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Original article

Migraine and associated comorbidities are three times more frequent in children with ADHD and their mothers

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Abstract

Objective: Attention deficit and hyperactivity disorder (ADHD) is a neuro-developmental disorder related to internalizing and externalizing disorders as well as somatic complaints and disorders. This study was conducted to evaluate the prevalence of headache subtypes, epilepsy, atopic disorders, motion sickness and recurrent abdominal pain among children and adolescents with ADHD and their parents.

Methods: In a multi-center, cross-sectional, familial association study using case-control design, treatment naïve children and adolescents between 6 and 18 years of age diagnosed with ADHD according to the DSM-5 criteria as well as age- and gender-matched healthy controls and their parents were evaluated by a neurologist and analyzed accordingly.

Results: 117 children and adolescents with ADHD and 111 controls were included. Headache disorder diagnosis was common for both patients and healthy controls (59.0% vs. 37.8%), with a significantly elevated rate in the ADHD group ($p = 0.002$). Migraine was found in 26.0% of ADHD patients and 9.9% of healthy controls. Tension headache was found in 32.4% of ADHD patients and 27.9% of healthy controls. Headache diagnosis was also found to be significantly more common in mothers of children with ADHD than control group mothers (90.5% vs. 36.6%, $p < 0.001$).

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Conclusion: Headache diagnoses and specifically migraines were significantly more common among children with ADHD and their mothers, while recurrent abdominal pain was elevated in both parents and ADHD patients. Migraine is an important part of ADHD comorbidity, not only for children but also for mothers. Motion sickness may be reduced among families of ADHD probands.

Keywords: Migraine; Attention deficit and disruptive behavior disorders; Tension-type headache

1. Introduction

Attention deficit/hyperactivity disorder (ADHD) is common among children and adolescents, with a prevalence of 5.3% globally, and is considered to be an important disorder leading to both poor academic performance and low quality of life [1]. It is also a widely accepted risk factor for the development of other externalizing and internalizing disorders as well as common chronic disorders throughout the life-span [1].

Primary headache disorders are subdivided into migraine, tension-type headaches (TTHs), cluster headaches, and other (less common) types. The most frequent types are migraine and tension-type headache, with a prevalence of 10.0–27.0% in children and adolescents [2,3]. There is a bidirectional relationship between headache and childhood psychopathology, with headache reducing quality of life and leading to psychiatric symptoms and conversely psychopathology, especially internalizing disorders being expressed with somatic complaints and headache [4]. Migraine itself is often accompanied by severe impairments, such as low quality of life, low academic performance and poor cognitive functioning, which are similarly seen in children and adolescents with ADHD [5–7]. Recent studies have reported that both learning disabilities and ADHD may be related to headache in pediatric populations [5]. Various hypotheses were proposed to explain this correlation, including a common involvement of dopaminergic systems, dysfunctional iron metabolism in the central nervous system and shared genetic pathways [8,9].

ADHD is also frequently comorbid with other medical conditions and disorders, such as epilepsy, atopic diseases, disorders and symptoms of the gastrointestinal tract (e.g., recurrent abdominal pain) and proneness to motion sickness. These conditions are also frequently seen in patients with pediatric migraine [10–15].

There is limited data regarding the frequency and correlates of migraine and ADHD association. The present study was carried out to evaluate rates of migraine and TTH as primary headache disorders, as well as to examine the comorbidity of epilepsy, atopic disorders, motion sickness and recurrent abdominal pain among children and adolescents with ADHD and their parents.

2. Materials and methods

2.1. Study center, patients and protocol

The protocol was designed as a cross-sectional, case-control, multi-center study. The study was conducted in the second half of 2016 at Mersin University and Baskent University Medical Faculties as a collaborative study by the Departments of Neurology and Child and Adolescent Psychiatry. Consecutive children who were diagnosed with ADHD according to DSM-5 criteria along with matched healthy controls selected from schools in the epidemiological catchment area are included in this study [16].

Children diagnosed as ADHD (any presentation type) according to DSM-5 criteria without mental retardation/intellectual disabilities and/or autism spectrum disorders were included in the study. Mental retardation/intellectual disabilities were ruled out with clinical examination and Turkish version of the Wechsler Intelligence Scale for Children-Revised [17] while children were diagnosed with the Turkish version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS-PL) [18,19]. The children should be either treatment naïve or free of treatments for ADHD for the last three months. The age range of the children was 6–18 years old. All the parents provided written informed consent to the study protocol. All the patients and parents underwent a face-to-face neurological examination following a complete psychiatric evaluation. Headache diagnosis was made according to the ICHD-3 beta criteria for children with ADHD and healthy controls and their parents [20].

