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Olfaction and Taste Processing in Autism

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Abstract

Background: Autism is often associated with sensory symptoms, but few studies have examined chemosensory functions in this population. We examined olfactory and taste functioning in individuals with autism to characterize chemosensory processing and test competing hypotheses about underlying brainstem versus cortical abnormalities.

Methods: Twenty-one participants (10-18 yrs) with autism were compared to 27 well-matched controls with typical development. Taste identification was tested via sucrose, NaCl, citric acid, and quinine solutions applied to standard locations on the anterior tongue. Taste detection thresholds were established in the same regions with electrogustometry, and olfactory identification was evaluated with “Sniffin’ Sticks.”

Results: Participants with autism were significantly less accurate than controls in identifying sour tastes and marginally less accurate for bitter tastes, but were not different in identifying sweet and salty stimuli. Taste detection thresholds via electrogustometry were equivalent. Olfactory identification was significantly worse among participants with autism.

Conclusions: True differences exist in taste and olfactory identification in autism. Impairment in taste identification with normal detection thresholds suggests cortical, rather than brainstem dysfunction. Further research is needed to determine the neurological bases of olfactory and taste impairments, as well as the relationship of chemosensory dysfunction to other characteristics of autism.

Keywords

autism; olfaction; taste; electrogustometry; sensory processing; psychophysics

Autism is a neurodevelopmental disorder characterized by deficits in socialization, communication, and range of interests. Children with autism often present with unusual responses to sensory stimuli. This is confirmed by parent report studies showing that children with autism experience increased sensory symptoms when compared to children with typical development or with general delays (1-3). However, individuals in other clinical groups such as Fragile X syndrome also present with abnormal sensory responsiveness (4), suggesting that sensory dysfunction, broadly defined, may not be specific to autism. The majority of laboratory studies have tested theories of hypo- and hyper-arousal as explanations for sensory dysfunction

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in this population. As a whole, these studies do not provide strong support for a global impairment in arousal in autism (5). Furthermore, hypo- or hyper-arousal models are generally not specific to one sensory modality.

A different approach to understanding sensory dysfunction in autism is to examine the integrity of specific sensory systems. Inconclusive results across previous studies may be clarified by focusing on response patterns within and across distinct modalities. Since the peripheral and central circuitries of sensory functions are well mapped in humans, this approach can also help to advance our knowledge of the neurobiology of autism. This type of modality-specific investigation has been successful in identifying atypical cortical activation in recent studies examining auditory processing in autism (6-8).

Another promising direction for establishing links between behavioral responses and the neurobiology of autism is the study of chemosensory processing. Considerable clinical evidence suggests that individuals with autism have atypical responses to tastes and odors. For example, a recent study examining the specificity of parent-reported sensory symptoms found that abnormal response to taste and smell was the only factor that differentiated children with autism from those with Fragile X syndrome, heterogeneous developmental disabilities, and typical development (2). Other parent report studies similarly documented increased abnormalities in autism relative to controls in the sense of smell (9). One study objectively tested olfactory functioning in 12 adults with Asperger syndrome and found they were significantly impaired in identifying common odors compared to matched, typical controls (10).

Taste and smell are both critical for ingestive behaviors, and there is a growing literature documenting high rates of restricted and atypical eating in autism (9,11-13). Feeding difficulties are estimated to occur in as many as 70 to 90% of children with autism (11,14), yet no empirical studies have examined possible neurobiological mechanisms involved in these difficulties.

While the ability to identify and detect tastes has not been examined in autism, neurobiological studies provide indirect support for the possibility of taste dysfunction. There is evidence of brainstem dysfunction in autism (15), including hypoplasia of the facial nerve (CN VII) nucleus (16). CN VII carries gustatory information from the anterior two-thirds of the tongue via the chorda tympani, and damage to this nucleus or pathway affects taste detection. Identification of tastants and the perception of flavor is mediated centrally by a complex network involving regions of the thalamus, insula/operculum, orbitofrontal cortex (OFC), and amygdala (17). Several of these regions have been implicated in autism, most notably the OFC and amygdala (see 18 for a review).

