OLFACTION IMPAIRMENT AND ITS ASSOCIATION WITH WEIGHT AND PROGRESSIVE WEIGHT LOSS IN OLDER ADULTS

By

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ABSTRACT

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Olfaction impairment (OI) is a very common, but underreported, sensory deficiency among older adults that can lead to a host of adverse health conditions, quality of life issues, and is a predictor of 5-year mortality. Similarly, body composition and weight are driving factors of poor health among older populations, with malign effects including decreased mobility and sarcopenia. We theorize that older adults with OI both weigh less, and lose weight faster than those with without any impairment. Our goal is to examine how OI associated with weight and weight loss two ways: 1) cross-sectional, where we assess the association during the year sense of smell was tested; and 2) longitudinally, where we inspect whether OI indicates more rapid weight loss over a seven-year period. The outcome variables of interest were total mass, total lean mass, total bone-free lean mass and total fat mass. Analyses were also performed in race-specific populations and in sex-specific populations. Data were obtained from the Health, Aging and Body Composition Study. The study found in the cross-sectional analysis that those with poor olfaction has significantly less total mass (-1.48 kg) and fat mass (-1.05 kg) than those with good olfaction. Longitudinally, those with poor olfaction showed a significantly faster decrease in total mass (-245.7 g/year), lean mass (-171.4 g/year) and bone free mass (-164.7 g/year) but not fat mass. Differing results were found in race-specific analyses but not in sex-specific analyses, with the decrease in weight appearing in whites but not blacks.

Dedicated to Heidi, Story and Collins.
For your support, love and understanding.

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INTRODUCTION

In older adults, olfaction impairment (OI) is a very common ailment that represents a crucial factor in many health issues, with studies indicating that the prevalence of OI increases with age. The prevalence of OI has been shown to be approximately 25%[1] in those aged 50 and older, but the prevalence increases to a range of 60%-75% when looking at adults 80 and older.[1,2] Disparities are present when examining OI by racial group, with the rate of OI in blacks approximately twice that of OI in similar white populations,[1,3,4] even after controlling for demographics, socio-economic considerations and health statuses. Poor olfaction can lead to a host of health problems that adversely affect older populations, including quality of life decline, safety concerns[5] and dietary changes.[6] Perhaps even more importantly, studies have also revealed that olfaction has a significant impact on cognitive health, with poor olfaction regarded as a potential prodromal symptom for neurodegenerative diseases like Parkinson's Disease an Alzheimer Disease,[7,8] and a risk factor for schizophrenia as well.[9] Indications also show that poor olfaction is a predictor of 5-year mortality in older adults.[10] This makes OI one of the leading factors of ill health in older adults. However, there is still much regarding the relationship between olfaction impairment and general health status in older populations that is unknown and needs to be explored further. This study will focus one area of potential concern, poor olfaction and its association with weight and weight loss.

Weight, body composition, and weight loss have been found to be significant factors related to the general health status and quality of life within this population. Losses in body weight can have significant negative effects on mobility,[11,12] lean muscle mass[13,14] and bone mineral density,[15] and is associated with many later-in-life conditions, including depression[16] and cognitive impairment.[17] It has also been theorized to be a potential non-cognitive indicator for Alzheimer's disease.[18] Additionally, weight loss (change >5%) can be an indicator for an increased risk of mortality.[19,20] Given the combination of these effects and associations, a person's weight and their ability to maintain a stable weight may be one of the most substantial concerns when considering elderly health.

Research examining the association between olfaction and weight changes in older populations have been limited, especially with regards to whether different races and sexes are affected the same way. If poor olfaction can be shown to be an indicator for lower weight and weight loss, it would be an important step in understanding the connection between olfaction impairment and poor health in older adults. Therefore, this study aims to examine this relationship, using a biracial community-based cohort of older adults in the United States, in two ways: 1) a cross-sectional approach to explore the how poor olfaction is associated with weight and body composition and 2) a longitudinal approach that further scrutinizes whether poor olfaction can be predictive of weight loss. Both analyses will examine the overall population, as well as race- and sex-specific populations.

