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A Comparative Study of Minor Physical Anomalies among Patients of Schizophrenia and Bipolar Affective Disorder

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Abstract:
Background*: Because the bodily structures involved in the expression of minor physical anomalies typically share their embryonic origin with that of the brain, minor physical anomalies represent potentially valuable indices of disturbances in early neurodevelopment. Here the aim is to determine and compare the frequency of minor physical anomalies (MPAs) in schizophrenia patients and Bipolar affective disorder patients*
Materials and Methods*: 100 schizophrenic patients (46 men, 54 women) and 100 Bipolar Affective Disorder patients (60 men, 40 women) were evaluated for Minor Physical Anomalies with a modified Version of Waldrop Scale*
Results*: Compared with BPAD patients, schizophrenia patients showed a higher incidence of almost all studied MPAs. The differences are statistically significant for 17 items out of 19. The two anomalies Epicanthus and low seated ears occurred with almost equal frequency in both the study groups. This pattern is true for mean MPA scores as well as for the number in each group with prominent MPAs.*
Conclusion: *Results suggest some degree of specificity for MPAs to schizophrenia compared with BPAD, perhaps indicating that neurodevelopmental factors are more relevant to the etiology of schizophrenia .*
Key Word*: Schizophrenia, Bipolar Affective Disorder, Minor Physical Anomalies*

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I. Introduction

Minor physical anomalies are slight dysmorphic features representing subtle alterations in the development of various bodily structures in the mouth, eye, ear, global head, hand and feat areas. Minor physical anomalies are considered to develop during the first and/or early second trimester of gestation. Because the bodily structures involved in the expression of minor physical anomalies typically share their embryonic origin with that of the brain, minor physical anomalies represent potentially valuable indices of disturbances in early neuro development.

Once formed minor physical anomalies persist in to adult life and are readily detected on simple visual examination of the particular body area. Because minor physical anomalies represent disturbed prenatal development, they have increasingly been studied in individuals with a range of mental, behavioral, and physical disorders such as autism, epilepsy, fetal alcohol syndrome, mental retardation, ADHD, cerebral palsy and schizophrenia. MPAs may be associated with other serious neuropsychiatric disorders such as bipolar disorders and unipolar depression[3].

The neurodevelopmental model of schizophrenia asserts that the etiological origins of the disease can be traced to events occurring prenatally.Minor physical anomalies (MPAs) are minor congenital malformations which are found with significantly increased frequency among both patients with schizophrenia and their siblings, suggesting the effect of early developmental disturbance in their families[1].Several diverse lines of evidence now support this model including epidemiological data, the presence of birth/pregnancy complications, the observed pattern of developmental brain anomalies, the presence of pre-morbid behavioral and neuromotor deficits and the gross somatic abnormalities that tend to accompany the disease.

Regarding this last category, particular emphasis has been placed on the presence of excess minor physical anomalies (MPAs) in those affected with schizophrenia. Some studies also proposed that MPAs and craniofacial features may serve as useful markers for identifying Treatment Resistant Schizophrenia at early stages of the illness[10]. Some findings suggest the selected MPAs could distinguish Early onset schizophrenia (EOS) and Adult onset Schizophrenia (AOS) patients from healthy individuals, with higher accuracy for EOS patients thus improving risk assessment[11]

II. Aims and Objectives

The aim of this study was to determine and compare the frequency of minor physical anomalies (MPAs) in schizophrenia patients and Bipolar affective disorder

III. Material And Methods

Study Design: Observational cross-sectional study.
Study Location: Government hospital for mental care, Visakhapatnam, Andhra Pradesh, India.
Study Duration: March 2019 to May 2019.
Sample size: 200 patients

Subjects & selection method: The study was conducted in the Government hospital for mental care, Visakhapatnam. The study included 100 schizophrenia patients (46 men and 54 women),and 100 bipolar affective disorder patients (60 men and 40 women) according to ICD-10 criteria both from inpatient and outpatient department of government hospital for mental care. This study is a cross-sectional study and used convenient sampling method.

