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## Validity and Reliability Testing of the National Health and Nutrition Examination Survey (NHANES) Taste and Smell Protocol

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### **ABSTRACT:**

The NHANES 2011–2014 protocol includes a taste and smell questionnaire (CSQ) in the home interview followed by brief olfactory and taste assessment in mobile exam centers. The CSQ asks self-reported taste and smell ability, and selected symptoms, comorbidities, and treatment for chemosensory disorders. In the taste assessment, participants rate intensities of 1 M NaCl and 1mM quinine hydrochloride applied to the tongue tip and these plus 0.32M NaCl sampled with the whole mouth. Smell function is assessed with two 4-item, scratch-and-sniff tests (Pocket Tests™ (PT), Sonosonics, Inc.) to classify normosmia and olfactory dysfunction from microsmia to anosmia. We examined the NHANES protocol test-retest reliability and compared the PT to an Olfactometer identification task. Seventy-seven adults (mean age=39, range: 18-87 years) were tested at baseline and 2.5 weeks. Taste intraclass correlations (one-way random, single measures) ranged from 0.47-0.71 (moderate to substantial agreement). Classification of olfactory function agreed for 97% of participants across two PT trials ( $\kappa = 0.65$ ). Compared to the Olfactometer at each testing session, the PT averaged 50% sensitivity (true positive rate) and 100% specificity (true negative rate) to identify olfactory dysfunction. All adults incorrectly classified by PT were mild microsmics. If detecting moderate to severe dysfunction, the PT averaged 100% sensitivity and 97% specificity. A subsample (50 adults) completed testing at 6.5 months to test the CSQ stability. The six CSQ items pertaining to

chemosensory impairment had moderate to near perfect agreement (ICC single measures, 0.57-0.94). These findings indicate that the NHANES chemosensory protocol has good test-retest reliability and is highly sensitive in identifying moderate to severe olfactory dysfunction.

## **INTRODUCTION:**

Chemosensation responds to chemicals within and outside of the body and serves to translate stimuli into metabolic, neurological, and behavioral responses.<sup>1</sup> As such, the chemosenses taste and smell are significant determinants of health. Complex interactions between the externally-perceived chemosensation create a unique perception of food flavor.<sup>2</sup> Individual differences in chemosensory ability and the perception of food flavor can impact dietary intake.<sup>3</sup> Chemosensory function varies with genetics and factors that influence the translation of a chemical message to a nervous signal for perception and response.

For taste, the density of taste buds, which hold taste receptors, and fungiform papillae varies from person to person.<sup>4,5</sup> Taste buds, located on the tongue, pharynx, larynx, and epiglottis, are chemically activated with chemical-receptor binding to stimulate three different cranial nerves. These nerves transmit taste signals to the brain for perception of salt, sweet, sour, bitter and possibly the savory taste of glutamate. The density of taste buds and papillae corresponds with taste intensity.<sup>6,7</sup> Genetic differences in the individual receptors for sweet, salty, sour, bitter, and umami tastes also impact taste perception.<sup>8-16</sup>

Smell is a dual sensory process, as odors are transported both orthonasally, through the nostrils, and retronasally, through the nasopharynx.<sup>17</sup> Retronasal olfaction occurs when the process of chewing and swallowing releases odorants in the back of the throat.<sup>18</sup> A single cranial

nerve (CN I) is responsible for carrying retronasal or orthonasal signals from receptors to the olfactory bulb and the olfactory cortex the brain. The ability to smell complex odors is mediated by genetic variation in olfactory receptor genes<sup>19</sup> as well as environmental and medical factors that influence the transmission of the olfactory message from the receptor to the olfactory cortex. The integration of orthonasal, retronasal, taste, and somatosensory reception in the CNS creates flavor perception and behavioral responses.<sup>20,21</sup>

Environmental factors that influence chemosensation include such as infection, chemical exposure, mechanical damage, and aging.<sup>1</sup> Due to its anatomical nature, the smell pathway is much more liable to damage than taste. Olfaction is carried by just one cranial nerve versus three for gustation.<sup>22,23</sup> Most reported changes in “taste” are in fact due to olfactory disturbances.<sup>24</sup> Thus, age-related loss of smell is most common. Specific risk factors for olfactory disturbances include exposure to toxins, upper respiratory tract infections, head trauma, chronic nasal or sinus diseases, and neurodegenerative diseases (Alzheimer disease, Parkinson disease, Huntington disease, Down syndrome).<sup>25</sup> Conditions impacting mucus production and oral health, such as head and neck cancers, cancer treatments, and poor oral hygiene, are also known to decrease olfactory ability. Smell loss is classified as hyposmia (decreased ability), anosmia (specific or total for all odors), or parosmia (altered quality).<sup>1,26,27</sup> Total taste loss (ageusia) is rare due to the redundancy of cranial nerves and the high turnover rate of taste receptor cells. Partial loss or total taste loss from damage to a single taste-related cranial nerve is more common.<sup>28,29</sup>

The perception of food sensations has an impact on food intake. The theory of sensory-specific satiety (SSS) hypothesizes that liking of flavors decreases in relation to foods unconsumed. For example, a variety of diverse flavors means it takes a person a longer time to

become satiated, whereas monotonous diets may decrease intake due to quicker satiation. Liking of individual flavors is also linked to health outcomes. Many vegetables, high in essential vitamins, minerals, and phytonutrients, are bitter tasting. Studies have shown that genetic tasters of propylthiouracil (a bitter chemical) perceive higher levels of bitter and consume fewer vegetables.<sup>30</sup> Lower intake of vegetables correlates with increased risk of chronic disease.<sup>31</sup>

There are a number of examples of how genetic or environmental variation in chemosensation influences what is liked. Sweet liking is negatively related to PROP tasting, and preference also varies by number of fungiform papilla. Salt intake is related to high blood pressure and cardiovascular risk, and salt liking varies across gender and taste phenotype.<sup>32</sup> Individuals also differ in sour liking, which impacts fruit consumption in infants and children.<sup>33,34</sup> Fat perception, which is primarily a textural sensation via mechanoreceptors, also varies genetically and with altered taste sensations. Individuals with damage to the chemosenses may have a heightened sensation and greater liking for fat. Increased fat preference is linked to dietary behaviors and higher rates of adiposity.<sup>35,36</sup> Thus, genetic or environmental caused variation in chemosensation can influence health outcomes through food preference as a driver of food intake.

