



HAL
open science

Odor detection threshold, but not odor identification, is impaired in children with autism

Iva Dudova, Jan Vodicka, Marketa Havlovicova, Zdenek Sedlacek, Tomas Urbanek, Michal Hrdlicka

► **To cite this version:**

Iva Dudova, Jan Vodicka, Marketa Havlovicova, Zdenek Sedlacek, Tomas Urbanek, et al.. Odor detection threshold, but not odor identification, is impaired in children with autism. *European Child and Adolescent Psychiatry*, 2011, 20 (7), pp.333-340. 10.1007/s00787-011-0177-1 . hal-00692192

HAL Id: hal-00692192

<https://hal.science/hal-00692192>

Submitted on 29 Apr 2012

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Iva Dudova, Jan Vodicka, Marketa Havlovicova, Zdenek Sedlacek, Tomas Urbanek, Michal Hrdlicka

Title: Odor detection threshold, but not odor identification, is impaired in children with autism

I. Dudova (✉), M. Hrdlicka

Department of Child Psychiatry, Charles University in Prague, 2nd Faculty of Medicine, V Uvalu 84, 15006 Prague, Czech Republic

e-mail: iva.dudova@lfmotol.cuni.cz

phone number: +420 224 433 400

fax number: +420 224 433 420

J. Vodicka

Department of Otorhinolaryngology and Head and Neck Surgery, University of Pardubice, Faculty of Health Studies, Kyjevska 44, 53203 Pardubice, Czech Republic

M. Havlovicova, Z. Sedlacek

Department of Biology and Medical Genetics, Charles University in Prague, 2nd Faculty of Medicine, V Uvalu 84, 15006 Prague, Czech Republic

T. Urbanek

Institute of Psychology, Academy of Sciences, Veveri 97, 60200 Brno, Czech Republic

M. Hrdlicka

Charles University, 1st Faculty of Medicine, Kateřinska 32, 12108 Prague, Czech Republic.

Abstract

Objective: The aim of our study was to examine odor detection thresholds and odor identification in autistic subjects.

Methods: Thirty-five patients with Asperger's syndrome and high functioning autism (mean age 10.8 ± 3.6 years; 31 boys) were compared with 35 healthy control subjects (mean age 10.4 ± 2.4 years; 28 boys). There were no significant differences between groups with regard to mean age ($p = 0.598$) and gender proportion ($p = 0.324$). Olfactory testing used the Sniffin' Sticks test (Threshold and Identification parts only).

Results: Participants with Asperger's syndrome and high functioning autism, in comparison with healthy controls, were significantly impaired relative to odor detection thresholds (6.3 ± 3.1 vs. 7.9 ± 2.0 ; $p = 0.025$). Autistic participants were significantly better in correctly identifying the odor of an orange (94% vs. 63%; $p < 0.05$) and significantly worse at correctly identifying the odor of cloves (40% vs. 74%; $p < 0.05$). With regard to identification of fourteen other substances, there were no significant differences. There was no significant difference between autistic and control subjects on the total score of olfactory identification ($p = 0.799$). Odor identification ability (as expressed by this total score) correlated significantly with age in the control group ($p = 0.049$) but not in the autism group ($p = 0.103$).

Conclusions: We found impaired odor detection and almost normal odor identification in children with autism. Implications for further research are discussed.

Key words: autism spectrum disorders, sensory abnormalities, olfactory, Sniffin' Sticks, odor threshold, odor identification.

Introduction

Olfactory functions have become a topic of interest in psychiatric research over the last two decades. The most successful work has been done in neurodegenerative disorders like Alzheimer's disease and Parkinson's disease [1, 2]. Neuropathological changes accompanying neurodegenerative disorders are implicated in causing deficits in olfactory abilities. Olfactory deficits may occur early in the course of Alzheimer's disease and discriminate it from multi-infarct and other dementias, although the available reports are inconclusive [3]. Impaired olfaction has been found to be most strongly associated with Parkinson's disease (PD), and it seems to be a biomarker of the disease. Olfactory testing has already become a recommended part of the diagnostic process with regard to its potential for distinguishing PD from other parkinsonian syndromes [4].

In contrast, the processes underlying olfactory abnormalities in disorders of early development are less clear. It was proposed that the neurobiology relevant to deficits observed in neurodevelopmental disorders, such as autism spectrum disorders (ASD), attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD) and schizophrenia might be more related to abnormalities in brain maturation processes than to a specific neuropathological process. Interruption of normal neurodevelopment, reflected by olfactory deficits, may manifest as developmental arrest, developmental lag or possible functional deterioration following the onset of these conditions [3]. In view of olfactory functions, schizophrenia has been the most frequently studied neurodevelopmental disorder. A meta-analytic review of olfaction in schizophrenia revealed that comparable deficits include all psychophysical measures - odor detection, identification and memory [5]. Similar findings in unaffected family members support a genetic contribution to these deficits and suggest an early neurodevelopmental etiology for schizophrenia [3].