Inclusion criteria:
The Subjects aged between 18 to 60 years and those who have satisfied ICD-10 criteria for the diagnosis of schizophrenia and Bipolar disorder are included in the study
Exclusion criteria:
Potential subjects were excluded if they had a history of any other comorbid psychiatric disorder, any neurological disorder, any signs of mental retardation or a somatic disorder with neurological components

Procedure methodology

A cross sectional study was done on the subjects by examining with a slightly modified version of the Waldrop Physical Anomaly Scale. The original scale includes 18 morphological abnormalities from six body regions: head, eyes, ears, mouth, hands, and feet[4]. Most of the abnormalities were scored qualitatively as present (1) or absent (0).The biomarkers fine electric hair, head circumference, epicanthus, intercanthal distance, high/arched palate and third toe >/- second were scored in a graded manner: 1 or 2, according to severity. Following changes are made in modified version – The categories adherent ear lobes and lower edges of the ears that extend backward/upward (two grades of a single item in the original scale) were defined as separate items because of the high prevalence of the former and only occasional occurrence of the latter. Furrowed tongue was graded by scoring 1 for randomly furrowed tongue (a normal variant) and scoring 2 for transversely furrowed tongue (frequently observed in pathological conditions)[5]. In the original scale both types are scored 1. The intercanthal distance as well as the head circumference were scored 1 if differed from Normal head circumference of same sex by 1.5 - 2 SD and 2 if they differed by more than 2 SD in both directions

Statistical analysis: The data were analysed with SPSS 23.0 using descriptive statistics; chi squared test- two-tailed for determining that the data are independent and using Independent samples t-test for comparing mean MPA scores of both the study groups. The level of statistical significance is set at $p<0.05$

IV. Results

Schizophrenia patients showed a higher incidence than bipolar affective disorder patients of all MPA biomarkers (excluding epicanthus and low-set ears). seventeen MPA biomarkers: fine electric hair ($p < 0.001$), abnormal hair whorls ($p < 0.001$),head circumference ($p < 0.05$), epicanthus ($p < 0.05$), Hypertelorism ($p < 0.05$),adherent ear-lobes ($p < 0.001$), lower edges of the ears that extend backward /upward ($p < 0.05$), malformed ears ($p < 0.05$), asymmetrical ears ($p < 0.05$) soft pliable ears ($p < 0.01$), high/arched palate ($p < 0.001$), furrowed tongue ($p < 0.001$), smooth/rough spots on the tongue ($p < 0.05$), curved 5th finger ($p < 0.001$), single transverse palmar crease

($p < 0.05$), third toe ≥ second toe ($p < 0.01$), partial syndactyly ($p < 0.05$) and big gap between first and second toe ($p < 0.001$) were significantly more common in schizophrenia patients compared with bipolar patients

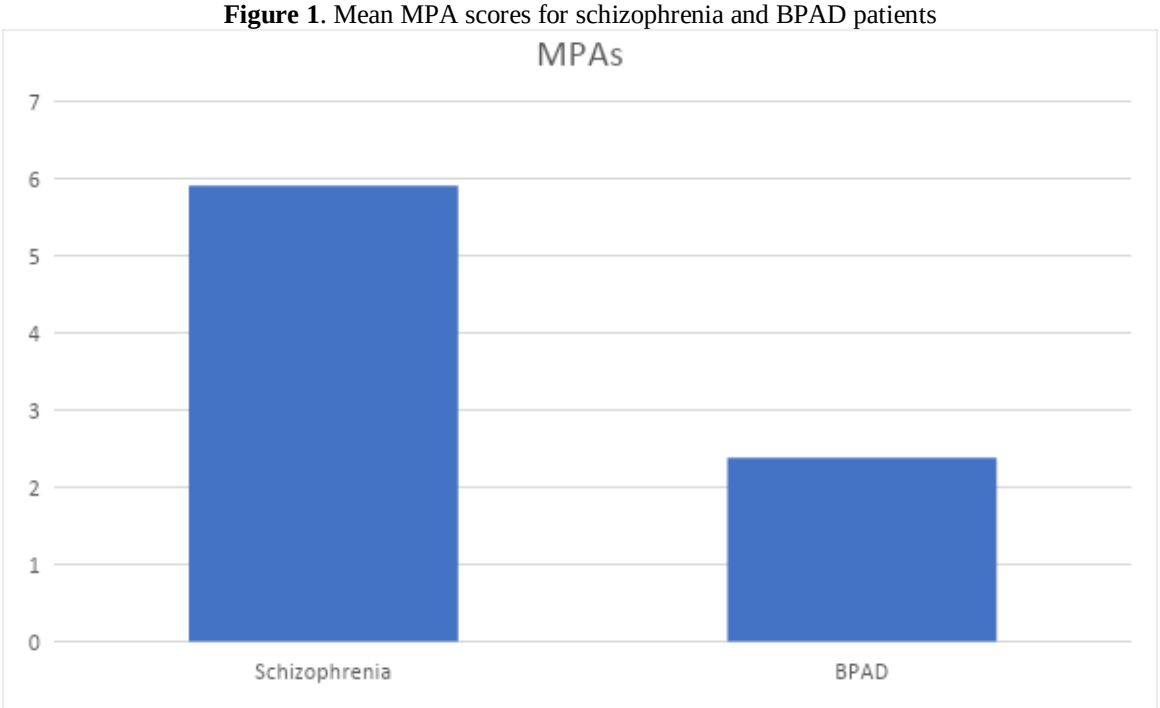
Table 1. comparison of prevalence rate of MPAs on the Waldrop scale between schizophrenia patients and BPAD patients

