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A Pilot Study of Self-Rated and Psychophysical Olfactory Dysfunction in Men Living with HIV

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Abstract

Background Olfactory loss is associated with poor quality of life, malnutrition, and increased risk of depression, yet few studies have examined unawareness of olfactory dysfunction in men living with HIV (MLWH).

Method MLWH ($n = 51$) completed olfaction self-ratings, psychophysical odor identification testing, cognitive measures, and questionnaires assessing smell habits, mood, cognitive failures, and quality of life. The sensitivity and specificity of olfactory self-ratings was calculated, and *t*-tests were used to examine factors contributing to discordance between self-rated and psychophysical olfaction dysfunction.

Results We found that 33.3% (17 of 51 MLWH) of our sample demonstrated discordance between self-reported and psychophysical olfactory scores. Those unaware of olfaction dysfunction reported using less scented products in daily life but showed no other differences across demographic, clinical, or cognitive indices.

Conclusions Our results cohere with prior studies of cognitively normal older adults, traumatic brain injury, and Parkinson's disease, which found that olfactory self-ratings may inadequately capture the full range of a person's olfactory status. Our work extends these findings to MLWH, with discordance rates ranging from 35 to 61% for self-rated and psychophysical olfactory dysfunction.

Implications Given the differing rates of self-rated and psychophysical olfaction in our sample, psychophysical olfactory measures may be useful to consider in the neuropsychological assessment and clinical care of PLWH.

Keywords Smell · Hyposmia · Chemosensory · Unawareness · HIV-associated neurocognitive disorder

Introduction

The consequences of olfactory dysfunction can include decreased appetite, reduced nutritional intake, unintentional weight loss, and difficulty detecting spoiled food and hazards in our environment such as fire and gas leaks (Croy et al. 2014, Fjaeldstad and Smith 2022). Olfactory dysfunction is heightened in healthy older adults who later develop Alzheimer's dementia (AD) or Parkinson's disease (PD), with smell loss emerging as an independent predictor of those patients at risk for accelerated cognitive decline (Chen et al. 2021). An unfortunate observation is that humans show striking rates of discordance between self-ratings of olfactory functioning and performance on quantitative psychophysical olfactory measures. Thus, without quantitative assessment, individuals may not seek evaluation and treatment for olfactory dysfunction.

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To date, multiple studies have shown disagreement between self-rated and quantitative psychophysical olfactory assessment. Nordin et al. (1995) found that 77% of healthy older adults and 74% of patients with AD with psychophysical olfactory dysfunction perceived their sense of smell to be normal. This discordance may contribute to underestimation in the prevalence rates of olfactory dysfunction. Indeed, prevalence estimates in persons 18 to 101 years of age differ significantly when self-report is used (9.5%) compared to estimates derived from formal olfactory assessments (21.2 to 35.8%) (Desiato et al. 2021). Interestingly, studies have further demonstrated that discordance can vary as a function of age and cognitive status. Despite similar overall rates of accuracy across age groups, older adults tend to overestimate their olfactory abilities, whereas young adults may underestimate their olfactory abilities (White and Kurtz 2003). In studies examining cognitive status, individuals with unawareness of olfactory loss demonstrate poorer scores on measures of memory recall and processing speed when compared to participants with awareness of olfactory dysfunction (Wehling et al. 2011).

People living with HIV (PLWH) have impairments on formal measures of odor identification and odor detection thresholds when compared to demographically matched controls (Brody et al. 1991; Mueller et al. 2002; Razani et al. 1996). The severity of olfactory dysfunction correlates with poorer auditory-verbal memory (Vance et al. 2019), and olfactory dysfunction has been put forth as a potential predictor of those PLWH at risk for poor cognitive outcomes (Sundermann et al. 2021). However, comparisons between self-rated and psychophysical olfactory performance are limited in PLWH, underscoring the need for further investigation. In the current study, we examined the discrepancy between self-ratings and quantitative psychophysical odor identification performance in men living with HIV (MLWH). Participants were categorized into one of four groups (true positives, false negative, false positives, and true negatives) based on (1) self-ratings (intact vs. impaired) and (2) psychophysical olfactory performance (dysfunction vs. normosmia). We then examined the sensitivity and specificity of olfactory self-ratings as compared to psychophysical olfactory functioning and the demographic, clinical, and cognitive factors that may contribute to inaccurate self-report in MLWH with psychophysical olfactory dysfunction.