Olfactory dysfunction is also implicated in public safety issues; Santos and colleagues found that patients with olfactory impairment suffer a significant increase in olfactory-related hazardous events than patients with normal olfaction. Events included cooking-related incidents, ingestion of spoiled food, inability to detect gas leaks, and inability to smell fire.<sup>37</sup>

There has been relatively little research concerning chemosensory dysfunction at a population level. Such research is needed due to the impact of taste and smell ability on dietary

intake, health outcomes, and public safety. A population-based survey would generate a large amount of data from which correlations between variations in chemosensory function and nutrition and health outcomes could be identified.<sup>38</sup> The Healthy People 2020 Goals have pinpointed chemosensory health as an area for improvement. Goals for taste and smell include to increase the proportion of adults with chemosensory disorders who have seen a health care provider and tried recommended methods of treatment for their disorder in the past 12 months. A third goal is to reduce the proportion of adults with chemosensory disorders who experience a resultant negative impact on health status, work, or quality of life.<sup>39</sup> The inclusion of chemosensation in the Healthy People 2020 Goals further reflects the necessity of further research to improve knowledge of this subject.

To accurately study chemosensation at an epidemiological level, the research design needs to address several methodological challenges. The measures used must be valid and reliable in order to translate findings from lab or clinical settings to the general population.<sup>38</sup> Unlike hearing or vision tests, the modalities used to measure smell and taste loss are varied with no singular standard procedure.<sup>40</sup> Studies conducted at a population-based level must be well-designed to ensure that any hypothesized associations or potential risk factors are actually contributing to chemosensory loss.<sup>23</sup>

For the first time, a chemosensory component was added to the 2012 National Health and Nutrition Examination Survey (NHANES) to assess the normal variation and prevalence of dysfunction in taste and smell ability. NHANES is a nationally-representative survey of the U.S. population based on home-based interviewing and measures taken at mobile examination centers (MECs). NHANES began in 1999 as a continuous survey conducted every two years to collect

data on health, nutritional, and medical conditions from 10,000 participants ages birth to 85 years. The population is selected through statistical algorithms. NHANES is conducted by the National Center for Health Statistics, CDC, with joint funding support through the National Institutes of Health.<sup>38</sup> The chemosensory component includes a home interview to collect self-reported data of chemosensory-related problems, and a taste and smell assessment to be completed in the MEC.

The Taste and Smell questionnaire (CSQ) in the home interview is used to assess perceived taste and smell problems over the past 12 months as well as changes since age 25 in smell and flavor perception, and ability to taste sweet, salty, sour, and bitter. Information about symptoms, treatments, and risk factors for chemosensory disorders is also collected.

The purpose of MEC exam is to assess taste ability through a taste intensity measure and olfactory dysfunction through a scratch and sniff test. Participants are first prescreened and orientation to the general Labeled Magnitude Scale (gLMS) used for intensity ratings. A taste exam is administered using solutions of NaCl and quinine applied to the tongue tip and whole mouth using a standard package designed by Dr. John Hayes from Penn State. Smell assessment is achieved through use of the Modified Pocket Smell Test<sup>TM</sup> (PT), Sensonics, Inc. an 8-item scratch-and-sniff odor identification test. The PT was developed under the guidance of Dr. Richard Doty from UPenn based on the University of Pennsylvania Smell Identification Test (UPSIT), a commonly used 40-item smell assessment test.

The gLMS scale used in the MEC exam is accepted as a fast, valid and reliable method for measuring and comparing the sensory intensities in large populations. This scale was also used in the NIH Toolbox for Assessment of Neurological and Behavioral Function (NIH

Toolbox) project. The NIH Toolbox consists of brief measures used to assess cognitive, emotional, motor, and sensory function in both clinical and epidemiological studies. The gLMS was selected for use in the Toolbox because it can be administered in brief sessions and is conducive to use by elderly populations. The gLMS is able to distinguish ranges of perception. The gustation tests of the NHANES chemosensory component are modeled off of the NIH Toolbox, further justifying the use of the gLMS scale.<sup>41</sup>

The scale consists of a vertical scale ranging from 0 at the bottom to 100 at the top, with descriptive adjectives (no-sensation, barely detectable, weak, moderate, strong, very strong) placed in a logarithmic distribution along the scale.<sup>42</sup> The scale corresponds directly with magnitude matching, the gold standard for assessing intensity ratings across individuals and groups.<sup>43,44</sup> gLMS also corresponds well with anatomical measures of taste receptor density,<sup>45</sup> and with taste receptor genotype. gLMS ratings have been shown to be accurate and reliable in classifying individuals as tasters and nontasters based on ability to taste PROP bitterness when compared to TAS2438 genotyping.<sup>46-48</sup> The gLMS has been used in multiple laboratory<sup>49-55</sup> and population-based studies<sup>56,57</sup> to assess taste, and has the added advantage of being easily used by low literacy populations.<sup>36</sup> The gLMS also has predictive validity in predicting health outcomes by linking PROP bitter perception with dietary intake behaviors that affect cancer, disease, and obesity risk.<sup>58,59</sup>

Quinine hydrochloride (QHCl) was selected as a suprathreshold probe of regional (tongue tip) and whole mouth taste. Suprathreshold measures are at concentrations high enough to produce perceptible physiological effects, and are more reflective of real world tastes than threshold measures. Quinine is also recognized by multiple bitter taste receptors, and so can be



used to detect localized taste damage.<sup>45,52</sup> Oral infections, medications, environmental exposures, and middle ear infections may damage the chorda tympani nerve responsible for taste reception from the anterior tongue. Such localized damage may disinhibit other nerves to the tongue to compensate for bitter taste reception, and so spatial taste testing with quinine is important.<sup>60,61</sup> Regional taste function has also been shown to impact dietary intake, such as increasing fat-palatability, increasing alcohol preference, and increasing vegetable bitterness which all contribute to increased risk for overweight and obesity.<sup>45,50,58,62</sup>

The olfactory component utilizes the Modified Pocket Smell Test, an 8-item scratch-and-sniff style test. Participants are asked to identify the odorant from four choices, and number of correctly identified odors is correlated with smell ability. The test-retest reliability and validity of the Modified Pocket Smell Test (PT) has not been evaluated in comparison to other standard olfactory measures. The PT is compared to OLFACT-ID™ test, a valid and reliable 40-item test administered through an Olfactometer (Osmic Enterprises, Inc.) to compare the use of greater olfactory stimulus control.

