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Association of Alterations in Smell and Taste with Depression in Older Adults

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Objective: Examine the relationship between depression and changes in smell or taste.

Study Design: Cross-sectional analysis of 2011–2012 and 2013–2014 National Health and Nutrition Examination Survey (NHANES).

Methods: We examined 5,275 adults ≥40 years old who completed smell and taste questionnaires as well as a validated depression assessment instrument, the Patient Health Questionnaire (PHQ-9). Analyses incorporated sampling weights to account for the complex sampling design and associations were analyzed using multivariate logistic regression adjusted for related demographics and socioeconomic data.

Results: The prevalence of altered smell and taste was 23.0% (95% CI: 20.7–25.3%) and 11.9% (95% CI: 10.7–13.1%), respectively. Among those who met criteria for major depressive disorder, the prevalence of altered smell and taste was higher at 39.8% (95% CI: 33.4–46.1%) and 23.7% (95% CI: 18.7–28.7%), respectively. In a multivariate model adjusting for age, gender, education, major comorbidities, smoking history, heavy alcohol use, sinus disease, cold symptoms, and trauma history, adults ≥40 and <65 years old who reported alterations in smell (OR: 1.64, $p = 0.004$) and adults ≥40 years old who reported alterations in taste (OR: 1.77, $p = 0.001$) were more likely to meet criteria for major depressive disorder.

Conclusion: There is a strong association between major depression and alterations in smell and taste among certain age groups in the general U.S. population. Primary care providers should screen for depression when patients report changes in smell or taste.

Key Words: Olfaction, gustation, depression, major depressive disorder, health disparities, smell, taste.

Level of Evidence: 4.

INTRODUCTION

The ability to smell and taste contributes significantly to a patient's quality of life. However, in the United States, an estimated 15 million individuals report problems with smell and 7.5 million individuals report having problems with taste in the previous 12 months, with the prevalence increasing with age.[1] Olfactory dysfunction can result from viral upper respiratory infections (URI), side effects of certain medications, head trauma, sinonasal disease, congenital anosmia, neurodegenerative disorders, or normal aging.[2–6] Disorders of taste are less common and are often difficult to distinguish from olfaction-related gustatory alterations.[7] Common causes of taste dysfunction include URI, head trauma, medications, and idiopathic causes.[5,6,8] Olfaction and gustation play an important role in eating, hazard detection (eg, poisonous fumes, smoke, spoiled food), social communication, and overall quality of life.[3,9,10]

While other major sensory impairments such as blindness and hearing loss are known to be associated with mental health disorders, the link between olfactory dysfunction and depression is not as well characterized.[11–13] Previous studies have associated impairment of olfactory function with worse cognitive function, feelings of vulnerability, increased loneliness, and depressive symptoms.[4,14–16] However, these studies had small sample sizes limited to an institution or specific population with oftentimes conflicting results. Many specifically only examined patients with chronic sinonasal disease or patients seeking medical attention for olfactory disorders. The relationship between major depression and changes in smell or taste has not been previously described in a nationally representative sample of U.S. adults.[17,18] Even less is known about the relationship between gustatory disorders and depression; limited studies show an association between taste perception and affective disorders, and anecdotally clinicians have observed patients developing depression subsequent to gustatory dysfunction.[19,20]

The National Health and Nutrition Examination Survey (NHANES) collected health surveys on taste and

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smell ability as well as related health conditions for the first time in representative samples in the U.S. in 2011–2012 and 2013–2014. In this study, we used extracted data from the NHANES survey to study the relationship between depression and alterations in smell and taste in adults ≥40 years old.

METHODS

Adult data was collected from the 2011–2012 and 2013–2014 NHANES, which uses a complex, multistage, probability sampling design to select participants from the civilian noninstitutionalized U.S. population. Since the data was already deidentified and is publicly available, this study was exempt from institutional review board approval.

