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Field Survey Measures of Olfaction: The Olfactory Function Field Exam (OFFE)

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Abstract

Population-based field research on human olfaction has been limited by a lack of feasible assessment tools. Previous olfactory survey research has measured only odor identification, with no research being done on odor detection (i.e., a person's sensitivity to detect a particular odor). Laboratory studies suggest that deficits in both aspects of olfactory function may be related to physical health, mental health and cognition, social function, including overall quality of life, and even mortality. However, field studies are needed to validate and extend these findings in large representative samples. Here we describe the olfactory function field exam, an instrument that can be deployed in field environments by lay interviewers to evaluate both odor identification and odor detection rapidly, practically, and accurately. Use of this new survey tool in future field-based population health studies will elucidate the impact of olfactory function on a myriad of health and social conditions.

Keywords

smell; odor sensitivity; odor identification; aging; humans

Introduction

Olfaction is not merely the ability to detect an odor but also the ability to recognize the odor and respond appropriately. Further, perception of odorants has significant implications for

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physical and mental health, cognition, social function, and quality of life (Frasnelli and Hummel 2005; Smeets et al. 2009).

Olfactory dysfunction impairs the detection of environmental hazards (Santos et al. 2004), and about half of older adults are unable to detect the mercaptans odor that is used to warn of gas leaks in otherwise odorless natural gas (Cain and Stevens 1989). Olfactory deficits directly affect diet and nutrition (Visvanathan and Chapman 2009), impede associated social behaviors such as dining out (Aschenbrenner et al. 2008), and even predict mortality (Gopinath et al. 2012; Wilson et al. 2011). Clinical research has indicated that difficulty identifying odors (which necessarily includes the cognitive demands of matching a name to an odor) is a harbinger of cognitive decline and dementia (Devanand et al. 2010). Olfactory function also plays a major role in unconscious behavior. In addition to established roles in sexuality (Saxton et al. 2008) that are most relevant during years of fertility, social odorants may play a critical role in navigating broader social interactions across one's entire life span (Hummer and McClintock 2009).

Despite its importance, field research in human olfaction has been hampered by an inability to collect representative data. Self-reported measures of olfactory ability are characteristically unreliable (Landis et al. 2003). Clinical or laboratory methods are not feasible, given the cost, length of the examination, complexity of administration, sensitivity of the technology, and size of the equipment.

The University of Pennsylvania Smell Identification Test (UPSIT; Doty et al. 1984) and the related Brief Smell Identification Test (B-SIT; Doty et al. 1996) are portable and validated. However, these methods measure olfactory identification (not detection/sensitivity) and are prohibitively costly as they are not reusable for multiple respondents, which may also limit data collection. Other available tests also focus on identification and are cumbersome for large-scale use (San Diego Odor Identification Test [SDOIT], Murphy et al. 2002; Scandinavian Odor-Identification Test [SOIT], Brämerson et al. 2004).

Olfactory sensitivity testing using the common testing odor *n*-butanol and psychophysical methods can take 20 minutes to administer and requires repeated trials with 16 concentrations (Hummel et al. 1997). Testing sensitivity to androstadienone (AND), a putative human pheromone, is similarly complex logistically. Laboratory studies have demonstrated physiological and neurological effects that accompany exposure to AND (Savic et al. 2001; Wyart et al. 2007), but prior research has attempted to explain AND's social function without measuring detection of the social chemical signal as an odor. As a result, to date, there are no population-based research studies investigating olfactory detection for either *n*-butanol or AND.

Because of these limitations, previous large-scale investigations have utilized samples of convenience (Wysocki and Gilbert 1989) or have focused on olfaction and its relationship to neurodegenerative diseases in clinically at-risk individuals (Siderowf et al. 2012). Survey research investigating olfactory identification has been conducted in relatively homogeneous samples (Brämerson et al. 2004; Murphy et al. 2002). Due to these limitations and with no

prior examination of detection, we have limited knowledge of olfaction in representative populations.

In sum, the standard laborious psychophysical measures used to evaluate olfaction are not feasible to administer as part of a field survey. Thus, we designed the olfactory function field exam (OFFE).

Methods

The National Social Life, Health, and Aging Project (NSHAP) is a nationally representative study of older adults and their partners (age range 36–99 years, mean = 72.4, SD = 8.1) conducted in subjects' homes. NSHAP was designed to assess social life and health during aging and offer insight into the function of the home-dwelling older adult U.S. population. The NSHAP wave 2 data are publicly available through the National Archive of Computerized Data on Aging (Waite et al. 2014; NACDA, <https://www.icpsr.umich.edu/icpsrweb/NACDA/>).

The study consisted of an extensive 2-hour interview during which biological samples were collected and cognitive and sensory functions were tested (Jaszczak et al. 2009) first in 2005–2006 (wave 1) and again in 2010–2011 (wave 2).