## **MATERIALS AND METHODS:**

### **Subjects:**

A convenience sample of 77 healthy adults, between the ages of 18 and 87 y (mean age =  $39.526 \pm 20.787$ ), was recruited from the UConn and Storrs, Mansfield community and invited for two testing sessions, occurring an average of two weeks apart. A subset of participants came back after 6 months. Most subjects were female (68.83%) and Caucasians (87.01%). All procedures were approved by the local IRB. Participants provided informed and written consent

and were paid for their time. Prior to testing, participants were screened for exclusion criteria (pregnancy, allergies to quinine, taking thyroid medication) and asked to report current nasal symptoms, including sneezing or blocked up nose. These exclusion criteria were selected as allergies to quinine, or having thyroid disease, to avoid including individuals who may have a sensitivity to PROP, a medication used to treat the thyroid condition, Graves Disease. Nasal symptoms may also impact both olfactory and gustatory perception of odorants/tastants.

### Intensity Scaling:

Participants used the general labeled magnitude scale (gLMS) as a cross-modality standard to rate the intensity of oral stimuli. The scale ranges from “non-sensation” at 0 to “strongest sensation of any kind” at 100 with descriptive adjectives (“barely detectable,” “weak,” “moderate,” “strong,” and “very strong”) in a semi-logarithmic order on the side of the scale. All subjects received a verbal orientation to the gLMS scale, in which they were asked to practice rating intensities of remembered sound and light sensations. Remembered sensations (brightness of a dimly lit restaurant, brightness of a well-lit room, brightest light ever seen) and sound tones (1000Hz, 50 to 98 dB) were used in place of standard NHANES protocol LED-generated lights due to lack of equipment. The subject first determined the appropriate descriptor of their choice, then clicked on either side of that adjective to approximate their rating of strength of sensation. Clicking caused the computer to generate a numerical value of the subject’s rating, manually recorded by the experimenter.

Procedure:

*Taste and Smell Questionnaire (CSQ)*

The CSQ was administered at first and second visits (2 weeks apart), as well as at 6 months follow-up for a subset of subjects. In the NHANES protocol, the questionnaire is a part of the home interview. For our purposes, participants individually completed the CSQ in the laboratory at each visit to assess reliability. Questions included yes/no responses for taste/smell ability and changes in the past year and since age 25. Participants were also asked to rate their overall chemosensory perception and ability to taste individual flavors since age 25 as better/worse/no change. Responses were numerically coded to allow for quantitative analysis.

*Intensity of taste stimuli on regional areas*

Intensity scaling and identification of solutions was performed both regionally and within the whole mouth. 1mM Quinine, 0.32 M NaCl, and 1 M NaCl were painted across the anterior tongue to stimulate the chorda tympani branch of cranial nerve VII. The same solutions, with the addition of 3.2mM PROP, were then sampled with the whole mouth, with instructions to rinse for approximately 5 seconds with 10ml of solution, then expectorate. Subjects rinsed with deionized water between each tasting to reduce any residual stimulus. The participant rated the intensity of the taste stimuli using gLMS, with the intensity rating verbally reported and then manually recorded by the experimenter. All participants sampled these tastants at first and second visits (2 weeks apart). A subset of participants (n=50) also sampled Sucrose (0.32M and 1M), 1g/L Alum and 32mM Citric Acid in the whole mouth. The tastants included in the original

NHANES protocol (Quinine and NaCl) were repeated for a subset of the population at 6 months to assess longer-term reliability.

### *Assessment of smell function*

Participants first completed the 8-item Modified Pocket Smell Test, developed by Sonosics and used by NHANES. The Modified Pocket Smell Test (PT) includes two booklets of 4 scratch-and-sniff odorants each. Subjects were asked to identify odors and rate intensity using the gLMS each time the experimenter scratched the card using a pencil and verbally provided smell options for each item. Each odorant listed four alternative responses, which were read aloud for the subject to choose from. The correct choices were chocolate, strawberry, smoke, leather, soap, grape, onion, and natural gas. Selecting 6 or more odorants correctly was classified as normosmia, with 5 or fewer identified classified as dysfunction. Smell function was also assessed using the 40-item odor identification test administered with an OEI Olfactometer. The 40-item test included all of the odorants used in the PT except for natural gas, which did not overlap between the tests. Participants were again asked to identify and rate the intensity of the smell using the gLMS, with the experimenter reading possible choices. Correctly identifying more than 33 odorants was classified as normosmia; identifying 32 or fewer odorants classified as dysfunction. Scores of 0-19 represent anosmia (complete lack of smell), 19-25 severe microsmia, 26-29 moderate microsmia, and 30-33 mild microsmia. Scoring is based on normative data presented in the UPSIT (University of Pennsylvania Smell Identification Test) manual, with reference to Segura et. al (2013), which used gender-blind classifications for UPSIT. UPSIT is a scratch-and-sniff with 40 odorants (4 booklets of 10 odorants), and so the

scoring system correlates well with the 40 item Olfactometer test. The PT and Olfactometer were repeated across 2 weeks for all participants.