Adults who were 40 years or older were eligible to participate in the taste and smell disorders component of the NHANES, which was administered in the 2011–2012 and 2013–2014 surveys for the first time. The analytic cohort was composed of 6,352 adults who had complete data on smell and taste alteration and depression. There were no exclusion criteria to the taste and smell questionnaire. Participants were categorized as having smell alteration if they reported a problem in smell in the past 12 months (yes/no), worse sense of smell since age 25 (better now/worse now/no change), or smelling an unpleasant, bad, or burning odor when nothing is there (yes/no).[21] Participants were categorized as having taste alteration if they reported a problem with taste in the mouth in the past 12 months (yes/no) or change in ability taste food flavors such as chocolate/vanilla/strawberry since age 25 (yes/no). "Associated medical history" variables included persistent cold/flu for longer than a month in the past 12 months (yes/no), ever having two or more sinus infections (yes/no), ever having a broken nose or other serious injury to face or skull (yes/no), and ever having a loss of consciousness because of a head injury (yes/no). Sociodemographic information was collected for each respondent including age, gender, race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican-American or other Hispanic, Asian, or others), education level (<12th grade, high school graduate, or some college or more), and annual household income (<US $20,000, $20,000–45,000, $45,000–75,000, ≥$75,000). "Comorbidity" variables known to be related to smell and taste alteration included in the study were diabetes (based on self-reported diagnosis and/or current use of insulin or other diabetic medications), cardiovascular disease (congestive heart failure, coronary artery disease, angina pectoris, or myocardial infarction), stroke (self-reported history), hypertension (told by physician on two more more visits about hypertension diagnosis), smoking status (current, former, and never), and heavy alcohol use (≥4 drinks per day).

The nine-item Patient Health Questionnaire (PHQ-9) was used to evaluate depressive disorders. The validated questionnaire is a self-administered version of the PRIME-MD diagnostic instrument for common mental disorders that measures the presence and severity of depression with scores ranging from 0–27.[22] A PHQ-9 score ≥10 is considered diagnostic for major depression with a sensitivity of 88% and specificity of 88%.[22] Participants were categorized as having any depressive symptoms or major depressive disorder if either of the initial questions addressing depressed mood was answered as "more than half the days" or "nearly every day" and the PHQ-9 score was ≥5 or ≥10, respectively.

Data was analyzed using Stata software (version 11.1, StataCorp, College Station, TX, U.S.A.). Survey variables that incorporated weighting, clustering, or stratification were used in the statistical analysis to produce national estimates for the prevalence of taste and smell disorders based on the survey design for NHANES. Unweighted numbers were reported in Table I to provide descriptive measures of the study cohort. Statistical analysis included the Student's t test for continuous variables and chi-square or Fisher's exact tests for categorical variables. The population prevalence of smell and taste alterations were estimated with 95% confidence intervals. Logistic regression analyses were used to examine the associations between smell/taste alteration and depression. Sociodemographic variables along with cardiovascular factors and other related medical risk factors were explored in association in association with the smell and taste alteration. All significant tests were two-sided with a type 1 error rate of 0.05.

RESULTS

The overall study population consisted of 5,275 adults 40 years or older who participated in the NHANES survey in 2011–2012 and 2013–2014. Of those who participated, 1,172 adults were classified as having self-reported smell alteration, and 652 were classified as having self-reported taste alteration. In adults who reported having alterations in smell, the average age was 59.5 years old, 49.3% were female, 50.9% were white, 55.0% had some college education or more, and 26.9% had an annual household income less than $20,000 a year. In adults who reported having alterations in taste, the average age was 60.0 years old, 50.3% were female, 48.2% were white, 50.6% had some college education or more, and 29.6% had an annual household income less than $20,000 a year. Also, adults with alterations in taste or smell had a significantly higher prevalence of hypertension, cardiovascular disease, diabetes, stroke, smoking, heavy alcohol use, two or more sinus infections, persistent cold symptoms, previous head injury, and nasal or facial fractures. Table I displays further details regarding the sociodemographic characteristics of this study's cohort.

Table II describes the prevalence of smell or taste alterations in three groups: the study cohort, those in the study with any depressive symptoms, and those in the study with major depressive disorder. The overall estimated prevalence of alterations in smell and taste in U.S. adults ≥40 years were 23.0% (20.7–25.3) and 11.9% (10.7–13.1), respectively. Among respondents with depressive symptoms, the prevalence of alterations in smell and taste were estimated to be 33.9% (27.8–39.9) and 19.3% (14.7–23.8), respectively, both higher than the overall population. The prevalence of alterations in smell and taste were also estimated to be higher among participants with major depressive disorder at 39.8% (33.4–46.1) and 23.7% (18.7–28.7), respectively.

Table III displays the results of the stepwise multivariate logistic regression analysis of the association between depressive disorders and alterations in smell and taste. After controlling for demographic factors, comorbidities, and associated medical history, adults with alterations in smell were more likely to have any depressive symptoms (OR: 1.35, $p = 0.02$) and major depressive disorder (OR: 1.67, $p < 0.001$), and adults who reported alterations in taste were more likely to have major depressive disorder (OR: 1.77, $p = 0.001$).

TABLE I.
Demographic Characteristics of Participants Age ≥40 Years NHANES 2011–2012 & 2013–2014.