MPA		Schizophrenia	BPAD	X^2	p
Head					
Fine electric hair	Awry soon after combing	36	8	22.844	0.000002
	Doen't comb down	0	0		
Hair whorls ≥ 2		50	22	17.014	0.000037

Head circumference	1.5 – 2 SD	14	6		
	> 2 SD	29	18	8.489	0.014
Eyes					
Epicanthus		27	18	2.653	0.128
Hyper(Hypo)telorism	1.5 – 2 SD	24	13	4.013	0.045
	> 2SD	0	0		
Ears					
Low seated ears		4	1	1.846	0.174
Adherent ear lobes		66	32	23.129	0.000002
Lower edges extend back or upwards		4	0	4.082	0.043
Malformed ears		6	0	6.186	0.013
Asymmetrical ears		6	0	6.186	0.013
Soft and pliable ears		10	0	10.526	0.001
Mouth					
High or steepled palate	Flat and narrow	22	6	25.766	0.000003
	Definitely steepled	14	1		
Furrowed tongue	Randomly furrowed	38	12	18.928	0.000078
	Transversely furrowed	2	6		
Tongue with smooth-rough spots		22	8	7.686	0.006
Hands					
Curved fifth finger		52	26	14.208	0.000164
Single transverse palmar crease		30	14	7.456	0.006
Feet					
Third toe	Equal to second	42	16	16.416	0.000051
	Longer than second	0	0		
Partial syndactylia of II and III toes		10	2	5.674	0.017
Big gap between I and II toes	0.1 to 0.5 cm	38	8	25.409	0.0001
	≥0.60 cm	0	0		

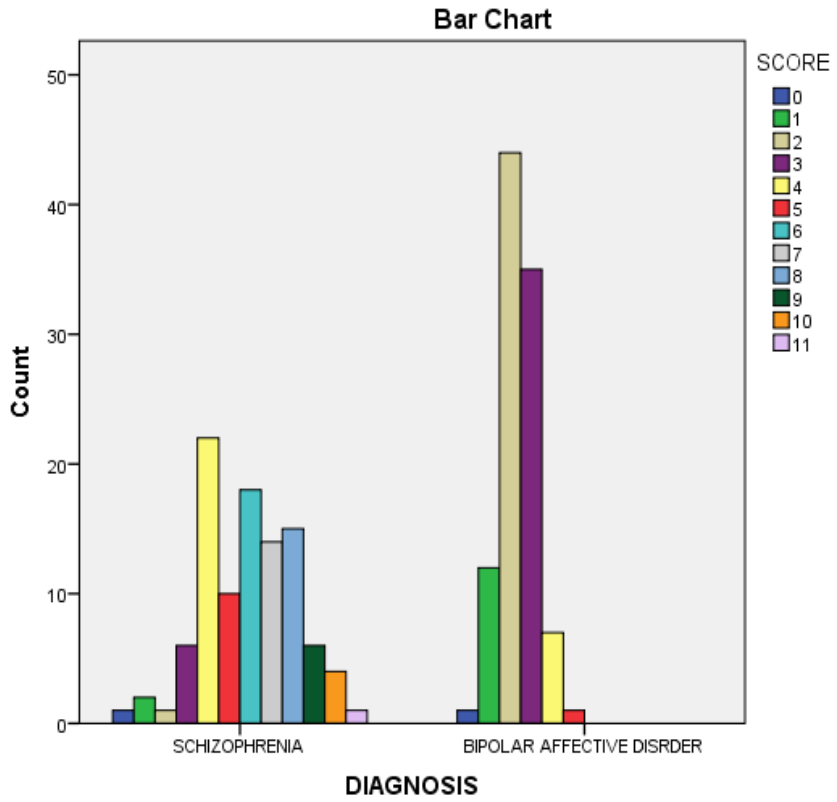
The Mean MPA score for the schizophrenia patients (5.98) was significantly higher than the scores for bipolar patients (2.38) with computed test statistic value $t = 15.225$, and $P < 0.001$

