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Evaluating the Prevalence of Olfactory Dysfunction in a Pediatric Population

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Introduction

Our sense of smell provides information about our environment and food quality that is critical to our health and safety, a nutritious diet, and psychological well-being. Although smell loss has several potential etiologies (e.g., head trauma, allergic rhinitis, and enlarged adenoids) that are common among children, studies evaluating the prevalence of olfactory dysfunction in the pediatric population are rare. Moreover, of the available tests for evaluating olfactory function in adults, children are likely to be unfamiliar with many of the odor stimuli used and have limited ability to read and identify labels to select from alternative choices, which is the typical adult response option. Consequently, specialized forms of olfactory tests must be developed for this population. Based on the format of the San Diego Odor Identification Test¹ and the delivery system of the Brief Smell Identification Test², this paper reviews the development of a short form odor identification test utilizing standardized odor stimuli suitable for administration to children between 3–17 years of age.

Why Study Olfaction in Children?

Routine evaluations of visual and auditory acuity are performed in childhood in order to identify deficits in sensory abilities that may impair normal development and learning. Given the importance of vision and hearing to normal functioning, it is not surprising that specialized tests for evaluating pediatric populations have been developed^{3–5}. In contrast, tests of olfactory function for very young children are neither routinely available nor administered. This likely represents an oversight in our appreciation of the importance of the olfactory system for identifying hazards in our environment and ensuring nutritious food choices. Given the evidence that olfactory learning may be particularly robust during childhood⁶, identifying deficits in this age group could be important for normal development.

Although congenital anosmia is estimated to be a relatively rare occurrence⁷, there are a number of conditions occur in early childhood that can lead to either partial or total loss or distortion in olfactory ability. For example, the olfactory system is particularly vulnerable to head injuries which may sever the olfactory nerve and result in a complete loss of olfactory ability. Even swelling in this area can prove temporarily disabling to the sense of smell. Several studies of children have shown measurable deficits in children with head injury or traumatic brain injury and the degree of performance decrement is associated with the severity of the head trauma^{8,9}. Conditions which produce significant nasal congestion or nasal passage obstructions, such as allergies or enlarged adenoids may also impair olfactory sensitivity. A study of children before and after adenoidectomy revealed that performance on an odor identification test improved following the procedure¹⁰.

Beyond these known risk factors, there may be additional disease or environmental factors that can impact olfactory ability among young children. As one example, animal studies have demonstrated that a variety of heavy metals (e.g., cadmium, manganese) that come into contact with the olfactory epithelium can be taken up in the primary olfactory neurons and be transported to the olfactory bulbs and even further into other areas of the brain^{11,12}. Given the large number of children who are still exposed to lead dust in their home environment, we might expect to observe some impact on olfactory performance among children with high blood lead levels. For these reasons, there is increasing interest and impetus to screen children at an early age for olfactory function.

The NIH Toolbox

The NIH Toolbox for assessment of neurological and behavioral function is a project funded by the NIH Blueprint for Neuroscience Research, an initiative sponsored by 16 NIH Institutes, Centers, and Offices that support neuroscience research¹³. The goal of the NIH Toolbox project is to develop brief but comprehensive measurement tools for assessing cognitive function, emotional health, sensory and motor function across the entire lifespan. The Toolbox aims to be responsive to the needs of researchers in a variety of settings, but with particular emphasis on measuring outcomes in clinical trials and functional status in large epidemiological and longitudinal studies.

The tests which will ultimately be included in the Toolbox must meet a number of specific criteria. They must be brief, easy to use and administer in a variety of settings and with different subgroups, but psychometrically sound. Additionally, they must be available for use without intellectual property issues and at minimal cost to the users, who may be incorporating items from the Toolbox as only a subset of measures to be used in their overall study.

The Toolbox project has placed special emphasis on developing or modifying tests for use among pediatric populations, recognizing that few standardized tests exist to assess normal children for motor and sensory function. Moreover, in many of the motor and sensory domains, there is a general reliance on proxy reporting and national 'norms' if they do exist, are typically based on English-speaking populations.

Issues in the Development of Pediatric Olfactory Assessment Tools

There are numerous challenges to evaluating olfactory function among children, particularly in the age ranges from 3–5 years old.

