	<2	22	23	
	3 - 5	6	6	0.837
	>6	2	1	
2	NSS			
	0 - 5	13	25	
	6 - 10	12	5	0.003*
	>11	5	0	

MPA- Minor Physical Anomalies, NSS- Neurological Soft Signs.

Table 5 shows eight schizophrenia patients 26.7% had 3 or more MPAs compared to seven siblings (23.3%) had 3 or more MPAs. Seventeen schizophrenia patients (56.7%) had 6 or more NSS compared to five siblings (16.7%) had 6 or more NSS. On statistical analysis NSS have been significantly high in schizophrenia patients than siblings, but MPAs did not show difference.

CHART – 1, Schizophrenia patients –MPA Scores



MPA- Minor Physical Anomalies.

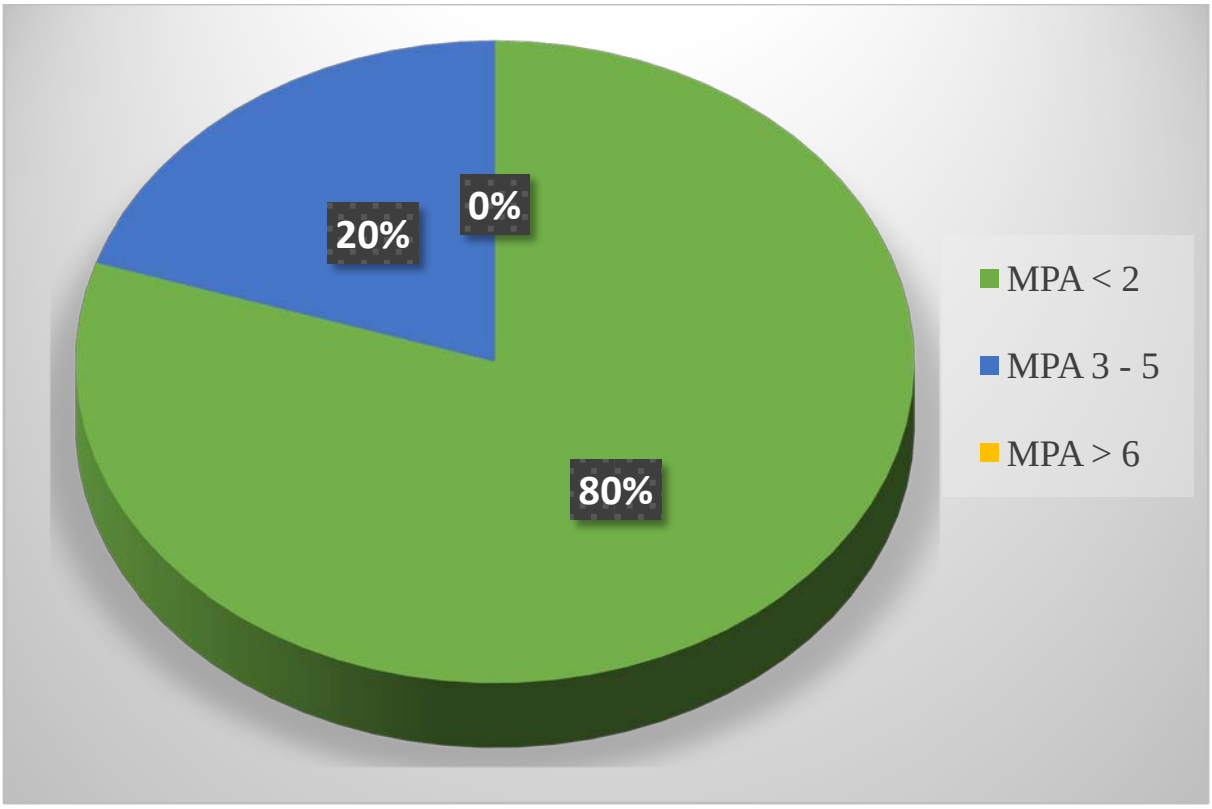
Table 6, Table showing Comparison of MPA –T and NSS score between bipolar patients and their siblings.

SL.No	Variable	Bipolar (N=30) n	Siblings (N=30) n	P value
1	MPA			
	< 2	24	26	
	3 - 5	6	4	0.351
	> 6	0	0	
2	NSS			
	0 - 5	22	27	
	6 - 10	7	2	0.193
	>11	1	1	

MPA- Minor Physical Anomalies , NSS- Neurological Soft Signs.

