

OLFACTORY FUNCTIONING IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER

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Summary

Introduction: Attention deficit hyperactivity disorder (ADHD) is characterized by a persistent pattern of behavior, present in two or more settings that can negatively impact on social, academic or occupational functioning. Children with ADHD tend to have one or more sensory processing problems. Very few studies have investigated olfactory impairment in children with ADHD and results are not consistent.

Objective: The aim of this study is to examine the olfactory functioning in group of children with ADHD compared with healthy children matched for age, gender and school achievement.

Method: We have analyzed a group of 24 children with diagnosis of ADHD according to DSM-V, aged 7-14 years, as well as 26 healthy control subjects with no data of any behavioral or psychological problem. Assessment of the olfactory identification and discrimination was performed using the Sniffin'Stick test of nasal chemosensory performance.

Results: There were no significant differences among two groups of participants in terms of age, gender and school achievement. The mean (SD) age of patients and healthy children was 11, 57 (2, 32) and 11, 95 (1, 77) respectively. Significant differences between the two groups were evident in the both domains of olfactory function. According to odor discrimination we found statistically significant difference between the ADHD and control group ($p < 0.05$) and according to odor identification we found high statistical significant difference ($p < 0.001$).

Conclusion: Olfactory function in children with ADHD has been a topic of increasing interest. The results of our study suggest olfactory impairment in two different domains of olfactory functioning. We believe that dopaminergic dysregulation is one of underlying mechanism of this phenomenon. Future studies with large sample size could include all three domain of olfactory functions as well as other sensory processing problems in children with ADHD.

Key words: ADHD, children, olfactory, functioning

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is characterized by a persistent pattern of behavior, present in two or more settings that can negatively impact on social, academic or occupational functioning [1]. (DSMV, 1)

The etiology and pathogenesis of ADHD is not yet fully understood. Genetic contribution, differences in brain structure and function, and neurotransmitter imbalances are suggested [2]. ADHD is linked to deficits in the functioning of several brain areas, including the prefrontal cortex, the basal ganglia, cerebellum, temporal and parietal cortex [3,4]. These areas are important in brain activities that may be impaired in ADHD. Individuals with ADHD present difficulties in several domains of attention

and other cognitive functions: problem solving, planning, orienting, alerting, cognitive flexibility, sustained attention, response inhibition, and working memory [5]. Other domains, involving affective components, such as motivation and delay aversion, are also affected [6]. Studies on different candidate genes for ADHD have been recently undertaken and mostly have focused on genes involved in the dopaminergic neurotransmission system [3,7,8].

Children with ADHD often experience a variety of sensory processing disorder symptoms [9]. Sensory processing disorders are impairments in responding to sensory stimuli such as deficits in detection, modulation or interpretation of stimuli [10]. These disorders, along with over-responsivity, under-responsivity, and sensory discrimination problems, impact the

Table 1. Demographic characteristic of the ADHD and control group
Tabela 1. Demografske karakteristike ADHD i kontrolne grupe

	ADHD group ADHD grupa	Control group Kontrolna grupa
Number of participants Broj ispitanika	24	26
Age, mean (SD) (%) Uzrast, prosečna vrednost (SD) (%)	11.57 (2.32)	11.59 (1.77)
Male N (%) Dečaci Br (%)	22 (91.7)	23 (88.47)
School achievement Školski uspeh	3.54 (0.83)	3.73 (0.87)
IQ	97.04 (12.50)	/

ADHD – Attention deficit hyperactivity disorder

ADHD – Hiperkinetski poremećaj sa poremećajem pažnje

responses of children to sensory events in daily life. [11].

Specific sensory problems in children with ADHD have been associated with an increased possibility of behavioral and social problems, difficulties in attention, and somatic complaints [9,12], as well as with higher anxiety levels [13]. In addition, sensory functioning has a strong correlation with academic achievement and cognitive processing in ADHD [10].

Children with ADHD also show functional manifestations of sensory problems, particularly in sensory seeking, auditory filtering, and in sensitivity

to tactile, auditory, visual, taste and olfactory stimuli [12]. Olfactory function reappeared clinically important as an early diagnostic pre-motor biomarker of Parkinson's disease [14]. Researchers have also more carefully assessed the sense of smell in patients with other neuropsychiatric disorders [14].

