



Association between attention deficit and hyperactivity disorder and Perthes disease

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Objective: The aim of this study was to determine whether or not there is an association between attention deficit and hyperactivity disorder (ADHD) and Perthes disease.

Methods: The study included 3 groups of patients: Perthes patients, trauma patients, and orthopedic patients without Perthes disease or history of trauma. Each group was comprised of 56 males and 4 females. Patients were evaluated for present or past diseases, exposure to second-hand smoke, the age at which they had begun to walk, history of trauma prior to Perthes diagnosis in the Perthes group, weight, height and body mass index (BMI). Eighteen questions on the DSM-4 (Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition) ADHD checklist was used in the psychiatric evaluation of patients. The rate of ADHD was compared between groups.

Results: Attention deficit and hyperactivity disorder was diagnosed in 7 patients in the Perthes group, 3 in the trauma group, and 3 in the non-trauma group; and this difference was not significant ($p=0.160$).

Conclusion: There were no significant differences in the rate of ADHD between trauma and non-trauma groups of Perthes patients, which suggests no association between ADHD and Perthes disease.

Key words: Attention deficit and hyperactivity disorder; Perthes disease; second-hand smoking; trauma.

Various theories concerning the etiology of Perthes disease have been reported. One such theory is that hyperactivity often results in trauma, occluding the blood vessels supplying the femoral head, and thus, resulting in femoral head avascular necrosis.^[1] Loder et al.^[2] reported that 33% of patients with Perthes disease also had attention deficit and hyperactivity disorder (ADHD).

Although recent studies have claimed that Perthes disease and ADHD are related, many had insufficient

statistical power due to the lack of control groups and small sample sizes.

Using a large sample of subjects, the aim of this study was to determine whether or not there is an association between ADHD and Perthes disease.

Patients and methods

Approval for this study was obtained from the Ethics Committee of the Göztepe Training and Research

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Hospital, Istanbul Medeniyet University (Protocol no: 14.02.2012 19/A).

The study included 3 groups of patients: Perthes patients, trauma patients, and orthopedic patients without Perthes disease or history of trauma.

The automation system of the hospital (SARUS®) was used to randomly select the first group from patients diagnosed with Perthes (ICD: M91.1) disease between 2001 and 2011. The presence of the disease was radiographically reassessed. The 4 patients misdiagnosed (two had developmental hip dysplasia, one multiple epiphyseal dysplasia and one sequelae to septic arthritis) were excluded from the study. Patients diagnosed with mental disorders other than ADHD were also excluded. Of the patients in the Perthes group (56 males, 4 females), 28 had right hip, 25 left hip and 7 bilateral disease and 33 cases had been treated conservatively and 27 surgically. The trauma group consisted of patients (56 male, 4 female) admitted to the orthopedic emergency service for any musculoskeletal trauma and the normal group (56 male, 4 female) included patients presenting to the pediatric orthopedic polyclinic with complaints other than trauma or hip pain.

The trauma and normal groups were selected at random on a first-come-first-serve method to match in terms of gender and age with those in the Perthes group.

After routine examination and treatment, all patients were psychiatrically evaluated. Patients and parents were questioned regarding present or past diseases, exposure to second-hand smoke, the age at which they had begun to walk and history of trauma prior to Perthes diagnosis in the Perthes group. Stages of Perthes disease were not taken into consideration. Weight, height and body mass index (BMI) were recorded. Patients' parents were asked to answer 18 questions on the DSM-4 ADHD checklist.^[3] The first half of the questionnaire aims to identify the presence of attention deficit disorder and the last half hyperactivity disorder (Table 1). The presence of 6 or more of the 9 symptoms was considered positive. Children with positive questionnaires were sent to the pediatric psychiatrist for further examination.

All psychiatric evaluations were conducted by the same pediatric psychiatrist (S.U.) who was blinded to the groups. The clinical interview included questions regarding the history and nature of the child's behavioral difficulties, quality of their relationship with family and peers, family's medical and personal history and the child's social performance in daily activities. ADHD diagnosis was made according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition).^[4] Patients were further diagnosed as having attention deficit or hyperactivity or both together.

Table 1. DSM-4 ADHD checklist.