Methods

Participants

This institutional review board-approved cross-sectional study was conducted from March 2014 to January 2015. Full details of the recruitment and inclusion criteria are described in prior work (Vance et al. 2019). Briefly, MLWH were recruited to participate using flyers circulated and posted in the University of Alabama at Birmingham Medical Center HIV/AIDS clinic. Following a telephone screening, participants who met eligibility criteria were scheduled for a study visit and instructed to reschedule if they developed a cold, flu, or other sinus-related symptoms. Informed consent was obtained from all participants, after an explanation of the study procedures.

All participants were screened for eligibility through a telephone screen. To meet study eligibility, all participants were HIV-positive men with a diagnosis lasting at least one year, a current patient of the HIV/AIDS clinic, age $\geq$ 40 years, and English proficient with current housing. Participants with severe neurological or sensory impairment (other than anosmia), including neurodegenerative conditions, head trauma with a loss of consciousness $\geq$ 30 min, schizophrenia, learning disability, or severe visual or hearing impairment, were excluded. Participants with sinonasal conditions (substance inhalation, sinus infection within the past 3 months, asthma, nasal obstruction, flu or cold symptoms, allergies, oral thrush, or oral candidiasis) or current chemotherapy/radiation treatment were also excluded. Following a telephone screening of 127 people who called the research office and were interested in the study, 51 participants who met eligibility criteria were scheduled for a study visit and instructed to reschedule if they developed a cold, flu, or other sinus-related symptoms. The final analytic sample was 51 MLWH (mean age = 54.02 years, 66.7% Black; see Table 1).

Olfactory Self-Rating Assessment

Prior to olfactory psychophysical testing, participants were asked two questions to capture self-ratings of olfactory ability. Participants were first asked: "How would you rate your sense of smell?" with the following response options: *poor* (1), *fair* (2), *good* (3), *very good* (4), and *excellent* (5). Consistent with prior work (Adams et al. 2017), answer choices "*excellent*," "*very good*," and "*good*" were classified as intact olfaction, whereas answer choices "*fair*" and "*poor*" were considered a self-rating of impaired olfactory function. Next, participants were asked: "In general, have you noticed changes in the strength of odors?" The following response options accompanied the question: *not at all* (1), a *little* (2), *moderately* (3), *very much* (4), and *extremely* (5). Answer choices "*not at all*" and "*a little*" were classified as intact olfaction, whereas answer choices "*moderately*," "*very much*," and "*extremely*" were considered a self-rating of impaired olfactory function. Subjects reporting intact olfaction for these questions were noted to have intact olfactory functioning.

Table 1 Demographic and clinical characteristics of the sample stratified by race

	Overall MLWH ($n=51$) Mean (SD)	Black MLWH ($n=34$) Mean (SD)	White MLWH ($n=17$) Mean (SD)	t-value / χ^2	p value
Age (years)	54.02 (6.27)	52.99 (6.12)	56.08 (6.23)	−1.69	0.10
Education level (years)	13.67 (2.92)	12.94 (2.63)	15.11 (3.02)	−2.84	*0.01*
Smoking burden (cigarettes/day)	2.27 (4.97)	2.91 (5.28)	1.00 (4.12)	1.30	0.20
Duration LWH (years)	18.78 (2.74)	17.71 (2.37)	20.93 (2.11)	−4.75	*0.001*
Most recent HIV viral load (copies/mL)	618.76 (3180.86)	71.41 (135.68)	892.44 (3884.54)	0.87	0.39
Most recent $CD4^+$ T cell count (cell/mm^3)	620.14 (369.997)	627.853 (399.14)	604.706 (314.39)	0.21	0.84
$CD4^+$ T cell count nadir (cell/mm^3)	179.96 (234.06)	166.79 (203.897)	206.29 (290.425)	−0.56	0.58
Odor Identification Score (total correct)	31.02 (5.87)	30.06 (5.38)	32.94 (6.50)	−1.68	0.10
HVLT delayed recall (total correct)	7.20 (3.00)	6.24 (2.82)	9.12 (2.42)	−3.60	*0.001*
Trail Making Test Part A (s)	40.24 (18.41)	43.80 (20.05)	33.12 (12.19)		
Trail Making Test Part B (s)	158.39 (133.62)	181.10 (155.43)	112.96 (51.73)		
Trail Making Test Part B minus Part A (s)	118.14 (122.82)	137.30 (143.91)	79.84 (45.69)	1.60	0.12
Smell Habits (total score)	12.47 (4.76)	13.68 (4.54)	10.06 (4.34)	2.72	*0.01*
CES-D (total score)	19.76 (11.01)	21.03 (10.70)	17.24 (11.51)	1.16	0.25
CASP quality of life (total score)	38.71 (11.53)	38.65 (12.17)	38.82 (10.50)	−0.05	0.96
Medication adherence (total score)	-0.02 (0.64)	-0.06 (0.58)	0.07 (0.76)	−0.64	0.52
Cognitive failures (total score)	39.88 (15.18)	39.38 (15.67)	40.88 (14.55)	−0.33	0.74

