An Investigation into Prevalence of Neurological Soft Signs in Children with Attention Deficit-Hyperactivity Disorder and Their Siblings

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ABSTRACT

Attention deficit-hyperactivity disorder (ADHD) is one of the most common psychiatric disorders in children, which is associated with a high level of comorbidity among siblings of individuals with ADHD. Given the strongly hereditary nature of ADHD, it may include a group of neurobehavioral defects that can be seen with a higher prevalence in the patients' siblings due to shared genetic origins. The present study was aimed at examining the prevalence rate and mean scores of neurological soft signs in children with ADHD and their siblings and comparing them with a healthy population. Thirty-two children and adolescents with ADHD and an age range of 7 to 16 years old and 32 siblings of them with the same age range were studied using attention deficit-hyperactivity checklist of DSM-IV-TR and K-SADS Questionnaire, and their neurological soft signs were evaluated using NES questionnaire. Afterwards, the results were compared with those of 32 healthy children and adolescents. The total scores on the test of assessing neurological soft signs were 8.34±4.9, 4.6±3.34, and 3±3.25 in the group with ADHD, the siblings, and the control group, respectively. There was a significant difference between the two groups and the control group ($p<0.001$). Examining neurological soft signs separately showed that the siblings obtained higher scores than the control group on the tests of fist-edge-palm, right-left separation, and audio-visual separation and coordination. In the present study, prevalence of neurological soft signs was higher among the siblings of the children with ADHD than the control group. These auxiliary signs may help find etiological signs of the disorder and identify individuals at risk.

Key Words: Attention Deficit-Hyperactivity Disorder, Neurological Soft Signs, Neurological Evaluation Scale

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Introduction

Attention deficit-hyperactivity disorder (ADHD) is a behavioral and neurocognitive disorder, which is characterized by inappropriate levels of motor hyperactivity, lack of concentration, and impulsivity (Sadock& Sadock, 2009). This disorder has been known as one of the most common neurobehavioral disorders among children, with a global prevalence of 5.29% (Sadock & Sadock, 2009). In spite of its onset in childhood, its symptoms continue until adulthood, and they cause a large number of complications for the patients, their families, and the society (Sadock & Sadock, 2009).

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There is no definitive diagnostic test for this disorder. To diagnose the afflicted children, they need to undergo comprehensive evaluations in different contexts including home, school, and society. Moreover, different individuals like parents, teachers, and peers should be used to collect the required data in order to obtain the diagnostic criteria. Nowadays, interviewing the parents forms the evaluation core (Greenhill, 1998). Moreover, a physical evaluation with a description and thorough examinations is used to reject physical disorders with similar symptoms (Sadock& Sadock, 2009). Regarding the course of the disorder, the high rate of comorbidities and complications such as academic failure, increased likelihood of smoking and consuming drugs, and increased exposure to events such as accidents and crimes (Greenhill, 1998) have been taken into account in clinical evaluations and early diagnosis in order to timely prevent and treat the children at risk.

Presence of neurological soft signs in children with ADHD is one of the areas that is nowadays taken into account. In general, different studies have shown the relationship and prevalence of this sign in ADHD (Uslu, *et al*., 2007; Martins *et al*., 2008). Given the high rate of comorbidity of this disorder among siblings, this question is posed whether prevalence of this disorder is more seen in siblings of children with ADHD or not. Because if it is proved that this disorder is more prevalent among the ADHD children's siblings compared to the healthy population, these signs can be proposed as a marker for genetic predisposition to develop this disorder. Since ever, there have been few studies focusing on neurological soft signs among children with ADHD, particularly among Iranian patients (Bombin *et al*., 2003). No studies have focused on the siblings of these children, either. In this regard, the present study was carried out in order to determine the prevalence rate of neurological soft signs among children with ADHD who had referred to Child and Adolescent Psychiatry Clinic, Imam Hussein (AS) Hospital and their siblings and compare them with healthy children.

Materials and methods

The present investigation was a descriptive cross-sectional study. The statistical population consisted of 7-to-16-year-old children and adolescents with diagnosis of ADHD referring to Child and Adolescent Psychiatry Clinic, Imam Hussein (AS) Hospital and their siblings with the same age range. Convenience sampling was utilized, such that all of the participants were selected based on the study inclusion criteria.

