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Original Research Article

A study on comparison of neurological soft signs and minor physical anomalies between siblings of attention deficit hyperactivity disorder and normal controls

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ABSTRACT

Background: The objective of the study was to compare the neurological soft signs and minor physical anomalies between ADHD siblings and normal controls, to observe the correlations among these parameters with sex and socioeconomic status of the subjects and to find out the interrelationship between neurological soft signs (NSS) and minor physical anomalies (MPAs) in both groups if at all there is a correlation.
Methods: This case control study was conducted in children of diagnosed ADHD and normal of age group 8-13 years at Institute of Child Health and Hospital for Children, Egmore, Chennai, during the period February 2013 to October 2014. The number of subjects from both case and control group were 57 each. All the patients were assessed for NSS by PANESS and MPAs by using Waldrop scale.
Results: Total number of children included in the study is 114. Male dominance was noted in the study (64.9%). Most of the patients belong to upper lower class (39.5%). ADHD siblings showed a significant increase in NSS especially in the field of overflow, gaits and stations, and timed when compared with the normal children ($P<0.05$). In both the groups, the difference in sex was not statistically significant in overflow, gait and stations, total timed, total PANESS and MPA scale ($p>0.05$). In case group parameters like gait and total time were significantly correlated with MPA scale. In control group, significant correlations were noted only between total PANESS and MPA scale. No positive correlation was observed between NSS and MPAs with socioeconomic status of the study participants in both the groups ($p>0.05$).
Conclusion: The current findings indicate that no significant correlation was existed between sex and socioeconomic status with NSS and MPAs in both the groups. ADHD siblings failed to show a significant increase in MPAs but showed a significant increase in NSS. However more number of studies is warranted for minor physical anomalies in ADHD siblings as early diagnosis of ADHD could be a possibility in children born with minor physical anomalies even before 3 years.

Keywords: ADHD, Minor physical anomalies, Neurological soft signs

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is said to be the most common neuro-behavioral disorder of childhood. It is prevalent among school going children and it is the most extensively studied mental disorder. It can continue through adolescence and adulthood too.[1] It is characterized by inattention, easy distractibility and difficulty in sustaining attention, poor impulse control and reduced self-inhibitory capacity. Usually seen

symptoms are motor over activity and motor restlessness. The common problems are academic under achievement, problems with interpersonal relationships with family members and peers, low self-esteem. The usual co-morbidities of ADHD are emotional problems, language disorders and learning disorders.[2,3]

There is no single factor that determines the expression of ADHD. It is the final common pathway for a variety of complex developmental process of the brain. Mothers of children with ADHD are said to have increased birth complications like pre-eclampsia, prolonged labour, and difficult delivery.[4] Maternal smoking, alcohol and drug usage during pregnancy are commonly linked to the development of ADHD in children.[5]

In India, there is not much data available for prevalence of ADHD but various studies show that prevalence of ADHD ranging from 2 to 17%.6 There was a significant difference in the prevalence of ADHD in the ratio of males and females, the ratio being 3:1.[7]

Neurological soft signs (NSS) are non-normative performance on a neurological evaluation of motor and sensory functioning in the absence of focal lesion. The poor coordination, speed, accuracy of limb or axial movements, dysrhythmias, and overflow are found during clinical examination of young children.[8]

NSS is studied in terms of timed and untimed motor activities. The most reliable of the timed movements are speed of movements followed by dysrhythmias. Of the individual soft signs synkinesias, and mirror movements have the highest incidence at younger age group. Overflow movements are those that are mirrored in other body parts and occur at the same time as in the parts intended to perform.[9]

Minor physical anomalies (MPAs) or dysmorphic features occur with higher than usual frequency in children with developmental disabilities, learning disorders and speech and language disturbance. As with soft signs, the documentation of minor physical anomalies is a part of neuropsychiatric assessment, but it is rarely helpful in the diagnostic process and does not confer good or bad prognosis in most of the situations.[1]

MPAs may have a genetic basis, they might also be caused by factors in the fetal environment: anoxia, bleeding, or infections have been linked to disorders of pregnancy and are thought by some to be a marker for insults to the fetal neural development towards the end of the first trimester.[10] Thus, in the neuro developmental literature, they are seen as indirect indications of inferences with brain development. In studies of children and adolescents with conduct problems, such markers have been linked to some extent to impulsivity and aggressiveness.

