

# Smell Identification Function in Children with Attention Deficit Hyperactivity Disorder

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**Objective** Deficits in olfactory function are common features in neurodegenerative and neuropsychiatric disorders. Olfactory processing is related to dopamine metabolism and orbitofrontal cortex functioning, both known to be involved in the neurobiology of ADHD. Some investigations suggested alterations in olfactory processing (identification and detection threshold) in patients with ADHD. Despite increasing knowledge, controversy about this topic still exists regarding children with ADHD. This study was conducted to help elucidate some of this controversy.

**Methods** 50 participants (8-15 years, mean=10.70±1.77) with ADHD were compared to 50 controls. The two groups were well matched for age, gender and Mean School Scores (MSS). We assessed odor identification and threshold through a smell test composed of two tests of identification and detection threshold. Odor detection threshold was assessed with the odorant phenyl ethyl alcohol solved in propylene glycol using a single staircase method. Odor identification was assessed with chemical essences of five common odorants.

**Results** The mean Sensory Identification Score for children with ADHD and the control groups were 3.76 (1.06) and 4.46 (0.76), respectively ( $p<0.001$ ). The mean for Sensory Threshold Score for ADHD and control group was 6.4 (3.35) and 9.75 (2.16), respectively ( $p<0.001$ ).

**Conclusion** This study replicated altered olfactory performance in ADHD. Substantial olfactory deficits across the two domains of identification and detection threshold are observed in children with ADHD. These deficits do not seem to be a result of olfactory task difficulty and are not influenced by age, gender and MSS. Further studies are required to investigate whether olfactory function can be used as a biological marker for early diagnosis, treatment and prognosis of ADHD.

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**Key Words** ADHD, Olfaction, Identification, Threshold, Smell test.

## INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is a very common psychiatric disorder in children and adolescents. ADHD is associated with impairments in different domains of sensory function.<sup>1-6</sup> Understanding sensory problems in ADHD may help us better understand the spectrum of problems included within the broad label of ADHD.

Unlike to other sensory systems, few synapses are located between the olfactory cortex and the peripheral olfactory receptors

leading to a direct relation between brain and environment.<sup>2,7</sup>

Regarding these facts, olfactory function is increasingly being used as a marker in neurodegenerative and neuropsychiatric disorders. Olfactory dysfunction is reported in many neurologic and psychiatric disorders such as Alzheimer's disease, Parkinson's disease (PD), Schizophrenia, Autism and Obsessive compulsive disorder (OCD).<sup>8-10</sup> For example, odor identification, odor detection threshold and odor memory are impaired in patients with schizophrenia.<sup>11</sup> The ability of children and adolescents with autism is less than healthy matched controls in identifying common odors.<sup>10</sup>

Olfactory function in patients with ADHD has been a topic of increasing interest. It is reported that processing of smells is mediated by a set of neuroanatomical and neurochemical structures that have been implicated in the pathophysiology of ADHD.<sup>12,13</sup>

Greater errors in odor identification are found in adults with ADHD comparing to healthy control group; although the dif-

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ference was not significant anymore when the two groups matched for IQ.<sup>2</sup> In another study Scheckelman and colleagues reported no altered olfactory performance in adult ADHD patients but they found an association of cortical olfactory processes with hyperactivity and impulsivity in adult ADHD.<sup>14</sup> Gansler reported that olfactory identification in adults with ADHD is less than the normal controls.<sup>15</sup>

There was found only two studies included children and adolescents with ADHD. Romanos et al reported significant improved odor sensitivity (threshold) in un-medicated ADHD children and adolescents compared to odor sensitivity of patients medicated with methylphenidate and healthy controls which are similar to each other.<sup>16</sup> Others reported that olfactory identification ability of children with ADHD is significantly poorer than healthy controls.<sup>17</sup>

Moreover, a study compared odor identification between ADHD adults and a control group. There was no significant interaction between group and gender.<sup>2</sup> Therefore, we hypothesized that there is no gender differences in olfactory processing between boys and girls with ADHD.

Overall, olfactory processing function is not typically studied in ADHD patients and the few existing researches on this topic have yielded inconsistent results.<sup>14,16-18</sup> In general, olfactory processing in children with ADHD, but not in adults with ADHD,<sup>19</sup> seems to be impaired. Therefore, we performed the current study to assess the olfactory function of ADHD children and compare it to healthy controls. Regarding the similarity of the pathways involved in the pathophysiology of ADHD and those of olfactory processing, we hypothesized that olfaction is diminished in ADHD patients in both genders. If this comes true, future studies may wish to make exploration into whether systematic clinical assessment of olfactory function can provide valuable information for the early detection and classification of ADHD patients or whether this sensory domain can be used to predict course of the illness or to monitor treatment response.