Figure 1. Mean MPA scores for schizophrenia and BPAD patients



Higher MPA scores are more seen in schizophrenia patients when as lower MPA scores are more seen in Bipolar patients.

Figure 2. Number of subjects in each group with particular MPA scores



V. Discussion

MPAs in the cefalo-facial area can occur along with *in utero* structural changes of the brain that show relation to schizophrenia development. According to Trixler et al. certain anomalies of the mouth and head have more significant relationship with neurodevelopmental anomalies than the cumulative prevalence of MPAs[12]. Similarly, Weinberg et al. suggest that information of the body areas showing a greater susceptibility to dysmorphic changes in the context of schizophrenia may be a key to the timing of anomalies and their relationship with neurodevelopment[8].There is a clear developmental logic in the occurrence of these anomalies. In the early prenatal period brain and skull development are so intimately connected that changes in brain morphology could find real expression in cefalo-facial morphogenesis.

Given the complex processes of cefalo-facial morphogenesis, development of these abnormalities is not unusual. Due to the overlaps in the timeline of ontogenetic development of different body structures, MPAs may also occur in areas (e.g. hands, feet) which are distant from the cefalo-facial area. Studies of MPA biomarkers in schizophrenia patients testify to violated neurodevelopment which increases the predisposition to the development of schizophrenia. MPAs may represent a putative endophenotype for schizophrenia[7].

A study by McGrath J et al. on 310 individuals with psychosis and 303 controls predicted that the patients with psychosis would have more qualitative abnormalities involving the eyes, ears, and palate compared with controls[2].A study by Alexander RC et al. on 41 schizophrenia subjects,8 Bipolar subjects,19 mentally retarded subjects ,and 14 normal controls, the mean total weighted waldrop score is higher for retarded group than the schizophrenic, bipolar and normal groups[9].The current study attempted to determine whether the increased MPAs are associated with schizophrenia in particular or with psychosis in general.

The data from our study show statistically higher prevalence of morphological abnormalities in schizophrenia patients compared with Bipolar patients suggesting some degree of specificity to schizophrenia. The pattern of changes in the morphological variables in the study is not unidirectional. This suggests that changes may be a random output of a general neurodevelopmental defect or may define different neurodevelopmental defects that ultimately allow better characterization of subgroups of schizophrenia patients

Strengths of the study: TO our knowledge, this is the first Indian study to compare MPAs among schizophrenia and Bipolar patients

Limitations of the study: Sample is drawn from a cross section of population attending a tertiary care hospital.Thus results cannot be applied to the community as a whole.

VI. CONCLUSION

Although there is still no clarity about the nature and role of the processes of disontogenesis in the etiology of schizophrenia, it may be assumed that MPAs reflect the impact of a certain neurodevelopmental risk factor, which in interaction with other genetic and non-genetic factors can lead to the development of the disease, at least in a subpopulation of schizophrenia patients. Identification of MPAs serve as markers for Treatment Resistant Schizophrenia at early stages of illness thus improving risk assessment and treatment plan.

Issues of conflict: None

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