METHODS AND MATERIALS

Study Population

The Health, Aging and Body Composition Study (HABC) was created as a way to delve into the multitude of factors that lead to the decline of functions in older adults, with its focus on the change in body composition in relation to age, behavioral and physiological conditions. The study began in 1997-1998, enrolling a total of 3075 community-dwelling, healthy older adults, aged 70-79. The eligibility criteria for entry included a self-reported ability to climb 10 stairs and walk ¼ mile with no difficulty, no mobility-related problems in performing every-day tasks, cancer-free for the previous three years and no intention of changing residence for at least three years. The participants were recruited from two separate sites, Memphis, Tennessee and Pittsburgh, Pennsylvania and were 45% women and 33% African-American. Contact was made with participants on an annual or biennial basis through clinical and home visits through year 10 and then again at year 16. Further contact made by semiannual phone calls to update contact information and health status through year 15, and then quarterly until year 17. Olfaction was examined during the year 3 clinical visit using the 12-item Brief Smell Identification Test (BSIT). Body composition and weight measurements were assessed during annual clinical visits beginning in year 1, and then were subsequently switched to biennial clinic visits starting after year 6. Institutional Review Boards at the University of Tennessee, the University of Pittsburgh and the University of California-San Francisco approved all study protocols and informed written consents were obtained for all participants. [21]

Anthropometric Outcomes

Four body composition measures of interest were identified that have shown to affect the health status of older adults: 1) total mass[12] (or whole body mass), 2) total lean mass (also called fat-free mass), 3) total bone-free lean mass[22] and 4) total fat mass.[14] These anthropometrics were collected annually for years 1-6, and then biennially for years 8 and 10, using whole body dual-energy X-ray absorptiometry (DXA). DXA is a non-invasive method that has the ability to measure both total body composition and regional subsections as well. Two separate x-rays are generated using different energy levels and then, through the comparison of the two results, accurate totals can be assessed for various body composition measures.[23] Total mass, lean mass and fat mass are obtained directly from the DXA while bone-free mass is calculated from the difference of lean mass and bone mineral content (also obtained directly through DXA). Validation for DXA in gathering lean mass measurements[24] and fat mass measurements[25] has been published previously.

Brief Smell Identification Test

The BSIT, an abbreviated version of the 40-item Pennsylvania Smell Identification Test, is a widely-used[10,12,26] exam for olfaction in epidemiological studies and was performed during the year 3 clinical visit. It is a cross-cultural test that asks respondents to identify 12 common odors, via a scratch-and-sniff form, and choose the correct answer from a selection of four options. Each correct answer is given a point and the final score is the total of all correct answers, ranging from 0-12, with a higher score indicating a better sense of smell.[27] Validation for this test of olfaction has been show in multiple studies.[27,28]

For the purposes of this study, a score >10 will be considered within the good olfaction group, a score ≥9 and ≤10 will be considered within the moderate olfaction group, and any score <9 will be considered a case within the poor olfaction group. The BSIT was successfully performed on 2537 participants, and all the data collected from year 3 will be considered their baseline data.

Covariates and Possible Confounders

Other covariates to be considered in this study will include demographic information (age, sex, race, clinic site, height, education and family income), lifestyle choices (smoking status and physical activity), and self-reported general health status and general appetite status. The demographic data was collected upon entry into the study in year 1 and remained unchanged when the olfaction test was given in year 3. Education was categorized by three levels (less than high school, high school graduate, and postsecondary) and annual family income was categorized by four levels (less than 10k, between 10k and 25k, between 25k and 50k, and greater than 50k). Lifestyle choices and the self-reported statuses were gathered in year 3. Smoking status has three levels (never smoker, former smoker, and current smoker), physical activity is binary based on whether the participant walks more than 90 minutes per week at a brisk pace, health status has three levels (excellent/very good, good, and fair/poor) and appetite status has three levels (very good, good, and moderate to poor).

We also controlled for diseases and conditions that are potential confounders within our analysis, following definitions set by already published criteria within the HABC cohort. Disease status at baseline was considered a binary variable for all conditions. Cancer[29] (excluding melanoma), cardiovascular disease[30] (coronary heart disease, congestive heart failure, cerebrovascular disease, and peripheral vascular disease) and cognitive conditions (Parkinson's Disease and dementia)[31] were assessed and adjudicated by experienced physicians using hospital records, current medication information, annual surveillance data and self-reported cases of doctor-diagnosed conditions. Specifically, for Parkinson's Disease, this was done through consensus agreement between two mobility disorder specialists after examination of the relevant records. Additionally, for cognitive conditions, the Modified Mini-Mental Status Examination (3MS)[32] was assessed in years 1, 3, 5, 8, and 10. Using this test (with scores ranging from 0-100), cases of cognitive dementia were assessed if 1) the 3MS score in year 1 was <80 or 2) the race-stratified cognitive decline was ≥1.5 standard deviations since year 1.

We also defined depressive symptoms[33] as a score ≥10 on the 15-question Center for Epidemiological Studies Depression (CES-D) scale. Diabetes[34] was assessed through self-reported diagnoses, if fasting blood glucose levels were ≥126 mg/dL or oral glucose tolerance test levels were ≥200 mg/dL, or through self-reported medication use. Finally, hypertension[35] was defined through self-reported diagnoses and medication use, or if systolic blood pressure was ≥140 mmHg or diastolic blood pressure was ≥90 mm Hg.