Table 6 shows six bipolar patients (20%) had 3 or more MPAs compared to four siblings (13.3%) had 3 or more MPA s. Eight patients with bipolar had 6 or more NSS compared to three (10%) siblings had 6 or more NSS. Both variable did not show significant difference.

CHART – 2, Bipolar patients –MPA Scores



MPA- Minor Physical Anomalies.

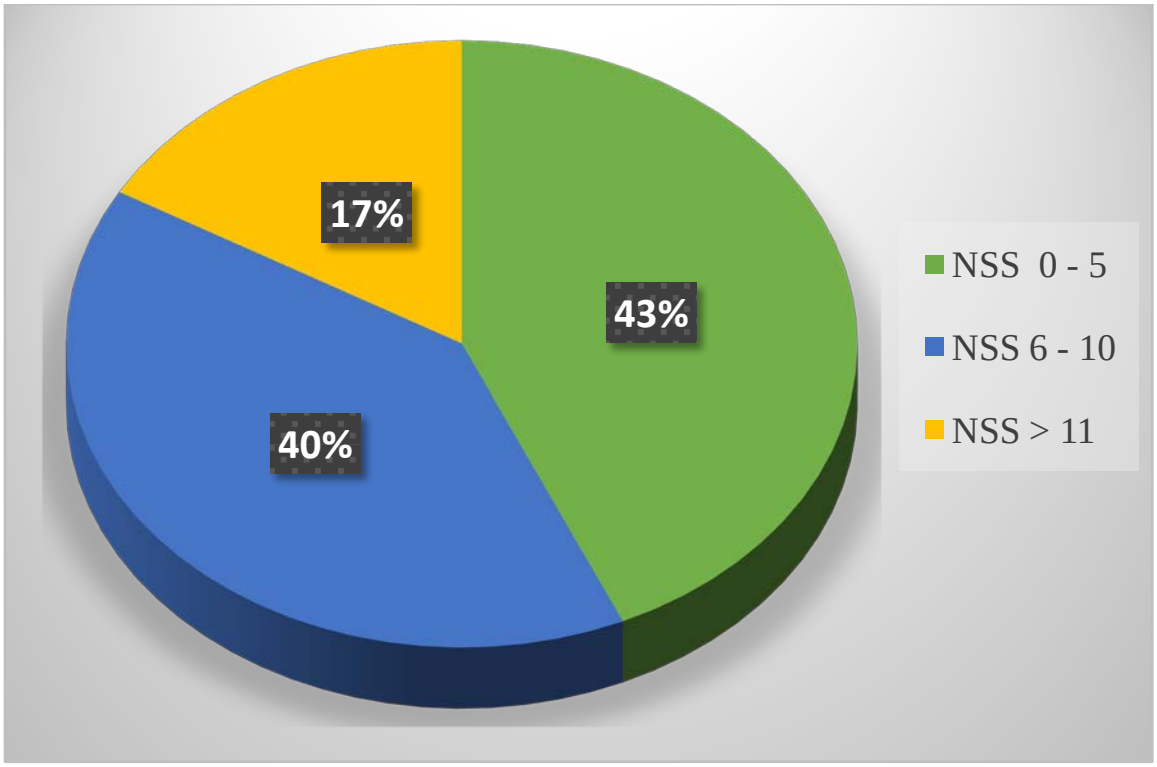
Table 7, Table showing Comparison of MPA –T and NSS score between schizophrenia patients and bipolar patients.

SL.No	Variable	Schizophrenia (N=30) n	Bipolar (N=30) n	P value
1	MPA			
	<2	22	24	0.352
	3 - 5	6	6	
	>6	2	0	
2	NSS			
	0 - 5	13	22	0.043*
	6 - 10	12	7	
	>11	5	1	

MPA- Minor Physical Anomalies , NSS- Neurological Soft Signs.