In the present investigation, 3 groups of 32 people were studied. The first group included ADHD patients who were under treatment. This group had been diagnosed with ADHD based on the description retrieved from their parents and the clinical observations and examinations conducted by a children psychiatrist (apart from the psychiatrist responsible for the present study) based on DSM-IV-TR diagnostic criteria.

The second group included 32 siblings of the first group children, aged 7 to 16 years old. However, this group did not have ADHD based on the evaluations conducted using K-SADS questionnaire and ADHD checklist of DSM-IV-TR.

The third group included 32 healthy individuals, aged 7 to 16 years old. The siblings of this group did not have ADHD based on the diagnostic criteria of the present study. This group was selected from among a generally healthy population.

The individuals of all 3 groups entered the study after their parents were talked to about the aims of the study and filled out a written consent letter. For all of the children, a demographic questionnaire, K-SADS questionnaire, and ADHD checklist of DSM-IV-TR were completed. Children suffering from mental retardation (IQ<70), Tourette's disorder, chronic tic disorder, obsessive-compulsive disorder, cerebral palsy, and any apparent neurological disorder that could disturb the results of the study were excluded from the study. The children who had entered the study were examined by a general psychiatric assistant using Neurological Evaluation Scale (NES for neurological soft signs).

K-SADS Questionnaire

K-SADS questionnaire is a semi-structured interview that was designed in order to assess the current and previous courses of mental diseases among children and adolescents based on DSM-IV and DSM-III. There are search and objective criteria to evaluate each sign. The interview is semi-structured, and it is not necessary to repeat its questions word by word. This questionnaire was completed based on interviewing parents and children, and summing up the data collected from all available resources.

First, the questionnaire was completed by each of the informed individuals separately, and after the data were summed up and contradictions were resolved, the checklist of diagnoses over lifetime and the total evaluation scoring scale

were completed for each children. The Persian translation of this questionnaire is also available, and its validity and reliability have been proved (Ghanizadeh, 2009).

NES Questionnaire

This questionnaire includes 28 neurological soft signs which generally indicate 3 main functional areas. These three areas are:

1. Sensory integration
2. Motor coordination and sequence of complex movements
3. Dominance of hemispheres, frontal lobe symptoms, and eye movements

Each sign is given a score of 0 (without problem), 1 (slight disorder), or 2 (outstanding disorder), except for sucking and snout reflexes that receive score 0 or 2. The scoring of each sign is descriptive, so that scoring can be standard. The minimum and maximum scores are 0 and 56, respectively.

Validity and reliability of this questionnaire in evaluating neurological soft signs were reported to be acceptable by Buchanan and Heinrichs, 1989.

Demographic questionnaire

This questionnaire was designed by the researcher. It includes age, gender, educational status, health history of mother, health history of child, etc.

Data analysis methods

To analyze the collected data in the present study, median, standard deviation, range, mean, and percentage were used. Generalized estimating equations (GEE) were utilized to compare the results of the groups. Bonferroni method was used for double comparison (comparing a variable that was once compared in the control group and the patient group and once in the control group and the siblings).

All analyses were carried out using SPSS 21.0. The level of statistical significance was set at $p < 0.05$.

Ethical considerations

The parents were provided with explanations on the study's procedures, and written consent was obtained from them. Moreover, no interference was made in the treatment process of the patients.

Results

In the present investigation, out of the 99 children who were studied, 66 were male (66.7%) and 33 were female (33.3%). Out of the 66 male children, 20 were in the control group, 27 in the patient group, and 19 in the sibling group. Out of the 33 female children, 12 were in the control group, 5 in the patient group, and 16 in the sibling group. There was a significant difference between the patient and control groups in terms of their gender ($p<0.001$). The difference between the siblings and the control group was not significant ($p=0.353$). There was no significant difference between the boys and the girls in terms of the total score of neurological soft signs ($p=0.931$). The total scores in the girls' and boys' groups were respectively 4.55±3.99 and 5.71±4.6.

In evaluating neurological soft signs through NES test, the total score of the experimental group was 8.34±4.9, in the sibling group 4.6±3.34, and in the control group 3±3.25, and the difference between the experimental group and the control group and the sibling group and the control group was significant ($p<0.001$).

Comparing the experimental group and the control group and the sibling group and the control group with regard to neurological soft signs led to the following results (See Table 1).

1. The mean score of dominance of hemispheres in the control group was 0.25±0.44, in the experimental group 0.06±0.25, and in the sibling group 0.17±0.38. The difference between the experimental group and the control group was significant ($p=0.02$), but there was no significant difference between the sibling group and the control group ($p=0.24$).