Inattention

- 1) Often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities.
 - 2) Often has difficulty sustaining attention in tasks or play activities.
 - 3) Often does not seem to listen when spoken to directly.
 - 4) Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions).
 - 5) Often has difficulty organizing tasks and activities.
 - 6) Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework).
 - 7) Often loses things necessary for tasks or activities (e.g. toys, school assignments, pencils, books, or tools).
 - 8) Is often easily distracted by extraneous stimuli.
 - 9) Is often forgetful in daily activities.
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Hyperactivity-impulsivity

- 1) Often fidgets with hands or feet or squirms in seat.
 - 2) Often leaves seat in classroom or in other situations in which remaining seated is expected.
 - 3) Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness).
 - 4) Often has difficulty playing or engaging in leisure activities quietly.
 - 5) Is often "on the go" or often acts as if "driven by a motor".
 - 6) Often talks excessively.
 - 7) Often blurts out answers before questions have been completed.
 - 8) Often has difficulty awaiting turn.
 - 9) Often interrupts or intrudes on others (e.g. butts into conversations or games).
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On the assumption that approximately ADHD is seen at a rate of 20% in the Perthes group and 5% in the other groups and taking a confidence interval of 95% and power of 80%, 59 patients were determined sufficient for each group.

Data was calculated as frequency, ratio, mean, and standard deviation. The Kolmogorov-Smirnov test was used for data distribution, the Kruskal-Wallis ANOVA test for height, weight, BMI and age at first steps, and the chi-square test in the analysis of ratio-dependent data. Data was analyzed using the SPSS statistical package v.19.0 (SPSS Inc., Chicago, IL, USA). P values of <0.05 were considered statistically significant.

Results

Height, weight, BMI, and age at first steps were not significantly different among the three groups ($p>0.05$) (Table 2).

The history of exposure to second-hand smoke in the normal group (43.3%) was significantly lower ($p=0.007$) than that of the Perthes (70.0%) and trauma groups (65.0%) (Table 3).

In the Perthes group, trauma was an etiological factor in 14 of 60 patients. Seven had additional diseases (two asthma, two familial Mediterranean fever, one growth hormone deficiency, one epilepsy, and one bilateral pes equinovarus deformity) (Fig. 1). None of the patients were related. Mean time elapsed between initial diagnosis of Perthes disease and evaluation was 4.58 ± 3.60 years (range: 3 months to 13 years).

Eight patients in the Perthes group, 3 in the trauma group and 3 in the normal group had positive questionnaire for ADHD. After clinical assessment, 7 patients with Perthes disease were diagnosed with ADHD; 4 with hyperactivity, 1 with attention deficit disorder and 2 with both hyperactivity and inattention. Of these, one patient was female and one had bilateral hip involvement. In the trauma group, 3 patients were diagnosed with ADHD, and all 3 had only attention deficit disorder. All ADHD patients were male with trauma to the upper extremities. In the normal group, 3 male patients diagnosed with ADHD had hyperactivity. The rate of ADHD was not statistically significantly different among the three groups ($p=0.160$) (Table 4).

Table 2. Height, weight, body mass index (BMI), and age at first steps (months) in the three groups.

	Perthes (Mean±SD)	Trauma (Mean±SD)	Non-Trauma (Mean±SD)	p
Height (cm)	141.93±22.09	146.78±20.41	144.73±21.96	0.465
Weight (kg)	43.78±17.94	43.90±16.60	41.97±15.82	0.779
BMI (kg/cm ²)	20.83±4.56	19.52±3.11	19.35±2.95	0.051
Steps (month)	12.00±1.64	11.72±0.85	12.08±0.98	0.115

Kruskal-Wallis ANOVA test (95% confidence interval). SD: Standard deviation.

Table 3. Exposure to second-hand smoke by group.

	Perthes		Trauma		Non-Trauma		p
	n	%	n	%	n	%	
Passive smoking							
Not exposed to	18	30.0	21	35.0	34	56.7	0.007
Exposed to	42	70.0	39	65.0	26	43.3	

Chi-square test (95% confidence interval).

Table 4. The ADHD rates of the three groups.

	Perthes		Trauma		Non-Trauma		p
	n	%	n	%	n	%	
Psychiatric condition							
Normal	53	88.3	57	95.0	57	95.0	0.160
ADHD	7	11.7	3	5.0	3	5.0	

Chi-square test (95% confidence interval).

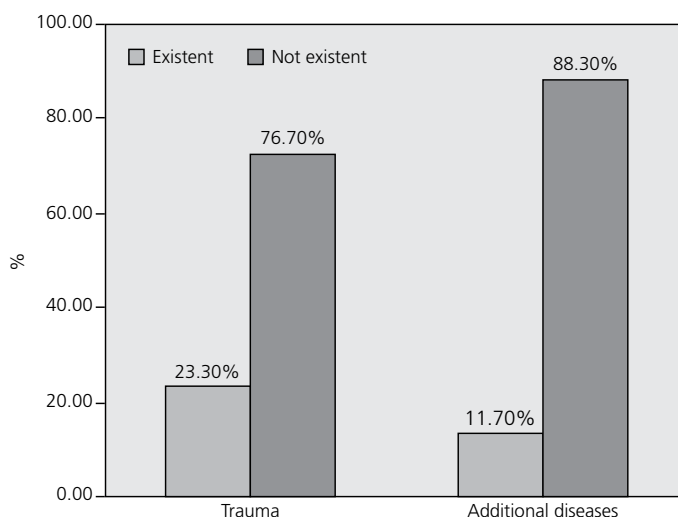


Fig. 1. Patients in the Perthes group with history of trauma and patients with additional diseases.