The socio-economical levels of subjects were determined according to the vocational and educational status of family members older than 18 years of age and living in the same household with the child as per the Turkish Family Structure Study conducted by the Ministry of Family and Social Policies [21].

2.1.1. Ethics

The study protocol was approved by the local ethics committee of the study center with a protocol number of MEU.0.01.00.06/265. All study procedures were in accordance with the Declaration of Helsinki and local

laws and regulations. All persons gave their informed consent prior to their inclusion in the study.

2.1.2. Statistics and power analysis

A priori analysis of chi-square tests to determine a difference in medium effect size (0.3) at alpha level of 0.05 with 95% power at 1 degree of freedom revealed a total (ADHD and control) sample size of 145 [22]. Within the specified time period, 117 patients with ADHD and 111 controls were included, leading to 99.5% power [22].

Statistical analysis was performed using the statistical package SPSS 23.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were described either as means and standard deviations or medians and inter-quartile ranges (IQR) depending on assumptions of normality ($p > 0.05$ via Kolmogorov-Smirnov or Shapiro-Wilks ($n < 30$) tests) and the presence of outliers. Bivariate comparisons between groups were conducted either with Student's *t* test for independent samples or Mann-Whitney U test depending on assumptions. Categorical variables between groups were analyzed by using the chi-square test. Yates' continuity correction or Fisher's Exact test were used if needed. Values of $p < 0.05$ were considered statistically significant, and all comparisons were two-tailed.

3. Results

The study group consisted of 117 patients diagnosed with ADHD and 111 healthy age- and sex-matched control subjects. Median ages were 11 years (IQR = 4.0) in the ADHD group and 12 years (IQR = 3.0) for healthy controls with no significant difference between groups (Student's *t* test, $p = 0.83$). Mean ages of mothers and fathers were 37.9 (S.D. = 5.7) and 42.7 (S.D. = 6.0) years; respectively. Thirty-six of children with ADHD (30.8%) had a comorbid diagnosis. Most common comorbidities, in order of frequency were tic disorders ($n = 17$, 14.5%), anxiety disorders ($n = 9$, 7.7%), conduct disorder ($n = 8$, 6.8%), phonological disorders and enuresis nocturna (one patient each, 0.9%). Families of both patients and controls were mostly from higher socio-economic strata (37.6% vs. 38.7%) with no significant difference between groups (Chi Square, $p = 0.50$).

In the whole sample 50.9% of children ($n = 116$) reported headache in the past three months whereas life time diagnosis of a primary headache disorder was found in 48.7% ($n = 111$). In the ADHD group, headache complaints within the past three months were reported by 60 children (51.3%), while 69 children (59.0%) met the criteria for a life-time primary headache disorder according to ICHD-3 beta. The corresponding rates for controls were 50.5% ($n = 56$) and 37.8% ($n = 42$); respectively. While headache complaints in the past three months did not differ between groups; a life time diagnosis of primary headache disorder was significantly more frequent among children with ADHD (Chi Square test, $p = 0.002$, Phi = 0.21).

Within the whole study sample, 42 children (18.4%) had migraine and 69 (30.3%) had tension-type headache (TTH). Migraine was found in 26.5% of ADHD patients and 9.9% of healthy controls. TTH was found 32.5% of ADHD patients and 27.9% of healthy controls. Thus, the odds ratio (OR) for primary headache disorder in children with ADHD in our sample was 2.4 (95.0% Confidence Interval = 1.4–4.0, $p = 0.002$) [23–25]. The ORs for migraine and TTH were 3.3 (95.0% Confidence Interval = 1.6–6.9, $p = 0.002$) and 1.2 (95% CI = 0.7–2.2, $p = 0.46$); respectively [23–25].

In the whole sample, atopic disorders were reported in 40.4% of children ($n = 92$). Rates of atopic disorders were 44.4% in ($n = 52$) children with ADHD and 36.0% ($n = 40$) of healthy controls, and no significant difference was found between the two groups (Chi Square test, $p = 0.20$).