STATISTICAL ANALYSIS

Summary Statistics

Using the above anthropometric outcomes variables, covariates and confounders, we reduced the 2537 participants who had taken the BSIT to a final analysis sample. We removed 136 participants due to either missing outcome variables or DXA readings that were invalidated due to artifacts found during screenings that prevented accurate measurements. Participants missing other covariates were also dropped from the analysis (each covariate had, at most, 7 missing data and some missing data overlapped). We believe this exclusion was justified due to the small percentage of missing values and does not affect the robustness or power of the analysis. A single exception was made regarding the variable for family income. This variable had 304 missing values, and we created a missing category in addition to the original 4 levels in order to ensure no further data was lost due their exclusion. The final sample size used in the statistical analysis was 2311 participants, with 1128 males and 1183 females, and 1438 white participants and 873 black participants.

Analysis of variance was conducted to analyze the means of continuous variables across the olfactory groups at baseline, while chi-square tests were performed to assess the proportion of subjects within categorical variables. (Table 1)

Cross-sectional Analysis

It is important to understand the relationship between OI and weight during the year that the smell test was given. As subsequent smell tests weren't given beyond baseline, this analysis will give us the clearest picture regarding the expected body composition by olfaction group, it will

Table 1 Participant characteristics by olfaction score on B-SIT				
	Poor: Score <9 N=753	Moderate: Score ≥9 and ≤10 N=785	Good: Score >10 N=773	p-value*
Continuous Variables, Mean (SD)				
Age (years)	76.1(2.93)	75.6(2.91)	75.1(2.61)	<.0001
Standing Height (m)	1.68(0.09)	1.66(0.10)	1.65(0.09)	0.0278
Daily Caloric Intake (Kcal)	1982.6(852.8)	1872.1(698.9)	1775.5(698.8)	0.0020
Categorical Variables, N (%)				
Sex				<.0001
Female	303(25.6)	400(33.8)	480(40.6)	
Male	450(39.9)	385(34.1)	293(26.0)	
Race				<.0001
White	411(28.6)	494(34.4)	533(37.1)	
Black	342(39.2)	291(33.3)	240(27.5)	
Clinic Site				0.0023
Pittsburgh	362(30.6)	395(33.4)	425(36.0)	
Memphis	391(34.6)	390(34.5)	348(30.8)	
Physical Activity				.1501
≥ 90 mins/week	71(29.1)	78(32.0)	95(38.9)	
< 90 mins/week	682(33.0)	707(34.2)	678(32.8)	
Smoking Status				0.0002
Never Smoker	307(29.6)	349(33.7)	380(36.7)	
Former Smoker	79(44.9)	59(33.5)	38(21.6)	
Current Smoker	367(33.4)	377(34.3)	355(32.3)	
Education				<.0001
Less than High School	242(45.9)	166(31.5)	119(22.6)	
High School Graduate	212(28.5)	269(36.2)	263(35.4)	
Postsecondary	299(28.8)	350(33.7)	391(37.6)	
Family Income				0.0002
Less than 10k	98(42.1)	76(32.6)	59(25.3)	
10k to 25k	270(35.5)	242(31.8)	249(32.7)	
25k to 50k	203(29.9)	247(36.3)	230(33.8)	
Greater than 50k	96(26.5)	117(32.2)	150(41.3)	
Missing	86(31.4)	103(37.6)	85(31.0)	
Health Status				<.0001
Excellent/Very Good	296(28.3)	354(33.8)	396(37.9)	
Good	287(33.1)	315(36.3)	266(30.7)	
Fair/Poor	170(42.8)	116(29.2)	111(28.0)	
Appetite Status				0.0019
Very Good	352(29.4)	422(35.2)	425(35.5)	
Good	288(35.0)	262(31.8)	273(33.2)	
Moderate to Poor	113(39.1)	101(35.0)	75(26.1)	
Diabetes at Baseline				0.0701
Yes	189(35.4)	187(35.1)	157(29.5)	
No	564(31.7)	598(33.6)	616(34.7)	
Hypertension at Baseline				0.2009
Yes	564(32.8)	597(34.7)	558(32.5)	
No	189(31.9)	188(31.8)	215(36.3)	
Cancer at Baseline				0.9278
Yes	146(32.1)	158(34.7)	151(33.2)	
No	607(32.7)	627(33.8)	622(33.5)	
CVD at Baseline				0.9574
Yes	220(33.0)	225(33.8)	221(33.2)	
No	533(32.4)	560(34.0)	552(33.6)	

Table 1 (cont'd) Participant characteristics by olfaction score on B-SIT Cont.				
	Poor: Score <9 N=753	Moderate: Score ≥9 and ≤10 N=785	Good: Score >10 N=773	p-value*
Dementia at Baseline				
Yes	196(56.7)	93(26.9)	57(16.4)	<.0001
No	557(28.4)	692(35.2)	716(36.4)	
Depression at Baseline				
Yes	126(38.2)	116(35.2)	88(26.6)	0.0103
No	627(31.7)	669(33.8)	685(34.5)	
*P-values for continuous variables were obtained through analysis of variance. P-values for categorical variables were obtained through chi-square tests.				

be informative for comparing the differences between olfaction groups, and it will allow us to compare the race- and sex-specific associations.