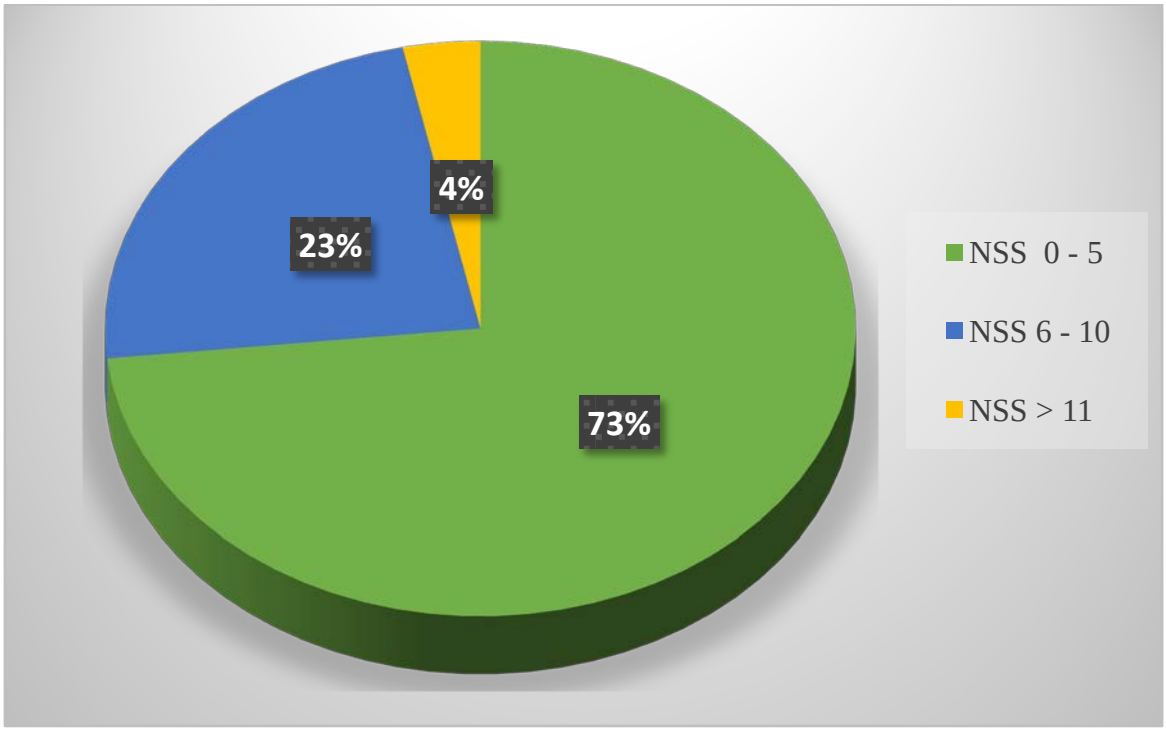
Table 7 shows eight schizophrenia patients (28.7%) compared to six bipolar had 3 or more MPAs . seventeen schizophrenia patients (56.7%) compared to eight bipolar patients had 6 or more NSS , show statistically significant difference.

CHART – 3, Schizophrenia patients –NSS Scores



NSS- Neurological Soft Signs.

CHART – 4, Bipolar patients –NSS Scores



NSS- Neurological Soft Signs.

Table 8, Table showing Comparison of visual memory, attention, and executive function between schizophrenia patients and their siblings.

Tests	Variables	Schizophrenia Mean	Schizophrenia SD	Siblings Mean	Sibling SD	t value
Visual memory	Rey copy	29.96	7.430	30.400	7.435	-0.226
	Rey IR	15.16	7.684	22.567	9.684	-3.279*
	Rey DR	13.76	7.873	21.567	9.522	-3.458**
Attention	Digit F	6.6	2.175	7.233	1.455	-1.326
	Digit B	2.76	1.406	3.567	1.501	-2.130
Executive function	Stroop I	61.833	14.669	73.067	16.630	-2.775
	Stroop II	34.267	9.355	48.767	11.044	-5.487**
	Stroop III	18.800	6.008	26.133	6.684	-4.469**
	Trail A	115.53	40.340	75.700	24.418	4.627**
	Trail B	175.93	58.439	126.867	44.621	3.655**

IR- Immediate recall, DR delayed Recall, Digit F- forward, Digit F – Backward.
*p<0.005 , ** p<0.001

Table 8 shows schizophrenia patients have significantly low scoring on visual memory compared to siblings, both on immediate and delayed recall domains. They did not show difference in attention impairment but patients have significant impairment in executive function compared to their siblings.