In the present study, we build on previous findings of parent-reported smell and taste abnormalities in autism (2,9) by characterizing chemosensory processing using objective, laboratory-based measures. We also extend Suzuki et al's (10) study of adults with Asperger syndrome by testing odor identification in a sample of children and adolescents with high-functioning autism compared to well matched, typically developing controls. Finally, by measuring both taste identification and detection, we test competing hypotheses about underlying brainstem versus cortical abnormalities. We hypothesized that participants with autism would be less accurate than controls in both odor and taste identification. We did not have a strong prediction about taste detection thresholds: impaired performance would suggest brainstem or peripheral involvement, whereas intact taste detection and impaired identification would implicate regions above the level of the chorda tympani and facial nerve nucleus.

Studies of olfaction in individuals with schizophrenia have demonstrated that odor identification deficits are related to negative symptoms in the disorder, such as social

impairment, affective flattening, and avolition (19-22). Because of the similarities between these symptoms in schizophrenia and autism (23-25), we were interested in whether olfaction was related to social impairment in autism as well.

Methods and Materials

Participants

Participants were 21 children and adolescents with high-functioning autism and 27 typically developing controls. Ages in both groups ranged from 10 to 18 years. Participants were recruited from the community or from a database of families who participated in previous studies.

Diagnoses of Autistic Disorder (based on DSM-IV-TR, 26) were established with the Autism Diagnostic Interview-Revised with the caregiver (ADI-R; 27) and the Autism Diagnostic Observation Schedule with the participant (ADOS; 28). These standardized measures yield diagnostic information as well as scores within core symptom domains (e.g., communication, socialization). Only participants who met diagnostic criteria on the ADI-R and ADOS, as well as clinician judgment, were invited to participate. Participants with autism had no diagnoses of genetic syndromes or definable postnatal etiologies for their developmental difficulties (e.g., head injury, tumor).

Typically-developing controls had no history or evidence of autism on the ADI-R or ADOS, no behavioral or psychiatric disorder as assessed by parent ratings on the Child Behavior Checklist (29), no learning disabilities, and no history of head trauma. There were also no concerns about autism spectrum disorders in their 1st or 2nd degree relatives.

Cognitive ability was measured with the Wechsler Intelligence Scale for Children, 4th Ed. (30) or the Wechsler Adult Intelligence Scale, 3rd Ed. (31). Because our identification tasks had a receptive language component, we administered the Peabody Picture Vocabulary Test, 3rd Ed. (PPVT-III; 32). All participants had cognitive ability and receptive language standard scores greater than 85. Participants with autism and controls were matched by group on chronological age, Full Scale IQ, PPVT-III Standard Score, socioeconomic status (33), gender, and handedness (see Table 1).

This research was approved by the University of Rochester's Research Subjects Review Board. Prior to testing, written informed consent was obtained from parents and from 18-year-old participants. Younger participants also gave written assent.

Materials

Taste Identification—We measured basic taste identification with a regional chemosensory exam. Four tastants were used: sweet (sucrose; 30%), salty (NaCl; 10%), sour (citric acid monohydrate; 10%), and bitter (quinine sulfate dihydrate; 0.25%). Concentrations were based on previous research (34,35) and piloting with children and young adults. Tastants were suspended in a 2% carboxymethylcellulose solution to minimize spread of the stimulus across the tongue; carboxymethylcellulose alone was used as a control. Solutions were prepared in the University of Rochester's Strong Memorial Hospital Pharmacy under sterile conditions and stored at 4°C. Solutions were brought to room temperature before use. The tastants were presented in one of two quasi-random orders, counterbalanced across groups and side of initial presentation. The orders included multiple presentations of each stimulus to prevent speculation about remaining stimuli. Quinine was always presented last because it can leave an aftertaste in the mouth that could affect subsequent trials.

Tastant solutions were applied to the right or left anterior two-thirds of the tongue via a sterile cotton swab. Participants rinsed with water and expectorated between trials. To reduce migration of the solutions to other areas of the tongue and soft palate, participants kept their mouths open and tongues slightly extended until they had responded by pointing to one of four choices. This allowed us to evaluate function only within the area innervated by one of the chorda tympani to facilitate comparison with the electrogustometry thresholds described below. Response choices were presented visually as printed words (which were also read aloud by the examiner) and paired with representative pictures (e.g., saltshaker) in order to reduce language and working memory demands. Accuracy was measured for each tastant and side of the tongue separately.