Fifty-six children (24.6%) in the whole sample reported recurrent abdominal pains. The corresponding rates in ADHD and control groups were 31.6% ($n = 37$) and 17.1% ($n = 19$); respectively with abdominal pain being significantly more common in the ADHD group (Chi Square, $p = 0.017$, Phi = 0.17). OR for recurrent abdominal pain was 2.2 (95% CI = 1.2–4.2, $p = 0.012$).

The ADHD group contained eight patients with epilepsy, while none were found in the control group (Chi Square, $p = 0.007$). In the whole sample 73 children reported motion sickness (30.0%). Rates of motion sickness in ADHD and controls were 24.8% ($n = 29$) and 39.6% ($n = 44$); respectively with significantly more common reports among controls (Chi Square, $p = 0.016$, Phi = 0.16). OR for motion sickness in children with ADHD was 0.5 (95% CI = 0.3–0.9, $p = 0.017$) (Tables 1 and 2).

Primary headache disorders were also significantly more common in mothers of children with ADHD

Table 1
Socio-demographic features and medical comorbidities of ADHD patients and age- and gender-matched healthy controls.

	ADHD (n = 117)	Control (n = 111)	P*
Boys	96	85	*0.391*
Age (years, range)	11 (6–18)	12 (8–16)	*0.650*
Education (years, range)	5 (1–12)	5 (2–10)	*0.749*
Primary headache disorder	69 (59.0%)	42 (37.8%)	***0.002*****
Migraine	31 (26.5%)	11 (9.9%)	***0.048*****
Tension-type headache	38 (32.5%)	31 (27.9%)	
Atopic disorders	52 (44.4%)	40 (36.0%)	*0.225*
Recurrent abdominal pain	37 (31.6%)	19 (17.1%)	***0.017*****
Motion sickness	29 (24.8%)	44 (39.6%)	***0.016*****
Epilepsy	8 (6.8%)	0 (0.0%)	***0.007*****

* Chi-square and Mann-Whitney U tests.
** Statistical significance level was considered as $P < 0.05$.

Table 2
Diagnosis of primary headache disorders according to ICHD-3 beta criteria among patients with ADHD and age- and gender-matched controls.

Headache subtypes	ADHD (n = 69)	Control (n = 42)	P*
Episodic migraine	29 (42.0%)	11 (26.2%)	***<0.001*** **
Chronic migraine	1 (1.4%)	0 (0.0%)	
Probable migraine	1 (1.4%)	0 (0.0%)	
Infrequent episodic TTH	25 (36.2%)	11 (26.2%)	
Frequent episodic TTH	7 (10.1%)	19 (45.2%)	
Chronic TTH	6 (8.7%)	1 (2.4%)	

* Chi-square test, ICHD: International classification of headache disorders, TTH: Tension-type headache.
** Statistical significance level was considered as $P < 0.05$.

Table 3
Socio-demographic features and medical comorbidities of mothers of patients with ADHD and those of controls.

	ADHD-M (n = 116)	C-M (n = 110)	*P**
Age (years, range)	37 (26–54)	39 (27–55)	*0.095*
Education (years, range)	8 (2–16)	12 (0–18)	*0.392*
Primary headache disorder	105 (90.5%)	72(65.5%)	***<0.001*** **
Migraine	80 (69.0%)	45 (40.9%)	***0.049*** **
TTH	25 (21.6%)	27 (24.5%)	
Atopic disorders	56 (48.3%)	54 (49.1%)	*0.902*
Recurrent abdominal pain	26 (22.4%)	10 (9.1%)	***0.011*** **
Motion sickness	53 (45.7%)	53 (48.2%)	*0.790*
Epilepsy	2 (1.7%)	0 (0.0%)	*0.498*

* Mann-Whitney U and chi-square tests, ADHD-M: Mothers of children with ADHD, C-M: Mothers of control children, TTH: Tension-type Headache.
** Statistical significance level was considered as $P < 0.05$.

Table 4
Diagnosis of primary headache disorders according to ICHD-3 beta criteria of mothers of ADHD patients and those of controls.

Headache subtypes	ADHD-M (n = 105)	C-M (n = 72)	*P**
Migraine without aura	56 (53.3%)	33 (45.8%)	***0.005*** **
Migraine with aura	3 (2.9%)	6 (8.3%)	
Chronic migraine	21 (20.0%)	6 (8.3%)	
Infrequent episodic TTH	14 (13.3%)	7 (9.7%)	
Frequent episodic TTH	6 (5.7%)	16 (22.2%)	
Chronic TTH	5 (4.8%)	4 (5.6%)	

* Chi-square test, ADHD-M: Mothers of children with ADHD, C-M: Mothers of control children, TTH: Tension-type Headache.
** Statistical significance level was set as $P < 0.05$.