Discussion

Previous studies have explored the possible correlation between Perthes and ADHD. However, such studies have compared only patients with Perthes disease with non-Perthes patients. The possibility of increased incidence of ADHD in trauma cases compared to the general public must be considered.^[5-9] A previous study reported that ADHD patients have a significantly higher incidence of traumatic injuries than the general population.^[10] Because children with ADHD are more active and inattentive than their counterparts, it has been hypothesized that a higher rate of trauma would follow. In the current study, 5% of both trauma and non-trauma patients were diagnosed with ADHD. Additionally, patients in the trauma group who had ADHD showed no apparent differences in the severity of trauma or in the proportion of injuries compared to unaffected children.

Trauma is a major component in the etiology of Perthes disease. Studies have shown that the arteries supplying blood to the proximal femur are occluded in patients following trauma.^[11,12] In the developing proximal femur, the major lateral epiphyseal artery courses through a narrow passage which renders it highly susceptible to disruption by trauma to this area. The risk of vascular interruption secondary to trauma is increased due to the penetration of these vessels through the thick cartilage of the femoral head.^[12] In our study, 14 of the patients in the Perthes group had a history of trauma, indicating that trauma likely plays a role in the etiology of Perthes disease.

The frequency of ADHD among children worldwide is thought to be 5 to 10% and the disorder generally con-

tinues to manifest throughout adulthood.^[13-15] Recent studies have reported that Perthes disease patients are more likely to have ADHD. According to Loder et al.,^[2] 33% of Perthes patients had ADHD. However, while this and other studies evaluated many behavioral characteristics of Perthes patients, no study to date has compared the frequency of ADHD among Perthes children and control groups. The present study compared Perthes children to both patients with and without a history of trauma. Although the incidence of ADHD was higher in the Perthes group, the difference was not statistically significant.

Some previous studies on Perthes disease have reported lower average birth weights, delayed skeletal maturation and lower weight-height percentiles in Perthes patients compared to healthy peers.^[16-18] However, other studies have reported no such correlation.^[19] In the present study, the average BMI and average age at first steps were not significantly different between Perthes patients and unaffected children.

Many links have been identified between second-hand smoke and various systemic diseases. Exposure to second-hand smoke likely contributes to Perthes disease, which is characterized by hip avascular necrosis.^[17] Glueck et al.^[20] and Garcia Mata et al.^[21] reported that cigarette smoke negatively affects the coagulation and fibrinolytic systems by inhibiting the plasminogen activator.^[22] Tsao et al. observed that venous occlusion in the hip causes intramedullary hypertension, leading to anoxia and avascular necrosis of bone.^[23] Our results support this hypothesis, as 70% of Perthes patients were exposed to second-hand smoke, compared to 43.3% in

the normal group and 65% in the trauma group. The trauma group's relatively high percentage could be attributable to behavioral changes that result from an increase in serum cotinine levels caused by exposure to second-hand smoke.^[24]

The present study had some limitations. Retrospective bias was possible as the medical questionnaire inquired about past events which are related to the time period prior to the diagnosis of Perthes disease, such as age at first steps, history of trauma and history of exposure to second-hand smoke. Although ADHD diagnoses were conducted in the clinical interview, the DSM-4 ADHD checklist was used to assess the patients sent to the interview process and the Conners' Teacher Questionnaire was not used. Although the pediatric psychiatrist was blinded to the groups, previous history regarding Perthes disease and trauma could have been provided by the family during the interview. Additionally, while exposure to second-hand smoke was defined as one or more smokers in the household, the degree of exposure to second-hand smoke was not quantified and the correlation between exposure to second-hand smoke and the severity of Perthes disease was not assessed. In each group, the majority of patients were male, which supports the observation that Perthes disease and ADHD are predominantly male diseases.^[9,25,26] Therefore, we do not feel that our study was hindered by the inclusion of mostly male patients.

In conclusion, the frequency of ADHD appears similar in Perthes patients and non-Perthes patients both with and without a history of trauma. Exposure to second-hand smoke in Perthes patients and trauma groups are higher than the control group.

Conflicts of Interest: No conflicts declared.

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