Unusual reactions to sensory stimuli are well known features of autism spectrum disorders, and questions regarding this feature have been incorporated into most diagnostic tests for ASD. Children with autism experience increased sensory symptoms compared to children with typical development or those having general delays. Leekam et al [6] reported that over 90% of children with autism had sensory abnormalities and had sensory symptoms in multiple sensory domains. Abnormal behavioral responses have been confirmed by parent report studies [7-9]. Results from these studies suggested that sensory abnormalities in autism are global in nature (involving several modalities) but have the potential to improve with age [10]. Sensory defensiveness defined as being sensory sensitive or having a low threshold for

response to stimuli is described especially as tactile, oral, visual and auditory defensiveness. In contrast, some children with autism are described as being “sensory seeking” defined as sensory insensitive or having a high threshold for response to stimuli [11]. Sometimes a combination of defensiveness and an apparent insensitivity may be described. Distinct sensory processing subtypes in autism, based on specific patterns of sensory processing including taste and smell sensitivity, were differentiated in studies by Lane et al. [12,13]. The degree of sensory difficulties in different domains can affect functioning in many different activities of daily living [14].

Auditory impairment is frequently studied among children with autism, ranging from peripheral and sensorineural hearing deficits or loss to auditory hypersensitivity with bizarre reactions to sounds. A review by Hitoglou et al. [15] addressed a number of studies that have investigated the reason for auditory deficits in patient with ASD. Neurophysiologic studies have reported aberrations in brainstem and cognitive auditory evoked potentials, reflecting maturational changes, whereas pathologic and imaging studies have revealed abnormalities within parts of the auditory system itself. Neurochemical findings suggest a role for serotonin dysfunction in auditory abnormalities [15]. Increased loudness perception of pure tone intensity in children and adolescents with autism, demonstrating the existence of hyperacusis in autism, was reported Khalfa et al. [16]. Tharpe et al. [17] described auditory characteristics in 22 autistic children and 22 of their typically developing peers. The audiologic test battery consisted of behavioral measures (i.e. visual reinforcement audiometry, tangible reinforcement operant conditioning audiometry, and conditioned play audiometry) and physiological measures (auditory brain stem response audiometry, distortion product otoacoustic emissions, and acoustic reflexes). Children with autism demonstrated essentially equivalent results on a battery of physiological auditory tests as those obtained from typically developing children. However, on average, behavioral responses of children with autism were elevated and less reliable relative to those of typically developing children [17]. Jones et al. [18] tested auditory discrimination ability in 72 adolescents with ASD (39 childhood autism; 33 other ASD) and 57 IQ and age-matched controls, assessing their capacity for successful discrimination of the frequency, intensity and duration differences in pairs of sounds. At the group level, auditory discrimination ability did not differ between the adolescents with and without ASD. However, auditory frequency discrimination was enhanced in a subgroup of individuals with ASD that share particular defining features, suggestive of a specific phenotype.

The ability to identify and detect tastes was examined by Bennetto et al. [19] in 21 participants with autism compared with 27 controls. Taste identification was tested via sucrose, NaCl, citric acid, and quinine solutions; taste detection thresholds were established with electrogustometry. Participants with autism were significantly less accurate than control participants in identifying sour tastes and marginally less accurate for bitter tastes. Taste detection thresholds were equivalent [19].

Abnormal reactions to olfactory stimuli in autistic children have been described in several studies [8, 20-22]; however, few studies have dealt with olfactory abnormalities in ASD using olfactory testing. The first of these studies measured odor detection thresholds and odor identification in 12 adult males with Asperger's syndrome (AS) with a mean age of 32.9 years and 12 matched control subjects [23]. The Cain two-bottle test and the University of Pennsylvania Smell Identification Test (UPSIT) [24] were used. Asperger's syndrome subjects were not impaired with regard to odor detection but were significantly impaired with regard to olfactory identification. Assuming that medial temporal lobe structures are implicated in odor detection, while the orbitofrontal cortex is implicated in olfactory identification, the authors suggested that AS was associated with orbitofrontal, but not medial temporal lobe, dysfunction. In 2007 Bennetto et al. [19] examined olfactory and taste functioning in individuals with autism. The study focused on olfactory identification and compared 21 participants with autism (mean age 14.4 years) with 27 well-matched controls. Using the Sniffin' Sticks test, they found that olfactory identification was significantly impaired in those participants with autism.