In the last years, an increasing interest has been paid to the olfactory function assessment in ADHD. Processing of smells is related to dopamine metabolism and orbitofrontal cortex functioning, both

Table 2. The comparison of Smell identification score and Smell discrimination score between ADHD and control group
Tabela 2. Poređenje Skora identifikacije mirisa i Skora diskriminacije mirisa između ADHD i kontrolne grupe

Sniffin' Sticks score Sniffin' Sticks skor	Participants Ispitanici	Mean (SD) Srednja vrednost (SD)	Minimum Minimum	Maximum Maksimum	p value p vrednost
Smell identification score Skor identifikacije mirisa	ADHD group Grupa sa ADHD	6.21 (2.64)	2	12	p < 0.001
	Control group Kontrolna grupa	8.88 (1.70)	5	12	
Smell discrimination score Skor diskriminacije mirisa	ADHD group Grupa sa ADHD	8.92 (1.91)	5	12	p < 0.05
	Control group Kontrolna grupa	9.81 (1.10)	8	12	

ADHD – Attention deficit hyperactivity disorder

ADHD – Deficit pažnje i poremećaj hiperaktivnosti

known to be involved in the neurobiology of ADHD [15,16].

Very few studies have investigated olfactory impairment in children with ADHD and results are not consistent. Olfactory identification ability of children with ADHD is not as good as healthy controls subjects [17]. Odor threshold is lower in ADHD than in healthy controls, but stimulants improve it [18]. Recent study [19] reported that there were no significant differences between ADHD and control subjects in three different domains of olfactory function.

OBJECTIVE

The aim of this study is to examine the olfactory function in group of children with ADHD compared with healthy children matched for age, gender, and in terms of school achievement.

METHODS

The ADHD group was recruited from the outpatients of Clinic of Neurology and Psychiatry for Children and Youth. Twenty-four children aged 7-14 years met the DSM-V criteria for ADHD diagnosis and achieved total IQ score of >70 on the REVISK Intelligence scale for children (a test comparable to the internationally known Wechsler Intelligence Scale for Children)[20]. Children with current upper respiratory tract infection or nasal allergies, as well as children with history of severe head trauma, epilepsy, and

thyroid disease, were excluded from the study. The control group was formed from twenty-six healthy children, with no data of any behavioral or psychological problem in the medical records. IQ data were not collected from the control group, but all of these children had a mandatory assessment of intellectual functioning admitting the elementary school and attending universal national educational program. The two groups were matched for age, gender, and in terms of school achievement. At the time of testing all patients were treated with Concerta (OROS methylphenidate), 18 or 36 mg once daily, at least 6 months.

Assessment of the olfactory functions was performed using the Sniffin' Sticks test of nasal chemosensory performance [21, 22]. The "Sniffin' Sticks" are felt tip pens filled with odors. For odor presentation the cap was removed by the examiner and each pen placed approximately 2 cm in front of the nostrils for 2-3 second. We assessed two different domains of olfactory function – odor identification and odor discrimination.

Odor identification was assessed for 14 common odors. The original test consists of 16 odors, but we eliminated two, because children were not been familiar with them (anise and rum). The test presented as multiple choice questions composed of correct answer and three distractors. The children were asked to select the best possible answer. The sum of the correct answers was regarded as the

odor identification score. The score ranges were between 0-14.

In the odor discrimination task, 16 triplets are presented to the subject, and the task was to determine which of three pans smell differently. Presentation of triplets was separated by at least 30s. During this part of test, participant is blindfolded wearing a sleeping mask, to prevent visual identification of the pens. Because 16 triplets were tested, the subject's scores ranged from 0-16.

The results were analyzed using standard statistical methods: Student's t-test and Mann Whitney test.

RESULTS

There were no significant differences among the two groups of participants in terms of age, gender, and school achievement (table 1).

At the time of testing, the mean (SD) age of patients and healthy children was 11.57 (2.32) and 11.95 (1.77) respectively. The two groups of participants have similar gender distribution also. Approximately 90% of all participants in each group were boys. The mean (SD) school marks in ADHD patients and control group was 3.54 (0.83) vs. 3.73 (0.87) respectively.

All patients had preserved the perception of odors.

Significant differences between the two groups were evident in the both domains of olfactory function. According to odor discrimination we found statistically significant diffe-

rence between ADHD and control group ($p < 0.05$) and according to odor identification we found high statistical significant difference ($p < 0.001$) (tabela 2).

DISCUSSION

Olfactory function in patients with ADHD has been a topic of increasing interest [17]. Test of smell identification are a well-recognized means of indirectly assessing the integrity of the orbital prefrontal cortex, a brain region that plays a key role in controlling emotions and suppressing aggressive and impulsive behaviors [23].

Most previous studies of olfactory function have investigated adult patients with ADHD [2,24,25,26]. Impairment of olfactory functions in children with ADHD was reported in only few recent studies, with quite inconsistent findings.

Our results suggest significant differences in odor identification ability and odor discrimination between children with ADHD treated with methylphenidate and healthy children. This finding is in accordance with data from some other studies. Karsz et al. examined olfactory identification in children with ADHD [17]. Authors found that the smell identification in ADHD subjects was significantly poorer when compared with the control subjects. They also found highly significant right nostril impairment among the children with ADHD. Granizadeh et al. [15] reported that children with ADHD have

significant impairment of odor identification and lower achievement in odor sensitivity tasks compared to healthy control participants.