Table 9, Table showing comparison of visual memory, attention, and executive function between bipolar patients and their siblings.

Tests	Variables	Bipolar Mean	Bipolar SD	Siblings Mean	Sibling SD	t value
Visual memory	Rey copy	27.100	7.658	30.633	6.542	-1.922
	Rey IR	15.467	7.592	24.800	8.846	-4.497**
	Rey DR	13.733	8.250	22.333	9.897	-3.656**
Attention	Digit F	6.467	1.776	6.600	1.734	-0.294
	Digit B	2.833	1.234	3.267	1.741	-1.112
Executive function	Stroop I	73.267	17.508	69.200	17.243	0.906
	Stroop II	40.667	9.639	46.033	11.574	-1.951
	Stroop III	20.933	8.043	22.900	6.984	-1.011
	Trail A	119.667	71.480	69.900	25.346	3.594**
	Trail B	191.767	92.317	132.333	56.670	3.005**

IR- Immediate recall, DR delayed Recall, Digit F- forward, Digit F – Backward.
*p<0.005 , ** p<0.001

Table 9 shows bipolar patients had significant impairment in visual memory both in Immediate recall and Delayed recall compared to their siblings, no difference were noticed in attentional impairment, but bipolar patients showed significant impairment in executive functions as suggested by trial A and trial B by tests compared to their siblings.

Table 10, Table showing Comparison of visual memory, attention, and executive function between schizophrenia Patients and bipolar patients.

Tests		Schizophrenia Mean	Schizophrenia SD	Bipolar Mean	Bipolar SD	t value
Visual memory Attention	Rey copy	29.96	7.430	27.100	7.658	-1.472
	Rey IR	15.16	7.684	15.467	7.592	-0.152
	Rey DR	13.76	7.873	13.733	8.250	0.016
	Digit F	6.6	2.175	6.467	1.776	0.260
	Digit B	2.76	1.406	2.833	1.234	-0.195
Executive function	Stroop I	61.833	14.669	73.267	17.508	-2.742
	Stroop II	34.267	9.355	40.667	9.639	-2.610
	Stroop III	18.800	6.008	20.933	8.043	-1.164
	Trail A	115.53	40.340	119.667	71.480	-0.276
	Trail B	175.93	58.439	191.767	92.317	-.0.794

IR- Immediate recall, DR delayed Recall, Digit F- forward, Digit F – Backward.

Table 10 shows on comparison of visual memory, attentional domain and executive domain, schizophrenia patients did not show any statistical difference compared to bipolar mood disorder patients.

CHART – 5, Comparison of Visual Memory, Attention, and Executive Function between Schizophrenia Patients and Bipolar Patients