In a randomly selected subset of wave 2 respondents ($n = 2,304$), 10 minutes were allotted to test olfactory function, including odor identification and detection of *n*-butanol and AND using OFFE.

NSHAP was administered by nonmedical professional interviewers utilizing computer-assisted personal interviewing (CAPI; Smith et al. 2009). Over 100 interviewers collected the data, requiring clear protocols to ensure reliability. CAPI reduced interviewer burden and error and permitted precise measurement of administration time.

Olfactory Protocols

The detection component of OFFE utilized two types of odorants: *n*-butanol, a physical odorant commonly used clinically for determining olfactory sensitivity (Hummel et al. 2007), and AND, a social odorant that modulates behavior (Hummer and McClintock 2009). Classically, olfactory sensitivity is determined using psychophysical testing. Therefore, our goal was to ensure that OFFE had the ability to quickly approximate measures of olfactory sensitivity. OFFE also measured odor identification with a shortened, validated version (Mueller and Renner 2006) of the 16-odor identification test developed by Hummel and colleagues (1997), which is used widely in laboratory and clinical settings (Philpott et al. 2008).

In contrast to typical psychophysical testing methods, OFFE tests did not use a forced-choice paradigm. Forced-choice paradigms are not feasible in a field survey setting due to time constraints and the need to maintain respondent cooperation. Respondents were strongly encouraged to offer an answer. If respondents still could not, interviewers recorded whether respondents refused or did not know. Therefore, refusals and responses of “don't

know” reflect legitimate uncertainty and offer additional information about the respondent's true ability as opposed to inflated scores that necessarily result as a product of guessing.

Odor detection—The odor detection component required respondents to detect *n*-butanol and AND in a series of ascending concentrations. *n*-Butanol is a natural ingredient in many foods and beverages and has a strong alcoholic aroma. It is a standard test odorant used to evaluate olfactory sensitivity (Hummel et al. 2007).

AND was chosen because it is produced by humans and is known to have both physiological and neurological effects (Hummer and McClintock 2009). AND was included to elucidate the role of olfaction in social function. Limited research has demonstrated that some individuals are unable to detect AND, regardless of how strong the concentration is (Lundström et al. 2003). A known genetic allele codes for the olfactory receptor necessary to detect AND, which is likely to explain this selective anosmia (Keller et al. 2007). AND detection ability at the population level is unknown.

Detection pens—All odors were presented via commercially available felt-tip Sniffin' Sticks pens from Burghart Medical Technology (Wedel, Germany), including a custom 8% *n*-butanol pen. The Sniffin' Sticks technology also permitted us to create our own AND stimuli by diluting AND in propylene glycol and filling blank Sniffin' Sticks as previously described (Lundström et al. 2003).

Detection test administration—When presenting a pen, the interviewer removed its cap and gently waved it approximately 0.5 inches below the respondent's nose. Respondents were instructed to breathe in slowly through their nose as the pen was presented for approximately 2 seconds. Field interviewers wore a cotton glove to minimize the effects of any odors associated with the interviewer.

Explicit demonstration of the target odor is a necessary attribute of psychophysical testing (Hayes and Jinks 2012; Hummel et al. 1997). Further, background odors exist in the field. So that respondents knew which odor they would be asked to detect, they were first presented with a practice target pen that contained the strongest *n*-butanol concentration. The practice target pen had a blue cap and blue bottom and was labeled in blue print with a number one. Respondents were asked if they were able to smell the odor in the practice target pen. Even if they could not or were unsure, all respondents were administered the *n*-butanol test.

After presenting the practice target pen, field interviewers explained the goal of the detection task and read the following, “Some of the pens are strong and some of the pens are weak so do not be discouraged if you cannot smell the odor in some of the pens because this is part of the measure. Just try your best to decide which pen has the odor.” The instructional period oriented the respondent to the task and served as a “washout” period after exposure to the high-concentration practice target pen. The respondent's detection ability was then determined by presenting a set of three numbered pens. Only one pen in the triad contained the target odor.

The interviewer presented the triad one pen at a time, then asked, “Which of the three pens contains the odor?” and entered the response into CAPI. The *n*-butanol detection test consisted of six triads (pens with red caps and red bottoms, labeled 1–18 in red print). The target pen was presented as the first, second, or third pen. Order of administration was independent of the result of the preceding triad. *n*-Butanol concentrations were practice target (8.0%), triad 1 (0.13%), triad 2 (0.25%), triad 3 (0.50%), triad 4 (2.00%), triad 5 (4.00%), and triad 6 (8.00%). These concentrations were chosen based on previous research investigating *n*-butanol sensitivity in this age-group. The weakest *n*-butanol concentration (0.13%) is one dilution stronger than the mean odor threshold (0.06%) that has been previously reported in older adults (Hummel et al. 2007). Utilizing concentrations that range from 0.13% to 8.0% enables the OFFE to quantify typical olfactory function as well as olfactory dysfunction in NSHAP's older population.

