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ORIGINAL ARTICLE

Correlation between clinical manifestations of nocturnal enuresis and attentional performance in children with attention deficit hyperactivity disorder (ADHD)

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KEYWORDS
attention deficit hyperactivity disorder (ADHD);
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Background/Purpose: Children with attention deficit hyperactivity disorder (ADHD) tend to be more vulnerable to various forms of voiding dysfunction and nocturnal enuresis (NE). We attempt to compare the clinical manifestations and attentional performance between ADHD children with NE and those without NE.
Methods: We consecutively enrolled children diagnosed with ADHD in child and adolescent psychiatric clinics. The questionnaires for evaluation of ADHD symptoms and voiding dysfunction symptoms were administered to all study participants. All participants also received the Test Battery for Attention Performance (TAP) for assessment of attentional function.
Results: A total of 53 children were enrolled in this study, comprising 47 boys and six girls. The prevalence rate of NE was 28.3%. Children in the NE group had statistically significant higher dysfunctional voiding symptom score (5.40 ± 3.66 vs.3.16 ± 2.74; $p = 0.018$) and two subscales of "When I wet myself, my underwear is soaked" ($p < 0.001$) and "I miss having a bowel movement every day" ($p = 0.047$). There were no significant differences with regard to all psychiatric evaluations between the NE and non-NE groups. In the TAP test, the NE group showed a significantly shorter reaction time in the domain of inhibitory control, working memory, and auditory sustained attention than the non-NE group.

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Conclusion: Children with ADHD have a high prevalence of NE. ADHD children with NE had a significantly higher dysfunctional voiding symptom score and shorter reaction time in most domains of the TAP test. Further study is needed to discern the impact of NE on the neuropsychological function of ADHD children.

Introduction

Attention deficit hyperactivity disorder (ADHD) is a common problem in child and adolescent psychiatric clinics.[1] It represents a syndromic diagnosis with three symptom domains: inattention, hyperactivity, and impulsivity.[2] Although there are effective treatments for ADHD, no established objective "test" can conclusively diagnose ADHD.[3] Test Battery for Attention Performance (TAP) is a neuropsychological testing used for the evaluation of inhibitory control and attentional performance in children with ADHD.[4,5]

The association between nocturnal enuresis (NE) and ADHD has been investigated in several previous studies.[6–11] Children with ADHD tend to be more vulnerable to various forms of urinary problems, such as NE, voiding dysfunction (VD), and diurnal incontinence.[9–13] The etiology of NE has been reported to be associated with neurological maturation. Previous studies have demonstrated that children with NE had higher incidence of delayed language and gross motor development.[14] However, surveys with neuropsychological attention tests in ADHD children with NE are lacking. Therefore, we conducted our study using TAP to evaluate neuropsychological function and attentional performance in children with ADHD. Moreover, our aim was to investigate the correlation between NE and attentional performance in children with ADHD.

Materials and methods

After obtaining approval from the institutional research ethics committee, informed consent was obtained from each participant before any evaluations or sample collections were conducted. Between January 2005 and December 2007, we consecutively enrolled 53 children, aged 6 to 10 years, diagnosed as having ADHD who first sought medical help without previous medications in the Child and Adolescent Psychiatric Clinics of Taipei Municipal Hospital. The diagnosis of ADHD was confirmed by experienced child and adolescent psychiatrist according to *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* criteria. Children with other mental disorders such as mental retardation, pervasive developmental disorder and psychosis, and organic brain diseases such as seizure were excluded from the study. Details on demographic data, perinatal history, medical history, the presence of sleep disorder, and developmental history were collected from parents or medical records. Sleep disorders including obstructive sleep apnea, nightmares, and sleepwalking were recorded and compared between the two groups.