Brewer et al. [25] investigated olfactory identification in 15 children with high functioning autism (HFA) (mean age 77.8 months) and 15 controls (matched for age, gender and IQ) utilizing a modified visual analogue of the UPSIT. No significant differences were found between the two groups regarding olfactory identification ability. However, smell identification was negatively correlated with age in the HFA group, a finding which was opposite to the relationship found in controls. Finally, May et al. [26] reported results of a 5-year follow-up of children with HFA that followed a previous study. They found that both HFA and controls had improved birhinal olfactory identification. Additionally, unirhinal olfactory identification was compared between HFA, AS and controls (12 participants per group). Unirhinal olfactory identification was reduced in HFA compared to AS and controls, suggesting an orbitofrontal compromise in HFA but orbitofrontal integrity in AS.

The aim of our study was to examine both odor threshold and identification using olfactory testing in a representative group of ASD subjects. Another part of the study, which

dealt with odor pleasantness in ASD, has already been published [27]. Patients with ASD assessed all the odors from the Identification part of the Sniffin' Sticks test, overall, as less pleasant than control subjects; however, the difference was significant only for the smell of cinnamon and pineapple and at the trend level for the smell of cloves.

Methods

Participants

Participants were children and adolescents with autism spectrum disorders, while children and adolescents with normal development were used as controls. Subjects with ASD came from the Department of Child Psychiatry, University Hospital Motol (Prague) and healthy controls were recruited during preventive visitations with their primary care pediatricians who were based in Pardubice Regional Hospital. Inclusion criteria for the autistic group were: (1) diagnosis of Asperger's syndrome, high functioning autism, or a high functioning autism spectrum disorder, confirmed using the Autism Diagnostic Interview – Revised (ADI-R) [28] and/or by the Childhood Autism Rating Scale (CARS) [29], (2) age 6 – 18 years (i.e. age < 19), and (3) IQ \geq 70. Subjects with an organic smell disturbance or an acute respiratory infection were excluded. Inclusion criterion for the control group was age 6 – 18 years (i.e. age < 19). Subjects with a prior psychiatric diagnosis, mental retardation, organic smell disturbance or an acute respiratory infection were excluded. Control participants had no history or evidence of autism. All participants from the control group were screened using the Childhood Autism Spectrum Test (CAST, formerly known as Childhood Asperger Syndrome Test) [30] for autism spectrum disorders. Only individuals with negative CAST results were enrolled in the study. Intelligence testing in the autistic group was performed using Stanford-Binet Intelligence Scale, 4th Edition. IQ data were not collected for the control group because of time constraints. However, all controls were attending mainstream schools with no evidence of intellectual impairment.

The sample consisted of 70 subjects. Power analysis, based on results from pilot data, estimated that a minimum of 34 subjects per group (i.e. 68 subjects in total) would be needed. The group of autistic children included 35 participants (31 boys); mean age 10.8 ± 3.6 years; diagnoses, according to International Classification of Diseases, 10th Revision (ICD-10) [31], included 27 patients with Asperger's syndrome, 5 patients with childhood autism, and 3 patients with pervasive developmental disorder unspecified. The total CARS score was 36.3 ± 3.6 . The control group included 35 subjects (28 boys); mean age 10.4 ± 2.4 years. All

participants were nonsmokers. There were no significant differences between groups with regard to mean age ($p = 0.598$) and gender proportion ($p = 0.324$); details are presented in Table 1. No significant differences regarding history of head trauma or somatic diagnoses were observed between groups. Although the rates of head trauma seemed to be quite high in both groups, they were only mild cases without known consequences. Allergy was the most frequent somatic diagnosis in the autism as well as the control group.

Relative to controls, autistic children had undergone more nasal operations ($p < 0.001$), with adenoidectomy being the most common procedure. Autistic children were also taking more medications ($p < 0.001$), and the difference was mostly due to use of psychotropic medications in this group, whereas no subjects from the control group were on psychotropic drugs. Twenty-two subjects from the autistic group were taking antipsychotics (risperidone, ziprasidone, quetiapine, levomepromazine), fifteen subjects were on selective serotonin reuptake inhibitors (sertraline, escitalopram), four on stimulant medication (methylphenidate), two were being treated with anticonvulsants (valproate, lamotrigine), two with nootropics (piracetam, ginkgo biloba) and one with atomoxetine. Antihistaminergic drugs (levocetirizine, cetirizine, desloratadine, ketotifene) were the most common somatic medications in both groups, and that corresponded to the high rate of allergies in autistic as well as control subjects.

The study was approved by the Ethics Committees of both hospitals. All participants and their legal guardians agreed to participate in the study; legal guardians signed informed consents for subjects under 18 years of age, per Czech law. Only one subject, aged 18.5 years, signed the consent himself.