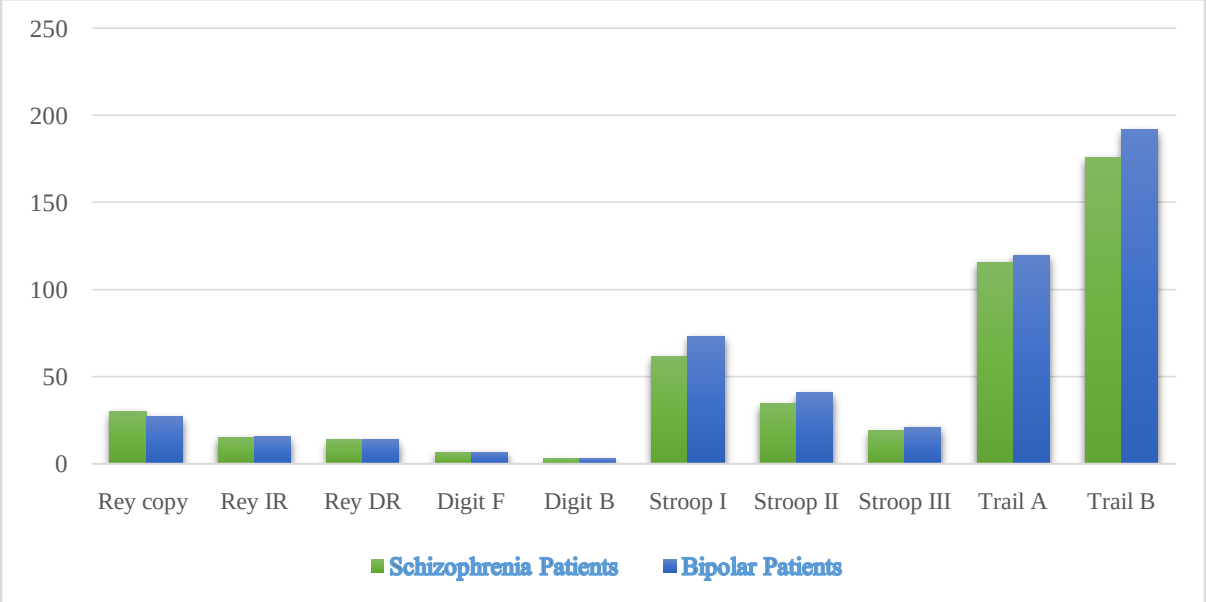


Table 11, Table showing Comparison of verbal memory and word fluency between schizophrenia patients and their siblings

Tests	Variable	Schizophrenia Mean	Schizophrenia SD	Siblings Mean	Sibling SD	t value
Verbal memory	AVLT 1	5.067	1.964	5.733	1.721	-1.398
	AVLT 2	5.933	2.164	7.000	2.364	-1.823
	AVLT 3	6.333	2.339	8.500	2.389	-3.550**
	AVLT 4	6.900	2.454	9.767	2.359	-4.612**
	AVLT 5	7.900	2.881	9.633	2.282	-2.583
	List B	3.567	4.804	4.167	1.533	-0.652
	IR	6.533	2.515	7.933	2.243	-2.275
	DR	5.700	3.678	7.867	2.675	-2.610
	Recognition	23.367	5.442	26.200	2.524	-2.587
	Omission	3.067	3.205	1.733	2.227	1.871
	Commission	1.867	2.886	1.067	0.826	1.460
verbal fluency	ANT	9.500	2.345	11.633	2.442	-3.451
	COWAT	10.633	7.924	16.200	8.438	-2.634

AVLT- Auditory verbal learning test, IR- Immediate recall, DR delayed Recall, ANT- Animal Naming Test, COWAT- Controlled Oral Word Association Test.
*p<0.005 , ** p<0.001

Table 11 shows schizophrenia patients had significant impairment in verbal recall compared to their siblings, but did not differ in relation to recognition . On comparison of word fluency both cases and controls did not show any difference.

Table 12, Table showing Comparison of verbal memory and word fluency between bipolar patients and their siblings

Tests	Variable	Bipolar Mean	Bipolar SD	Siblings Mean	Sibling SD	t value
Verbal Memory	AVLT 1	5.100	1.768	5.667	1.900	-1.196
	AVLT 2	6.667	2.090	6.967	2.484	-0.506
	AVLT 3	6.167	2.365	8.467	2.315	-3.806**
	AVLT 4	7.300	2.562	8.567	2.269	-2.027
	AVLT 5	7.770	2.409	9.233	2.431	-2.454
	List B	2.700	1.622	4.233	1.888	-3.374**
	IR	6.500	2.688	7.233	2.569	-1.080
	DR	5.500	2.701	7.200	2.340	-2.606
	Recognition	22.900	4.130	25.367	3.102	-2.616
	Omission	3.733	3.373	2.033	1.938	2.394
	Commission	2.367	3.388	0.900	0.995	2.275
verbal fluency	ANT	10.367	2.442	10.833	2.394	-0.747
	COWAT	13.967	5.014	15.533	6.442	-1.051

AVLT- Auditory verbal learning test, IR- Immediate recall, DR delayed Recall, ANT- Animal Naming Test, COWAT- Controlled Oral Word Association Test.
*p<0.005 , ** p<0.001

Table 12 shows on comparison of bipolar patients and their siblings, bipolar patients had significant impairment in verbal recall compared to sibling but difference was noticed on comparison of word fluency.