Various studies have proved that ADHD have a link with neurological soft signs and minor physical anomalies. Therefore this study was conducted with objective to compare the neurological soft signs and minor physical anomalies between ADHD siblings and normal controls, to observe the correlations among these parameters with sex and socioeconomic status of the subjects and to find out the interrelationship between NSS and minor physical anomalies in both groups if at all there is a correlation.

METHODS

This was a case control study conducted in children of diagnosed ADHD and normal of age group 8-13 years at Institute of Child Health and Hospital for Children, Egmore, Chennai, during the period February 2013 to October 2014. Selection criteria for cases and controls were tabulated in Table 1.

Table 1: Selection criteria of both groups.

Groups	Inclusion criteria	Exclusion criteria
Cases	Siblings of ADHD children	Children with CP, DD, post meningitic sequelae and any other gross neurological deficit
	Age group of 8-14	Features of psychiatric disorder
	Not positive for ADHD	Family history of schizophrenia
Control	Age between 8-14	Children with CP, DD, post meningitic sequelae or any other gross neurological deficit
	Not suffering from ADHD	Features of psychiatric disorder
		Family history of schizophrenia

The number of subjects from both case and control group were 57 each. Case group consists of children between age groups 8-13 who are a sibling of children diagnosed of ADHD now or previously by a psychiatrist or by examiner who is well trained in administering DSM-IV criteria. Subjects are then given DSM IV criteria and subjects not be positive for ADHD are included in the study. Subjects included in the study are then assessed using PANESS for neurological soft signs and Waldrop for minor physical anomalies.[11,12]

Similarly, subjects in control group falling in age group from 8-13 who are negative for DSM-IV criteria are included and considered as controls. These children are then assessed by PANESS for neurological soft signs and Waldrop for minor physical anomalies.

The results of both the groups are compared and statistical significance if at all any is identified.

PANESS is an observational scale for assessing physical and neurological examination for soft signs developed by Martha Denckla. It consists of 21 questions covering gait, stance, laterality, quality of rapid movements, impersistence score, involuntary movement score, repetitive speed of movement score, and sequenced speed of movement score, asymmetrical movement score. The result was assessed in terms of laterality, timed and untimed motor movements. It has been found to have adequate test retest reliability, inter-rater reliability, and internal consistency. It is particularly useful for assessment of motor speed in children because it is brief, minimizes the need for equipment, provides lateralized data, and is applicable to children as young as 5 years.

MPAs are evaluated by Waldrop minor physical anomalies score. The maximum numbers of score that one can obtain in minor physical anomalies are 15 and minimum number of score could be zero. Minor physical anomalies included in this study include head circumference and hair and its consistency whether is soft, fine, brittle, curly. The maximum score of 2 is given for certain items like head circumference >1.5 S.D

Statistical analysis

Data are collected and continuous variable (over flow items, total PANESS, minor physical anomalies) between cases and controls were reported. To find out the significant difference between in neurological soft signs and minor physical anomalies, standard deviation (SD) and mean (x) was calculated for each group. Null hypothesis was assumed (neurological soft signs and minor physical anomalies were equal among both groups). Independent t test was applied to compare the mean between the two groups. Using specific formula t value is calculated which is compared with t values from the table and to see if t calc >t to say that the differences were statistically significant. The SD were compared by Levens test for equality of variance by calculating F and assuming a 95% confidence interval (95%) and if the variances have a statistically significant difference between the 2 groups are identified. 2-tailed method is used to find out the statistical significance. The p value of <0.05 is considered significant. Also, frequency tables for age and gender are plotted using graphs and bars and if any age and gender variation if at all present is identified. All analysis is performed using SPSS (statistical package for social sciences) version 10.0.