(ADHD-M) (90.5% vs. 36.6%, $p < 0.001$). Migraine was found in 68.9% of ADHD-M and 40.9% of mothers of controls. TTH was found in 21.5% of ADHD-M and 24.5% of mothers of controls. Recurrent abdominal pain was also significantly more common in ADHD-M ($p = 0.011$). The odds ratio (OR) for primary headache disorder in mothers of children with ADHD in our sample was 2.4 (95.0% Confidence Interval = 1.4–4.0, $p = 0.002$). The corresponding ORs for migraine and TTH were 3.2 (95% CI = 1.9–5.5, $p < 0.001$) and 0.9 (95% CI = 0.5–1.6, $p = 0.59$). Lastly, for recurrent abdominal pain OR was 2.9 (95% CI = 1.3–6.3, $p = 0.008$; Tables 3 and 4).

For fathers, the prevalence of headache was similar between groups. Migraine was found in 20.9% of fathers of ADHD patients (ADHD-F) and 13.7% of control fathers. TTH rates were 31.4% for ADHD-F versus 34.3% for controls. Recurrent abdominal pain and motion sickness were also significantly common in ADHD-F. The odds ratio (OR) for primary headache disorder in fathers of children with ADHD in our sample was 1.2 (95.0% Confidence Interval = 0.7–2.1, $p = 0.53$). ORs for recurrent abdominal pain and motion sickness were 2.7 (95% CI = 1.1–6.8, $p = 0.03$) and 0.3 (95% CI = 0.1–0.7, $p = 0.003$); respectively (Tables 5 and 6).

4. Discussion

This multi-center, cross-sectional case-control study evaluated headache, recurrent abdominal pain, motion sickness, epilepsy and atopic disorders among children with ADHD and age- and gender-matched controls and their parents. Primary headache disorders, migraine, TTH, recurrent abdominal pain and epilepsy were significantly more common in children with ADHD, while atopic disorders did not differ between groups and motion sickness was significantly more common among control children. Among mothers of children with ADHD, primary headache disorders, migraine, TTH and recurrent abdominal pain were significantly more common. As for fathers, only recurrent abdominal pain was more common among fathers in the ADHD group, while motion sickness was once again more common among controls. Although it is known that headaches may be associated with ADHD our

Table 5
Socio-demographic features and medical comorbidities of fathers of patients with ADHD and those of healthy controls.

	ADHD-F (n = 105)	C-F (n = 99)	*P**
Age (years, range)	41 (31–61)	42 (32–65)	*0.164*
Education (years, range)	12 (1–16)	12 (0–18)	*0.855*
Primary headache disorder	55 (52.4%)	49 (49.5%)	*0.789*
Migraine	22 (21.0%)	14 (14.1%)	*0.309*
TTH	33 (31.4%)	35 (35.4%)	
Atopic disorders	24 (22.9%)	34 (34.3%)	*0.121*
Recurrent abdominal pain	18 (17.1%)	7 (7.1%)	***0.040*** **
Motion sickness	10 (9.5%)	26 (26.3%)	***0.003*** **
Epilepsy	0 (0.0%)	1 (1.0%)	*0.493*

* Mann-Whitney U and chi-square tests, ADHD-F: Fathers of children with ADHD, C-F: Fathers of control children, TTH: Tension-type Headache.
** Statistical significance level was set as $P < 0.05$.

Table 6
Diagnosis of primary headache disorders according to ICHD-3 beta criteria in fathers of patients with ADHD and those of controls.

Headache subtypes	ADHD-F (n = 55)	C-F (n = 49)	P*
Migraine without aura	16 (29.1%)	12 (24.5%)	***0.004*****
Migraine with aura	2 (3.6%)	2 (4.1%)	
Chronic migraine	4 (7.3%)	0 (0.0%)	
Infrequent episodic TTH	24 (43.6%)	13 (26.5%)	
Frequent episodic TTH	5 (9.1%)	20 (40.8%)	
Chronic TTH	4 (7.3%)	2 (4.1%)	

* Chi-square test, ADHD-F: Fathers of children with ADHD, C-F: Fathers of control children, TTH: Tension-type Headache.
** Statistical significance levels was considered as $P < 0.05$.

results extend those findings and suggest a differential effect of parental gender [5].