Electrogustometry Detection Thresholds—To examine whether taste identification deficits could be secondary to dysfunction earlier in the taste pathway (e.g., chorda tympani), we used electrogustometry to establish taste detection thresholds (TR-06 Rion Electrogonometer, Sensonics Inc., Haddon Heights, NJ). Thresholds were measured in the same anterior region evaluated in the Taste Identification test. Weak anodal stimuli ($<400\mu\text{A}$) were presented via an electrode placed on the tongue. Liberation of protons at the site activates ionic taste receptors, producing a sour/metallic taste or sensation (36). We measured detection thresholds rather than sour taste identification, since the higher currents needed to elicit reliable, accurate labeling may also stimulate the trigeminal nerve (37).

Electrical stimuli were delivered for a duration of 1-sec via flat, circular electrodes (5 mm diameter) attached to a probe held by the examiner. We used a dual electrode method, in which stimuli were presented randomly to the right or left side of the tongue (1.5 cm from anterior midline and 1.5 cm from front). Participants indicated the side on which the taste/sensation was detected with a hand raise.

Thresholds for the right and left sides were established concurrently, using a two-alternative forced-choice adaptive staircase procedure as described in Loucks and Doty (38). Initial stimulus presentation was at 10 dB, which is in the middle of the range measured by the instrument (-6 to 34 dB, corresponding to 4 to $400\mu\text{A}$). Stimulus intensities were increased in 2dB steps following incorrect responses, or repeated at the same intensity following correct responses, until participants reached an initial criterion of five consecutive correct responses. After this basal was met, stimulus intensities were decreased or increased (i.e., staircase was reversed) in 2dB steps as follows: after two correct responses on one side at a stimulus level the intensity of next presentation on that side was decreased, and after one incorrect response the stimulus intensity was increased. This procedure yields efficient and reliable estimates of psychophysiological thresholds (39). The side of presentation was randomized by computer for each trial. Performance was measured as detection thresholds, which were the average of the last four of seven staircase reversal points.

Olfactory Identification—Olfactory identification was assessed with the “Sniffin’ Sticks” Odor Identification Screening Test, a commercially-available, standardized test of olfaction (Burghart Medical Technology, Wedel, Germany; 40,41). This test evaluates receptive identification of 12 common odors. It is appropriate for children and adults (41), and has been used widely to evaluate olfactory dysfunction in patient groups. Odorants are presented in felt-tip pens; instead of ink, the absorbent material in the pen is saturated with an odorant. The pens were uncapped by the examiner for 3 sec, then placed 1-2 cm in front of the participant's nostrils. Participants indicated the odorant among a field of four choices. In the standard administration, the choices are presented as written words. To decrease language demands, we adapted the response format: participants pointed to color photographs of the choices and foils. The choice words were also printed below each picture, and read aloud by the examiner. Our pilot studies indicated that this adaptation was important for reducing verbal demands for children with

autism. A similar adaptation found that photographs did not improve odor identification performance in healthy volunteers (42), so our adaptation was not likely to significantly increase performance in the control group. We also presented this task in two random orders, which were counterbalanced across groups. As is standard in other studies, performance was measured by average percent accuracy across the 12 trials.

Procedures

Participants did not eat or drink anything except water at least one hour prior to testing. We rescheduled testing if participants reported or showed evidence of nasal congestion or other respiratory illness. None of the participants were taking prescription or over-the-counter medication for upper respiratory infections, allergies, or other medical illnesses at the time of testing. None of the control participants were taking psychotropic medications for psychiatric diagnoses; however, it was not feasible to identify a sufficient number of potential volunteers with autism who were not prescribed psychotropic medications. Although some psychotropic medications have been shown to affect taste and saliva production, they are less commonly associated with decreased olfaction (43). Because stimulant medications (e.g., methylphenidate) are short acting, any participants taking these medications stopped taking them 24 hours prior to testing. Nine of the participants with autism were taking either a selective serotonin reuptake inhibitor (e.g., fluoxetine, citalopram; $n=7$) or risperidone ($n=2$). Because we could not withhold these medications without disrupting treatment, we repeated all the between-group analyses, comparing those patients with and without medications. We found no significant differences between the groups (in fact, mean performance levels were equivalent or even slightly better in the medicated group). Our null results for medications are consistent with research on schizophrenia, in which medication status does not attenuate performance differences on a range of olfaction tests (44).