Smell Assessment Test	Classification	Number of Odors Correctly Identified
Modified Pocket Smell Test (PT)	Normosmia	$\geq 6$
	Dysfunction	$\leq 5$
OEI Olfactometer	Normosmia	$\geq 33$
	Mild Microsmia	30-33
	Moderate Microsmia	26-29
	Severe Microsmia	19-25
	Anosmia	$\leq 19$

#### Statistical methods:

SPSS and Excel were used to analyze validity and reliability measures of the chemosensory component. For agreement of olfactory and taste measures across two trials (1<sup>st</sup> and 2<sup>nd</sup> visits averaging 2 weeks apart), Intraclass Correlation (ICC) single-measures, one-way random, Cohen's Kappa, and Pearson's r were used to assess intra-rater agreement. ICC was utilized for continuous measures (such as taste, olfactory intensity, light, and sound tones) measured by gLMS rating (1-100 scale). Interpretation of ICC, Kappa, and r were based on the following guidelines from Cicchetti and Sparrow (1981), consistent with recommendations from Burdock et al. (1973), Gelfand and Hartmann (1975) and Landis and Kolch (1977):<sup>63</sup>

< 0.40 = Poor Agreement

0.40 – 0.59 = Fair Agreement

0.60 – 0.74 = Good Agreement

>0.75 = Excellent Agreement

Agreement Coefficient ( $AC_1$ ) was used rather than ICC to look at agreement between CSQ (Taste and Smell Questionnaire) answers across 6 months because possible answers were categorical (yes/no, better/worse/no change). Kappa was not used for CSQ data a large majority of participants answered “no” to questions regarding taste/smell dysfunction and kappa has a tendency to yield skewed data in such data sets. Agreement Coefficient is designed to help overcome the limitations of kappa by being more sensitive to marginal probabilities, yielding more valid and reliable measures.<sup>64</sup>

## **RESULTS:**

### PT reliability

The Modified Pocket Smell Test (PT) was administered to all participants at first and second visits (about 2 weeks apart). Of the 77 participants, 69 (89.6%) returned for the 2<sup>nd</sup> visit after 2 weeks. The PT was repeated at two visits to examine its reliability as a measure of smell function. Agreement across two weeks was 95% based on cross-tabulation, with 1 participant classified as dysfunction at first visit but normosmic at second visit. This reflects near perfect agreement of the PT across two visits (Table 1).

When looking at individual odors, correct and incorrect identification was also consistent between the two visits, averaging 87% agreement (Figure 1). Chocolate had the lowest percentage agreement between the two visits (67.65%), with soap having the highest agreement (98.53%). It is important to note that the environmental hazard odorants, natural gas (91.18%) and smoke (95.59%), also had high percent agreements across the trials (Figure 1).

The perceived intensities of odorants were also in moderate to good agreement. Most odorants had moderate correlation based on Pearson's correlation (range 0.45\*\*-0.59\*\*) and ICC single-measures one-way random. Natural Gas had the strongest agreement (good; based on ICC 0.61) (Table 2). The intensity ratings of the PT odorants in each visit were not significantly different ( $p > 0.05$  for each odorant, Figure 2).

### PT versus Olfactometer

The PT was compared to the more widely tested and sensitive Olfactometer to establish validity. PT scores from the 1<sup>st</sup> visit had moderate agreement with the Olfactometer classifications ( $\kappa = 0.72$ ). Data collected from the second visit (PT and Olfactometer) was consistent with the trends seen at first visit. However, fewer subjects with microsmia/anosmia returned for the second visit, and so this data was not included as it does not reflect the ability of the tests to identify dysfunction.

The PT and Olfactometer at first trial agreed for 94.5% of participants, with 60% sensitivity (true positive rate) and 100% specificity (true negative rate). The Olfactometer identified 4 additional participants as having dysfunction (mild microsmia, scoring between 30-33 out of 40) than the PT. To determine the sensitivity and specificity of pocket smell test in detecting moderate-severe olfactory dysfunction, dysfunction by Olfactometer was reclassified as identifying 0-29 odors correctly (moderate-severe dysfunction), and normosmia as identifying 29-40 odors correctly (mild microsmia – normosmia). This improved agreement of classification between the PT and Olfactometer to 99% of participants at first visit, with only one participant in discordance. Sensitivity was improved to 100%, and specificity to 98% (Table 4).

The mean intensities of the Olfactometer odors, as measured by gLMS, were generally higher than PT odor intensities, except for leather ( $24.96 \pm 17.45$  Olfactometer,  $25.64 \pm 14.69$  PT) and soap ( $30.88 \pm 20.21$  Olfactometer,  $36.29 \pm 18.12$  PT). Intensity rating and identification of odorant were also positively correlated, for both the PT and Olfactometer. Soap, smoke, and onion, the odorants with the highest mean odor intensities, also had the highest percentage agreements for PT odor identification between visits 1 and 2 and positive odor identification when compared to the Olfactometer (Table 5). It should be noted that only seven odorants were compared between the two tests because the Olfactometer does not include Natural Gas as an available odorant.

The correct and incorrect identification of odorants between the two PT visits and Olfactometer are compared in Figure 3. As with previous measures, chocolate had the lowest average % agreement (68.925%), and onion had the highest (89.505%), closely followed by smoke (87.68%) and grape (87.09%).

#### Test-Retest Reliability for NHANES Taste Protocol and CSQ Items

The NHANES taste protocol consisted of five tastants, which were administered at first and second visits (approximately two weeks apart) in this trial. The gLMS rating of intensity of taste probes at the two visits had moderate to strong agreement for all tastants according to ICC single measures, one way random (Table 6). 1mM Quinine whole mouth had the highest ICC between trials (0.71). 1mM Quinine tongue tip had the second highest correlation (0.58), and 0.32M NaCl whole mouth the lowest (0.47).



1mM Quinine was correlated across tastants (controlling for age sex, and tone ratings). The NHANES protocol includes 1mM Quinine and 1M and 0.32M NaCl, bitter and salty tastants. Quinine was compared to a larger set of tastes (salty, bitter, sour, sweet, astringent) to assess its reliability in measuring overall taste function. The tastants with the highest correlations were 1M NaCl (0.61\*\*), 1M Sucrose (0.55\*\*), and 0.32M NaCl (0.54\*\*). 3.2 mM PROP had the lowest correlation with quinine (0.31\*\*). Quinine was significantly correlated with each tastant, suggesting its use as a probe for supertasting (Table 7).