MLWH, men living with HIV; LWH, living with HIV; HVLT, Hopkins Verbal Learning Test; CES-D, Center for Epidemiological Studies Depression Scale; CASP, Control, Autonomy, Self-Realization and Pleasure Quality of Life; SD, standard deviation

Psychophysical Olfactory Assessment

The ability to identify odors was measured with the 40-item University of Pennsylvania Smell Identification Test (UPSIT; Doty et al. 1984) purchased from Sensonics, Inc. The UPSIT is comprised of four booklets, ten odorants per book, presented in a four-alternative forced-choice test format. Each odor is presented on a single page embedded in a "scratch and sniff" microcapsule affixed to the bottom of each page. The psychometric properties of the UPSIT are well-described in prior studies (Doty et al. 1989, 1984). The UPSIT was administered birhinally, and correct responses were tallied for each participant, with a total possible score of 40. Sex-adjusted normative data from the UPSIT manual were used to dichotomize our sample into those with and without odor identification difficulties (Doty et al. 1984). A recommended UPSIT score ≤ 33 was used to capture men with olfactory dysfunction (hyposmia/anosmia).

Self-Report Questionnaires

Cognitive Failures Questionnaire (CFQ; Broadbent et al. 1982*).* As a measure of self-rated cognitive function, on this 25-item self-report questionnaire, participants rated how frequently they experience lapses in daily cognitive abilities including perception, memory, and motor function (e.g., "Do you find you forget appointments?"). Participants rated the frequency of cognitive failures on a five-point Likert scale (e.g., *very often*, *quite often*, *occasionally*, *very rarely*, and *never*). Higher scores represent more frequent perceived lapses in day-to-day cognitive function.

*Simplified Medication Adherence Scale (*Knobel et al. 2002*).* This 6-item self-report measure assesses adherence to medications (e.g., "Do you ever forget to take your medication?"). This questionnaire was developed for use in PLWH (Knobel et al. 2002). Responses were summed to generate a composite score; higher scores indicate greater non-adherence.

Center for Epidemiological Studies Depression Scale (CES-D; Radloff 1977*).* The CES-D is a 20-item self-report measure developed to identify depressive symptoms in the general population. Participants rated how often they experienced symptoms associated with depression over the past week. Higher scores indicate more depressive symptomatology.

Control, Autonomy, Self-Realization and Pleasure Quality of Life Scale (CASP-19; Hyde et al. 2003*).* The CASP-19 is a 19-item self-report measure of four domains of quality of life for individuals including (1) control, (2) autonomy, (3) pleasure, and (4) self-realization. Participants rated how often they experienced or felt each of the items (i.e., "I feel that my life has meaning") on a 4-point Likert scale ranging from 0 (i.e., "never") to 3 (i.e., "often"). Items are summed to yield a composite score that ranges from 0 to 57. Higher scores indicate higher levels of satisfaction with quality of life.

Smell Habit Questionnaire. The Smell Habit Questionnaire is a 6-item self-report measure developed for use in this study to assess use of scented products in the participant's daily life (e.g., "How often do you use cologne or perfume?") (see Supplementary Materials, eTable 1). Participants rated frequency of use on a 5-point Likert scale (e.g., *never (1)*, *once a week (2)*, *twice a week (3)*, *3 times a week (4)*, and *4 or more times a week (5)*). Higher scores represent more frequent use of scented products.