Materials

Olfactory threshold and identification were examined using Sniffin' Sticks, a commercially available test of olfaction (Burghardt Medical Technology, Wedel, Germany) that contains three parts: Threshold, Discrimination, and Identification. The test has been reliably standardized and is appropriate for both adults and children [32, 33] and has been previously used in the Czech population [34]. Two parts of the test (Threshold and Identification) were used in our study. During testing, odorants were presented using modified felt-tip pens. Instead of ink, the felt tampon was saturated with 4 ml of liquid odorants or odorants dissolved in propylene glycol. For odor presentation, the cap was removed by the investigator and after approximately 3 seconds, the pen's tip was placed centrally, approximately 2 cm in front of the nose.

Procedure

Participants did not eat or drink anything except water for a period of 1 hour before testing. Participants displaying any symptoms of rhinosinusitis (e.g. nasal blockage/obstruction/congestion or nasal discharge, facial pain/pressure and reduction or loss of smell) at the time of testing, were excluded. None of the participants were taking medication for upper respiratory infections, allergies or other medical illnesses on the day of testing. This was verified by the examiner immediately before the start of procedure. The examination was performed in quiet, well-ventilated rooms. The tests were administered in sequence starting with testing of odor thresholds, followed by testing of odor identification (this sequence matches the manufactures guidelines).

Threshold testing. First, patients were acquainted with the odor of n-butanol using a pen that contained n-butanol at its highest concentration. During testing subjects wore a black sleeping mask (i.e. were blindfolded) to prevent visual identification of the odorant-containing pens. Odor thresholds for n-butanol were assessed using a single-staircase, triple-forced choice procedure. Sixteen dilutions were prepared in a geometric series starting with a 4% n-butanol solution (dilution ratio 1:2 in deionized water). Three pens were presented in a randomized order, with two containing the solvent and the third containing the odorant at a specific dilution. The subject's task was to identify the odor-containing pen. Pen presentation (3 pens) to subjects took place every 20 s. Each pen was presented only once. Pens were presented in ascending concentrations until the patient correctly identified the pen filled with odorant in two subsequent trials. Two successful trials triggered the reversal of the staircase and the next lower concentration was then presented. This was continued until the patient missed one concentration; the miss triggered a staircase reversal. The next presentation was a 1-dilution step higher concentration. If this concentration was missed again, the next higher concentration was administered until a dilution step was correctly identified; then a lower concentration was presented. Threshold was defined as the geometric mean of the last four staircase reversal points for a total of seven reversals. The subjects' scores ranged between 0 and 16 [32].

Testing of odor identification. Odor identification was assessed using 16 common odors. Multiple choice task identification, of individual odorants, was performed from a list of four descriptors. In the standard administration, choices were presented as written words. To decrease language demands, autistic participants pointed to color photographs of the choices. The choice words were also printed below each picture and read aloud by the examiner [19].

The same procedure was used with the control group. Subjects had to identify the item that best described the presented odor. The interval between odor presentations was 20 – 30 s. Each one-item score was either 0 (false) or 1 (true). A total score of identification represented the sum of all correct answers. The total score for each participant could range from 0 to 16 [32].

Data analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS, version 15.0). Descriptive statistics for the sample were used. Age difference between groups was analyzed using the Independent–Samples T–test. Differences between groups regarding gender proportion, head trauma, somatic illness and nasal operation, as well as the use of medication, were analyzed using the Chi-Square test. Differences in odor threshold and odor identification (in total) were analyzed using the Mann–Whitney Test. Analysis of single item olfactory identification was carried out using the Chi-Square test, and the results were corrected for multiple comparisons using the Tukey adjustment [35]. Associations of odor threshold and odor identification with age were analyzed using the Pearson correlation.

Results

Odor Threshold

Participants with Asperger’s syndrome and high functioning autism, in comparison with healthy controls, were significantly impaired regarding odor detection threshold (6.3 ± 3.1 vs. 7.9 ± 2.0 ; $p = 0.025$; Table 2). Odor threshold did not correlate with age in the autism group ($r = 0.0006$, $p = 0.974$) or the control group ($r = 0.033$, $p = 0.852$).

Odor Identification

There was no significant difference between autistic and control subjects in total olfactory identification ($p = 0.799$; Table 2). Autistic participants were significantly better in correctly identifying the odor of an orange (94% vs. 63%; $p < 0.05$) and significantly worse in correctly identifying the odor of cloves (40% vs. 74%; $p < 0.05$). Differences in identification of the other fourteen substances were not significant (Table 3).

Odor identification ability (as expressed by the total score of olfactory identification) correlated significantly with age in the control group ($r = 0.355$, $p = 0.049$), however, this was not the case in the autism group ($r = 0.280$, $p = 0.103$).