Data Analysis

Prior to inferential statistics, we examined performance based on presentation order for the two identification tasks. Performance did not differ based on order, so results were collapsed for further analyses. Group differences on all tasks were evaluated with Analysis of Variance (ANOVA). Effect sizes were calculated with partial eta squared (η^2_{partial}). Values between .01 and .06 are generally considered a small effect, between .06 and .14 a medium effect, and those above .14 are regarded as a large effect. Finally, we used Pearson correlations to examine the relationship between taste detection threshold and taste identification in both groups, and between olfactory identification and social impairment in the group with autism.

Results

Taste Identification

We found no significant effects of side of presentation, so results were collapsed across right and left sides. Group performance was evaluated separately for each tastant by ANOVA (Figure 1). Participants with autism were significantly worse than controls at identifying citric acid, $F(1,46)=5.14$, $p=.03$, $\eta^2_{\text{partial}}=.11$, and marginally worse at identifying quinine, $F(1,46)=3.41$, $p=.07$, $\eta^2_{\text{partial}}=.08$. The groups were not different in accuracy for the other tastes: sucrose, $F(1,46)=.04$, $p=.84$, $\eta^2_{\text{partial}}<.01$; salt, $F(1,46)=1.43$, $p=.24$, $\eta^2_{\text{partial}}=.03$. The average accuracy scores for these tastants suggest that these null findings are not attributable to ceiling effects.

Electrogustometry Detection Thresholds

We found no significant effects of side of presentation on this task, so results were collapsed across sides. An ANOVA showed no significant difference between participants with autism and controls in taste detection thresholds, $F(1,46)=.53$, $p=.47$, $\eta^2_{\text{partial}}=.02$ (Figure 2).

We also examined the relationship between electrogustometry thresholds and localized sour taste identification since anodal electrogustometry activates sour taste receptors. Since participants with autism were significantly worse than controls in sour taste identification, this analysis was conducted separately for each group. As expected, there was a significant negative correlation between detection threshold and sour taste identification in the control group, $r(25) = -.48, p = .01$, indicating that control participants with lower (better) thresholds were more accurate in sour taste identification. In contrast, these measures were unrelated in the group with autism, $r(19) = .09, p = .71$. The difference between these correlations was significant when converted with Fisher's r to z' transformation (45), $Z = 1.97, p < .05$. The lack of a relationship between detection and identification in the autism group supports the idea that autism-specific impairment in taste identification is not attributable to impaired detection.

Olfactory Identification

An ANOVA showed that participants with autism were significantly less accurate than controls on olfactory identification, $F(1, 46) = 7.97, p = .007, \eta^2_{\text{partial}} = .15$ (see Figure 3).

Previous research has found links between olfactory identification and negative symptoms in schizophrenia (19,20,22). A recent study that examined this relationship in schizophrenia showed that the overall link between smell identification deficits and negative symptoms was driven primarily by diminished social drive, and particularly by lack of spontaneity and flow of conversation and impaired volition (46). We performed a secondary analysis to examine the relationship between olfactory identification and comparable scores taken from the ADI-R, the standardized parent interview we used for autism diagnosis. The scores on the ADI-R that most closely approximate the key negative symptoms identified above involved participants' current social interchanges and initiation and maintenance of conversations. In participants with autism, olfactory identification was marginally related to their ability to engage in social verbalization or chatting, $r(19) = -.44, p = .05$, and significantly related to their skill at maintaining a reciprocal conversation, $r(19) = -.56, p = .01$, where children with worse performance on the olfactory identification test were more likely to have greater social impairment. As a contrast, we also tested the relationship of olfaction to blunted affect, the negative symptom that showed the *smallest* (and nonsignificant) relationship to olfactory identification in Malaspina and Coleman's study. Similarly, in our study, the ADI-R score for range of facial expressions was not significantly related to olfactory identification in participants with autism, $r(19) = -.17, p = .45$.