Cognitive Tests

The Revised Hopkins Verbal Learning Test (HVLT-R; Brandt and Benedict 2001) was administered to capture encoding, retrieval, and recognition of rote auditory-verbal information. Individuals were read 12 words and asked to learn these words across three learning trials. Following a 20- to 25-min delay, participants were asked to recall as many words as possible from the list. The total number of words recalled represents the total delayed recall score. The Trail Making Test (TMT) was administered to capture psychomotor processing speed and visual set-shifting abilities (Reitan and Wolfson 1985; Reitan 1955). The task has two timed components. In part A, participants were asked to connect numbers spread across a page as quickly as possible in numerical order. In part B, participants were asked to connect numbers and letters spread across a page alternating between numbers and letters in alphanumeric order as quickly as possible. Time to complete is recorded for each trial, with shorter duration typically representing a better score.

Statistical Analyses

Similar to methods established in prior studies, participants were categorized into one of four groups based on their self-rated (intact vs. impaired) and psychophysical olfactory performance (dysfunction vs. normosmia):

1. True positives (TP): impaired self-rated olfaction and psychophysical olfactory dysfunction
2. False negatives (FN): intact self-rated olfaction and psychophysical olfactory dysfunction
3. False positives (FP): impaired self-rated olfaction and psychophysical normosmia
4. True negatives (TN): intact self-rated olfaction and psychophysical normosmia

Established formulas were used to calculate sensitivity (true positive rate), specificity (true negative rate), positive predictive value (PPV; probability of having olfactory dysfunction), and negative predictive value (NPV; probability of not having olfactory dysfunction) (Monaghan et al. 2021).

1. Sensitivity = %TP = TP/(TP + FN)
2. Specificity = %TN = TN/(TN + FP)
3. PPV = TP/(TP + FP)
4. NPV = TN/(TN + FN)

We next examined the demographic, clinical, and cognitive factors that may contribute to inaccurate self-report in MLWH with psychophysical olfactory dysfunction (excluding those with normosmia [FP, TN]). Using analysis of variance (ANOVA), participants demonstrating unawareness of olfactory impairment (FN) were compared to participants with awareness of olfactory impairment (TP) on the aforementioned cognitive and self-report assessments. Our sample had few participants ($n = 3$) who reported smell dysfunction despite intact smell on psychophysical assessment (FP), which prevented our ability to examine factors that contributed to discordance between the FP and TN groups. A statistical significance of $p < 0.05$ was used for all analyses.

Results

Participant Characteristics

Sample characteristics are shown in Table 1. The mean age of the overall sample was 54 years; 100% of the participants were men, and 67% were Black. The mean education level was 13.67 years. Compared to White MLWH, Black MLWH had similar age, smoking levels, and BMI but lower educational attainment and shorter disease duration. No significant differences were observed with respect to HIV-related disease characteristics (HIV viral load, $CD4^+$ T cell count, and $CD4^+$ T cell count nadir).

Prevalence of Self-Rated and Psychophysical Olfactory Impairment in MLWH

The prevalence of olfactory impairment based on psychophysical assessment on the UPSIT and self-ratings are presented in Table 2. In the current sample, 19.6% of participants self-rated their sense of smell as "fair" or "poor" and 25.5% self-rated moderate to extreme changes in the strength of odors. Across both items, 35.3% self-rated olfactory dysfunction. Significant differences were observed by race ($\chi^2(1) = 9.22$, $p = 0.002$), with higher rates of self-rated olfactory dysfunction observed in Black MLWH (41.2%) as compared to White MLWH (35.3%). On psychophysical assessments of odor identification accuracy, 60.8% of the overall sample demonstrated olfactory dysfunction, with significantly greater dysfunction observed in Black MLWH (73.5%) as compared to White MLWH (35.3%).

Table 2 Prevalence of psychophysical and self-rated olfactory impairment in Black and White men living with HIV

Olfactory impairment	White participants ($n=17$)	Black participants ($n=34$)	Total sample ($n=51$)
Psychophysical smell loss[a]	6 (35.3%)	25 (73.5%)	31 (60.8%)
Self-rated smell loss[b]	4 (23.5%)	14 (41.2%)	18 (35.3%)