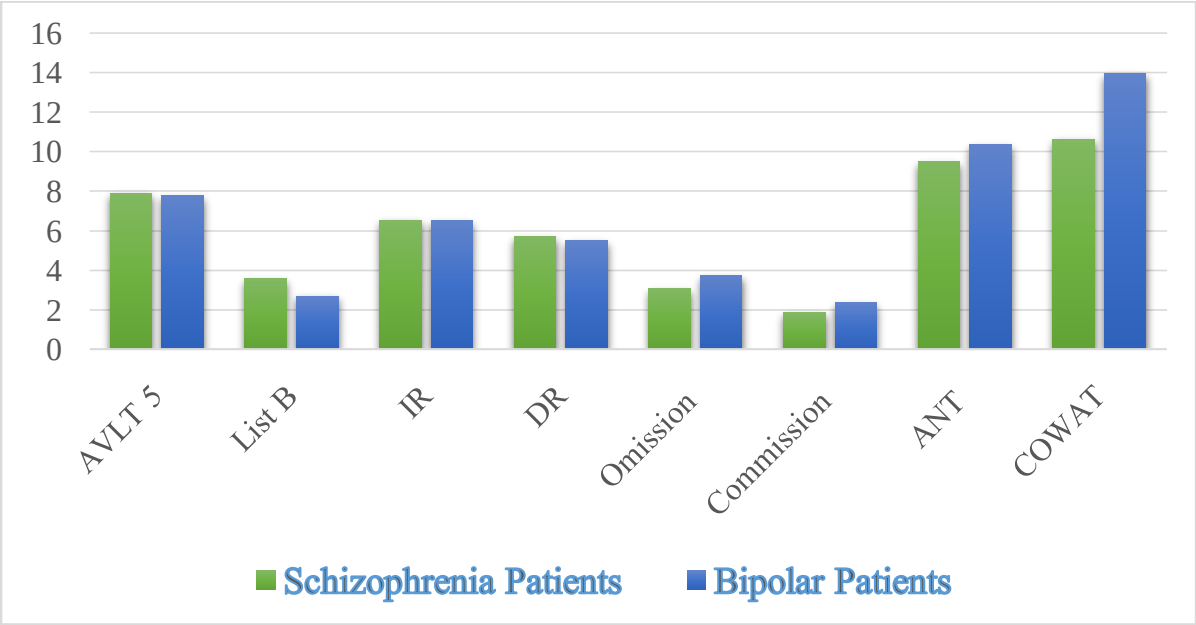
Table 13, Table showing Comparison of verbal memory and word fluency between schizophrenia patients and bipolar patients.

Tests	Variable	Schizophrenia Mean	Schizophrenia SD	Bipolar Mean	Bipolar SD	t value
Verbal Memory	AVLT 1	5.067	1.964	5.100	1.768	-0.069
	AVLT 2	5.933	2.164	6.667	2.090	-1.325
	AVLT 3	6.333	2.339	6.167	2.365	0.274
	AVLT 4	6.900	2.454	7.300	2.562	-0.618
	AVLT 5	7.900	2.881	7.770	2.409	0.292
	List B	3.567	4.804	2.700	1.622	0.936
	IR	6.533	2.515	6.500	2.688	0.049
	DR	5.700	3.678	5.500	2.701	0.240
	Recognition	23.367	5.442	22.900	4.130	0.374
	Omission	3.067	3.205	3.733	3.373	-0.785
	Commission	1.867	2.886	2.367	3.388	-0.615
verbal fluency	ANT	9.500	2.345	10.367	2.442	-1.402
	COWAT	10.633	7.924	13.967	5.014	-1.947

AVLT- Auditory verbal learning test, IR- Immediate recall, DR delayed Recall, ANT- Animal Naming Test, COWAT- Controlled Oral Word Association Test.

Table 13 shows on comparison of schizophrenia patients and bipolar patients both group didn't show significant difference in relation to verbal memory and word fluency.

CHART – 6, Comparison of verbal memory and word fluency between schizophrenia patients and bipolar patients.



DISCUSSION

Our sample consisted of thirty cases each of schizophrenia and bipolar patients as per ICD 10 DCR criteria; with same number of their corresponding siblings chosen as controls.

On detailed analysis of the sociodemographic profile (table 1), majority of schizophrenia patients in our sample are of younger age (76.7%). Two third of our sample are male gender, majority had education less than 10years (60%), more than half were unmarried, unemployed and from rural background. Among patients with bipolar illness majority (60%) are of younger age , predominantly male gender, predominantly employed and from rural back ground, marital and educational status were equally distributed . On comparison of cases and controls of both groups, no significant difference was noticed. On comparison of sociodemographic profile between schizophrenia patients and bipolar patients, both are equally matched, except bipolar patients had significantly higher proportion of employment status compared to schizophrenia patients.