2. Of the whole children, 16.2% had a disorder in the test of audio-visual coordination; 3.1% of the control group with a mean score of 0.06±0.35, 28.1% of the experimental group with a mean score of 0.34±0.6, and 17.1% of the sibling group with a mean score of 0.2±0.47 were proved to have disorder in this test. This difference between the experimental and control groups ($p<0.001$) and the sibling group and the control group ($p<0.001$) was significant.

3. The mean scores on Graphesthesia test were 0.22±0.55, 0.5±0.76, and 0.34±0.54 in the control group, the experimental group, and the sibling group, respectively. The difference between the experimental and control groups ($p<0.003$) and the sibling group and the control group ($p=0.02$) was significant.

4. In the Fist-Ring test, the total prevalence of the disorder was 18.2. In the control group, 6.3% of the children, in the experimental group 34.4%, and in the sibling group 14.3% had disorder. The mean scores in the control,

experimental, and sibling groups were respectively 0.06±0.25, 0.44±0.67, and 0.14±0.36. The difference between the experimental and control groups was significant (p<0.001). However, the difference between the sibling group and the control group was not significant (p=0.066).

5. In the test of fist-edge-palm, 34.3% of the children had disorder. In the control, experimental, and sibling groups, respectively 12.5%, 46.9%, and 42.9% of the children had disorder while taking this test. The mean score in the control group was 0.13±0.34, in the experimental group 0.56±0.67, and in the sibling group 0.34±0.5. This difference among the groups was significant (p<0.001).

6. The mean scores of Oseretsky Test in the control, experimental, and sibling groups were respectively 0.31±0.54, 0.94±0.72, and 0.46±0.51. The difference between the experimental and control groups was significant (p<0.001). The difference between the sibling group and the control group was also significant (p=0.03).

7. Rhythm tapping test was carried out in two sections, and the mean score of the first section in the control group was 0.06±0.25, in the experimental group 0.34±0.65, and in the sibling group 0.2±0.47.

8. In the mirror movement test, the mean score of the control group was 0.34±0.48. The mean scores of the experimental and sibling groups were respectively 0.72±0.63 and 0.49±0.56. The difference between the experimental and control groups was significant (p<0.001), but the difference between the control group and the sibling group was not significant (p=0.128).

9. Total prevalence of disorder in separating right and left among the children was 20.2%; in the control group 3.1%, in the experimental group 34.4%, and in the sibling group 22.9%. The mean scores in the control, experimental, and sibling groups were respectively 0.06±0.35, 0.35±0.8, and 0.26±0.51, and this difference was significant in all groups (p<0.001).

10. Prevalence of disorder in Gaze impersistence test was 28.1% in the control group, 56.3% in the experimental group, and 37.1% in the sibling group. The mean scores of this test were 0.38±0.66, 0.84±0.85, and 0.49±0.7 in the control, experimental, and sibling groups, respectively. The difference between the experimental and control groups was significant (p<0.001), but the difference between the sibling group and control group was not significant (p=0.266).

11. Among the three reflexes of snout, grasp, and sucking, grasp reflex with a mean score of 0.03±0.18 in the control group, 0.13±0.34 in the experimental group, and 0.06±0.24 in the sibling group was significant between the experimental and control group. The other two reflexes were not significant (p=0.99 & p=0.989).

Discussion and conclusion

The results of the present study showed that by considering the total mean score of NES test, the neurological soft signs were significantly higher in the experimental and sibling groups than the control group.

The results obtained from comparing the ADHD children and the control children are in line with those of the study carried out by Razjouyan *et al* in Shahid Beheshti University of Medical Sciences, in which neurological soft signs were more prevalent among the ADHD children than the control group (Razjouyan *et al*., 2007). Moreover, the results of the present study are in agreement with those of the studies carried out by Chan *et al* 2010 and Patankar *et al* 2010, who showed a higher prevalence of neurological signs among patients with ADHD. In the study carried out by Patankar *et al*; however, children with ADHD were divided into two groups; one with attention deficit and a hyperactive-impulsive one, and the relationship of the signs with each subgroup was examined, which was not taken into consideration in the present study.

No studies have ever focused on examining and comparing neurological deficits among siblings of children with ADHD and healthy populations, and in this regard the present study is noticeable. The results of the present study showed that neurological soft signs with a total mean score of 4.6±3.34 was significantly higher than the control group (p<0.001).