## METHODS

The participants were 100 children and adolescents including 50 individuals with ADHD and 50 children and adolescents as the control group. The two groups were match for age, gender and mean school scores (MSS). This study involved a comparison of two groups of children between the ages 8-15 (SD=1.7) years. There were 15 girls and 35 boys in each group. All the patients did not take stimulants for at least seven hours prior to testing.

Inclusive criteria were:

- 1- Chronological age between 8-15 years
- 2- No evidence or history of recent upper respiratory tract infection, sinusitis or nasal allergies.

- 3- No past history of severe head trauma, hypothyroidism, neurologic disorder or gestational and birth problems.

ADHD was diagnosed using the kiddie schedule for affective disorders and schizophrenia (KSADS) according to Diagnostic and Statistical Manual of Mental Disorders, 4th. Edition (DSM-IV).<sup>20</sup> The ADHD children and their parents were interviewed face to face. The parents of the patient participants joined the test but the healthy one's did not. Olfactory identification and threshold were assessed through a smell-test kit provided by the Center of Medicinal and Natural Products Chemistry Research affiliated to Shiraz University of Medical Sciences. The test was composed of two different tasks that were initially explained for the participants by detail. All of the children understood what they had to do. One task was to examine smell identification ability and the other one to assess smell threshold ability. The smell identification part consisted of five glass sniff-bottles, each one containing 4 mL of a specific odorant. Five common odorants including essences of apple, banana, lemon, orange and rose were chosen in respect to their familiarity to almost all individuals (16). The participant's task was to sniff the bottle for 3 seconds and choose the answer from a list of 4 descriptors reported by examiner. The number of correct answers was registered as the sensory identification score of the participant.

The olfactory threshold was assessed by serving a perfume grade Phenyl Ethyl Alcohol (PEA) as the odorant. The diluent used in this study was Propylene Glycol (PG) a relatively odorless and non-toxic material in which PEA is soluble (17). Detection thresholds were determined using a single staircase procedure (18). 16 triplets of bottles were prepared based on 16 different dilutions of PEA in PG in a geometric series with dilution ratio of 2/1. Each triplet was composed of three glass sniff-bottles: one of them containing 4 mL of a particular concentration of the odorant (PEA) dissolved in the diluent (PG), the other two bottles containing 4 mL of the diluents (PG) alone. The participant's task was to sniff each bottle for 3 seconds and identify the bottle that contained the odorant (or the bottle that had smell). If a correct answer was given in 2 successive trials, it would trigger the reversal of the staircase to the next lower concentration. If a wrong answer was given on any trial the next higher concentration was presented. There was a total 4 staircase reversals. The geometric mean of the last 3 reversal points was defined as the threshold estimate of the participant. The testing procedure lasted about 25 minutes. This study was approved by Shiraz university of Medical sciences. Participation was voluntary. The Univariate Analysis of Variance were used to compare the smell identification score (SIS) and smell threshold score (STS) of the two groups considering age and mean school scores covariates. Pearson correlation was performed to assess test-retest reliability.

**Table 1** .The comparison of Smell Identification Score and Smell Threshold Score between patients and controls

	Group	Mean (SD)	Minimum	Maximum
Smell identification score	Control	4.46 (0.76)	2	5
	Patient	3.76 (1.06)	0	5
Smell threshold score	Control	9.75 (2.16)	4	13.6
	Patient	6.4 (3.35)	0	13

**Table 2** .The comparison of Smell Identification Score & Smell Threshold Score between genders within attention deficit hyperactivity disorder group

	Gender	Mean (SD)	p value
Smell identification score	Girl	3.93 (0.96)	0.45
	boy	3.68 (1.1)	
Smell threshold score	Girl	6.28 (3.94)	0.78
	Boy	6.57 (3.12)	

## RESULTS

The two groups of participants did not differ in terms of age, gender and MSS. Their age ranged from 8-15 (Mean=10.8, SD±1.7). The mean (SD) of age for the patients and control group was 10.7 (1.7) and 10.7 (1.6), respectively. The mean of age was not different between the two groups ( $t=0.11$ ,  $df=98$ ,  $p=0.9$ ). 30% ( $n=15$ ) of all participants in each group were girls and 70% were boys. The mean (SD) of MSS for patients and control group was 18.1 (2.2) and 18.8 (2.0), respectively ( $t=1.6$ ,  $df=98$ ,  $p=0.1$ ).