Results from another study indicate significantly better odor sensitivity in unmedicated ADHD patients, without differences in odor discrimination and identification. The same study reported that stimulants normalized the odor sensitivity threshold in children with ADHD [18]. Methylphenidate as an indirect dopamine receptor agonist might have influence to odor sensitivity since olfaction is mediated by dopamine [2]. Two other studies reported no differences in olfactory functions among ADHD children compared with healthy controls. Romanos et al. [18] found no differences in both, odor discrimination and identification. Sari and Taskintuna [19] found no statistically differences between the ADHD and control groups in terms of all three domains of olfactory function. Some another studies reported that boys more than girls suffered from olfactory impairment [10, 18].

The different findings reported in these studies about olfactory functioning in children with ADHD, may be explained by differences in the methods used for assessment.

In conclusion, our investigation suggests olfactory impairment in two different domains of olfactory functioning. We believe that dopaminergic dysregulation is one of underlying mechanism of this phenomenon [19].

Poor performance in ADHD group in both domains of olfactory functioning is unlikely to be result of the difficulty of the task. The test was short and it was designed to engage the children's interest and attention.

This study has several limitations that may affect the interpretation of the findings: First, we did not assessed IQ in the control group so it is unknown how well the two groups were matched on this variable. Both affected and healthy children had normal pre-school intelligence as required for the regular education. No history of intellectual deterioration in all subjects. Despite of that, some variations in the actual IQ ranges could have some impact on the study results. Second, the sample size of girls in each group of participants is small; therefore no valid conclusions can be drawn from our results for female participants. Third, only ADHD children treated with methylphenidate were included in this study. Dopaminergic medication might have influence to odor determination since olfaction is mediated by dopamine.

Future studies with larger sample sizes and better balance in gender, could include all tree domains of olfactory functions, as well as some other sensory processing problem. Advanced research should include minimal neuropsychological test battery because attention, memory and language function may influence the olfactory test's results.

OLFAKTIVNO FUNKCIONISANJE DECE SA DEFICITOM PAŽNJE/HIPERAKTIVNIM POREMEĆAJEM

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Kratak sadržaj

Uvod: Hiperkinetski poremećaj sa poremećajem pažnje (ADHD) karakteriše se simptomima hiperaktivnosti, impulsivnosti i/ili poremećaja pažnje koji se javljaju u najmanje dve sredine, a negativno utiču na socijalno, akademsko ili profesionalno funkcionisanje. Deca sa ADHD mogu imati pridružen jedan ili više problema senzorne percepcije, uključujući i poremećaj na nivou percepcije mirisa. Mali broj dosadašnjih studija odnosi se na procenu olfaktivnog funkcionisanja deca sa ADHD, a dobijeni rezultati su nekonzistentni.

Cilj: Procena olfaktivnog funkcionisanja grupe deca sa ADHD u poređenju sa grupom zdrave dece, poredive po uzrastu, polu i školskom uspehu.

Metod: Analizirali smo mirisnu funkciju 24-oro deca sa nedvosmislenom dijagnozom ADHD i 26-oro zdrave školske dece, uzrasta 7-14 godina, očuvanog intelektualnog funkcionisanja. Sposobnost olfaktivne identifikacije i sposobnost olfaktivne diskriminacije procenjeni su primenom Sniffin'Stick testa za procenu olfaktivnog funkcionisanja.

Rezultati: Nije ustanovljena značajna razlika između dve grupe ispitanika u odnosu na uzrast, pol i školski uspeh. Prosečan uzrast (SD) deca sa ADHD u odnosu na zdrave ispitanike bio je 11,57 (2,32) vs 11,95 (1,79). Približno 90 procenata ispitanika u obe grupe činili su dečaci. Deca sa ADHD ostvarila su značajno niža postignuća u oba ispitavana domena mirisne funkcije, olfaktivnoj diskriminaciji ($p < 0,05$) i olfaktivnoj identifikaciji ($p < 0,001$).

Zaključak: Poremećaji senzorne percepcije mogu uticati na svakodnevno funkcionisanje deca sa ADHD i stoga ih je neophodno na vreme otkriti. Rezultati našeg ispitivanja ukazali su da ova deca mogu imati značajne poremećaje određenih sposobnosti olfaktivnog funkcionisanja, u čijoj osnovi se nalazi pretpostavljena redukovana dopaminergička aktivnost. Neophodno je da naredna istraživanja obuhvate veći broj ispitanika, više aspekata olfaktivnog funkcionisanja, kao i druge probleme senzorne percepcije deca sa ADHD.

Ključne reči: ADHD, deca, olfaktivno, funkcionisanje

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