Characteristics	Smell Alteration			Taste Alteration		
	Yes (n = 1172)	No (n = 4103)	*p*	Yes (n = 652)	No (n = 4623)	*p*
Gender, n (%)						
Male	594 (50.7)	2173 (53.0)		324 (49.7)	2443 (52.8)	
Female	578 (49.3)	1930 (47.0)	0.17	328 (50.3)	2180 (47.2)	0.13
Age, mean (SD)	59.5 (12.0)	58.8 (11.8)	<0.001*	60.0 (11.7)	58.9 (11.8)	0.001*
Race, n (%)						
White	596 (50.9)	1796 (43.8)		314 (48.2)	2078 (45.0)	
Black	247 (21.1)	1003 (24.4)		162 (24.8)	1088 (23.5)	
Hispanic	222 (18.9)	833 (20.3)		118 (18.1)	937 (20.3)	
Asian	68 (5.8)	389 (9.5)		35 (5.4)	422 (9.1)	
Other	39 (3.3)	82 (2.0)	<0.001*	23 (3.5)	98 (2.1)	0.002*
Education, n (%)						
Less than high school	262 (22.4)	928 (22.6)		192 (29.5)	998 (21.6)	
High school graduate	265 (22.6)	907 (22.1)		130 (19.9)	1042 (22.5)	
Some college or more	645 (55.0)	2268 (55.3)	0.93	330 (50.6)	2583 (55.9)	<0.001*
Comorbidities, n (%)						
Hypertension	612 (52.2)	1866 (45.5)	<0.001*	368 (56.4)	2110 (45.6)	<0.001*
Diabetes	247 (21.1)	746 (18.2)	0.03*	159 (24.4)	834 (18.0)	<0.001*
Cardiovascular disease	191 (16.3)	413 (10.1)	<0.001*	115 (17.6)	489 (10.6)	<0.001*
Stroke history	83 (7.1)	185 (4.6)	<0.001*	51 (7.8)	217 (4.7)	0.001*
Smoking, n (%)						
Never	470 (40.1)	1985 (48.4)		264 (40.5)	2191 (47.4)	
Former	416 (35.5)	1305 (31.8)		226 (34.7)	1495 (32.3)	
Current	286 (24.4)	813 (19.8)	<0.001*	162 (24.8)	937 (20.3)	0.002*
Annual household income, n (%)						
<$20,000	315 (26.9)	782 (19.1)		193 (29.6)	904 (19.6)	
$20,000–45,000	332 (28.3)	1067 (26.0)		190 (29.1)	1209 (26.2)	
$45,000–75,000	179 (15.3)	749 (18.3)		94 (14.4)	834 (18.0)	
>$75,000	275 (23.5)	1165 (28.4)		133 (20.4)	1307 (28.3)	
Refused/unsure	71 (6.1)	340 (8.3)	<0.001*	42 (6.4)	369 (8.0)	<0.001*
Medical history, n (%)						
Sinus infection	515 (43.9)	1262 (30.8)	<0.001*	272 (41.7)	1505 (32.6)	<0.001*
Previous head injury	251 (21.4)	514 (12.5)	<0.001*	130 (19.9)	635 (13.7)	<0.001*
Persistent cold symptoms	133 (11.4)	213 (5.2)	<0.001*	76 (11.7)	271 (5.9)	<0.001*
Nasal or facial fracture	248 (21.2)	585 (14.3)	<0.001*	143 (21.9)	690 (14.9)	<0.001*
Heavy alcohol use	268 (22.9)	688 (16.8)	<0.001*	141 (21.6)	815 (17.6)	0.01*

*$p < 0.05$
Defined as having four or more drinks of any alcoholic beverage daily.
SD = standard deviation.

Table IV displays the results of the same stepwise multivariate logistic regression model performed in Table III after stratifying the study cohort into two age groups. Adults <65 years old with alterations in smell were more likely to have any depressive symptoms (OR: 1.36, $p = 0.03$) and major depressive disorder (OR: 1.64, $p = 0.004$). However, adults ≥65 years old with alterations in smell had no significant association with major depressive disorder after controlling for comorbitidies (OR: 1.72, $p = 0.075$). The association between alterations in taste and major depressive disorder was not affected by the age stratification.

TABLE II.
Prevalence of Smell and Taste Alterations in Participants Age ≥40 Years NHANES 2011–2012 & 2013–2014 (weighted estimates).