Discussion

The present study provides empirical support for clinical and caregiver observations of atypical chemosensory processing in autism. We found that children and adolescents with high-functioning autism were significantly less accurate than matched controls in identifying basic tastes and odors. Matching on receptive language and Full Scale IQ, as well as the nonverbal response format of our tasks, suggests that these performance differences were not the result of cognitive limitations. These results also help to clarify the inconsistencies across previous reports of sensory dysfunction in autism. Our participants with autism were not impaired on all tasks measured; even within the domain of taste identification, we found a pattern of impaired and intact ability. Participants with autism were significantly worse than controls at identifying citric acid and marginally worse at identifying quinine, but the groups did not differ in their accuracy for sucrose or salt.

Another goal of this study was to evaluate whether taste processing patterns in autism were consistent with damage at the brainstem level. We found no differences between our groups on a psychophysiological measure of taste detection. Since we measured electrogustometry thresholds for detection rather than identification, it is unlikely that participants' performances

were affected by trigeminal stimulation. Electrogustometry is effective in detecting chorda tympani nerve damage (47); thus the lack of group differences on this measure suggests that our finding of impaired taste identification in autism is not secondary to dysfunction at the level of the chorda tympani or facial nucleus. While electrogustometry is generally considered effective in testing the integrity of taste pathways (48), anodal stimulation only activates sour taste receptors. Thus, we cannot make assumptions about the function of other classes of taste receptors. Despite these limitations, our clear pattern of impaired sour taste identification with intact electrogustometry detection implicates cortical dysfunction for individuals with autism. Furthermore, while electrogustometry was related to sour taste identification in the controls, these abilities were not associated in the group with autism, further suggesting that dysfunction above the level of the brainstem is driving performance decrements in this group.

Our data also provide strong support for the presence of olfactory deficits in autism. Participants with autism were significantly less accurate than controls in identifying common odors. This finding is consistent with Suzuki et al's (10) report of odor identification deficits in Asperger syndrome, as well as parent reports of atypical smell processing in questionnaire studies (2, 9). Our data do not allow us to draw conclusions about the level at which odor identification deficits are likely to arise in the nervous system because we did not measure olfactory detection thresholds. Previous research shows that adults with Asperger Syndrome, while impaired on olfactory identification relative to matched controls, demonstrated intact olfactory detection (10). However, that study was based on a relatively small sample ($n=12$ per group), and detection thresholds were established with 1-butanol, which can be a trigeminal stimulant (49). Thus, further studies are needed to evaluate the role of detection in olfactory identification deficits in autism.

There has been considerable recent interest in the role of olfactory dysfunction in other neurobehavioral disorders, including schizophrenia (50,51) and obsessive-compulsive disorder (52,53), as well as neurodegenerative disorders, including Parkinson's disease (54), Alzheimer's disease (55), and adulthood Down syndrome (56). Because the neural circuitry of this system is well characterized, olfactory functioning is increasingly being used as a behavioral probe for the functional integrity of brain regions in these disorders. In addition, there is evidence for moderate heritability of olfactory identification in a study of healthy twins (57). Studies of schizophrenia found that unaffected family members, including monozygotic twins (58) and other 1st or 2nd degree relatives (59), performed worse on olfactory identification than healthy controls, but somewhat better than their affected relatives, suggesting that olfactory dysfunction could be related to a predisposition for psychosis. Individuals with familial risk for Alzheimer's disease also show impairments in olfactory functions (60,61). Together, these studies suggest a genetic vulnerability to olfactory dysfunction in other disorders, so further investigation may be warranted in autism.