The reported prevalence of headache among school children varies greatly depending on samples and study centers, although a rate of 10.0–20.0% is commonly cited [20–22]. The most frequent types are migraine and tension-type headache, which occur in 2.0–17.0% and in 0.9–24.0% in children and adolescents, respectively [26–28]. Previous studies conducted among children and adolescents from the same geographic region of Turkey reported rates of 10.4–17.8% for migraine and 24.0–31.9% for TTH [2,3,29,30]. For the control group in our study, rates of primary headache disorders, migraine and TTH were 37.8%, 9.9% and 27.9%, respectively, and those rates are in accordance with previously reported results.

Leviton et al. first reported in a study on 150 elementary school children with recurrent headaches that approximately 40.0% experienced academic difficulties [31]. Strine et al. demonstrated in a population of children aged 4–17 that those who were referred for neurological assessment for frequent headaches were 2.6 times more likely to suffer from inattention and hyperactivity [32]. Meanwhile, in a recent retrospective study of 243 children and adolescents aged 6–18, Genizi et al. demonstrated that learning disabilities and ADHD are more common in children and adolescents who are referred for neurological assessment for primary headaches compared with the general pediatric population [5]. Of interest is the fact that the authors reported that patients with TTH in their sample were more likely to have ADHD than migraineurs (36.5% vs. 19.8%). Within our sample of children with ADHD, primary headache disorder was found in 59.0%. Of those, 26.5% met the criteria for migraine, while 32.5% met the criteria for TTH. The OR for ADHD symptoms in children with headaches and for primary headache disorders in ADHD appear to be broadly similar (i.e., 2.6 and 2.4) and clinically important (i.e., excludes OR = 1.0). That is, children with frequent headaches may be 2.6 times more likely to experience symptoms of inattention and hyperactivity, while children with ADHD may be 2.4 times more likely to have primary headache disorders. Therefore, we can say that the rates we determined are similar to those previously reported for children with ADHD.

According to the World Health Organization's ranking of causes of disability, headache disorders are among the ten most disabling conditions for adults of both genders, and among the five most disabling for women in particular. Globally, the percentages of the adult population with an active headache disorder are 46.0% for headache in general, 42.0% for TTH and 11.0% for migraine [33]. A nationwide study of adults in Turkey reported rates of 16.0% for migraine and 31.7% for TTH [34]. In our study, primary headache disorders were also significantly more common in mothers of children with ADHD (ADHD-M) (90.5% vs. 36.6%, $p < 0.001$), the most prevalent type being migraine (68.9%). However, no significant difference was found between fathers of children with ADHD and those of controls. Fathers of children with ADHD mostly reported TTH (60.0%). The OR for headache disorders in mothers of children with ADHD is similar to that of their children in our sample, and it differs significantly from that of fathers. As this is a novel finding, it may require further explanation and replication. The similarity of primary headache disorders between children with ADHD and their mothers may reflect the effects of genetics, and the difference seen in fathers may reflect the importance of genomic imprinting [35]. Alternatively, the concordance between mothers and children may reflect environmental effects, such as observational learning. Parents of both control children and those with ADHD had elevated rates of primary headache study compared with previous results from national surveys. Those differences may reflect both sampling bias (in parents of children with ADHD) as well as differential methods of ascertainment (i.e. previous surveys used questionnaires while in the present study clinical evaluation was used).

Recurrent pains, especially in the abdominal region, are common among school children. They appear to have negative effects on development, with associated school problems, and are frequently the cause of absence from school [36] Population-based studies reported that recurrent abdominal pain may be frequent among children with ADHD, with ADHD patients reporting this complaint twice as often as controls [37]. Similarly, we found that recurrent abdominal pain was significantly more common among children with ADHD, their mothers and their fathers. As was argued regarding primary headache disorders, this finding is novel and should be replicated and may reflect genetic and/or environmental factors.

Motion sickness is a complex syndrome with a hypothesized population prevalence of 0.01% [38].