Some believe that neurological soft signs occur mostly and naturally at young ages and depend on the evolutionary stage (Sadock& Sadock, 2009).

In the present study, to prevent the interference of this factor, children of higher age range, i.e. 7 to 16 years old, were selected. The total mean age in the present study was 10.8±3 years. In the control group, the mean age was 10.7±1.9 years, in the experimental group 9.6±3 years, and in the sibling group 12.1±3.5 years, and this difference was not statistically significant.

Table 1. Comparison of frequency of neurological soft signs in the experimental, control, and sibling groups

		Total	Group						P		
			Control (I)		ADHD (II)		Sibling (III)		Total	I VS II	I VS III
Tandem walk	0	90 (90.9%)		32 (100.0 %)			26 (81.3%)	32 (91.4 %)	0.785		
	1	8 (8.1%)	0 (0.0%)		5 (15.6%)		3 (8.6%)				
	2	1 (1.0%)	0 (0.0%)		1 (3.1%)		0 (0.0%)				
Romberg test	0	98 (99.0%)	32 (100.0 %)				31 (96.9%)	35 (100. 0%)	>0.99		
	1	1 (1.0%)	0 (0.0%)		1 (3.1%)		0 (0.0%)				
	2	0 (0.0%)	0 (0.0%)		0 (0.0%)		0 (0.0%)				
Adventitious over Flow	0	76 (76.8%)	26 (81.3%)				26 (81.3%)	24 (68.6 %)	0.161		
	1	22 (22.2%)	6 (18.8%)			6 (18.8 %)		10 (28.6 %)			
	2	1 (1.0%)	0 (0.0%)		0 (0.0%)		1 (2.9%)				
Tremor	0	92 (92.9%)	31 (96.9%)		30 (93.8%)			31 (88.6 %)	0.321		
	1	7 (7.1%)	1 (3.1%)		2 (6.3%)		4(11.2%)				
	2	0 (0.0%)	0 (0.0%)		0 (0.0%)		0 (0.0%)				
Cerebral dominance	left	83 (83.8%)	24 (75.0%)		30 (93.8%)			29 (82.9 %)	0.031	0.028	0.243
	right	16 (16.2%)	8 (25.0%)		2 (6.3%)		6 (17.1%)				
Audio-Visual Integration	0	83 (83.8%)	31 (96.9%)		23 (71.9%)			29 (82.9 %)	<0.001	<0.001	<0.001
	1	12 (12.1%)	0 (0.0%)		7 (21.9%)		5 (14.3%)				
	2	4 (4.0%)	1 (3.1%)		2 (6.3%)		1 (2.9%)				
Streognosis	0	95 (96.0%)	32 (100.0 %)		28 (87.5%)		35 (100.0%)		0.925		
	1	3 (3.0%)	0 (0.0%)		3 (9.4%)		0 (0.0%)				
	2	1 (1.0%)	0 (0.0%)		1 (3.1%)		0 (0.0%)				
Graphetesia	0	72 (72.7%)	27 (84.4%)		21 (65.6%)		24 (68.6%)		0.002	0.003	0.025
	1	19 (19.2%)	3 (9.4%)		6 (18.8%)		10 (28.6%)				
	2	8 (8.1%)	2 (6.3%)		5 (15.6%)		1 (2.9%)				
Fist-Ring Test	0	81 (81.8%)	30 (93.8%)		21 (65.6%)		30 (85.7%)		<0.001	<0.001	0.066
	1	15 (15.2%)	2 (6.3%)		8 (25.0%)		5 (14.3%)				