Minor physical anomalies were present in 63.3% of our sample of patients with schizophrenia illness and 50 % was found in their sibling. Our study is in concordance with study done by O'Callagan 1995 showed higher rate of MPAs in schizophrenia patients in comparison with their siblings. But not in concordance with a study done by Alexander RC et al., 1994 who showed no difference between the two groups[7]. MPAs were present in 50% of patients with bipolar illness and 36.7% of their sibling. Lohr and Flynn et al 1993 , had similar findings with the presence of MPAs is more in bipolar patients than their first degree relatives[1]. Tables 2 to 7 for MPAs and NSS.

Our study finding show on statistical analysis the difference in the presence of MPA in schizophrenia patients (63.3%) compared to bipolar illness (50%) was not significantly higher. Whereas PaulSats et al., 1994 showed schizophrenia patients have high prevalence of MPAs than bipolar patients[9].

20% of patients of with schizophrenic illness and their sibling had 3-5 MPAs and 6.7% of our sample with Schizophrenic illness had more than 6 MPAs compared to single sibling who had more than 6 MPAS, which is similar to the study done by Green et al 1995[4].

20 % of bipolar patients and 13% of their siblings had MPA between 3-5 and none of them had MPA more than 6. McNeal et al 1998 found no significance in MPA score between bipolar patients and their siblings[8].

The difference in the presence of MPA between schizophrenia and bipolar patient, schizophrenia patient and sibling, bipolar patient and sibling did not show any significant difference. The findings are similar with the study done by Ismail et al 1988 [8], he showed MPA in mood disorder did not differ significantly from those of schizophrenia patients. And

McNeal et al 1998 found no significance in MPA score between bipolar patients and their siblings[8].

Regarding Neurological soft signs, 28 patients (93.3%) of diagnosis with schizophrenia had NSS, 19 (63.3%) sibling of schizophrenia had NSS, 22 patients (73.3%) with bipolar illness had NSS and 11 of their bipolar siblings (36.7%) had NSS. There is significantly higher presence of NSS between schizophrenia patients and siblings, bipolar patients and siblings, schizophrenia patient and bipolar patients in our sample. The same trend was observed by Bachmann Setal 2002 who found high prevalence of NSS in patients with schizophrenia and their biological relatives without significant difference[12]. Likewise Jacobson et al 2003 showed high prevalence of NSS in bipolar patients than their siblings[14], and Manschercek et al 1994 et al had reported NSS in 92% of schizophrenia patients, 52% of bipolar patients, and 5% of control subjects.

Regarding the NSS score seventeen schizophrenia patients had 6 or more, whereas only five patients with schizophrenia sibling had more than 6 NSS which on comparison showed higher prevalence in schizophrenia. The results are similar to study done by Nasrallahet al 2001, found high total score in schizophrenic group in comparison with their first degree relatives[15]. Similarly Goswami U et al., 1998 suggested that presence of neurological soft signs in relatives increase with the potential genetic loading[16]. Venkatasubramanian G et al 2003 showed presence of NSS in never treated schizophrenia[36.]

There is significant high score in NSS in schizophrenia patients compared to bipolar patients. Similar to our study Whitty et al 2000 found significant difference in NSS score between those two groups[6]. Compare to our study Boks et al.,2000 in found there is no statistical difference between schizophrenia and bipolar patients[9].

On analysis of Neurocognitive dysfunction, there is a significantly higher prevalence of visual memory impairment of immediate and delayed recall, executive dysfunction among schizophrenia patients compared to their siblings (see Table 8). Seidman et al., 2001 also showed similar findings of high prevalence of visual memory deficits in schizophrenia[11]. Likewise in relation to the executive dysfunction Cannon TD et al 2002 showed 56% of the schizophrenia patients, 50 % of their healthy siblings showed executive dysfunction[17]. Jabben N et al 2006 reported the similar findings[18].

The same trend of visual memory impairment and executive dysfunction was noticed on comparing bipolar patients and their siblings in our study (Table 9). Frank et al 2006 found similar results in executive dysfunction between bipolar patients and their siblings[10]. In relation to visual memory Seidman et al., 2001 and Bora et al., 2003 showed impairment in visual memory is more with bipolar group than their sibling [18,19].