The degree of olfactory identification dysfunction in our autism sample (Cohen's $d=.86$) approached the strength of the effect size reported in a meta-analysis of 18 studies of olfactory identification in schizophrenia (mean weighted $d = .94$; 44). Because of the link between olfaction and social drive in schizophrenia, and the similarities between some of the social withdrawal symptoms in the two disorders, we examined this relationship between olfaction and social drive in our sample. Our results suggest a similar relationship between olfactory identification and current ratings of initiation and maintenance of conversation and social interchange in autism. These correlations are notable, considering the small sample size and relatively restricted range on the social variables. Although these findings are very preliminary, they do suggest that future studies of olfaction in autism should include careful measurement of social functioning to investigate this issue further.

Our findings of impaired taste and odor identification with intact performance on electrogustometry suggest that chemosensory processing problems in autism occur at the cortical rather than brainstem level. Several regions may be plausible candidates for further consideration. For example, the OFC contains secondary taste cortex (62) and olfactory cortex (63), and plays a key role in flavor perception through the integration of taste and olfactory information (64,65), although other brain areas are also involved (66). The OFC is also involved in stimulus-reinforcement association learning, including the association of olfactory stimuli and the primary reinforcement value of taste (67). Several groups have proposed dysfunction in OFC or OFC-amygdala circuitry in autism (18,68,69), and recent neuroimaging studies reported evidence of developmental abnormalities in OFC volume (70,71).

While the current study found clear differences in chemosensory processing compared to typically developing controls, individuals with other developmental disabilities may also show impairments in these specific functions, as they do with more general sensory symptoms (4). Future studies should include control groups of individuals with other developmental disabilities such as Fragile X syndrome and Down syndrome to evaluate the specificity of these deficits. Future investigations should also extend these findings to younger children with autism, and those with more significant neurocognitive impairments. Sensory symptoms are often more clinically problematic in these groups, so evaluation of chemosensory abilities as well as other symptoms (e.g., repetitive behaviors) will help to determine which factors relate most to sensory impairments in autism.

Difficulty in identifying basic tastes and smells may contribute to high rates of food refusal and selectivity reported in children with autism. The development of food preferences begins in early toddlerhood, and depends on a complex interaction between biological predispositions (e.g., taste or olfactory processing), tendencies toward food neophobia (i.e., rejection of novel foods), the ability to learn associations between foods and contexts, and the eating environment itself (see 72 for a review).

Future study of chemosensory processing in autism may reveal important links between brain function, clinically relevant behavior, and treatment. Furthermore, recent advances in the genetics of both taste and olfaction, as well as the relationship between olfactory impairments and neuropsychological and social dysfunction in other disorders, raise the possibility that chemosensory dysfunction could serve as a biobehavioral marker in autism.

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Figure 1. Taste Identification Accuracy

Group means for percent accuracy on individual tastants, collapsed across side of presentation. Error bars represent standard error of the mean. * $p < .05$, † $p < .10$

Figure 2. Electrogustometry Detection Thresholds

Boxplots show each group's full range of threshold detection points for the anterior tongue (chorda tympani region), collapsed across side of presentation. Boxes represent the interquartile ranges, whiskers are the 10th and 90th percentiles, and open circles are scores beyond these points. Group means are indicated by a dashed line, and medians by a solid line. Output current for thresholds is reported in decibels (possible range was -6 to 34 dB).

Figure 3. Olfactory Identification

Group means for percent accuracy on “Sniffin’ Sticks” Odor Identification Test. Error bars represent standard error of the mean. ** $p < .01$

Table 1
Descriptive characteristics of the autism and control groups

	Autism <i>M (SD)</i>	Control <i>M (SD)</i>	<i>F</i> or χ^2	<i>p</i>
<i>n</i>	21	27		
Age	14.35 (2.46)	14.48 (2.16)	.04	.85
Full Scale IQ	105.62 (11.37)	109.73 (7.88)	1.91	.17
PPVT-III	113.76 (11.28)	118.26 (11.14)	1.45	.24
Socioeconomic Status	52.12 (10.45)	54.18 (8.63)	.39	.53
Handedness (R:L)	16:5	23:4	.63	.43
Gender (M:F)	17:4	20:7	.32	.57

Note. PPVT-III = Peabody Picture Vocabulary Test, 3rd Ed. (standard scores). Socioeconomic status was measured with Hollingshead's (1975) Index.