	Smell Alteration (95% CI)	Taste Alteration (95% CI)
Total prevalence	23.0 (20.7–25.3)	11.9 (10.7–13.1)
Any depressive symptoms*	33.9 (27.8–39.9)	19.3 (14.7–23.8)
Major depressive disorder*	39.8 (33.4–46.1)	23.7 (18.7–28.7)

†Defined as in Methods.
CI = confidence interval.

TABLE III.
Stepwise Regression Models of the Association between Major Depressive Disorder or Any Depressive Symptoms with Smell and Taste Alterations.

	Smell Alteration				Taste Alteration			
	Any Depressive Symptoms[†]		Major Depressive Disorder[†]		Any Depressive Symptoms[†]		Major Depressive Disorder[†]	
Variable	OR (95% CI)	*p*	OR (95% CI)	*P*	OR (95% CI)	*p*	OR (95% CI)	*p*
Base model	1.84 (1.42–2.39)	<0.001**	2.37 (1.80–3.11)	<0.001**	1.91 (1.36–2.69)	0.001**	2.49 (1.78–3.49)	<0.001**
Base + demographic factors[‡]	1.66 (1.27–2.19)	0.001**	2.13 (1.64–2.77)	<0.001**	1.64 (1.14–2.35)	0.009**	2.16 (1.53–3.04)	<0.001**
Base + demographic factors[‡] + comorbidities[§]	1.48 (1.15–1.90)	0.003**	1.86 (1.44–2.41)	<0.001**	1.49 (1.07–2.08)	0.021*	1.94 (1.40–2.70)	<0.001**
Base + demographic factors[‡] + comorbidities[§] + associated medical history[#]	1.35 (1.05–1.74)	0.02*	1.67 (1.28–2.19)	<0.001**	1.37 (0.98–1.91)	0.066	1.77 (1.27–2.46)	0.001**

*$p < 0.05$; **$p < 0.01$
[†]Defined in Methods.
[‡]Demographic factors include age, gender, education, and income.
[§]Comorbidities include hypertension, cardiovascular disease, diabetes, stroke, smoking, and heavy alcohol use.
[#]Associated medical history includes previous sinus infections, persistent cold symptoms, previous head injury, and nasal/facial fracture.
CI = confidence interval; OR = odds ratio.

DISCUSSION

To our knowledge, this is the first study in the literature to investigate the relationship between major depression and self-reported alterations in olfaction and gustation using a large nationally representative sample that included a validated questionnaire to diagnose major depressive disorder. One previous study by Boesveldt et al. analyzing data from a nationally representative probability sample of 3005 older American adults reported an association between any depressive symptoms and olfactory dysfunction, which is consistent with our results.[23] That study, however, did not evaluate for major depression.[23] All other previous studies evaluating the relationship between depression and olfaction or taste were small case-control studies with varied results.[24,25]

The overall prevalence of altered smell and taste were estimated to be 23.0% and 11.9% among U.S. adults, respectively. This corresponds to studies of olfactory dysfunction that reported a prevalence of 19% to 24% in adults.[26–28] Few published reports have described the prevalence of gustatory dysfunction; major chemosensory clinical centers report that while approximately 70% of patients with gustatory complaints demonstrated olfactory loss, fewer than 10% demonstrated quantifiable taste loss.[29,30] Given the relatively low incidence of taste disorders in the general population and that most subjective taste complaints can be attributed

TABLE IV.
Regression Model of the Association between Major Depressive Disorder or Any Depressive Symptoms with Smell and Taste Alterations Stratified by Age.

		Smell Alteration				Taste Alteration			
		Any Depressive Symptoms[†]		Major Depressive Disorder[†]		Any Depressive Symptoms[†]		Major Depressive Disorder[†]	
	Variable	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
<65 years	Base + demographic factors[‡] + comorbidities[§] + associated medical history[#]	1.36 (1.03–1.81)	0.031*	1.64 (1.19–2.26)	0.004**	1.32 (0.88–1.98)	0.172	1.66 (1.12–2.47)	0.014*
≥65 years	Base + demographic factors[‡] + comorbidities[§] + associated medical history[#]	1.24 (0.77–2.00)	0.362	1.72 (0.94–3.12)	0.075	1.54 (0.99–2.40)	0.056	2.14 (1.07–4.30)*	0.033*

*$p < 0.05$; ** $p < 0.01$
[†]Defined in Methods.
[‡]Demographic factors include age, gender, education, and income
[§]Comorbidities include hypertension, cardiovascular disease, diabetes, stroke, smoking, and heavy alcohol use
[#]Associated medical history includes previous sinus infections, persistent cold symptoms, previous head injury, and nasal/facial fracture
CI = confidence interval; OR = odds ratio.