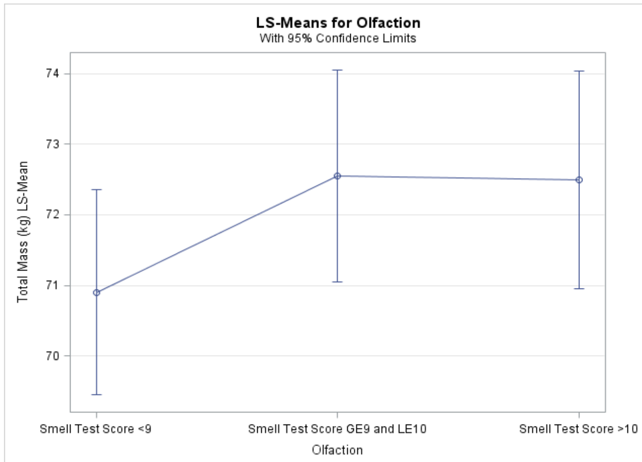
The analysis was completed by means of multiple linear regression, using data from year 3, for four outcomes: 1) total mass, 2) total lean mass, 3) total bone-free lean mass, and 4) total fat mass. Within the exposure variable, the group with the best sense of smell (olfaction score >10) was used as the reference group and all outcomes were adjusted to control for demographics, lifestyle choices, and health, appetite and disease status. The model, in an abbreviated form, can be written as:

$$Y = \beta_0 + \beta_1, \beta_2(Olfaction\ Group) + \beta_3(Age) + \beta_4(Race) + \ \beta_5(Sex) + \beta_6(Height) + \ \beta_7(Site) + \beta_8(Physical\ Activity)$$
$$+ \beta_9, \beta_{10}(Smoke) + \beta_{11}, \beta_{12}(Education) + \beta_{13}, \beta_{14}, \beta_{15}, \beta_{16}(Income) + \beta_{17}, \beta_{18}(Health\ Status)$$
$$+ \beta_{19}, \beta_{20}(Appetite\ Status) + \beta_{21}(Cancer) + \beta_{22}(Diabetes) + \beta_{23}(CVD) + \beta_{24}(Cognitive)$$
$$+ \beta_{25}(Depression) + \beta_{26}(Hypertension) + \varepsilon$$

where ε denotes model error. Dummy variables were created for categorical variables and where multiple β's exist in the model, they represent the individual estimate for each dummy. The following reference levels were used—race: black, sex: female, site: Pittsburgh, physical activity: <90mins/week, smoke: never smoker, education: less than high school, income: less than 10k, health status: fair-poor, appetite status: moderate-poor, all disease statuses: not present.

Least square means (or adjusted means) were estimated from the model and the difference between them were calculated as well. (Figure 1)

Figure 1 Least square means by olfaction group for total mass



Longitudinal Analysis

As previously mentioned, weight loss in older populations is often considered a critical indicator of poor health. A longitudinal analysis will allow us to examine how weight changes over time for all olfaction groups and inspect how the rate of weight loss is different when assessed between separate groups. Again, race- and sex-specific analyses will be explored as well.

For the analysis, year 3 was used as the baseline and year 10 as the final measurement, with the interest being the comparison of linear weight change over time between olfaction groups. To perform the analysis, a mixed model regression with random effects was constructed with estimations obtained through maximum likelihood, rather than the restricted maximum likelihood. This was done for two reasons: 1) It allowed for performances of the likelihood ratio test (LRT) to examine whether parsimonious models existed and 2) even though maximum likelihood produces biased estimates for the standard errors, this bias is reduced when sample sizes are large enough. Our sample size (n=2311) should be sufficient. Fixed effects were defined as the same covariates which were used in the cross-sectional analysis (disease status was updated to include incident cases that occurred during the seven years of interest) and the outcomes examined remained the same as well. Additionally, year was added to fixed effects, as was the interaction between year and olfaction groups. Summary statistics for each outcome in Year 3 and Year 10 can be seen in Table 2.