Discussion

This study provides detailed data on olfactory abilities in autistic children. We found impaired odor detection and almost normal odor identification (fourteen items were without difference, while one item was identified better and one item was identified worse in ASD vs. controls). Brewer et al. hypothesized that understanding the maturation of various olfactory abilities in the context of brain structural and functional changes will be important in understanding the nature and pattern of deficits observed in neurodevelopmental disorders. Childhood-onset disorders like ASD involving brain structures relevant to olfaction are likely to have a greater impact on olfactory functions maturing during childhood (e.g. detection as measured by sensitivity to threshold) as well as adversely affecting functions maturing later during adolescence (e.g. olfactory identification). Early developmental insults affecting olfactory – related neural systems may only manifest as olfactory deficits at a time when such functions would normally be reaching maturity (“growing into deficit”) [3].

Four previous studies have identified intact odor detection and reported both impaired and intact olfactory identification in patients with ASD. In the first study, Suzuki et al. [23] reported normal odor detection, but impaired olfactory identification in adults with Asperger’s syndrome; these results are at odds with our observations but consistent with previous observations which suggested that olfactory identification deficits relating to ASD may progressively deteriorate with age. However, the Suzuki et al. study was based on a relatively small sample (12 subjects in the Asperger’s group and 12 in the control group) and consisted of only male adults (mean age = 33 years). This may also explain the differences between Suzuki et al. and our study.

Impaired olfactory identification in children with high functioning autism was reported by Bennetto et al. [19]. The researchers used older participants than we did (mean age 14.4 versus 10.8 years in our study); thus, it is plausible that the autistic group in our study may “grow into deficit” as they become older. The study examined both olfactory and taste functioning in individuals with autism, but focused mainly on taste examination (taste identification and electrogustometry detection thresholds vs. olfactory identification). Olfactory identification was assessed using Sniffin’ Sticks Odor Identification Screening Test which evaluates receptive identification of 12 common odors. However, the study did not present olfactory identification in total or values for single items, which would have been useful for comparing their results with our results.

Brewer et al. [25] examined children with high functioning autism aged 5 – 9 years and found no significant difference between HFA and control groups with regard to olfactory identification (measured using a visual analogue of the UPSIT). While results from Suzuki et al. and Bennetto et al. differed from our results, the Brewer et al. study was consistent with our research. The absence of an olfactory identification deficit in HFA was suggested to be caused by immature olfactory identification at younger ages. The study employed a previously unused picture format of the UPSIT; additionally, the group of tested participants was small (30 subjects in total).

The hypothesis that olfactory identification abilities, in HFA children, can deteriorate with age, in some HFA participants, was confirmed in a 5-year follow-up in children with HFA by May et al. [26]. They found that olfactory identification improved in both groups (HFA and controls) during the follow-up but development was more heterogeneous in children with HFA. This is in agreement with our data, which was obtained in a group of participants of similar age. We found odor identification ability to be positively correlated with age, in the control group, but not in the autism group.

The second part of the May et al. [26] investigation compared unirhinal olfactory identification in children with HFA, AS and controls; 12 subjects per group, with an average age of 10.8 years in the AS group, 10.6 years in the HFA group and 9.7 years in the control group. Olfactory identification was poorer in HFA compared to AS and controls. Our clinical group included children with both diagnoses (most had AS, but there were five with HFA); therefore, results of intact olfactory identification measured birhinally are consistent with the findings of May et al. Additionally, May et al. found more left nostril deficits in HFA, whereas AS and controls demonstrated better left nostril olfactory identification; however, these differences were not significant. The above mentioned olfactory identification deficits probably indicate impairment of left and right orbitofrontal regions in children with HFA relative to controls.

Another aspect of olfaction involves an estimation of odor pleasantness. Hrdlicka et al. [27] assessed odor pleasantness on a 5-point scale using the Identification part of the Sniffin' Sticks test. Subjects with AS and HFA, compared to healthy controls, perceived the smell of cinnamon and pineapple as significantly less pleasant; while at the trend level, the same was true of cloves. Autistic subjects assessed all odors, overall, as less pleasant than control subjects, but the differences were not significant. In absolute values, orange was perceived as the most pleasant odor among autistic participants and banana for controls. Clove was perceived as the most unpleasant smell for the autistic group and turpentine for the control

group. This observation could lead to an explanation of the current results. The most easily identified item (orange) for the autistic group was also judged as the most pleasant odor, while the item most difficult to identify (clove) was the one judged to be the least pleasant odor. It seems plausible that odor identification ability in autistic children could be related to its pleasantness, at least at the extreme poles of a pleasantness scale.