- There are no tests which have been validated or provide normative data among children this young.

- Most of the existing tests utilize odor stimuli that would be unfamiliar to many children. In fact, the cultural and experiential specificity of certain items in many odor identification tests limit their use across diverse populations, and often necessitate the development of culture-specific test versions ^{14,15}.
- The cognitive and linguistic demands of many existing tests confound the interpretation of the results from young children.
- Children's attentional resources also need to be considered in limiting the number of items in a test, even while recognizing that the reliability and specificity of any test increases with the number of items.

Chemosensory researchers who have worked extensively with young children have argued that age-appropriate, game-like tasks that are fun for children and minimize the impact of cognitive and language development are necessary in order to ensure that what is being measured is olfactory ability, not cognition ^{16,17}. Hedonic judgments disguised as a game (for example, give odors you like to Big Bird, odors you don't like to Oscar the Grouch) have been shown to be reliable methods for children as young as three years of age. In slightly older children, matching odors to pictures is a successful method, provided the child has experience with the particular odor stimuli being evaluated ¹⁸.

For purposes of the Toolbox effort, we identified several published or commercially-available tests which could serve as the building blocks for a pediatric specific test that meets the Toolbox criteria. The Brief Smell Identification Test ² is a 12-item scratch and sniff test representing a subset of the items from the 40-item Smell Identification Test. Items in the B-SIT have been selected to have broader cross-cultural familiarity. The micro-encapsulated stickers provide an efficient and easy way to administer standardized odor stimuli and individuals are asked to select from four possible labels, which one best corresponds to the source of what they smell. The test has excellent reliability (>.80) and although less specificity than its parent (the 40-item SIT), can be administered to adults and older children in under 5 minutes. However, data on this test exist only for children aged 5 and older, and performance for children aged 5–9 is similar to adults in their 8th decade where true deficits in olfaction are known to exist ¹⁹. This raises the question as to whether the test is actually measuring olfactory ability among children this young or whether cognitive or language confounds are responsible for the relatively poor performance. In addition to the linguistic response requirements in the current version, however, the costs of this commercially-available test may limit its use in studies where olfaction is not the primary endpoint.

Recognizing that instrument costs in large scale epidemiological trials could produce an obstacle to their adoption, Murphy and colleagues ¹ developed a version of odor identification test using grocery store items which are then placed in opaque plastic bottles. In the San Diego Odor Identification Test (SDOIT), 8 everyday items are sniffed and matched to the appropriate line drawing (out of 20 possible), keeping costs low and removing the reading and language issue which can confound the assessment in young children. Performance on this test is quite good and reliability is high (>.80). However, given that the test uses actual food items, concerns about standardization of stimuli and the need for investigators to prepare the stimuli themselves may prove to be barriers to the use of this test in many situations.

Based on the existing tests and methodologies, the goal of the olfactory domain team was to refine a child-specific test that utilizes standard, easily obtained stimuli, can be administered in less than 5 minutes, uses both pictures and words as response options and maintains good reliability, sensitivity and specificity.

The Toolbox Pediatric Odor Identification Test

The version of the test which is currently under development uses items which have been identified as highly familiar to children in the 5-9 year age group. Our goal is to identify up to 6 items whose odors are readily recognized by most American children from 3-9 years old and that can be easily depicted in picture form. Currently, there are two versions of the test, each containing six odor stimuli. Table 1 lists the odor stimuli and identifies which of them are used in the SDOIT and the B-SIT. For standardization purposes and ease of administration, we have produced micro-encapsulated versions of each odorant in a sticker format which can be scratched by the administrator or the test taker to release the odor.

The test uses both pictures and words of each stimulus as response options. The high resolution quality of the pictures will enable us to conform to the Toolbox format by having the children view the picture alternatives and respond on a touch screen to facilitate data collection. To ensure that the pictures are recognized appropriately, children are first given a pre-test in which they are asked to point to the picture that the experimenter names. If they incorrectly identify a picture, they are told the correct name and given the opportunity to point to the correct picture again. If they fail to identify the picture after feedback, responses to that item will be disregarded.