Table 2 Whole cohort summary statistics for outcome measures in Year 3 and Year 10 in kg

	Mean	Standard Deviation	Range
Year 3			
Total mass	75.2	14.5	41.3-133.2
Total lean mass	48.6	10.2	25.8-84.5
Total bone-free lean mass	46.4	9.7	24.3-81.2
Total fat mass	26.7	8.5	7.0-67.3
Year 10			
Total mass	72.4	14.4	35.3-126.3
Total lean mass	46.9	9.7	24.6-77.2
Total bone-free lean mass	44.9	9.4	23.5-74.8
Total fat mass	25.5	8.2	6.1-64.9

To develop a mixed model that was as reduced as possible, we began with the most complicated form: a full mean function, random effects for both intercept and slope and an unstructured variance, and an unstructured covariance matrix that is not common to each olfactory group. Starting with this most complex model, LRTs were used to reduce the model beginning with the mean function, then turning to the random effects and covariance structures. A summary of these tests can be seen in Table 3, using total mass as the anthropometric example. Similar assessments were made with similar results for the other outcomes.

Table 3 Mixed model comparisons using likelihood ratio tests for Total Mass			
	Chi-Square Statistic*	DF	P-value
Mean Stucture			
Unstructured vs. Different linear average trends	18.2	12	0.6684
Different linear average trends vs Same linear average trends	5.5	1	0.0190
Random Effects			
Both intercept and slope vs Just intercept	No difference	1	NA
Both intercept and slope vs Just slope	823.1	1	<.0001
Just intercept vs No random effects	3682.2	1	<.0001
Covariance Structure			
Common covariance vs. Separate covariance	5791.9	42	<.0001
Unstructured variance vs Toeplitz	331.8	45	<.0001
Calculated from the difference of the -2 log likelihood for the nested model and the full model			

Based on the table above, the most parsimonious mixed model will have a mean structure with different linear average trends, will include a random intercept and have an unstructured variance structure for each of the olfaction groups. Written out, an abbreviated form would be represented by:

$$Y_{ij} = X_i\beta_i^* + \beta_{27i}(Time) + \beta_{28}, \beta_{29}(Time * Olfaction\ group) + b_i + \varepsilon_{ij},$$

where *ij* represents the ith subject at time j=3,4,5,6,8,10, ε_{ij}denotes the model errors, $X_i\beta_i^*$ represents similar covariates shared with the cross-sectional model and b_i represents the random intercept. SAS 9.4 was used for all analyses.

RESULTS

Summary Statistics

In our analysis, (Table 1) olfaction was associated with age, daily caloric intake, sex, race, self-reported health status, self-reported appetite status, and education level. Specifically, poor olfaction was an indicator of older age, a higher daily caloric intake, male sex, black race, a self-reported health status of fair/poor, a self-reported appetite status of moderate to poor and lower education level. For the disease statuses included, associations with olfaction could be observed for dementia and depressive states, but it was not associated for cardiovascular disease, hypertension, diabetes and cancer.

Cross-sectional Analysis

When examining the whole cohort, poor olfaction was significantly associated with lower total mass and lower fat mass when compared to the reference group (good olfaction). (Table 4) Specifically, older adults in the poor olfaction group would have a total mass that, on average, was 1.48kg less than those in the good olfaction group, and a total fat mass that was 1.05kg less. No significance was determined when contrasting good and moderate olfaction scores for total mass or total fat mass, nor was there any significance when comparing any olfaction group for lean mass or bone-free lean mass.

Interestingly, this relationship changes when we separate the analysis by race. When looking only at the white population of older adults, a poor sense of smell is significantly associated with lower expected mass for all four measures of body composition, when compared to those

Table 4 Multivariable linear regression results for mean response by olfaction group in for the whole cohort, race-specific analyses and sex specific analyses