Traditional accounts focused their explanations on the mismatch between visual and vestibular inputs, although recent accounts have suggested that visceral afferent feedback may also be important [38]. As far as we are aware, no systematic evaluation has been previously attempted of motion sickness in children with ADHD and their parents, although older case reports of children with learning disabilities and ADHD responding to anti-motion sickness medications do exist [39]. In our study, we found that motion sickness was significantly less common among fathers and mothers of children with ADHD as well as in children with ADHD themselves (OR ADHD = 0.5, 95% CI = 0.3–0.9, p = 0.02; OR ADHD-M = 0.91, 95% CI = 0.5–1.5, p = 0.71; OR ADHD-F = 0.4, 95% CI = 0.2–0.8, p = 0.01). According to our figures, children with ADHD and their fathers may be significantly less likely to experience motion sickness. This finding may also be related to genetic and/or environmental factors, and should be replicated.

Most previous studies and meta-analyses supported the observation that ADHD showed higher comorbidity with atopic disorders, such as asthma, eczema and rhinitis, and that this comorbidity was bi-directional [40–42]. In our study, no significant differences were found in atopic disorders between children with ADHD and control children. There were also no significant differences in parents. This difference may be due to sampling, reporting and/or recall bias, and should be replicated.

Compared to controls, children with epilepsy had a greater prevalence of ADHD and conduct disorder. Several studies have shown that ADHD, especially the inattentive type, is associated with a statistically significant risk of developing epilepsy [43,44]. In our study, eight epileptic patients were found in the ADHD group, and none were found in healthy control group. Similar to previous studies, five of the eight epileptic patients had ADHD inattentive type. Two of the mothers of children with ADHD had epilepsy, versus none of the fathers. We did not attempt statistical comparisons due to the low number of observations. Further studies of epilepsy and related conditions among index patients and first-degree relatives of children with ADHD are recommended.

Our results should be evaluated while keeping in mind the limitations of this study. First, our findings are valid for children and adolescents at the study centers for ADHD treatment within the specified time frame, and may not be valid for other clinical and/or population samples. Second, headaches and other medical disorders and complaints in both children and their parents may be prone to recall and reporting bias. Although we attempted to overcome this limitation for primary headache disorders through clinical evaluation with neurologists/ pediatric neurologists, reports of recurrent abdominal pain, atopic disorders and motion sickness could not be corroborated. Third, it is known that somatic complaints are especially common in prepubertal children, and may be reduced in adolescents [45]. The inclusion of adolescents in our sample may have affected the results. We avoided further sub-group analyses to control Type I errors and suggest further studies to evaluate the effects of puberty and/or adolescence on medical comorbidities in ADHD. Fourth, the relationships between primary headache disorders and other medical complaints and comorbidities may be affected by ADHD subtypes, and this factor was not controlled for in our analyses. Fifth, it is known that ADHD in children is a significant stressor for their parents and other family members, and failure to control for stress and/or burnout levels in our sample may be a confounding factor. Sixth, we did not evaluate the parents themselves for ADHD. Regardless of these limitations, our results suggest that primary headache disorders may be elevated in both children with ADHD and their mothers, that recurrent abdominal pain is common in both children with ADHD and their parents.

5. Conclusion

In this study, it was found that headache is more prevalent in children with ADHD than healthy controls and also that headache disorders are more common among mothers of children with ADHD. Migraine was nearly three times more frequent in children with ADHD than in healthy controls (26.0%, 9.9%), and migraine was also more prevalent in mothers of children with ADHD than mothers of healthy controls. We also observed that recurrent abdominal pain was significantly more common among children with ADHD and their parents as well as parents of healthy controls. On the other hand, ADHD seemed to be a protective factor for motion sickness in children and their parents. We did not find significant differences for atopic disorders, while samples in cells were too few to analyze statistically for epilepsy. To the best of our knowledge, our findings have not been reported previously in the literature. This difference could support common pathophysiologic mechanisms and genetic susceptibility of these disorders, or alternatively, it may suggest environmental factors.

Understanding the patterns of medical comorbidity in ADHD patients and the families of index patients with ADHD may lead to better treatment of affected individuals and aid in etiologic studies of the disease. Differing patterns of comorbidity among patient subgroups may lead to better care for patients and provide clues regarding the sources of heterogeneity of ADHD.

6. Conflict of interest statement

On behalf of all authors, the corresponding author states that there is no conflict of interest.

7. Ethical standard

The study protocol has been approved by the institutional ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All persons gave their informed consent prior to their inclusion in the study

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