RESULTS

Total number of children included in the study is 114. And no children were missing or disqualified during the study. The total number of males in both case and control group are 74 which is 64.9% and total number of females in both case and control group are 40 which accounts for 35.1%. Male dominance was noted in the study as given in Table 1.

Table 2 presents the socioeconomic status of both cases and controls that were classified into 5 groups based on Modified Kuppusamy Scale. The number of children included in the upper class (Class 1) is 6 and in the upper middle class (Class 2) 30, lower middle class (Class 3) is 29, upper lower class (Class 4) is 45, lower class (Class 5) is 4. Most of the patients belong to upper lower class (39.5%).

Table 1: Sex distribution of study participants.

Sex	No. of patients	Percentage (%)
Male	74	64.9
Female	40	35.1
Total	114	100

Table 2: Socioeconomic status of study participants.

Socioeconomic class	Group		Total (%)
	Cases (%)	Control (%)	
Upper	3 (5.7)	3 (5.7)	6 (5.3)
Upper middle	12 (21.5)	18 (31.5)	30 (26.3)
Lower middle	17 (29.8)	12 (21.5)	29 (25.4)
Upper lower	24 (42.1)	21 (36.8)	45 (39.5)
Lower	1 (1.7)	3 (5.7)	4 (3.5)
Total	57 (100)	57 (100)	114 (100)

The parameters assessed in the study by using PANESS and Waldrop score was analysed and compared statistically by using independent T test (Table 3). All the factors except MPAs were found to be not significant ($p<0.05$) when both groups are compared.

Table 3: Comparison of parameters between cases and controls.

Parameters	Groups	Mean	SD	P value
Overflow (0-31)	Cases	3.456	1.037	0.001
	Controls	3.456	1.037	0.001
Gaits and stations (0-49)	Cases	3.456	1.037	0.001
	Controls	2.088	0.879	0.019
Total timed (0-70)	Cases	2.088	0.879	0.020
	Controls	7.877	1.954	0.000
Total PANESS (0-119)	Cases	7.877	1.954	0.000
	Controls	9.842	2.475	0.000
MPA scale 0-33	Cases	9.842	2.475	0.000
	Controls	0.281	0.355	0.431
Age	Cases	0.281	0.355	0.431
	Controls	1.585	0.210	10.33

Table 4 presents the association of parameters with sex distribution. In both the groups, the difference in males and females was not statistically significant in overflow, gait and stations, total timed, total PANESS and MPA scale ($p>0.05$). The correlation between various

parameters of PANESS with total PANESS and MPA scale in both groups were given in Table 5. In case group, all the parameters were significantly correlated with total PANESS ($p<0.05$).

Table 4: Comparison between parameters and sex distribution of both study groups.

Parameters	Sex	Cases			Controls		
		N	Mean	SD	N	Mean	SD
Overflow (0-31)	Male	38	11.24	5.533	38	7.22	5.083
	Female	19	10.26	6.539	19	7.86	5.525
Gaits and stations (0-49)	Male	38	6.97	6.197	38	4.22	3.235
	Female	19	5.11	4.267	19	4.33	3.903
Total timed (0-70)	Male	38	27.42	11.222	38	18.50	10.227
	Female	19	27.89	10.862	19	21.76	8.949
Total PANESS (0-119)	Male	38	34.47	14.921	38	23.33	12.786
	Female	19	33.00	13.715	19	25.52	10.269
MPA scale 0-33	Male	38	3.92	1.792	38	3.72	2.337
	Female	19	3.89	1.410	19	3.48	1.662

Table 5: Pearson correlation between various parameters of PANESS with total PANESS and MPA in both groups.