We are aware of some methodological limitations in our study. We did not perform exact IQ testing in the control group, and relied only on normal school performance of the subjects. Subjects were not medication free, especially in the autism group. Because of potential association with medication taking and olfactory abilities, we performed a literature search and found only minimal effects of antipsychotic and other psychotropic medications on olfactory performance [5, 19, 36, 37]. There was also a high rate of allergies in both groups that corresponded with the use of anti-allergy medication. However, the studies that have evaluated the impact of smell dysfunction associated with allergic rhinitis have generally found an association between the degree of smell loss and the severity of nasal symptoms [38]. In addition, the duration and severity of this olfactory loss were associated with the presence of severe sinonasal disease in patients with allergic rhinitis [39]. None of the participants in our study reported smell loss or showed symptoms of acute rhinosinusitis [40].

Some authors have concluded that examination of olfactory disturbances could provide early markers of impending neurological or psychiatric illness and, in some disorders, including schizophrenia and ASD, could serve as trait markers of cognition [3]. However, research in the field of autism and olfaction is still in its infancy, and further studies on the topic are needed.

Acknowledgments

Supported by the Ministry of Education, Youth and Sports, Czech Republic (research grant MSM 0021620849), the Ministry of Health, Czech Republic (research grants MZOFNM2005 and 1A-8667/4), and by the Institute of Psychology, Academy of Science, Czech Republic (research plan AV0Z70250504). We thank the Autism Research Center (University of Cambridge, UK) for use of the CAST screening tool that was used in our research.

References

1. Mesholam RI, Moberg PJ, Mahr RN, Doty RL (1998) Olfaction in neurodegenerative disease. A meta-analysis of olfactory functioning in Alzheimer's and Parkinson's diseases. *Arch Neurol* 55:84-90.

2. Hawkes C (2003) Olfaction in neurodegenerative disorder. *Mov Disord* 18:364-372.
3. Brewer WJ, Castle D, Pantelis Ch (2006) *Olfaction and the Brain*. Cambridge University Press, New York.
4. Suchowersky O, Reich S, Perlmutter J, Zesiewicz T, Gronseth G, Weiner WJ (2006) Practice parameter: diagnosis and prognosis of new onset Parkinson disease (an-evidence based review). *Neurology* 66:968-975.
5. Moberg PJ, Agrin R, Gur RE, Gur RC, Turetsky BI, Doty RL (1999) Olfactory dysfunction in schizophrenia: a qualitative and quantitative review. *Neuropsychopharmacol* 21:325-340.
6. Leekam SR, Nieto C, Libby SJ, Wing L, Gould J (2007) Describing the sensory abnormalities of children and adults with autism. *J Autism Dev Disord* 37: 894-910.
7. Kientz MA, Dunn W (1997) A comparison of the performance of children with and without autism on the sensory profile. *Am J Occup Ther* 51:530-537.
8. Rogers SJ, Hepburn S, Wehner E (2003) Parent reports of sensory symptoms in toddlers with autism and those with other developmental disorders. *J Autism Dev Disord* 33:631-642.
9. Baranek GT, David FJ, Poe MD, Stone WL, Watson LR (2006) Sensory experiences questionnaire: Discriminating sensory features in young children with autism, developmental delays, and typical development. *J Child Psychol Psychiatry* 47:591-601.
10. Kern JK, TrivediMH, Garver CR, Grannemann BD, Andrews AA, Savla JS, Johnson DG, Mehta JA, Schroeder JL (2006) The pattern of sensory processing abnormalities in autism. *Autism* 10:480-494.
11. Watling RL, Deitz J, White O (2001) Comparison of sensory profile scores of young children with and without autism spectrum disorder. *Am J Occup Ther* 55:416-423.
12. Lane AE, Young RL, Baker AE, Angley MT (2010) Sensory processing subtypes in autism: association with adaptive behavior. *J Autism Dev Disord* 40:112-122.
13. Lane AE, Dennis SJ, Geraghty ME (2010) Brief report: Further evidence of sensory subtypes in autism. *J Autism Dev Disord* DOI 10.1007/ s10803-010-1103-y.
14. Frith U (1992) *Autism: Explaining the Enigma*. Blackwell, Oxford.
15. Hitoglou M, Ververi A, Antoniadis A, Zafeiriou DI (2010) Childhood autism and auditory system abnormalities. *Pediatr Neurol* 42:309-314.
16. Khalifa S, Bruneau N, Roge B, Georgieff N, Veuillet E, Adrien JL, Barthelemy C, Collet L (2004) Increased perception of loudness in autism. *Hear Res* 198:87-92.