The psychiatric interviews of these children were obtained from their parents using the validated, Chinese version of the Kiddi Schedule for Affective Disorders and Schizophrenia-Epidemiologic version (K-SADS-E).[15] Data on behavior problems such as ADHD, oppositional defiant disorder symptoms, conduct disorder, depression, mania, and anxiety disorders were also collected. The IQ of all study participants was assessed using the Chinese version of Wechsler intelligence Scale for Children,[16] which was conducted with the assistance of an experienced child psychologist. NE was defined as nighttime wetting with or without daytime incontinence, at least twice a week over a period of 3 months or longer, but without anatomical abnormalities. The evaluation of NE and VD was examined by urinalysis, renal echo, and structured questionnaire of NE and dysfunctional voiding symptom score (DVSS) questionnaire, Chinese-language version, which has been validated for quantification of voiding symptoms in children.[17,18] The DVSS consists of 10 questions that assess daytime incontinence, NE, constipation, urgency, voiding frequency, and dysuria, each was scored from 0 to 3 (0 = almost never,1 = less than half the time, 2 = about half the time, 3 = almost every time) for a maximum total score of 30 (most severe symptoms). An additional 11th question assesses recent stressful events within the family. Scores for the NE and non-NE groups were compared for each subscale and in aggregate. The diagnosis of VD was based on DVSS with a threshold score of 6 for females and 9 for males, and abnormal uroflowmetry curve shapes during micturition.

Each of the questionnaires used in this study was explained to the parent(s) of the participants and handed to them for completion. Participants ordinarily participated with their parents in responding to the questionnaires.

Test of attentional performance test

TAP test is a computer-driven test battery for the assessment of attentional function and inhibitory control.[4,5] All participants completed the TAP test in the morning with the assistance of a well-trained personnel. TAP test is a valid tool for the clinical assessment of attention function of children. Our study adopted the following five components:

(1) Alertness

There are two conditions in this test. For condition A, the children were instructed to press a button as fast as possible when a cross appeared (×). Under condition B, the children heard an arousal signal (60 dBA) first, then they were to press a button when a cross (×) appears.

(2) Auditory sustained attention

Two kinds of auditory stimulations (440 and 1000 Hz; 60 db) appeared randomly. The children were instructed to press the button when two |S1|signals were the same.

(3) Visual sustained attention

There are 16 points on the screen that form a square. Four asterisks appear in four of the 16 positions. The children were instructed to press the button when these four asterisks form a square.

(4) Inhibitory control (go/no-go task)

An upright cross and a cross rotated are presented sequentially in a pseudorandom order. Children are instructed to press the button when the upright cross appears (go). When a cross rotated 45° appears on the screen, the children should not press the button (no go). Reaction time, omission, and false alarm were recorded.

(5) Working memory

In order to evaluate working memory, numbers in pseudorandom order appeared in the middle of the screen. If a sequential number was the same, children were asked to press the button. Reaction time, omission, and false alarm were recorded.

Statistical analysis

Mean values of continuous variables were compared using an independent sample *t*-test. The chi-square analyses were performed to compare differences between categorized variables. All analyses were performed with Statistical Package for the Social Sciences software (SPSS 13th ed., Chicago, IL). A *p* value of less than 0.05 was regarded as significant.

Regarding sample size determination, based on some published series,[17,18] we set the cutoff point of DVSS difference as 3, within-group standard deviation as 3, alpha level 0.05, and power value of 0.8, and the estimated sample size as 16 in each group.

Results

A consecutive series of 53 children with ADHD aged 6 to 10 years were enrolled in the study. The demographic data of the 53 participants are listed in Table 1. The prevalence rate of NE in 53 children with ADHD was 28.3% (15/53). All demographic parameters were similar between the two groups. Table 2 demonstrates the results of DVSS and each subscale in the two groups. There are five children with VD in the NE group and four in the non-NE group (33% vs. 10.5%; $p = 0.046$). The ADHD children with NE had statistically significant higher total DVSS scores (5.40 $\pm$ 3.66 vs.3.16 $\pm$ 2.74; $p = 0.018$). In addition, children tin he NE group tended to have higher scores in the "When I wet myself, my underwear is soaked" and "I miss having a bowel movement every day" subscales of DVSS ($p < 0.001$ and $p = 0.047$).

Table 3 lists the clinical characteristics of all 53 participants. There were no significant differences in terms of K-SADS-E Symptom Profile, type of ADHD, type of comorbid psychiatric diagnosis, motor or language developmental delay, sleep disorders, and IQ score between the NE and non-NE groups.