Parameters	Correlation	Cases		Controls	
		Total PANESS (0-119)	MPA scale (0-33)	Total PANESS (0-119)	MPA scale (0-33)
Overflow (0-31)	Pearson correlation	0.805**	0.817**	0.817**	0.210
	Sig. (2-tailed)	0.000	0.000	0.000	0.117
	N	57	57	57	57
Gaits and stations (0-49)	Pearson correlation	0.729**	0.501**	0.501**	0.085
	Sig. (2-tailed)	0.000	0.000	0.000	0.531
	N	57	57	57	57
Total timed (0-70)	Pearson correlation	0.933**	0.906**	0.906**	0.209
	Sig. (2-tailed)	0.000	0.000	0.000	0.118
	N	57	57	57	57
Total PANESS (0-119)	Pearson correlation	1	1	1	0.305*
	Sig. (2-tailed)	-	-	-	0.021
	N	57	57	57	57
MPA scale (0-33)	Pearson correlation	0.444**	0.305*	0.305*	1
	Sig. (2-tailed)	0.001	0.021	0.021	-
	N	57	57	57	57

*Correlation is significant at the 0.05 level (2-tailed); **Correlation is significant at the 0.01 level (2-tailed).

Parameters like gait and total time were significantly correlated with MPA scale. In control group, significant correlations were noted only between total PANESS and MPA scale (Pearson correlation 0.305).

Table 6 shows the correlation between parameters and socioeconomic status of the study participants in both the groups and no positive correlations was noted.

DISCUSSION

Although most current knowledge about ADHD developed from clinical observation research, the understanding of the research in adults is growing rapidly. There are various studies regarding aetiology, clinical features, and treatment issues for attention deficit hyper-activity disorder in children. It is being discovered that adults and children with ADHD share similar clinical features, co-morbidities and failures in major life domains like academics and work and possibly brain abnormalities regarding this issue. It has become clear that a gain of full understanding of ADHD, the disorder must be studied from a lifespan perspective integrating what is known about how it affects adults and children.

Of the 114 children recruited in the study of the case-control format, 74 are males and 40 are females. There is no randomization done during the study. ADHD newly diagnosed and diagnosed previously on follow-up were asked to attend the clinics with their siblings falling into the age 8-13 years. The siblings were given DSM-IV criteria. The siblings who are all negative for ADHD in

DSM-IV criteria are included in the study as the control group. Other group consists of normal children negative for any neurological and psychiatric problems with negative family history of neurological disorders are given DSM-IV criteria. The children negative for DSM-IV criteria are included in control group.

DSM-IV criteria is employed in this study for both case and control for the diagnosis of ADHD and at least 6 of 9 symptoms of inattention are at least 6 of 9 hyperactive or impulsive symptoms were observed. The previously diagnosed ADHD children were included in the study that were on follow up and on drug treatment are also included in the study. Though the previously diagnosed children were not given DSM-IV criteria now, the diagnosis that was done earlier was by DSM-IV criteria by the psychiatrist of our hospital whereas the siblings and the normal controls were given DSM-IV criteria during the study. Sonia et al in her study suggested that neurological soft sign is dependent on family income, psychiatry disorders and age.[13] The result of his study suggested the neurological soft signs in ADHD are more prevalent among lower socio and economic groups.

On contrary, study by Martin et al showed the socio-economic status is independent of neurological soft status, but it depends on the aetiology especially anti-natal care, smoking, alcohol and drug usage.8 Socio-economic status also influences the treatment outcome and follow up of the children with ADHD.

Table 6: Correlation between parameters and socioeconomic status in both groups.