	Whole Cohort		Race				Sex			
			White N=1438		Black N=873		Male N=1128		Female N=1183	
	Estimate(SE)	P-value	Estimate(SE)	P-value	Estimate(SE)	P-value	Estimate(SE)	P-value	Estimate(SE)	P-value
Outcome Measure										
Total mass (kg)										
B-SIT score <9	-1.48(0.64)	0.0205	-2.55(0.73)	0.0005	0.54(1.17)	0.6441	-1.07(0.88)	0.2245	-1.50(0.91)	0.0995
B-SIT score ≥9 and ≤10	0.06(0.60)	0.9191	-0.52(0.67)	0.4393	0.95(1.15)	0.4709	0.04(0.88)	0.9624	0.08(0.82)	0.9263
B-SIT score >10	Ref		Ref		Ref		Ref		Ref	
Total lean mass (kg)										
B-SIT score <9	-0.43(0.28)	0.1291	-0.78(0.33)	0.0173	0.22(0.51)	0.6600	-0.32(0.44)	0.4642	-0.36(0.35)	0.3042
B-SIT score ≥9 and ≤10	0.001(0.27)	0.9966	-0.11(0.30)	0.7210	0.11(0.50)	0.8272	-0.17(0.44)	0.7078	0.09(0.31)	0.7657
B-SIT score >10	Ref		Ref		Ref		Ref		Ref	
Total bone-free lean mass (kg)										
B-SIT score <9	-0.41(0.27)	0.1347	-0.79(0.32)	0.0138	0.28(0.50)	0.5776	-0.32(0.43)	0.4602	-0.33(0.34)	0.3286
B-SIT score ≥9 and ≤10	0.002(0.26)	0.9928	-0.10(0.30)	0.7261	0.10(0.49)	0.8335	-0.15(0.43)	0.7234	0.09(0.31)	0.7741
B-SIT score >10	Ref		Ref		Ref		Ref		Ref	
Total fat mass (kg)										
B-SIT score <9	-1.05(0.42)	0.0126	-1.77(0.48)	0.0003	0.31(0.77)	0.6813	-0.75(0.54)	0.1695	-1.14(0.63)	0.0708
B-SIT score ≥9 and ≤10	0.06(0.40)	0.8800	-0.41(0.44)	0.3557	0.84(0.76)	0.2658	0.21(0.54)	0.7022	-0.02	0.9751
B-SIT score >10	Ref		Ref		Ref		Ref		Ref	

Model fully adjusted for demographics (age, sex, race, height, education, clinic site), lifestyle choice (smoking status, physical activity, average daily caloric intake) and health factors (health status, appetite status, disease status)

with a good sense of smell. Conversely, the opposite is true when turn to a solely black population. No olfaction group was found to have a significantly different expected mass for any of the four outcomes of interest. Even though the results are not significant, there are indications that total mass, lean mass, bone-free mass and fat mass might actually increase for those with poor olfaction, instead of decrease.

The sex-specific analysis showed little variation when comparing olfactory groups. In fact, no significance was seen in any of the expected body composition masses, for either males or females, when comparing poor olfaction to good olfaction.

Longitudinal Analysis

When comparing the rates of change in total mass between the poor olfaction group and the good olfaction group, we found that the poor olfaction group declined more rapidly, by approximately 245g per year. This indicates that at the end of the seven years used in this study, a person with a poor sense of smell would have lost about 1.715kg more total mass than if they'd had a good sense of smell. (Figure 2) Similarly, older adults in the moderate olfaction group also showed a faster decrease (180.3g per year) in total mass than those in the good olfaction group. Poor olfaction was also found to be a predictor of faster weight loss for lean mass and bone-free lean mass, comparatively to good olfaction, but not for fat mass. (Table 5) Within our race-specific analysis, we found results that mirrored our cross-sectional analysis. White participants followed the same pattern as the overall cohort, with both poor and moderate olfaction groups showing a significantly faster decline in their total mass when compared to the good olfaction group. Additionally, the same was true solely for poor olfaction when examining lean mass and bone-free lean mass. No associations were found regarding