Following the *n*-butanol detection test, the AND practice screener pen (blue cap and blue bottom labeled with a number two in blue print) containing the largest concentration of AND was presented. Respondents proceeded to the full AND detection test if they indicated they could smell the AND screener pen or said that they did not know or were unsure. Respondents were not given the full AND test only if they explicitly indicated they could not smell the screener pen. This was done to reduce frustration in the substantial subset of AND-anosmic respondents who otherwise would have been asked repeatedly to detect an odor that they had already indicated they could not detect at the highest concentration to be presented, presumably in large part due to the genetic variation in AND detection ability.

The AND detection test consisted of four triads (pens with green caps and green bottoms, labeled 1–12 in green print) administered with the same protocol as the *n*-butanol test. AND concentrations were practice screener (5.3%), triad 1 (0.13%), triad 2 (0.50%), triad 3 (2.0%), and triad 4 (5.3%). AND concentrations represent the ranges for three distinct groups identified in a laboratory study (Lundström et al. 2003): (1) incapable of AND detection; (2) AND detection only at high concentrations; and (3) AND detection at low concentrations.

OFFE concentrations were presented in increasing order to reduce the risk that a weaker concentration was made more difficult to detect after experiencing a stronger concentration (habituation; Doty et al. 2003). The color coding, labeling, and serial presentation of the OFFE pens aided the interviewers and ensured the accuracy and efficiency of administration.

Odor identification—The odor identification portion of OFFE is based on an abbreviated 5-odor test validated against the full 16-odor test (Mueller and Renner 2006). We dramatically simplified the protocol used previously. Rather than decipher each odor label from a 20-item word bank, respondents chose among four word/picture choices for each OFFE identification odor (rose, leather, orange, fish, and peppermint). Providing pictures reduced bias from language skills, an important feature for administration to a diverse population, and one used previously (Hummel et al. 1997; Murphy et al. 2002).

The pens used in the identification test had black caps and bottoms and were labeled 1–5 in black print. The OFFE identification test was also used successfully in NSHAP wave 1 (Boesveldt et al. 2011; Pinto et al. 2014; Schumm et al. 2009).

Scoring and Classification

Each of the three tests of OFFE is scored separately by summing the number of correct responses. In all three tests, a response of “don't know” or refusal is scored as incorrect. For each test, respondents were placed into one of the three olfactory function categories: (1) anosmic, (2) hyposmic, and (3) normosmic based on comparisons with other published studies (Cain 1989; Hummel et al. 2007; Mueller and Renner 2006). Anosmic indicates a lack of olfactory function; hyposmic indicates reduced olfactory function; and normosmic indicates olfactory function for a healthy normal adult.

Relevant Respondent History

NSHAP documented any history of severe head injury or nose surgeries. Respondents were also asked, “Today, do you have a head cold or chest cold?” A list of current medications and self-reported smoking history were also recorded. Finally, an open-ended notes section available in CAPI allowed interviewers to record any explanation respondents offered regarding smell deficits or loss.

Results

Cooperation Rates

Ninety-six percent of the sample consented for participation (1,006 men and 1,206 women; mean age 72.5, SD = 8.1). Of these, 99.4% ($n = 2,199$) completed all three tasks (separately: *n*-butanol 99.8% [$n = 2,207$], AND 99.6% [$n = 2,204$], and identification 99.7% [$n = 2,205$]). Interviewer notes indicate that respondents who did not complete after consenting were frustrated or disinterested.

Administration Time

The distribution of times to complete OFFE, including obtaining consent for each measure and explaining the instructions, is generated from CAPI data and depicted in Figure 1. The median time to complete OFFE and each component test is presented here followed parenthetically by the first and third quartile of the sample. The median time to complete OFFE was 11.28 minutes (9.37; 13.53). The median times to administer the individual tests of OFFE were consent and instructions, 0.65 minutes (0.20; 2.12); *n*-butanol, 5.03 minutes (3.83; 6.43); AND, 2.57 minutes (1.52; 3.38); and identification, 2.17 minutes (1.82; 2.72).

Detection: Functional Classification

***n*-Butanol**—The percentage of OFFE respondents classified by level of olfactory function for each test is presented in Figure 2. A quarter of the sample (26%) correctly detected five or six *n*-butanol pens, which we classified as normosmic. These respondents were able to detect concentrations that approximate the average threshold previously reported in a small clinical subset ($n = 289$) of older adults in Germany (Hummel et al. 2007). Nearly half of the

sample (45%) was only able to detect three or four pens, which we classified as hyposmic (i.e., they are experiencing some form of olfactory dysfunction). Finally, 29% of the sample was unable to detect more than two *n*-butanol target pens. The strongest concentration typically used clinically is 4.0% *n*-butanol (Hummel et al. 2007). An inability to detect this concentration is regarded as dysfunction in clinical samples (Cain 1989). Since OFFE includes target pens containing 4.0% and 8.0% *n*-butanol, we classified respondents who are unable to detect more than two pens as anosmic.