The tones and remembered light sensations measured by gLMS had fair to moderate agreement between the two visits (Table 6). Pearson's correlation (Figure 4) of the individual taste probes also showed moderate to strong agreement between first and second visit (2 weeks apart). Longer term test-retest reliability of the NHANES Taste component was also assessed at 6 months follow-up for a subset of population (50 participants) (Table 8). All taste probes had a slightly decreased, though still overall moderate agreement according to ICC. Consistent with the short-term reliability, 1mM Quinine whole mouth had the highest correlation at follow-up (0.55).

The CSQ (Taste and Smell Questionnaire) was also administered to the subgroup at 6-month follow-up. Questions regarding taste and smell function/loss, and individual taste components (sweet, sour, salty, bitter) were selected for analysis. Items regarding change in chemosensory change with aging were answered only by participants over age 40 (7 participants). All of the items had substantial to almost perfect agreement over the 6-month period based on Agreement Coefficient (Table 8).

## **DISCUSSION:**

Smell and taste dysfunction have an important impact on health. Previous clinical trials have demonstrated that chemosensory ability varies with age, medical conditions, and environmental exposure.<sup>8,11,13,15,16</sup> Variability in taste and smell function correlates with flavor perception and dietary intake. Smell also serves as an important warning system for public safety.<sup>10,11,14</sup> Despite the importance of chemosensation, relatively few population-based studies have been conducted.<sup>61</sup> In the present study, we evaluated the validity and reliability of the NHANES 2012 Chemosensory protocol by comparing its across two trials and to standardized measures. It was found that the NHANES chemosensory protocol showed good reliability for both short-term (2 week) and longer-term (6 month) measures when administered to healthy, educated adults in a lab-based setting. The methods and procedure of the component can then be translated to population-based studies to generate epidemiological data at a national level.

The smell assessment was administered to all participants at the initial and 2 weeks follow-up visit. Of the 8 odors in the Pocket Smell Test, chocolate and grape showed the least, but still moderate, agreement in identification and perceived intensities. Natural gas and smoke, two important odors for public safety, showed high agreement for identification and perceived intensities. The original NHANES chemosensory protocol does not include a rating of olfactory intensity. However, adding perceived intensity to either identification task (PT or Olfactometer) added minimal time to the procedure, and increased the variability in olfactory functioning scores. Perceived intensity of taste/flavor, commonly referred to as supertasting or non-tasting, has been shown to explain some variation in diet and health indices.<sup>65</sup>

Similar quick smell assessment tests to the Modified Pocket Smell Test do show higher levels of sensitivity. The Sniffin Sticks 16 item test was highly correlated with the 40-item UPSIT.<sup>66</sup> SS-16 showed higher sensitivity (81.1%), but lower specificity (89%) than our study. However, the study used a larger population with a greater level of olfactory dysfunction and used diagnosis of Parkinson's Disease (PD) as the outcome variable for analysis, rather than the range of normosmia-microsmia-anosmia used in the present study. Because microsmia is known to be associated with PD, researchers looked at the number of correctly identified odorants by control subjects versus number of incorrectly identified odorants by subjects with PD without regard to actual measurements of microsmia.<sup>66</sup>

The 8-item San Diego Odor Identification Test (SDOIT) and 12-item Brief-Smell Identification Test are more similar to the Pocket Smell Test. A comparison of SDOIT and B-SIT found that the shorter SDOIT had 90.9% sensitivity and 96% specificity in identifying subjects as having impaired or unimpaired smell.<sup>67</sup> This is a much higher sensitivity than the 60% reported for the total population by our study, although the difference may be accounted by the fact that SDOIT and B-SIT are both shortened tests of similar lengths whereas the PT was compared to the much lengthier 40-item Olfactometer test. Therefore, they are likely unable to identify mild microsmia similar to the PT. In this case, the modified comparison of moderate-severe microsmia yielding 100% sensitivity is a more appropriate comparison to the SDOIT and B-SIT. This could suggest that the PT is potentially more valid in identifying olfactory dysfunction.

When compared to the more sensitive 40-item Olfactometer test, the PT had good agreement (94.5% at first visit). At first visit, the PT identified 5 participants as normosmics

which the Olfactometer identified as dysfunction. All of those five subjects were mild microsmics according to the Olfactometer (scoring between 30-33). The PT, having only 8 odorants, is a much less sensitive test (60% Sensitivity) but highly specific in identifying true negatives (those without disorders – 100% Specificity) (Table 3).

As expected a short assessment test would have lower sensitivity than a more extensive test. Yet because the PT is highly correlated with the Olfactometer, it is possible to predict overall olfactory function from the PT. One study looked at the internal consistency reliability (ICR) of 10, 20, and 30 item fragments of the 40-item UPSIT. ICRs for all fractions were very high (0.752 for 10 items, 0.855 for 20 items, 0.898 for 30 items, and 0.922 for 40-items). This shows that individual UPSIT booklets (similar to the 8-item scratch and sniff PT) can be used to assess smell function in a reliable manner, especially when time constraints are present and in non-laboratory settings like the Mobile Examination Centers for testing the NHANES chemosensory component.<sup>68</sup>

The group who came back for a second visit at 2-week follow-up contained fewer microsmics, and so data concerning the more diverse group from 1<sup>st</sup> visit was only included in analysis as this population best reflects the test's ability to identify olfactory dysfunction. When mild microsmics identified by Olfactometer were classified as normosmic (30-40 normosmic) for the sake of statistical analysis, the sensitivity increased to 100% (Table 4). This demonstrates that the PT is most beneficial in identifying moderate to severe microsmics. This population is most important to identify as they are most likely to experience related health risks and are most important to be able to refer to further services.

The Pocket Smell Test may have use in identifying those with olfactory dysfunction who were previously unaware of their condition, so that they may be referred for further testing. In this way, the NHANES Chemosensory component can help to achieve the Healthy People 2020 Goals of increasing the proportion of adults with taste and smell disorders who seek and receive treatment. This is highly relevant for quick-screening methods, as it has been found that self-reported olfactory function does not correlate well with measured olfactory function.<sup>69</sup> Furthermore, we have shown that the PT is highly sensitive and specific in identifying subjects with moderate to severe microsmia, the group most important to identify as they are at highest health risk.