The pearson correlation between SIS results during the first and the second sessions was ( $r=0.55$ ,  $p=0.001$ ). Regarding the STS the correlation results between the 2 sessions was ( $r=0.28$ ,  $p=0.10$ ).

The mean (SD) of SIS and STS are showed in Table 1. Significant differences between the two groups were evident in the two domains of olfactory function. After adjusting for age and Mean school score, both STS and SIC in ADHD group were statistically less than the control group ( $p<0.001$ ,  $p<0.001$ , respectively).

These deficits were not associated with age and Mean School Scores (MSS). None of SIS and STS was related to gender in the ADHD group (Table 2).

## DISCUSSION

The findings from this clinical study show that children with ADHD have significant impairments on odor identification and odor threshold tasks compared to healthy control participants. Such findings corroborate past theoretical predictions that ADHD should be associated with olfactory dysfunction due to their neuro-anatomical and neuro-chemical similarities. Because the prefrontal lobe that is long-standing assumed

to have diminished functioning in ADHD, contains primary and secondary areas for olfactory processing. These olfactory deficits are not associated with age, gender and MSS totally and are not a result of olfactory task difficulty. Another explanation for these impairments could be simply inattention of ADHD children during the olfactory task.

Prior research findings for olfactory function of children with ADHD have been quite inconsistent. The findings of this study lend confidence to one earlier study by Karsz et al.<sup>17</sup> showing that patients with ADHD performed significantly worse than control participants on the olfactory identification test, however, they did not evaluate olfactory thresholds in that study and gender effects on odor identification ability could not be evaluated due to small sample size for girls. Two other studies reported no differences in olfactory function among ADHD patients compared to typical controls.<sup>2,14</sup> One recent study suggested improved olfactory threshold in un-medicated ADHD patients compared to medicated ones and healthy controls.<sup>16</sup> Our result is inconsistent with that study.<sup>16</sup> We could not find any study reported this result.

Determining whether some children with ADHD have olfactory dysfunction has implications for recommending rehabilitation treatment approaches. Suggestion that olfactory dysfunction may predict other behavioral problems or psychopathy in ADHD should be explored further. Although our sample size was small to divide the group with ADHD into intact and impaired on olfactory tasks, a larger sample size may confirm that two distinct subgroups exist within the population with ADHD regarding olfactory function and may these subgroups are related to the traditional three subgroups mentioned for ADHD.

The current study did not support a diagnosis specific gender difference in olfactory testing. There was no differential deficit in odor identification and threshold performance between boys and girls in both patient and control groups. It is in agreement with a recent study of patients with ADHD reported that gender was not a predictor for smell detection ability in ADHD patients according to parent reports.<sup>18</sup> It is nevertheless contrary to results of one previous study done by Murphy et al.<sup>2</sup> which reported that girls with ADHD performed better on olfactory identification tasks compared to boys, however, that study tested adult-age ADHD patients and current study included small sample size .

The impairment in olfactory function in ADHD patients does not seem to be a result of olfactory task difficulty, as some of participants with high MSS performed poorer on both identification and threshold tasks than some of those with low MSS. Moreover, the MSS of participants did not correlate with either SIS or STS totally; suggesting that the decline in olfactory function demonstrated in ADHD is relatively independent of the

difficulty of the tasks. the smell test administered here prepared in accordance with the standard method described by Doty et al and Hummel et al.<sup>21-23</sup>

In sum, our results suggest olfactory deficits are present in ADHD in both domains of smell identification and smell detection threshold. These deficits are not associated with age, gender and MSS totally.

The MSS used here could better be replaced by intelligence test but it was not possible due to limitations in time and fund. The discrepant findings about olfactory function in ADHD patients that have been reported in all respective studies may be due to differences in the measures and procedures employed. Therefore, establishment of an easy administrable, worldwide affordable, and standard test of olfactory function seems warranted. In hopes that true evaluation of olfactory functioning in patients with ADHD enables us to use such assessments in early diagnosis, treatment and prognosis of the disorder. Further studies with larger sample sizes need to be conducted before a differential deficit or intact ability in these olfactory functions can be confidently declared. Future studies are required to obtain more evidence with regard to diagnostic sensitivity, specificity and validity to establish olfactory function as a biological marker of ADHD.

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