AND—The AND concentrations chosen for OFFE were similarly selected to identify three types of individuals previously reported when tested for sensitivity to AND: “supersmellers,” “smellers,” and “anosmics” (Lundström et al. 2003). The capacity to identify these three phenotypes will offer the opportunity to investigate AND detection abilities that may be associated with clinical or physiological effects. Only 2% of the sample detected all four AND pens. We classify these most sensitive respondents as normosmic (supersmellers). Approximately one-third of the sample (35%) detected two or three AND pens. We consider these individuals who display an ability to detect AND as hyposmic (smellers). Finally, 36% of the sample detected one or none of the AND pens. The strongest AND concentrations administered were 2.0% and 5.3%. We consider those who are unable to detect AND at these high concentration as anosmic to AND.

Additionally, 585 respondents (27% of the sample) who indicated that they were unable to smell AND in the screener pen, even when explicitly told of its presence, did not receive the remaining triads. These respondents are also considered anosmic to AND.

Identification: Functional Classification

Mueller and Renner (2006) compared identification abilities of subjects for the same five identification odors used in OFFE and the full 16-item identification test and found that nearly all subjects who correctly identified four or five odors also scored in the normative range on the larger test. In contrast, those who were unable to identify any of the five identification pens scored similarly to anosmics on the established 16-odor test. More than three-quarters of the NSHAP sample (76%) identified four or five of the identification odors. We similarly classify these individuals as normosmic. Approximately 18% of the sample identified two or three odors and are considered hyposmic. Respondents who only identified one odor, or who failed to identify any of the OFFE odors (6% of the sample) are considered anosmic.

Discussion

The OFFE detection tests provide a method to evaluate olfactory detection abilities in a field setting for the first time and allow researchers to continue to assess the role of olfaction in everyday life. *n*-Butanol detection abilities are meaningful when considering environmental hazards, nutritional needs, and physical health. Evaluation of AND detection abilities will be critical to the continued investigation of the role of olfaction in the social world. The disparate distributions of these two abilities in our results reinforce that olfactory function is not a monolithic process consisting of a single component.

Previous survey research has focused almost exclusively on tasks of olfactory identification. Older adults in Beaver Dam, Wisconsin, were administered the eight-item SDOIT, which has 96% agreement with the B-SIT when classifying dysfunction and abnormal olfactory function (Krantz et al. 2009). Twenty-four and a half percent of Beaver Dam older adults identified five SDOIT odors correctly (62.5% correct) and were considered to have olfactory dysfunction (Murphy et al. 2002).

We categorized olfactory dysfunction on the OFFE identification test as being able to correctly identify three odors out of a total of five (60% correct). Twenty-four percent of OFFE respondents fit these criteria and are categorized as having olfactory dysfunction (18% hyposmic and 6% anosmic). Using Sniffin' Sticks pens in OFFE instead of opaque jars with odor-filled gauze (SDOIT), or microencapsulated, single-use scratch and sniff odors (B-SIT), we report a nearly identical percentage of olfactory dysfunction using fewer odors and fewer trials than other tests.

The term presbyosmia (age-related olfactory loss) recognizes that functional decline in olfaction is typical of aging. Our *n*-butanol detection data demonstrate that three-quarters of the older adults have some form of olfactory dysfunction. These individuals were unable to detect concentrations several steps stronger than the average threshold previously reported among older adults, suggesting that this cutoff may even be conservative and therefore underestimate the proportion of adults experiencing some form of dysfunction. This is especially relevant if future longitudinal research reveals mild dysfunction to be a precursor of more substantial declines.

OFFE can be deployed in field environments by lay interviewers to evaluate both olfactory identification and olfactory detection in a practical and accurate fashion. OFFE also offers a viable alternative for use in clinical practice where training and time constraints may preclude olfactory evaluation. Use of self-contained, reusable smell pens makes field or clinical olfactory testing both feasible and efficient. Straightforward, rapid, and noninvasive measures ensure a high cooperation rate and reliable administration. OFFE yields high-quality data at a low cost in a short time. Measuring olfaction in large, representative field samples will allow researchers to investigate relationships between this understudied sensory modality and a host of health outcomes and social interactions.

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Figure 1.

Distribution of times for olfactory function field exam completion (Kaplan–Meier survival estimate). The reference lines indicate the upper bound of the fastest quartile (9.37 minutes), median/second quartile (11.28 minutes), and the third quartile (13.53 minutes).

Figure 2.
Classification of olfactory function: odor identification and detection (*n*-butanol and androstadienone).