to olfactory loss, it has been recommended that olfaction be the primary investigative focus for clinicians.[31]

In our study cohort, we found significantly higher rates of comorbidities and other medical conditions in adults with alterations in smell or taste. This is consistent with previous studies analyzing national surveys on this topic.[32,33] Persistent cold/flu symptoms, sinonasal disease, and head trauma have been reported as being associated with olfactory and gustatory dysfunction likely due to disruption or obstruction of the olfactory mucosa.[1–3,8] Comorbidities and exposure to environmental toxins such as smoking and alcohol also likely increase the risk of damage to the olfactory mucosa leading to dysfunction.[34]

Older age has been consistently shown to correlate with a decreased ability to both smell and taste, with older males most affected.[16,26–28,35,36] However, findings are inconsistent regarding the effect of age on the psychological impact of olfactory dysfunction. While some studies found that elderly people with olfactory impairment were more likely to report depression and low quality of life, others found this association to be confounded by low cognitive function or other general health-related problems.[14–16,35,37] In this study, alterations in smell impairment was a strong predictor for depressive symptoms and major depressive disorder in adults less than 65 years old but not for adults $\geq$65 years old suggesting the association is likely confounded by the age-related physical and mental health changes seen in the geriatric population. The association between alterations in taste and major depressive disorder, on the other hand, was not affected by age stratification suggesting that alterations in taste may be a stronger predictor than alterations in smell for depression in the geriatric population.

We found that among those who met the criteria for major depressive disorder, the prevalence of altered smell and taste was higher at 39.8% and 23.7%, respectively. Even after controlling for sociodemographic factors, comorbidities, and associated medical risk factors, adults with olfactory or gustatory dysfunction were more likely to have major depressive disorder compared to adults without olfactory or gustatory dysfunction. The literature on olfactory or gustatory dysfunction in depressed populations is limited; however, a recent systematic review found several case-control studies that demonstrated patients with depression exhibited multiple aspects of smell dysfunction, including decreased scores for olfactory threshold, discrimination and identification, compared to controls.[24] Only one case-control study investigating the association between taste and depression was identified in the literature. The study of 39 patients in 1969 found that depressed patients required a significantly higher threshold concentration to perceive all basic taste modalities (sweet, salty, sour, and bitter) compared to nondepressed patients.[25]

Possible pathophysiologic mechanisms for the development of olfactory dysfunction secondary to depression or vice versa have been proposed. Depression is associated with elevated levels of inflammatory cytokines such as interleukin-6, tumor necrosis factor α, interleukin-1β, and glucocorticoids which can inhibit neurogenesis leading to limited proliferation of olfactory neurons.[24,38,39] Olfactory dysfunction causing secondary development of depression has also been suggested. In animal models where the olfactory bulbs have been ablated, the resulting chemical and behavioral states are similar to the profile of a depressed state.[24,39,40]

A pathophysiologic mechanism for the association between gustatory dysfunction and depression may involve the development of anhedonia, a core symptom of major depressive disorder, which can be detected in a decreased response to palatable food in rat models. One study demonstrated reduced expression of 5-HT1A receptors for serotonin in the taste cells of rats that develop anhedonia, suggesting that biological changes in taste cells may be a contributing factor to the development of depressive symptoms.[41]

The association between major depressive disorder and olfactory and taste dysfunction in older adults is further supported by a recent study on whether olfactory training improves quality of life and reduces the likelihood of depressive symptoms. A randomized unblinded study in Germany of 91 older participants (54 to 84 years) demonstrated that olfactory training for five months improved olfactory function and decreased depressive symptoms.[42] Further study is necessary to determine the role and clinical impact of olfactory training in reducing the odds of major depressive disorder, but it may be a promising inexpensive intervention in the future.

There are some limitations to this study that should be considered when interpreting the results. First, the reliance on self-reporting by individuals raises the possibility of recall bias. Alterations in smell and taste were not confirmed with objective standardized clinical tests, and the severity of smell and taste disturbances was not assessed. Second, the cross-sectional design of the study precludes the ability to draw valid conclusions on causality. Finally, the results are generalizable only to older adults in the U.S. population.

CONCLUSION

There is a strong association between major depression and olfactory and gustatory dysfunction among adults in certain age groups in the general U.S. population. Healthcare practitioners may be able to improve the quality of life of patients reporting alterations in taste or smell by screening for depressive symptoms and referring patients to mental health services. Further prospective studies are warranted to determine whether improving olfactory and gustatory function in older adults reduces the odds of major depressive disorder.

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