Parameters	Spearman's rho Correlation	Socioeconomic status	
		Cases	Controls
Overflow (0-31)	Correlation coefficient	0.008	0.202
	Sig. (2-tailed)	0.952	0.132
	N	57	57
Gaits and stations (0-49)	Correlation coefficient	0.071	-0.045
	Sig. (2-tailed)	0.602	0.741
	N	57	57
Total timed (0-70)	Correlation coefficient	0.171	0.113
	Sig. (2-tailed)	0.203	0.404
	N	57	57
Total PANESS (0-119)	Correlation coefficient	0.148	0.081
	Sig. (2-tailed)	0.271	0.549
	N	57	57
MPA scale (0-33)	Correlation coefficient	-0.068	0.179
	Sig. (2-tailed)	0.615	0.182
	N	57	57
Socioeconomic	Correlation coefficient	1.000	-
	Sig. (2-tailed)	-	-
	N	57	-

In the present study, the 114 children were classified into 5 groups based on their socio-economic status by modified Kuppuswamy scale. Each child was allotted one class based on their family income, education and occupation. The socio-economic classes were compared between two groups. Although the proportion of the upper (Class 1) and lower (Class 5) were less in both the groups, they were comparable in both groups. The upper middle class (Class 2), lower middle class (Class 3), upper lower class (Class 4) form the major class of our study in both case and control groups.

In the present study, correlations were noted by Pearson correlation were drawn for socio-economic status and other variables like overflow, gaits and stations, total timed, total PANESS and MPA scale. No significant positive correlations were noted. The reason probably is not an equal number of children were based in all the classes in both groups and decreased sample size even though correlation was established it cannot be taken into account due to the less sample size In this study, independent T-test were separately applied to both case and control group comparing girls and boys for overflow, gaits and stations, total timed, total PANESS, MPA scale had no significant differences. Although many studies did not find any difference in sex in executive functioning but the study of Newcorn et al suggest a decrease NSS in girls compared with boys with ADHD.[14-16] The total number of boys and girls in the present study were not similar and matched between the two groups. So, the insignificant results comparing the neurological soft signs and minor physical anomalies between the two groups shouldn't be taken into account. To clearly delineate the

differences if at all present, we need a large sample that is adequately matched between the two groups.

In the present study, we used ADHD siblings in the case group keeping in mind siblings have a similar genetic influence and brain abnormalities similar to ADHD children. So neurological soft signs are studied in ADHD siblings and significant statistical differences were noted. It gives the scope for future research that a common genetic factor is a similar regional brain abnormality could be responsible for the neurological soft signs. Previous studies of Semrud-Clikeman et al found a significant relationship between caudate, asymmetry and executive motor signs. They observed three small signs of adults using functional MRI and positron emission tomography provided evidence that anterior singulate and pre-frontal cortex are dysfunctional when performing response inhibition and timed motor task.[17] There is some limited evidence from studies of children with ADHD that motor functions associated with ADHD are correlated with brain volume abnormalities.

In the present study, MPAs are evaluated by Waldrop physical anomaly scale and studied for both case and control group. The study shows no significant statistical difference between the two groups though neurological soft signs showed a statistical significant difference. The correlation between minor physical anomalies and different variables of neurological soft signs were separately studied. In case group there is a positive correlation of MPA scale with overflow items, total timed and total PANESS were noted, whereas in control group no such correlations were noted and there is a positive correlation for total PANESS with MPAs. These findings are in accordance with the study of Holden et al. He studied the reliability of PANESS and also the correlation between the minor physical anomalies and ADHD and found a significant correlation between them.[18]

CONCLUSION

Present study concludes that is no significant correlation was associated between NSS and MPAs with socio-economic class and sex of the study subjects. ADHD siblings showed a significant increase in NSS especially in the field of overflow, gaits and stations, timed and a significant decrease in MPAs when compared with the normal children. The inter correlation of MPAs with various domains of PANESS showed a positivity for overflow and timed for ADHD siblings and with total PANESS in case of normal children. This positive correlation in among ADHD siblings with MPA scale gives a positive outlook for further future studies on MPAs as early diagnosis of ADHD could be a possibility in children born with MPAs even before 3 years.

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