The five NHANES tastants had moderate to strong reliability over 2 weeks, consistent with that reported for the NIH Toolbox taste measures for the whole mouth, and exceeded that for the tongue tip.<sup>41</sup> The difference may have resulted from a different level of training in administering tastants to the tongue tip. Longer term (6 month) test-retest reliability of all five taste probes still showed moderate agreement, though slightly decreased from that between the 1<sup>st</sup> and 2<sup>nd</sup> visits. Six items in the CSQ pertaining to chemosensory impairments also showed moderate to near perfect agreement across 6 months, indicating good long-term test-retest reliability of the Taste and Smell Questionnaire.

Whole mouth intensity for 1mM quinine correlated significantly with other tastants not included in the NHANES protocol. These included sweet, sour, and astringency standards as measured by 0.32M and 1M Sucrose, 32mM Citric Acid, and 3.2mM PROP respectively. These findings support the ability of the quinine probe to capture a broader range of taste variability (Fischer 1963).<sup>70</sup> Quinine's use as a suprathreshold taste measure may help to predict dietary

behaviors and disease risk. For example, supertasters may have decrease vegetable consumption, while participants with impaired regional taste function have been seen to have higher intakes of high fat-sweet foods and alcohol, which are linked to overweight and obesity.<sup>50,58,71</sup>

In conclusion, the 2012 NHANES Chemosensory Component was found to be a valid and reliable and reliable assessment of olfactory and taste ability. The test measures are appropriate given time and equipment restraints. This is the first time that NHANES is including a taste and smell component and will be able to assess the prevalence of taste and smell disorders at a national level. The data generated from the survey will be able to be used to assess associations between chemosensory function and other nutritional and health measures measured by NHANES. The eventual findings of the component will help to achieve the Healthy People 2020 goals regarding chemosensory health.<sup>72</sup> It is important to assess the national prevalence of taste and smell disorders in a valid and reliable manner given the demonstrated impact the senses have on dietary intake, public safety, and health outcomes.

**TABLES AND FIGURES:**

PT Test-Retest Reliability

Pocket Score 2 <sup>nd</sup> Visit Classification	Pocket Score 1 <sup>st</sup> Visit Classification	
	Normosmics	Dysfunction
Normosmia	63	1
Dysfunction	0	3

Table 1: Olfactory Function Classification for PT across 2 weeks agreed for 98.5% of participants ( $\kappa = 0.85$ , 95% CI: 0.71-0.99)

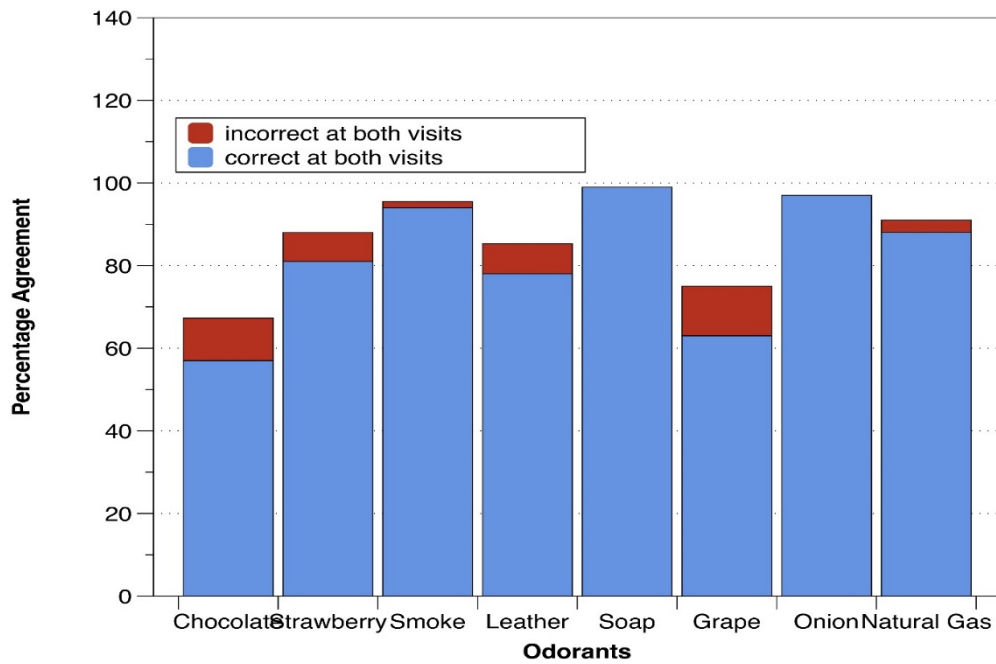


Figure 1: Correct and incorrect Odor Identification consistent across two PT trials, averaging 87.32% agreement

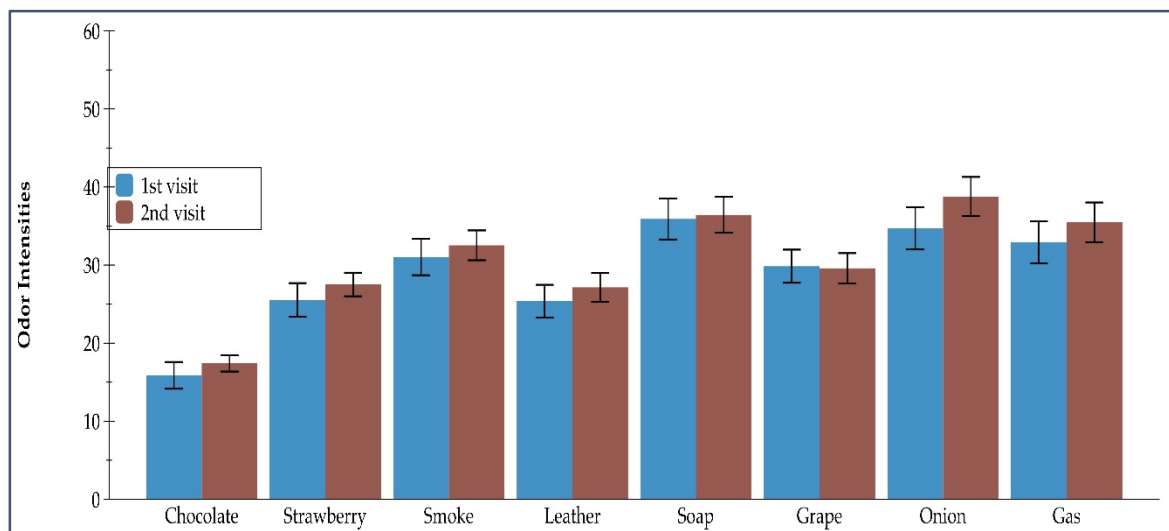


Figure 2: Comparison of the mean perceived intensities of PT odorants across 2 weeks were not significantly different.