Figure 2

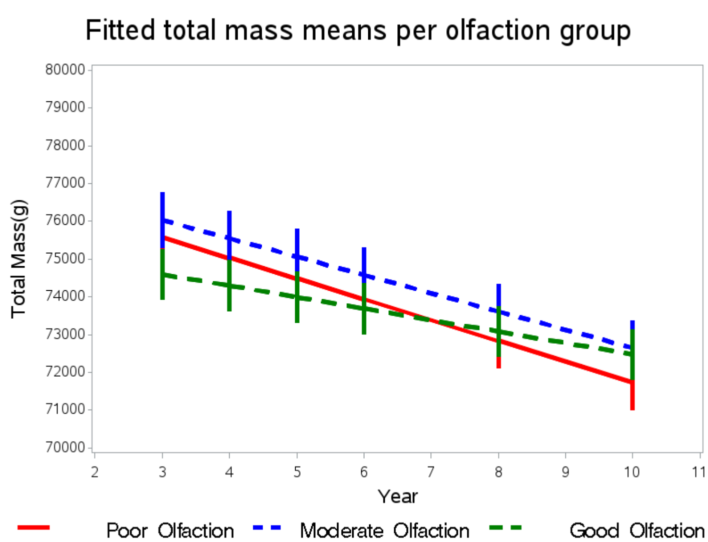


Table 5 Mixed model longitudinal regression results for linear trend of weight over time by olfaction group in for the whole cohort, race-specific analyses and sex specific analyses										
	Whole Cohort		Race				Sex			
			White N=1438		Black N=873		Male N=1128		Female N=1183	
	Estimate(SE)	P-value	Estimate(SE)	P-value	Estimate(SE)	P-value	Estimate(SE)	P-value	Estimate(SE)	P-value
Outcome Measure										
Total mass (g)										
B-SIT score <9*Year	-245.7(93.6)	0.0087	-189.8(83.9)	0.0238	-226.1(352.5)	0.5213	-252.7(250.8)	0.3138	-245.2(139.6)	0.0791
B-SIT score ≥9 and ≤10*Year	-180.3(87.2)	0.0387	-176.2(73.2)	0.0161	-201.3(280.3)	0.4726	-128.6(248.7)	0.6052	-274.1(105.4)	0.0094
B-SIT score >10*Year	Ref		Ref		Ref		Ref		Ref	
Total lean mass (g)										
B-SIT score <9*Year	-171.4(44.3)	0.0001	-132.6(49.4)	0.0073	-159.8(140.7)	0.2561	-103.9(124.4)	0.4035	-92.6(42.8)	0.0307
B-SIT score ≥9 and ≤10*Year	-74.2(41.8)	0.0759	-89.8(49.4)	0.0717	-43.3(135.6)	0.7495	-37.2(124.10	0.7651	-44.8(34.6)	0.1956
B-SIT score >10*Year	Ref		Ref		Ref		Ref		Ref	
Total bone-free lean mass (g)										
B-SIT score <9*Year	-164.7(42.3)	<.0001	-129.3(34.6)	0.0002	-152.5(139)	0.2725	-128.0(82.5)	0.1206	-88.0(42.1)	0.0369
B-SIT score ≥9 and ≤10*Year	-78.1(40.8)	0.0555	-79.4(41.0)	0.0530	-38.7(124.8)	0.7565	-67.5(83.2)	0.4172	-43.8(35.0)	0.2104
B-SIT score >10*Year	Ref		Ref		Ref		Ref		Ref	
Total fat mass (g)										
B-SIT score <9*Year	-92.1(77.6)	0.2355	-97.9(78.9)	0.2147	-82.5(184.9)	0.6553	-125.9(150.5)	0.4029	-205.6(117.4)	0.0799
B-SIT score ≥9 and ≤10*Year	-107.6(74.6)	0.1493	-74.2(58.1)	0.2012	-140.4(181.2)	0.4384	-100.1(117.9)	0.3959	-196.6(94.3)	0.0373
B-SIT score >10*Year	Ref		Ref		Ref		Ref		Ref	
Model fully adjusted for fixed effects demographics (age, sex, race, height, education, clinic site, previous year weight measures), lifestyle choice (smoking status, physical activity, average daily caloric intake) and health factors (health status, appetite status, disease status). Random effects included intercept. Covariance structure is unstructured across olfaction groups.										

olfaction groups and the decrease of fat mass. For black participants, poor olfaction had no significant effect on any body composition measure of weight loss over time.

Olfaction was not also associated with change in weight over time for any outcome when considering the male population. Women showed significance between poor olfaction and good olfaction for lean mass and bone-free mass, and between moderate olfaction and good olfaction for total mass and fat mass.

DISCUSSION

Outcome Evaluation

In this biracial cohort of healthy, community-dwelling older adults, we examined the relationship between olfaction and baseline body weight, as well as weight change over a period of seven years. Our initial analysis found similar OI distribution differences between males and females and blacks and whites as in previously published studies,[1,3] with prevalence of OI among blacks higher than among whites and prevalence of OI among men higher than among women. Overall, we found that poor olfaction in older adults was associated with a lower total mass and lower fat mass, but not for lean mass or bone-free mass. Prospectively, poor olfaction is also an indicator of a quicker change in total mass, lean mass and bone-free lean mass when compared to good olfaction.

This result is important as loss of lean mass, especially relative to the retention of fat mass, is considered to be one of the greatest health risks to older adults, as other studies have shown that the deterioration of muscle can lead to a multitude of public health and quality of life issues.[14,22] By showing that this relationship between olfaction and the loss of lean mass exists, it brings us one step closer to fully understanding the implications poor sense of smell has on health in an older population.

Stratum-specific examinations by race and sex allowed use to examine how the relationship between poor sense of smell and our body composition measures for each of the subgroups. For example, whites in both the cross-sectional and longitudinal analyses exhibited significance for almost every outcome (with the exception of change in fat mass over time in the longitudinal analysis) when comparing poor olfaction and good olfaction. However, blacks lacked significance in all race-specific analyses. Other researchers have studied the racial disparities of OI[1,3,4] but none have examined how those distinctions translate to body composition.