17. Tharpe AM, Bess FH, Sladen DP, Schissel H, Couch S, Schery T (2006) Auditory characteristics of children with autism. *Ear Hear* 27:430-441.
18. Jones CRG, Happe F, Baird G, Simonoff E, Marsden AJS, Tregay J, Phillips R, Goswami U, Thomson JM, Charman T (2009) Auditory discrimination and auditory sensory behaviours in autism spectrum disorders. *Neuropsychologia* 47:2850-2858.
19. Bennetto L, Kuschner ES, Hyman SL (2007) Olfaction and taste processing in autism. *Biol Psychiatry* 62:1015-1021.
20. Volkmar FR, Paul R, Klin A, Cohen D, editors (2005). *Handbook of Autism and Pervasive Developmental Disorders*. (3rd ed.). John Wiley & Sons, New York.
21. Leekam SR, Nieto C, Libby SJ, Wing L, Gould J (2007) Describing the sensory abnormalities of children and adults with autism. *J Autism Dev Disord* 37:894-910.
22. Wiggins LD, Robins DL, Bakeman R, Adamson LB (2009) Brief report: Sensory abnormalities as distinguishing symptoms of autism spectrum disorders in young children. *J Autism Dev Disord* 39:1087-1091.
23. Suzuki Y, Critchley HD, Rowe A, Howlin P, McMurphy DGM (2003) Impaired olfactory identification in Asperger's syndrome. *J Neuropsychiatry Clin Neurosci* 15:105-107.
24. Doty RL, Shaman P, Dann M (1984) Development of the University of Pennsylvania Smell Identification Test: a standardized microencapsulated test of olfactory function. *Physiol Behav* 32:489-502.
25. Brewer WJ, Brereton A, Tonge BJ (2008) Dissociation of age and ability on a visual analogue of the University of Pennsylvania Smell Identification Test in children with autism. *Res Autism Spectr Disord* 2:612-620.
26. May T, Brewer WJ, Rinehart NJ, Enticott PG, Brereton AV, Tonge BJ (2010) Differential olfactory identification in children with autism and Asperger's disorder: a comparative and longitudinal study. *J Autism Dev Disord*, doi: 10.1007/s10803-010-1101-0.
27. Hrdlicka M, Vodicka J, Havlovicova M, Urbanek T, Blatny M, Dudova I (2011) Brief report: Significant differences in perceived odor pleasantness found in children with ASD. *J Autism Dev Disord* 41:524-527.
28. Lord C, Rutter M, LeCouteur A (1994) Autism diagnostic interview - revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *J Autism Dev Disord* 24:659-685.
29. Schopler E, Reichler RJ, DeVellis RF, Daly K (1980) Toward objective classification of childhood autism: childhood autism rating scale (CARS). *J Autism Dev Disord* 10: 91-103.

30. Williams J, Scott F, Stott C, Allison C, Bolton P, Baron-Cohen S, et al. (2005) The CAST (Childhood Asperger Syndrome Test). *Autism* 9:45-68.
31. World Health Organization (1992) *International Classification of Diseases* (10th ed.). WHO, Geneva.
32. Hummel T, Sekinger B, Wolf SR, Pauli E, Kobal G (1997) 'Sniffin' Sticks': olfactory performance assessed by the combined testing of odor identification, odor discrimination and olfactory threshold. *Chem Senses* 22:39-52.
33. Kobal G, Klimek L, Wolfensberger M, Gudziol H, Temmel A, Owen CM, et al. (2000) Multicenter investigation of 1,036 subjects using a standardized method for the assessment of olfactory function combining tests of odor identification, odor discrimination, and olfactory thresholds. *Eur Arch Otorhinolaryngol* 257:205-211.
34. Vodicka J, Pellant A, Chrobok V (2007) Screening of olfactory function using odourized markers. *Rhinology* 45:164-168.
35. Moya LA (2003) *Multiple Analyses in Clinical Trials*. Springer, New York.
36. Doty RL (2003) *Handbook of Olfaction and Gustation*, 2nd ed. Marcel Dekker, New York.
37. Naik BS, Shetty N, Maben EVS (2010) Drug-induced taste disorders. *Eur J Intern Med* 21:240-243.
38. Passali GC, Ralli M, Galli J, Calo L, Paludetti G (2) How relevant is the impairment of smell for the quality of life in allergic rhinitis? *Curr Opin Allergy Clin Immunol* 8:238-242.
39. Guilemany JM, Garcia-Pinero A, Alobid I, Cardelus S, Centellas S, Bartra J, Valero A, Picado C, Mullol J (2009) Persistent allergic rhinitis has a moderate impact on the sense of smell, depending on both nasal congestion and inflammation. *Laryngoscope* 119:233-238.
40. Fokkens WJ, Lund VJ, Mullol J et al. (2007) European position paper on nasal polyps. *Rhinology* 45: 1-139.