	2	3 (3.0%)	0 (0.0%)		3 (9.4%)		0 (0.0%)				
Fist-Edge-Palm	0	65 (65.7%)	28 (87.5%)		17 (53.1%)		20 (57.1%)		<0.001	<0.001	<0.001
	1	31 (31.3%)	4 (12.5%)		12 (37.5%)		15 (42.9%)				
	2	3 (3.0%)	0 (0.0%)		3 (9.4%)		0 (0.0%)				
Ozeretski Test	0	51 (51.5%)	23 (71.9%)		9 (28.1%)		19 (54.3%)		<0.001	<0.001	0.039
	1	40 (40.4%)	8 (25.0%)		16 (50.0%)		16 (45.7%)				
	2	8 (8.1%)	1 (3.1%)		7 (21.9%)		0 (0.0%)				
Memory(5 min)	0	80 (80.8%)	24 (75.0%)		24 (75.0%)		32 (91.4%)		0.195		
	1	13 (13.1%)	6 (18.8%)		4 (12.5%)		3 (8.6%)				
	2	6 (6.1%)	2 (6.3%)		4 (12.5%)		0 (0.0%)				
Memory(10 min)	0	76 (76.8%)	24 (75.0%)		20 (62.5%)		32 (91.4%)		0.009	0.153	0.02
	1	15 (15.2%)	4 (12.5%)		8 (25.0%)		3 (8.6%)				
	2	8 (8.1%)	4 (12.5%)		4 (12.5%)		0 (0.0%)				
Rhythm tap(A)	0	83 (83.8%)	30 (93.8%)		24 (75.0%)		29 (82.9%)		<0.001	<0.001	0.014
	1	12 (12.1%)	2 (6.3%)		5 (15.6%)		5 (14.3%)				
	2	4 (4.0%)	0 (0.0%)		3 (9.4%)		1 (2.9%)				
Rhythm tap(B)	0	79 (79.8%)	29 (90.6%)		22 (68.8%)		28 (80.0%)		<0.001	<0.001	0.041
	1	14 (14.1%)	3 (9.4%)		5 (15.6%)		6 (17.1%)				
	2	6 (6.1%)	0 (0.0%)		5 (15.6%)		1 (2.9%)				
Rapid Alternative Movement	0	82 (82.8%)	28 (87.5%)		25 (78.1%)		29 (82.9%)		0.217		
	1	16 (16.2%)	4 (12.5%)		6 (18.8%)		6 (17.1%)				
	2	1 (1.0%)	0 (0.0%)		1 (3.1%)		0 (0.0%)				
Finger-Thumb opposition	0	97 (98.0%)	32 (100.0%)		30 (93.8%)		35 (100.0%)		0.918		
	1	2 (2.0%)	0 (0.0%)		2 (6.3%)		0 (0.0%)				
	2	0 (0.0%)	0 (0.0%)		0 (0.0%)		0 (0.0%)				

Mirror Movement	0	52 (52.5%)	21 (65.6%)		12 (37.5%)		19 (54.3%)		0.002	0.001	0.128
	1	43 (43.4%)	11 (34.4%)		17 (53.1%)		15 (42.9%)				
	2	4 (4.0%)	0 (0.0%)		3 (9.4%)		1 (2.9%)				
Extinction	0	89 (89.9%)	32 (100.0%)		24 (75.0%)		33 (94.3%)		0.878		
	1	7 (7.1%)	0 (0.0%)		6 (18.8%)		1 (2.9%)				
	2	3 (3.0%)	0 (0.0%)		2 (6.3%)		1 (2.9%)				
Right-Left Confusion	0	79 (79.8%)	31 (96.9%)		21 (65.6%)		27 (77.1%)		<0.001	<0.001	<0.001
	1	12 (12.1%)	0 (0.0%)		5 (15.6%)		7 (20.0%)				
	2	8 (8.1%)	1 (3.1%)		6 (18.8%)		1 (2.9%)				
Synkinesis	0	95 (96.0%)	32 (100.0%)		29 (90.6%)		34 (97.1%)		0.903		
	1	4 (4.0%)	0 (0.0%)		3 (9.4%)		1 (2.9%)				
	2	0 (0.0%)	0 (0.0%)		0 (0.0%)		0 (0.0%)				
Convergence	0	96 (97.0%)	32 (100.0%)		31 (96.9%)		33 (94.3%)		0.853		
	1	3 (3.0%)	0 (0.0%)		1 (3.1%)		2 (5.7%)				
	2	0 (0.0%)	0 (0.0%)		0 (0.0%)		0 (0.0%)				
Gaze impersistence	0	59 (59.6%)	23 (71.9%)		14 (43.8%)		22 (62.9%)		<0.001	<0.001	0.266
	1	24 (24.2%)	6 (18.8%)		9 (28.1%)		9 (25.7%)				
	2	16 (16.2%)	3 (9.4%)		9 (28.1%)		4 (11.4%)				
Finger to Nose Test	0	99 (100.0%)	32 (100.0%)		32 (100.0%)		35 (100.0%)		1		
	1	0 (0.0%)	0 (0.0%)		0 (0.0%)		0 (0.0%)				
	2	0 (0.0%)	0 (0.0%)		0 (0.0%)		0 (0.0%)				
Glabellar Test	0	94 (94.9%)	31 (96.9%)		30 (93.8%)		33 (94.3%)		0.407		
	1	3 (3.0%)	0 (0.0%)		1 (3.1%)		2 (5.7%)				
	2	2 (2.0%)	1 (3.1%)		1 (3.1%)		0 (0.0%)				
Snout Reflex	0	98 (99.0%)	32 (100.0%)		31 (96.9%)		35 (100.0%)		>0.99		
	1	1 (1.0%)	0 (0.0%)		1 (3.1%)		0 (0.0%)				
	2	0 (0.0%)	0 (0.0%)		0 (0.0%)		0 (0.0%)				