Attentional impairment was noticed in both group of schizophrenia and bipolar patients compared to their respective siblings but not statistically significant (see Table 9). Similar to our findings Zlin, J Zlao et al 2003 showed 44% of schizophrenia patients and 14 % of their siblings showed attentional deficit[20], Whereas Altshuler LL et al 1994 showed no difference in attentional deficit in both groups[21]. In relation to bipolar disorder Clarke et al 2002 and Finkelstein JRJ et al 1997 reported high prevalence of attentional dysfunction in comparison with their healthy siblings[6,33].

Though neurocognitive dysfunctions pertaining to visual memory, attentional impairment, executive dysfunction were on higher side in schizophrenia patient group, there is no statistical difference was noticed between schizophrenia patients and bipolar patients. In concordance with our study Byrne M et al., 2003 and Martinez-Aran A et al 2002 found no difference in executive dysfunction, attentional deficit between schizophrenia and bipolar patients[22,34], whereas Goodwin GM et al ., 2006 and David AS et al 1995 showed significant between two groups in executive dysfunction[23,32].

Verbal memory was impaired in significantly higher proportion in schizophrenia patients compared to their siblings, bipolar patient and their siblings, but there was no difference was inferred in comparing schizophrenia patients and bipolar patients (see Table 10 to 13). In similar to our study Keri S et al., 2004 and Aleman, Aet al., 1999 found greater deficits in verbal memory in schizophrenia patients than their siblings[24,30], which also shown by Kolur US J et al 2003 Ali SO et al 2000, showed higher rate of verbal memory deficits in bipolar patients than their siblings[25,31]. Also John et al., 2009 reported high rate of deficits in bipolar patients[25].

There was no significant difference noticed on comparing of word fluency between patient group and their siblings. In concordance with our study Saykin AJ et al., 2006 reported both schizophrenia and bipolar patients exhibited deficits in word fluency in comparison with their first degree relatives[26]. A similar report also shown by Tridevi JK et al., 2008 and Savitz J et al. 2005[27,28]. The difference between patients and controls in word fluency is in concordance with the result of Toomey R et al 1995 , who also reports that word fluency is significantly impaired in patients than controls[29]. Thompson JM et al showed significant abnormality in bipolar patients[35.]

Our study was aimed to assess the neurodevelopmental abnormalities, by assessing neurological soft signs, Minor physical anomalies and to further explore and conclude possible neurodevelopment dysfunction by assessment and comparison with neuropsychological dysfunction.

The study findings reveal possibility of serious CNS insult as causation of illness as evidenced by significant higher presence of NSS and further expressed by significant high expression of endopheno type in the form of neurocognitive dysfunction.

CONCLUSION

Based on our findings and on comparison between schizophrenia patient and their siblings, bipolar patient and their siblings, schizophrenia patients and bipolar patients the following conclusions are made.

1. **Neurological soft signs**, but not Minor physical anomalies and Neurocognitive dysfunction are **significantly higher** in schizophrenia patients compared to bipolar patients.
2. **Neurological soft signs**, **Neurocognitive dysfunction** but not Minor physical anomalies are **significantly higher** in schizophrenia patients compared to their siblings.
3. **Neurocognitive dysfunction** and **Neurological soft signs** are **significantly high** in bipolar patients compared to their siblings but such trend is not found in respect to Minor physical anomalies.
4. Attentional dysfunction, executive dysfunction are the common cognitive dysfunction found in schizophrenia and executive **dysfunction are significantly higher** in schizophrenia compared to siblings.
5. Verbal memory, and word fluency impairment are widely prevalent in both schizophrenia and bipolar illness and no difference was noticed.
6. **Verbal memory impairment and executive dysfunction is significantly** high in bipolar patients compared to their healthy siblings.

There is a need for future study with large sample size of both the group of illness and to be compared with first degree relatives and healthy controls in relation to NSS, MPAs and neurocognitive dysfunction, may help for understanding etiopathogenesis, symptom dimension and treatment response of both illness. This will help in identifying high risk individuals and possible intervention may be initiated early to prevent the occurrence of illness.

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Conflict of Interest

The authors colorfully declare this paper to bear not conflict of interests

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