Table 4 shows the results of the TAP test in all study participants. There were no significant differences between the NE and non-NE groups in the domain of alertness. However, in the domain of inhibitory control (go/no-go task), ADHD children with NE showed a significantly shorter reaction time than those without NE (461 $\pm$ 134vs. 534 $\pm$ 82.2 seconds; $p = 0.023$). Similarly, ADHD children with NE had a shorter reaction time than those without NE in the tests of working memory (757 $\pm$ 200 vs. 917 $\pm$ 226 seconds; $p = 0.022$) and auditory sustained attention (640 $\pm$ 104 vs. 718 $\pm$ 105 seconds; $p = 0.02$).

Discussion

ADHD is a childhood psychiatric disorder and affects around 3–7% of the childhood population.[1,19,20] Children with ADHD tend to be more vulnerable to various forms of NE and VD.[10–13] The prevalence rate of enuresis in children with ADHD was reported as 12.5% in a national survey in the United States[14] and 32% in another series.[12] In the present study, the prevalence rate of NE in patients with ADHD was high (28.3%). Since participants with ADHD in child and adolescent psychiatric clinics were mostly referred by pediatricians or general practitioners from local hospitals, their ADHD symptoms might be more severe. Second, the participants in this study were younger and had more severe symptoms of ADHD. These different characteristics might explain the higher prevalence of NE in our study sample compared to that of other studies.

Why do ADHD children have higher incidence of NE and VD? The exact pathogenesis is still not clear at this time. It has been suggested that voiding disturbances, particularly NE, in children with ADHD are due to nocturnal polyuria and detrusor overactivity.[21] Some investigators suggested that the delays in central nervous system maturation could account for this association between enuresis and ADHD.[22–25] Several previous studies have suggested that primary NE happens because a child with ADHD is less able to wake up when the urinary bladder is full or be awake enough to get up and go to the toilet when the urge to urinate is present.[11,24–26]

Elia et al[11] conducted a study to clarify NE as an endophenotype marker in 344 ADHD children ages 6 to 12 years. The enuresis group had a higher likelihood of inattentive symptoms than the nonenuretic group. Night wakings and the ability of children to wake themselves up in the morning were both significantly decreased in children with enuresis compared with children in the control group in the Child Sleep Habits Questionnaire Night Wakings subscale. The authors concluded that deficits in arousal may contribute to both enuresis and inattentive ADHD. NE may be a useful clinical marker in identifying a subgroup of the inattentive phenotype in ADHD genetic studies.[11] In the

Table 1 Clinical and demographic characteristics in 53 ADHD children stratified by the presence of nocturnal enuresis.

	NE (n = 15)	Non-NE (n = 38)	p
Age (y)	7.53 ± 1.06	7.26 ± 1.03	0.40
Paternal age (y)	40.4 ± 5.88	40.7 ± 4.61	0.87
Maternal age (y)	36.7 ± 5.20	38.0 ± 4.51	0.39
Birth weight (g)	3126 ± 517	3054 ± 554	0.67
Gender, F/M (%)	0/15 (0/100)	6/32 (15.8/84.2)	0.10
Gestational age (%)			
Full term	10 (66.7)	34 (89.4)	0.08
Premature (<3 wk)	4 (26.7)	2 (5.3)	
Post-term (>40 wk)	1 (6.7)	2 (5.3)	
Maternal education (%)			
College	4 (26.7)	9 (23.7)	0.92
High school	9 (60)	25 (65.8)	
Elementary school	2 (13.3)	4 (10.5)	
Household incomes (%)			
Low	1 (6.7)	4 (10.5)	0.74
Middle	10 (66.7)	21 (55.3)	
High	4 (26.7)	13 (34.2)	
Marital status (%)			
Intact marriage	12 (80)	33 (86.8)	0.16
Separated	0 (0)	3 (7.9)	
Divorced	3 (20)	2 (5.3)	
Patient with siblings	10 (66.7)	31 (81.6)	0.24
Type of delivery (%)			
Normal spontaneous delivery	8 (53.3)	24 (63.2)	0.51
Cesarean section	7 (46.7)	14 (36.8)	
Perinatal insult (%)	5 (33.3)	10 (26.3)	0.61
Newborn jaundice (%)	7 (46.7)	16 (31.6)	0.76

Household incomes: low mean monthly incomes < NT$30,000; moderate mean incomes between NT$30,000 and 75,000; high means incomes ≥ NT$75,000.
Numerical data are expressed as mean ± SD and compared with t-test.
Categorical data are expressed as number (percentage) and compared with Chi-square test.