For each odor stimulus, there are four response options shown: one is correct and three are distractors. Among the distractors, however, one is categorically or perceptually similar to the correct item (i.e., chocolate vs. coffee) and is considered a 'near-miss'. The other two are very dissimilar and are considered true distractors. This methodology is based on the Monell-Jefferson Chemosensory Clinical Research Center odor identification test²⁰ and allows us to determine if the child can identify the perceptual features of the odor sufficiently to classify it as a similar odor source. As with the Monell-Jefferson CCRC test, correct responses are given a score of '1' while near-misses are given a score of 0.5. This modification also allows us to obtain additional resolution on a test with a small number of items.

Finally, the use of picture and word response options will enable us to conform to the Toolbox format by having the children view and select response alternatives on a touch screen to facilitate data collection.

Test Plan and Populations

Children between the ages of 3 and 17 will be tested, with a particular emphasis on obtaining sufficient numbers of children in the 3-9 year range. To determine familiarity with the odor stimuli, the accompanying parent or guardian will also take the same version of the test as the child and answer a questionnaire about their and the child's familiarity with the food or odor items on the test. This will allow us to correctly interpret whether misses on the test are due to unfamiliarity with the odor stimulus or a true measure of olfactory dysfunction. The parent or guardian will also complete a short health questionnaire for the child focusing on conditions which are known to impair olfactory ability, such as allergic status, frequency of colds and prior head injuries.

We are currently testing at two sites: the pre-operative outpatient facility at the A.I. duPont Hospital for Children in Wilmington, Delaware and at the Monell Chemical Senses Center in Philadelphia, PA. At the duPont Hospital, patients are drawn from the Delaware Valley region having a pediatric population of 2.2 million children under the age of 18. Approximately 14,000 children per year undergo procedures at this facility and 12,500 of those go through the pre-op outpatient facility where testing will take place. Of those undergoing surgery, 35% have ENT-related surgery and this is the population among which

we might expect to see some olfactory disturbances. Our current plan estimates that 50 children and their parent/guardian can be evaluated each week, and within the hospital network, additional sites can be recruited as needed.

At the Monell Center, children are drawn from the Philadelphia metropolitan area. From past experience, approximately 600 children are tested annually in other studies. The brevity of this olfactory assessment makes it easy to append to existing studies to increase the clinical population sample. An additional advantage at the Monell Center, however, is that there are fewer time constraints on testing than at the hospital site.

The preliminary results from pre-testing at both the duPont Hospital and the Monell Center have shown that children as young as three years old can complete the pre-test and the olfactory test well within a 5-minute period and appear to be enjoying the game-like experience. Children aged 6 and up, complete the odor identification portion of the test in less than 2 minutes. Table 2 presents a brief summary of the preliminary results, stratified according to age group. Summarizing across both stimulus sets, the number of correct responses increases with age categories. However, the initial analysis suggests that certain items are better recognized among even the oldest age group than others and the outcome of these results will be the most important for determining the final stimulus selection. The current plan is to continue the pre-testing phase in order to determine the optimal stimulus selection, at which time the test stimuli will be finalized. Following that, the collection of normative data for children at all age groups will take place at multiple sites, including those already identified.

Summary

Increased awareness of the role of the olfactory system for safety, adequate nutrition and many aspects of quality of life should impel far more widespread evaluation of this sensory ability across large population groups. Evaluations of young children and identification of any deficits may be particularly important if critical periods for olfactory system development exist as have been shown for the gustatory system^{6,17}. The support from the NIH Toolbox is providing a significant opportunity to develop, validate and provide normative data for evaluation of olfactory function. The emphasis on the development of pediatric-specific tests which can be readily incorporated into large-scale clinical trials or epidemiological studies is a significant opportunity to advance our understanding of olfactory function and dysfunction across the lifespan.

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Table 1

Odor Stimuli

Set A	Set B
Banana ²	Peanut Butter ¹
Lemon ^{1,2}	Chocolate ^{1,2}
Play Doh™ ¹	Flower ²
Coffee ¹	Mint ¹
Cinnamon ^{1,2}	Play Doh™ ¹
Bubble Gum ¹	Grape

¹Used in SDOIT

²Used in B-SIT

Table 2

Odor identification results stratified by age group across the two stimulus sets.

Age Group	n	# Correct (of 6)
3–5	30	2.93
6–8	44	3.77
9–11	35	3.90
12–14	14	4.08
15–17	16	4.09