Odorants	Pearsons's Correlations	Intraclass correlations (ICCs) Single Measures, One Way Random	Agreement
Chocolate	0.46**	0.42 (0.20-0.60)	Moderate
Strawberry	0.50**	0.47 (0.26-0.64)	Moderate
Smoke	0.59**	0.58 (0.40-0.72)	Moderate
Leather	0.56**	0.56 (0.37-0.70)	Moderate
Soap	0.48**	0.48 (0.27-0.65)	Moderate
Grape	0.45**	0.46 (0.25-0.63)	Moderate
Onion	0.50**	0.49 (0.30-0.66)	Moderate
Natural Gas	0.60**	0.61 (0.43-0.74)	Good

Table 2: Pearson's correlations and ICCs for perceived odor intensities between two PT trials, (\* p<0.05; \*\*p<0.01).



PT vs. Olfactometer:

Pocket Score 1 <sup>st</sup> Visit Classification	Olfactometer Classification	
	Normosmia	Dysfunction
Normosmia	63	4
Dysfunction	0	6

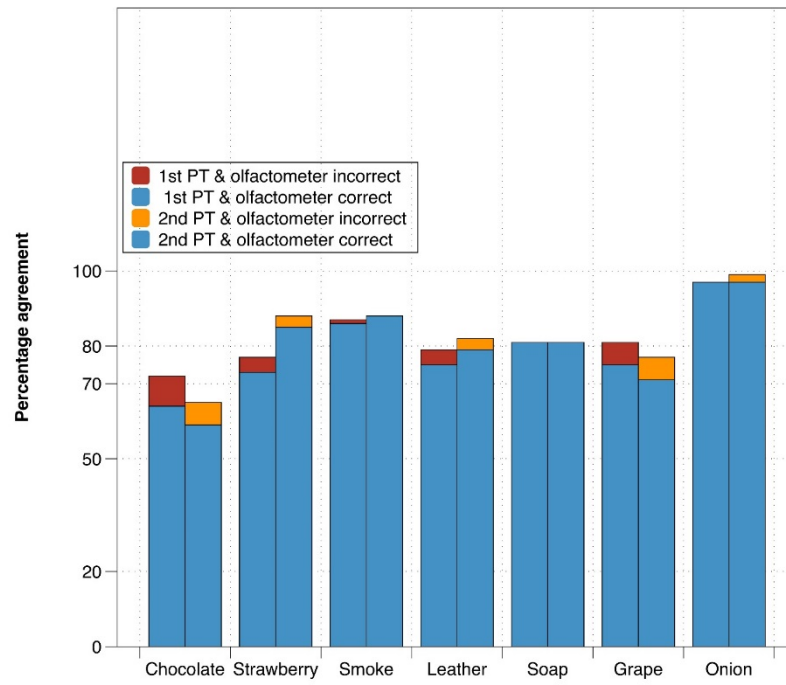
Table 3: Olfactory Function Classification for Olfactometer and PT at 1st visit agreed for 94.5% of participants ( $\kappa = 0.72$ , 95% CI: 0.59-0.85); 60% Sensitivity, 100% Specificity

Pocket Score 1 <sup>st</sup> Visit Classification	Olfactometer Classification	
	Normosmia	Moderate/ Severe Dysfunction
Normosmia	67	0
Dysfunction	1	5

Table 4: Olfactometer scoring was re-classified as: Dysfunction (0-29), Normal (29-40). For detecting moderate to severe dysfunction, olfactory function by Olfactometer and PT agreed for 99% of participants. ( $\kappa = 0.90$ , 95% CI: 0.80-1.00); 100% Sensitivity, 98% Specificity

Odorants	Mean PT Odor Intensities (SD)	Mean Olfactometer Odor Intensities (SD)	Correlation Coefficient
Chocolate	16.05 ± 9.53	21.50 ± 16.31	0.30*
Strawberry	24.96 ± 13.50	24.11 ± 17.45	0.67**
Smoke	31.02 ± 16.63	38.56 ± 20.49	0.49**
Leather	25.64 ± 14.69	24.96 ± 16.22	0.43**
Soap	36.29 ± 18.12	30.88 ± 20.21	0.62**
Grape	28.90 ± 14.68	34.86 ± 19.59	0.62**
Onion	35.53 ± 19.07	43.42 ± 23.67	0.43**

Table 5: Correlations between PT and Olfactometer Odor Intensities (\*  $p < 0.05$ ; \*\*  $p < 0.01$ ).



**Figure 3:** Correct and incorrect odor identification was consistent across the PT and Olfactometer tests, averaging 82.41%

Test-Retest Reliability for NHANES Taste Protocol and CSQ Items

<b>Across 2 weeks (n=77)</b>	<b>Intraclass correlations (ICCs) Single Measures, One Way Random</b>	<b>Agreement</b>
<b>Taste Probes</b>		
1 mM Quinine tongue tip	0.58 (0.40-0.72)	Moderate
1 M NaCl tongue tip	0.51 (0.31-0.67)	Moderate
1 M NaCl whole mouth	0.55 (0.35-0.70)	Moderate
1 mM Quinine whole mouth	0.71 (0.57-0.81)	Good
0.32 M NaCl whole mouth	0.47 (0.26-0.64)	Moderate
<b>Sound tones</b>		
50 dB	0.37 (0.14-0.56)	Poor
62 dB	0.44 (0.23-0.62)	Moderate
74 dB	0.47 (0.26-0.64)	Moderate
86 dB	0.53 (0.33-0.69)	Moderate
98 dB	0.63 (0.45-0.76)	Moderate
<b>Remembered Sensations</b>		
Dimly lit restaurant	0.44 (0.22-0.61)	Moderate
Well-lit room	0.36 (0.13-0.55)	Poor
Brightest light ever seen	0.44 (0.22-0.61)	Moderate

Table 6: ICCs for intensities of taste probes, sound tones and remembered sensations across 2 weeks.