Table 2 DVSS score of study participants (53 ADHD children) stratified by the presence of nocturnal enuresis.

	NE (n = 15)	Non-NE (n = 38)	p
	Mean ± SD	Mean ± SD	
Total DVSS	5.40 ± 3.66	3.16 ± 2.74	0.018
Subscale			
Wet underwear	0.07 ± 0.26	0.00	0.33
Soak underwear	1.13 ± 0.64	0.03 ± 0.16	<0.001
No daily bowel movement	0.33 ± 0.49	0.11 ± 0.31	0.047
Push to have bowel movement	0.73 ± 0.88	0.58 ± 0.72	0.51
Pee 1–2 times/day	0.33 ± 0.49	0.45 ± 0.83	0.62
Hold pee	0.60 ± 0.83	0.58 ± 1.00	0.94
Can't wait	0.07 ± 0.26	0.00	0.33
Push to pee	0.93 ± 0.88	0.55 ± 0.76	0.12
Hurt when pee	0.00	0.00	—
Stressful events	1.20 ± 1.52	0.87 ± 1.38	0.45
Voiding dysfunction (DVSS ≥ 6 in girls or DVSS ≥ 9 in boys)	5 (33.3)	4 (10.5)	0.046

Numerical data are expressed as mean and SD and compared with t-test.
Categorical data are expressed as number (percentage) and compared with Chi-square test.
DVSS = dysfunctional voiding symptom score; SD = standard deviation.

Table 3 Clinical characteristics (based on psychiatric evaluation) of 53 ADHD children stratified by the presence of nocturnal enuresis.

	NE ($n = 15$)	Non-NE ($n = 38$)	p
K-SADS-E Symptom Profile			
Inattention	6.07 ± 1.44	5.55 ± 1.98	0.37
Hyperactivity	2.53 ± 2.13	2.71 ± 1.99	0.78
Impulsivity	1.20 ± 0.94	1.13 ± 0.96	0.82
Type of ADHD			
Combined	1 (6.7)	10 (26.3)	0.28
Inattentive	11 (73.3)	22 (57.9)	
Hyperactivity/impulsivity	3 (20)	6 (15.8)	
Type of comorbid psychiatric diagnosis			
Opposional defined disorder	4 (26.7)	10 (26.3)	0.98
Conduct disorder	1 (6.7)	1 (2.6)	0.49
Depression	0 (0)	2 (5.3)	0.37
Mania	1 (6.7)	1 (2.6)	0.49
Phobia	1 (6.7)	6 (15.8)	0.38
Patient with sleep disorder	4 (26.7)	4 (10.5)	0.14
Patient with motor developmental delay	1 (6.7)	5 (13.2)	0.50
Patient with language developmental delay	3 (20.0)	4 (10.5)	0.36
IQ			
Verbal IQ	95.9 ± 11.8	92.8 ± 13.7	0.53
Performance IQ	97.6 ± 9.31	98.1 ± 16.0	0.92
Full IQ	97.6 ± 11.6	94.5 ± 14.3	0.51

Numerical data are expressed as mean ± SD and compared with t-test.
Categorical data are expressed as number (percentage) and compared with Chi-square test.
ADHD = attention deficit hyperactivity disorder; K-SADS-E = Kiddi Schedule for Affective Disorders and Schizophrenia-Epidemiologic version SD = standard deviation.

Table 4 Results of TAP test in 53 ADHD children stratified by the presence of nocturnal enuresis.