Grasp Reflex	0	92 (92.9%)	31 (96.9%)		28 (87.5%)		33 (94.3%)		0.021	0.005	0.389
	1	7 (7.1%)	1 (3.1%)		4 (12.5%)		2 (5.7%)				
	2	0 (0.0%)	0 (0.0%)		0 (0.0%)		0 (0.0%)				
Suck Reflex	0	97 (98.0%)	32 (100.0%)		31 (96.9%)		34 (97.1%)		0.989		
	1	1 (1.0%)	0 (0.0%)		0 (0.0%)		1 (2.9%)				
	2	1 (1.0%)	0 (0.0%)		1 (3.1%)		0 (0.0%)				

Table 2. General frequency and score of neurological soft signs in each group

		Score		Number of positive test		
		Mean ± SD	**simultaneous P**	**Mean ± SD**	**P**	**simultaneous P**
Group	Control	3.09 ± 3.25		2.6 ± 2.3	ref	Ref
	ADHD	8.34 ± 4.9	<0.001	6.4 ± 3.4	<0.001	<0.001
	Sibling	4.6 ± 3.34	<0.001	4.3 ± 2.9	0.001	<0.001

Table 3. The score of neurological soft signs given the demographic factors

		Score			Number of positive case		
		Mean ± SD	**P**	**simultaneous P**	**Mean ± SD**	**P**	**simultaneous P**
Group	Control	3.09 ± 3.25	Ref		2.6 ± 2.3	ref	Ref
	ADHD	8.34 ± 4.9	<0.001	<0.001	6.4 ± 3.4	<0.001	<0.001
	Sibling	4.6 ± 3.34	<0.001	<0.001	4.3 ± 2.9	0.001	<0.001
Age	<= 12.0	5.79 ± 4.69	Ref		4.7 ± 3.4	ref	
	13.0+	4.07 ± 3.37	0.186	.117	3.7 ± 2.7	0.342	.176
Gender	M	5.71 ± 4.6	Ref		4.7 ± 3.3	ref	
	F	4.55 ± 3.99	0.128	.931	4 ± 3.1	0.215	.926

It has been stated that neurological soft signs have a relationship with some psychiatric syndromes especially schizophrenia and obsessive-compulsive disorder Heinrichs *et al*, 2010. In this regard, all major psychiatric disorders and medical disorders that can cause obvious neurological signs were considered as the exclusion criteria of the present study. Only ODD disorder and learning disorder due to its high morbidity with ADHD was not considered as the exclusion criterion in any of the groups, which can be one of the limitations of the present study (Thienemann *et al*., 1995).

Some possibilities have been proposed with regard to the effect of Ritalin on improvement of neurological soft signs. For example, in a study conducted by Lerer in 1976, 72.5% obvious improvement or removal of neurological soft signs were reported as re result of Ritalin treatment. Since all of the experimental children were treated using Ritalin, the effect of this factor spread uniformly among all of the children with ADHD. On the other hand, prevalence of neurological soft signs was still higher in the experimental group than the control group in spite of its treatment with Ritalin. This finding is somewhat in contrast with that of the study conducted by Lerer &Lerer, 1976. With regard to medicine consumption, none of the siblings were treated with Ritalin. Among these children, 2.9% consumed medicine whose consumption was not due to the disorders that were among the exclusion criteria of the present study. None of the control children consumed medicine.

Analyzing each of the neurological soft signs showed that there was no significant difference between the groups in the results obtained from the tests of tandem walk, Romberg, adventitious over flow, tremor, memory (5 min), finger-thumb opposition, rapid alternative movements, synkinesis, convergence streognosis, finger-to-nose test, and glabellar, snout, and sucking reflexes.