[a]University of Pennsylvania Identification Test (UPSIT) score ≤ 33; [b]for olfactory self-ratings, participants were asked: "How would you rate your sense of smell?" Answer choices "*excellent*," "*very good*," and "*good*" were classified as intact olfaction, whereas answer choices "*fair*" and "*poor*" were considered a self-rating of impaired olfactory function. Participants were asked: "In general, have you noticed changes in the strength of odors?" Answer choices "*not at all*" and "*a little*" were classified as intact olfaction, whereas answer choices "*moderately*," "*very much*," and "*extremely*" were considered a self-rating of impaired olfactory function

Discordance in Self-Report of Olfactory Functioning

As shown in Table 3, one third of respondents demonstrated discordance between self-rated and psychophysical olfactory function: 29.4% of the sample had psychophysical olfactory dysfunction yet did not recognize it (i.e., FN), while 3.9% self-reported impaired olfaction yet tested within the normal range (i.e., FP). The remainder of the sample had concordance in their self-rated and psychophysical olfaction: 35.3% self-reported normal olfaction and had normal scores on the psychophysical assessment (i.e., TN), while 31.4% self-reported olfactory dysfunction and had psychophysical olfactory dysfunction (i.e., TP).

Sensitivity and Specificity

The sensitivity of self-reported olfaction was 51.6%, with approximately half of the impaired sample recognizing their psychophysical olfactory dysfunction. The specificity of self-reported olfactory abilities was much higher, as 90.0% of MLWH with intact olfaction correctly rated their sense of smell as intact (see Supplementary Materials, eTable 2).

Unawareness of Olfactory Impairment and Discordance Between Self-Rated and Psychophysical Olfactory Functioning

As shown in Table 4, participants demonstrating unawareness of olfactory impairment (FN) were compared to participants with awareness of olfactory dysfunction (TP). The TP group reported higher smell habits on the Smell Habits Questionnaire. Although we found slower performances on an executive measure of visual set-shifting (Trail Making Test Part B–Part A) in the TP group, this finding was driven by three individuals with exceedingly slow performances (e.g., time to complete greater than 350 s). Following removal of these three outliers, group differences were no longer statistically significant. No other differences were observed between the groups across demographic (age, race, and educational attainment) or health-related (smoking status, BMI, and HIV-related disease characteristics) factors. In addition, no differences emerged between groups with respect to delayed word-list recall or self-report of depressive symptoms, quality of life, cognitive failures, or medication adherence (Table 4).

Table 3 Self-rated olfactory dysfunction compared with measured psychophysical impairment in men living with HIV

		Measured psychophysical olfaction	
		Dysfunction	Intact
Self-rated olfaction	Impaired	31.4%	3.9%
		($n=16$)	($n=2$)
		True positive, TP	False positive, FP
	Intact	29.4%	35.3%
		($n=15$)	($n=18$)
		False negative, FN	True negative, TN

Measured psychophysical olfactory impairment was assessed with the University of Pennsylvania Smell Identification Test. Percentage of misclassification of correct reporting (TP, FN), over-reporting (FP), and under-reporting (FN)

Table 4 Demographic and clinical characteristics of the true positives and false negatives

	True positives ($n=16$) Mean (SD)	False negatives ($n=15$) Mean (SD)	t-value /χ^2	p value
Age (years)	53.85 (3.11)	53.96 (7.92)	−0.05	0.52
Race (% Black)	87.50	73.33	>0.99	0.32
Education level (years)	13.31 (2.73)	13.00 (2.78)	0.07	0.95
Smoking burden (cigarettes/day)	1.69 (3.42)	2.87 (6.36)	−0.65	0.52
Duration LWH (years)	18.17 (2.74)	18.59 (3.33)	−0.39	0.70
Most recent HIV viral load (copies/mL)	1461.69 (5585.02)	140.47 (435.24)	0.91	0.37
Most recent $CD4^+$ T cell count (cell/mm^3)	581.31 (375.62)	552.07 (278.05)	0.25	0.81
$CD4^+$ T cell count nadir (cell/mm^3)	184.63 (256.70)	184.60 (255.82)	<0.01	>0.99
Odor Identification Score (total correct)	27.38 (5.35)	27.93 (5.04)	−0.30	0.77
HVLT delayed recall (total correct)	5.50 (2.42)	6.47 (3.18)	−0.96	0.35
Trail Making Test Part A (s)	49.51 (21.28)	37.30 (11.03)		
Trail Making Test Part B (s)	148.69 (59.41)*	119.39 (40.07)		
Trail Making Test Part B minus Part A (s)	104.81 (82.10)*	82.10 (58.30)	2.07	0.21
Smell Habits (total score)	14.94 (3.86)	11.27 (4.70)	2.39	*0.02*
CES-D (total score)	22.56 (11.31)	17.93 (9.94)	1.20	0.23
CASP quality of life (total score)	36.50 (12.42)	37.80 (13.21)	0.28	0.77
Medication adherence (total score)	0.07 (0.55)	-0.04 (0.69)	0.49	0.63
Cognitive failures (total score)	40.31 (15.94)	41.40 (13.595)	−0.20	0.84