Table 1: Descriptive characteristics of the autism and control groups.

| | Autism (n=35) | Controls (n=35) | Statistics | | |
|----------------------------|------------------|--------------------|-----------------|----|--------|
| | | | t or χ^2 | df | p |
| Age (M, SD) | 10.8±3.6 | 10.4±2.4 | t=0.530 | 68 | 0.598 |
| Gender (boys: girls) | 31:4 | 28:7 | $\chi^2=0.971$ | 1 | 0.324 |
| Head trauma * (Y:N) | 9:26 | 9:26 | $\chi^2<0.001$ | 1 | 1.000 |
| Somatic diagnosis (Y:N) | 15:20 | 8:27 | $\chi^2=3.173$ | 1 | 0.075 |
| Nasal operation * (Y:N) | 16:19 | 2:33 | $\chi^2=14.658$ | 1 | <0.001 |
| Medication (Y:N) | 30:5 | 5:30 | $\chi^2=35.714$ | 1 | <0.001 |

M – mean, SD – standard deviation, Y – yes, N – no

* All cases were without subsequent impairment of olfactory functions.

Table 2: Odor threshold and identification in autism and control groups.

| | Autism (M, SD) | Controls (M, SD) | Mann-Whitney test | |
|-----------------------------------|-------------------|---------------------|-------------------|-------|
| | | | U | p |
| Odor threshold | 6.3±3.1 | 7.9±2.0 | 421.5 | 0.025 |
| Odor identification (total score) | 10.7±2.6 | 10.6±2.8 | 591.0 | 0.799 |

M – mean, SD – standard deviation

Table 3: Olfactory identification of single items in autistic and control groups as measured with the Sniffin‘Sticks test.

| Item No. (odor) | Correct identification | Autism | Controls | χ^2 test ^a | |
|-----------------|------------------------|------------|------------|----------------------------|--------|
| | | | | χ^2 | p |
| 1 (orange) | Y | 33 (94.3%) | 22 (62.9%) | 10.26 | 0.001* |
| | N | 2 (5.7%) | 13 (37.1%) | | |
| 2 (leather) | Y | 15 (42.9%) | 15 (42.9%) | 0.000 | 1.0 |
| | N | 20 (57.1%) | 20 (57.1%) | | |
| 3 (cinnamon) | Y | 22 (62.9%) | 27 (77.1%) | 1.701 | 0.192 |
| | N | 13 (37.1%) | 8 (22.9%) | | |
| 4 (peppermint) | Y | 33 (94.3%) | 31 (88.6%) | 0.729 | 0.393 |
| | N | 2 (5.7%) | 4 (11.4%) | | |
| 5 (banana) | Y | 28 (80.0%) | 30 (85.7%) | 0.402 | 0.402 |
| | N | 7 (20.0%) | 5 (14.3%) | | |
| 6 (lemon) | Y | 20 (57.1%) | 18 (51.4%) | 0.230 | 0.631 |
| | N | 15 (42.9%) | 17 (48.6%) | | |
| 7 (liquorice) | Y | 23 (65.7%) | 20 (57.1%) | 0.543 | 0.461 |
| | N | 12 (34.3%) | 15 (42.9%) | | |
| 8 (turpentine) | Y | 21 (60.0%) | 18 (51.4%) | 0.521 | 0.470 |
| | N | 14 (40.0%) | 17 (48.6%) | | |
| 9 (garlic) | Y | 22 (62.9%) | 24 (68.6%) | 0.254 | 0.615 |
| | N | 13 (37.1%) | 11 (31.4%) | | |
| 10 (coffee) | Y | 30 (85.7%) | 31 (88.6%) | 0.128 | 0.721 |
| | N | 5 (14.3%) | 4 (11.4%) | | |
| 11 (apple) | Y | 9 (27.5%) | 13 (37.1%) | 1.061 | 0.303 |
| | N | 26 (74.3%) | 22 (62.9%) | | |
| 12 (cloves) | Y | 14 (40.0%) | 26 (74.3%) | 8.400 | 0.004* |
| | N | 21 (60.0%) | 9 (27.5%) | | |
| 13 (pineapple) | Y | 26 (74.3%) | 24 (68.6%) | 0.280 | 0.597 |
| | N | 9 (27.5%) | 11 (31.4%) | | |
| 14 (rose) | Y | 27 (77.1%) | 21 (60.0%) | 2.386 | 0.122 |
| | N | 8 (22.9%) | 14 (40.0%) | | |

| | | | | | |
|------------|---|------------|------------|-------|-------|
| 15 (anise) | Y | 18 (51.4%) | 17 (50%) | 0.014 | 0.906 |
| | N | 17 (48.6%) | 17 (50%) | | |
| 16 (fish) | Y | 33 (94.3%) | 34 (97.1%) | 0.348 | 0.348 |
| | N | 2 (5.7%) | 1 (2.9%) | | |

Y – yes, N – no

^a df = 1

* Significant result ($p < 0.05$) after Tukey correction.