The tests that showed a significant difference between the ADHD group and the control group but showed no significant difference between the sibling group and the control group

include cerebral dominance, fist-ring test, mirror movements, grasp reflex, and gaze impersistence.

There was a significant difference between the two groups and the control group with regard to the results obtained from the tests of audio-visual integration, Graphetesia, fist-edge-palm, Ozeretski, right-left confusion, rhythm tapping, and A&B.

Different studies have focused on the type of neurological soft signs that are more common among children with ADHD. An example of such studies is the one carried out by Uslu in Turkey, which focused on dysrhythmia-related factors, speed of movements, and overflow with timed movement and reported a higher prevalence in children with ADHD (Uslu *et al*,. 2007). In the study carried out by Patankar, dysrhythmia and walking disorders were vividly related to ADHD (Patankar *et al*., 2010).

Although some of these signs are not in line with the results of the present study, for example, walking disorders in the recent study showed no significant difference between the groups, all of these results show the presence of disorder at all three stages of sensory integration, motor coordination, and the task of consecutive movements in children with ADHD.

The tests in the sibling group that showed disorder in sensory category (like right-left separation) and motor coordination (fist-edge-palm test) indicated a significant difference between the sibling group and the control group. Although no regions of the nervous system have been known to be related to neurological soft signs, finding similar signs among the members of a family suggests the presence of common underlying pathology that transmits in families. However, it is notable that in comparing the sibling group and the group with ADHD, there was not consistency regarding the type of disturbed signs, and a more significant difference was seen between the experimental and control groups in consistent cases. This finding may refer to the relationship between intensity of ADHD and the number of neurological soft signs and some signs more specifically. Response to this issue; however, was proposed as a question for the researcher, and it can be focused on in future studies.

Conclusion

According to the results of the present study, neurological soft signs were seen more among individuals at the risk of developing ADHD such as healthy siblings of the children with ADHD. However, further studies with larger samples are required to be able to refer to these signs as a hereditary marker of underlying pathology and an early diagnostic tool. In addition, genetic evaluations along with clinical investigations into these children can provide clinicians with more accurate data on whether this disorder is hereditary, transmitted as trait markers in risky families, or dependent on status or evolution.

References

Bombin I, Arango C, Buchanan RW. Assessment of neurological soft signs in schizophrenia. Psychiatric Annuals 2003; 33:170-176.

Buchanan RW, Heinrichs DW. The Neurological Evaluation Scale: a structured instrument for the assessment of neurological soft signs. Psychiatry Research 1989; 27:335-350.

Chan RCK, McAlonan GM, Yang B, Lin L, Shum D, Manschreck TC. Prevalence of Neurological Soft Signs and Their Neuropsychological Correlates in Typically Developing Chinese Children and Chinese Children with ADHD. Developmental Neuropsychology 2010;35(6):698–711.

Ghanizadeh A. Psychiatric comorbidity differences in clinic-referred children and adolescents with ADHD according to the subtypes and gender. Journal of Child Neurology 2009; 24(6):679-84.

Greenhill LL. Diagnosing ADHD in children, Journal of Clinical Psychiatry 1998;56:31-41.

Heinrichs DW, Buchanan RW. Significance and meaning of neurological signs in schizophrenia. American Journal of Psychiatry 1998;145: 11-18.

Lerer RJ, Lerer MP. The effect of methylphenidate on the soft signs of hyperactive children .The American Academy of Pediatrics 1976; 57:521-525.

Martins I, Lauterbach M, Slade P. A longitudinal study of neurological soft signs from late childhood into early adulthood. Developmental Medicine& Child Neurology 2008; 50:602-607.

Patankar VC, Sangle JP, Shah HR, Dave M, Kamath RM. Neurological soft signs in children with attention deficit hyperactivity disorder. Indian Journal of Psychiatry 2012;54(2):159-165.

Sadock B, Sadock V. Comprehensive textbook of psychiatry, ninth edition, 2009; 3560-3572

Thienemann M, Koran LM. Do soft signs predict treatment outcome in obsessive-compulsive disorder? The Journal Neuropsychiatry & Clinical Neurosciences 1995; 7(2): 218-222.

Uslu R, Kapçi EG, Öztop D. Neurological soft signs in comorbid learning and attention deficit hyperactivity disorders. The Turkish Journal of Pediatrics 2007;49(3):263.