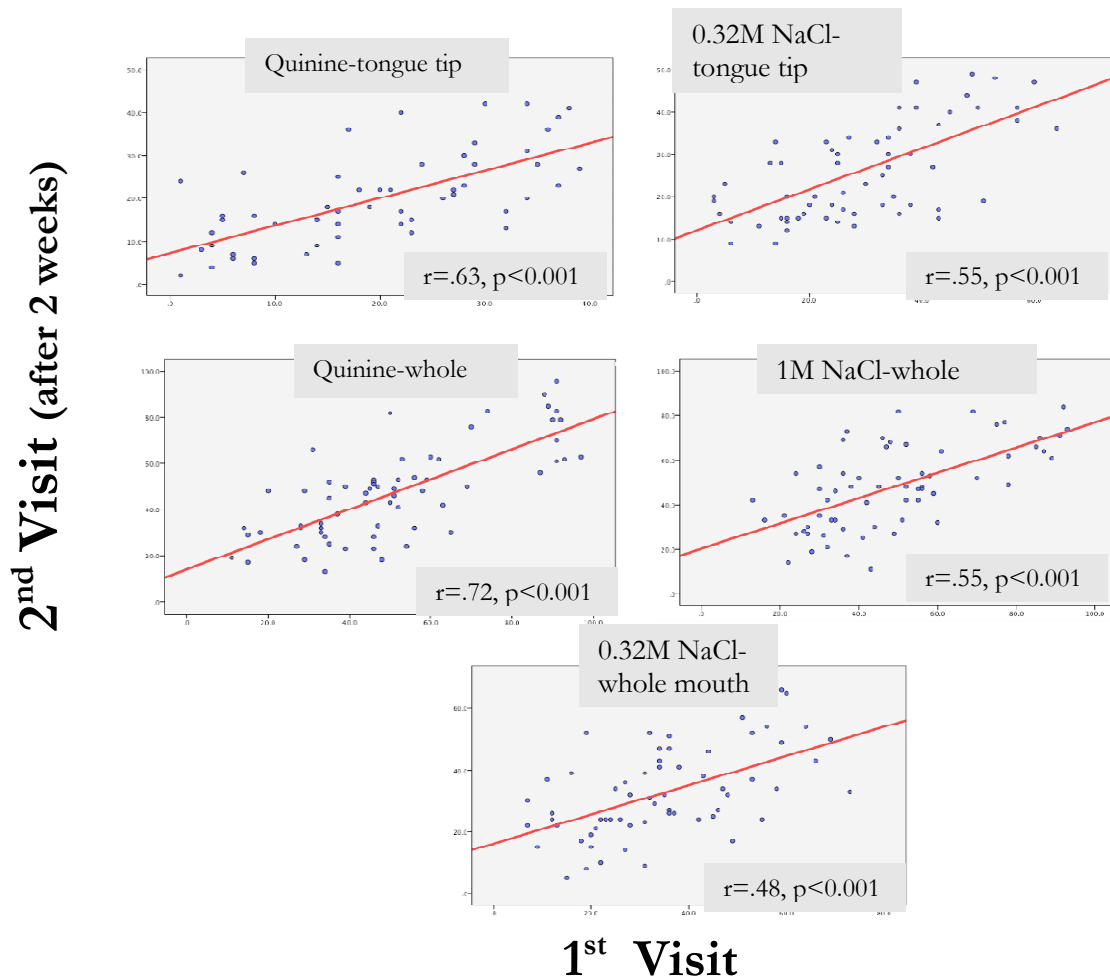


Figure 4: Pearson's correlations between the taste probes across the two visits (2 weeks apart).

	1 mM Quinine
1 mM Quinine	1
0.32 M NaCl	0.54**
1 M NaCl	0.61**
3.2 mM PROP	0.31**
0.32 M Sucrose	0.44**
1 M Sucrose	0.55**
32 mM Citric Acid	0.49**
1 g/L Alum	0.43**

Table 7: Quinine was significantly correlated with almost all tastants (controlling for age, sex and tones), suggesting its use as a probe for supertasting.

<b>Across 6 months (n=50)</b>	<b>Intraclass correlations (ICCs) Single Measures, One Way Random</b>	<b>Agreement</b>
<b>Taste Measures Test-Retest Reliability</b>		
1 mM Quinine tongue tip	0.47 (0.23-0.67)	Moderate
1 M NaCl tongue tip	0.48 (0.25-0.68)	Moderate
1 M NaCl whole mouth	0.49 (0.26-0.68)	Moderate
1 mM Quinine whole mouth	0.55 (0.30-0.72)	Moderate
0.32 M NaCl whole mouth	0.42 (0.24-0.63)	Moderate
<b>CSQ Items Test-Retest Reliability</b>		
	<b>Agreement Coefficient (AC<sub>1</sub>)</b>	
Smell problems during past 12 months (Y/N)	0.86 (0.78-0.91)	Almost perfect
Smell loss since 25 years old (Better/Worse/No Change)	0.90 (0.80-0.99)	Almost perfect
Taste problems during past 12 months (Y/N)	0.78 (0.64-0.92)	Substantial
Salt taste loss since 25 years old (Better/Worse/No Change)	0.76 (0.53-0.99)	Substantial
Sour taste loss since 25 years old (Better/Worse/No Change)	0.86 (0.75-0.97)	Almost perfect
Sweet taste loss since 25 years old (Better/Worse/No Change)	0.69 (0.51-0.87)	Substantial
Bitter taste loss since 25 years old (Better/Worse/No Change)	0.76 (0.52-0.99)	Substantial
Flavor taste loss since 25 years old (Better/Worse/No Change)	0.66 (0.52-0.80)	Substantial

**Table 8:** Taste measures and CSQ Items showed reasonable test-retest reliability over a period of 6 months.

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