Perhaps one explanation for this can be found when exploring how a person's diet is affected by the loss or reduction of the sense of smell. If we examine the racial breakdown in our baseline population by family income, we see a disproportionate number of blacks who fall into the lowest income bracket of less than $10000 per year (~25%) while the number of whites in the same category is much lower (~4%). Income can be tied to the quantities and varieties of food which can be purchased, leading to a potentially different diet based on said income. Although caloric intake was accounted for in this analysis, different food groups and cooking methods could lead to similar calorie counts while at the same time contributing to different areas of a person's body composition.

However, diet may not be the only concern. In an animal trials using mice, researchers showed that a poor sense of smell resulted in a significant decrease in weight, even though the caloric intake was held constant among all mice.[36] In humans, we've also seen that olfaction levels can be altered due to various metabolic disorders, including obesity, anorexia and diabetes.[36,37,38] This could indicate that olfaction is directly related to metabolic processes, although the physiological process of why this may occur is still not well known.

Study Strengths

There are a few strengths to this study. First, the Health ABC study is an extremely well-designed prospective cohort, with frequent points of data collection and contact with the study participants on a regular basis. The data addressed a wide range of topics and areas of interest, allowing us to examine a variety of covariates and control for potential confounders. Adjudications by experienced professionals regarding disease status added to the reliability of the data used in this study. Potential bias due to inaccurate or missing information should be considered minimal.

Additionally, the large sample size (N=2311) allowed for any concerns regarding power to be mitigated. Even when splitting the analysis into race- and sex-based stratum, the number of study participants in each group remains large enough to ensure that the results are meaningful and accurate.

Limitations

Although we believe our results to be valid, there are a few limitations to our current study. First, the olfaction test used in the HABC Study was given to participants whose mean age was ~75 at baseline. Even though OI increases with age, it would be appropriate to also examine younger individuals and track their olfaction decline to assess whether even earlier cases of OI could be predictive of weight and body composition problems as they age. Otherwise, the generalizability to a younger population would be limited and the results are only indicative of the association of olfaction and weight loss in an older population.

Secondly, sense of smell can change over time and the BSIT in this study was only administered in a single year. Without additional tests, any mistakes or errors that occurred when testing could not be assessed or potentially even know. Further, without repeated measurements for olfaction, we cannot examine how the temporal trend for sense of smell might affect weight and weight loss.

Thirdly, the BSIT only tests whether or not a person can identify a particular smell. It does not assess the sensitivity of a person's sense of smell. This distinction can lead to varying definitions for olfaction impairment and caution should be used in clearly defining different levels of impairment.

Finally, the loss of sense of smell can be due to reasons other than aging, which the BSIT does not adequately account for. This study did not seek to determine whether these other causes influenced the measures of body composition.

Future Analyses/Studies

Even though the Health ABC study enrolled participants who were healthy at enrollment, the target population of those aged >70 are inherently at risk for negative health status changes. So even by year 3, when the baseline began for this analysis, many of the participants had had adverse health events. To counter the effects of these events, preliminary work on sensitivity analysis has begun by creating a new 'healthy' population by removing participants who report a poor health status or who are suffering from a disease known to have a direct impact on both sense of smell and weight loss (or from its treatment, like cancer). This will allow for conclusions to be drawn indicating that the association between poor olfaction and weight loss is not due to the poor health status of a participant at baseline.

Another issue that arises with a population of older adults, especially in prospective studies, is how to account for mortality. An analysis covering the entire course of the study shows that by the end of the 17th year, approximately 65% of the original participants had passed away, and that doesn't include those lost to follow-up. A joint survival/longitudinal analysis has been proposed to examine this issue and create a model that can express the relationship between the censoring caused by mortality while assessing olfaction and the change in body composition over time.

As mentioned previously, animal studies have shown that olfaction may have a closer relationship to metabolic processes than previously supposed. The Health ABC study conducted a sub-study in years 2 and 3 which looks specifically at energy expenditure, in-depth food frequency questions and metabolic rates. Although the sample size is smaller than the original study (N=322), the subset of data could be very informative to explore the olfaction-metabolism relationship and assess whether results can be achieved that mirror the animal studies. Additionally, with the dietary information provided, an opportunity exists to examine whether difference in diets can adequately explain the differences found in this study among blacks and whites in regard to olfaction and weight.

CONCLUSION

Poor olfaction in older adults has been shown to be associated with lower weight (for total mass and fat mass) and a more rapid decline of weight loss (for total mass, lean mass and bone-free mass) when compared to good olfaction groups. As these changes in body composition can lead to many health hazards, it is important to understand the processes that lead to them and potentially find ways to identify those at greatest risk. Differences between whites and blacks offer new and interesting areas of research that could further explore the intricacies of how olfaction, and potentially diet and metabolism, can affect the weight and body composition of older adults.

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