	NE ($n = 15$)	Non-NE ($n = 38$)	p
Alertness			
Reaction time without warning (s)	375 ± 142	396 ± 108	0.56
Omission (no.)	0.20 ± 0.56	0.44 ± 0.86	0.33
Reaction time with warning (s)	324 ± 104	371 ± 84.9	0.11
Omission with warning (no.)	0.40 ± 0.74	0.32 ± 0.68	0.73
Inhibitory control (go/no-go task)			
Reaction time (s)	461 ± 134	534 ± 82.2	0.023
Omission (no.)	3.20 ± 3.63	2.38 ± 3.17	0.43
False alarm (no.)	7.27 ± 3.99	6.12 ± 3.98	0.36
Working memory			
Reaction time (s)	757 ± 200	917 ± 226	0.022
Omission (no.)	0.33 ± 0.49	0.71 ± 0.94	0.15
False alarm (no.)	1.00 ± 3.61	1.50 ± 3.96	0.68
Visual sustained attention			
Reaction time (s)	1211 ± 159	1208 ± 175	0.95
Omission (no.)	4.47 ± 2.72	5.35 ± 3.23	0.36
False alarm (no.)	1.87 ± 2.56	2.56 ± 4.10	0.55
Auditory sustained attention			
Reaction time (s)	640 ± 104	718 ± 105	0.02
Omission (no.)	1.33 ± 2.77	1.47 ± 1.85	0.84
False alarm (no.)	0.87 ± 1.77	1.38 ± 2.24	0.44

Numerical data are expressed as mean ± SD and compared with t-test.
Categorical data are expressed as number (percentage) and compared with Chi-square test.
ADHD = attention deficit hyperactivity disorder; TAP = Test of Attentional Performance.

present study, the inattentive K-SADS-E Symptom score was higher in the NE group, although not at a statistically significant level. More samples may be needed to clarify the correlation between NE and inattentive ADHD.

In their study, Bosson et al[24] suggested the presence or absence of boundary errors in both copy and memory reproductions by using a specific neuropsychological (Rey-Osterrieth) test that could reflect a delay in maturation and/or a disorganization of the retinal—hypothalamic—cortical pathways in the brain of children with NE.[24] Similarly, we applied the TAP test to children with ADHD with or without NE to analyze the impact of NE on the clinical manifestations and attention performance. This is the first study to use a neuropsychological test to evaluate children with ADHD and NE.

In the present study, we evaluated the five different domains of TAP test: alertness, inhibition control, working memory impairment, and attentional deficit. There were no significant group differences on alertness. However, there was evidence of the reaction times in the other three domains being shorter in the NE group. The inaccurate rate in response in each domain was similar in the NE and non-NE groups. As well known, hyperactive children are variable in their speed, and are generally slow and inaccurate in responding. In the present study, ADHD patients with NE reacted faster on TAP tests, yielding a statistical significance for the go/no-go test, working memory, and auditory sustained attention. This pattern of responses may indicate the neuropsychological differences among ADHD patients with and without NE. In our previous study, we found that ADHD children had an increased rate of error in various kinds of attention domains in TAP test as compared to healthy participants (data not shown here). In the present study, the NE group has a similar accuracy with faster response. Since neurological-developmental delay has been mentioned to be the cause of NE,[22,23] the results in the present study do not seem to be reasonable in consideration of this point. However, no previous study has focused on using attentional performance test in ADHD children with or without NE. In this pilot study, we just described the observational results based on a limited number of cases. Our results suggest a differential pattern of attentional functions in ADHD patients with NE and without NE. Further large-scale studyis warranted to clarify the exact pathophysiology between NE and performance of TAP attention test in ADHD.

We also examined whether the VD symptoms were different between ADHD children with NE and those without NE. The DVSS has been validated and is commonly used to evaluate lower urinary tract symptoms such as urinary urgency or straining in children.[18] In the present study, ADHD children with NE had a significantly higher DVSS score. Further investigations for other comorbid voiding problems by using other diagnostic tools such as urodynamic study may be necessary.

In terms of mean scores of all DVSS subscales, the subscale of item "When I wet myself, my underwear is soaked" and item "I miss having a bowel movement every day" were significantly higher in the NE group. These symptoms can be very stressful for children. Thus, we recommend that ADHD patients with nocturia presenting in the clinic require careful evaluation for other symptoms of VD.

An important limitation of this pilot study is the lack of healthy control patients. In addition, the number of participants in the NE group was limited. Furthermore, we could not provide information on the causal links between these conditions because of the cross-sectional nature of the study.

In conclusion, children with ADHD have a high prevalence of NE. Children with ADHD may benefit from a multidisciplinary approach.Simultaneous evaluation of VD and NE in children with ADHD is an important issue in clinical practice.This research represents a pilot study in preparation for a more comprehensive study of a larger cohort of children with ADHD. Further study is warranted to discern the impact of NE on the neuropsychological function of ADHD children.

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