*Three individuals produced TMT-B scores that were significantly slower than the remainder of the entire sample (e.g., time to complete greater than 350 s). Raw scores and group comparisons are reported with these three individuals removed. LWH, living with HIV; HVLT, Hopkins Verbal Learning Test; CES-D, Center for Epidemiological Studies Depression Scale; CASP, Control, Autonomy, Self-Realization and Pleasure Quality of Life; SD, standard deviation

Discussion

In PLWH, psychophysical olfactory dysfunction is a well-documented finding, with olfactory difficulties worsening as a function of age, nasal pathology, cognitive dysfunction, and disease stage (Brody et al. 1991; Hornung et al. 1998; Mueller et al. 2002; Razani et al. 1996). However, few studies have examined concordance rates between self-ratings and psychophysical performance in this population. In the current study, we found discordance between self-ratings and psychophysical assessment of olfactory functioning in MLWH. Though 35% of our sample reported olfactory dysfunction, 61% demonstrated olfactory impairment on a formal measure of odor identification accuracy. Of note, higher rates of measured and self-rated olfactory dysfunction were observed in Black MLWH as compared to their White counterparts. One-third of participants demonstrated discordance between self-assessment and psychophysically measured olfactory ability. In particular, 29% of the sample did not recognize their olfactory impairment and another 4% perceived reduced olfactory functioning despite testing within the normal range. Moreover, approximately 50% of those with olfactory dysfunction recognized it, and 90% with intact olfaction correctly rated their sense of smell as intact.

Prior studies have shown discordance between rates of self-reported and psychophysical olfactory dysfunction in healthy individuals and in persons with sinonasal and neurologic conditions (Doty et al. 1988; Murphy et al. 2002; Nordin et al. 1995; Wehling et al. 2011). To our knowledge, Fasunla et al. (2016) is the only other study to examine both self-rated and psychophysical olfactory performance in an HIV sample; the authors characterized psychophysical olfactory performance using the full Sniffin' Sticks battery in Nigerian women living with HIV (WLWH) and without HIV. Interestingly, WLWH showed comparable self-ratings to uninfected women but had significantly poorer psychophysical olfactory scores. In particular, 40% had psychophysical olfactory dysfunction compared to 51% in our MLWH sample. Differences in the olfactory tests administered, the observed female-advantage for olfactory abilities (26), and potential cultural differences in exposure to odorants between cohorts may explain these discrepancies. When compared to the rates of self-reported and psychophysical olfaction dysfunction in our cohort, we found similar rates of psychophysical olfactory dysfunction in MLWH as in PD (52%), advanced cancer (53%), and traumatic brain injury (TBI) (56%) (Callahan and Hinkebein 2002; McGettigan et al. 2019; Schmidt et al. 2020) but lower rates of self-rated olfactory dysfunction in MLWH compared to advanced cancer patients (70%) and PD (69%) (Hannum et al. 2020;

McGettigan et al. 2019; Schmidt et al. 2020). These findings indicate potential differences in the level of awareness of olfactory difficulties in PLWH when compared to other neurologic and clinical conditions.

We found low sensitivity (51.6%) and high specificity (90%) of self-report of olfactory dysfunction in our sample. These findings are comparable to prior findings of low sensitivity and high specificity for self-report of olfactory function observed in older adults (Adams et al. 2017; Loudghi et al. 2019; Wehling et al. 2011). These findings suggest that individuals with intact olfactory performance on psychophysical measures are more accurate at identifying their olfactory ability than participants with olfactory dysfunction. These results mirror recent meta-analytic findings in COVID-19 samples, which found that self-rated olfactory dysfunction was identified in 44% of patients using self-report with 77% of cases demonstrating psychophysical olfactory dysfunction using psychophysical measures (Hannum et al. 2020). Moreover, a recent study in PD found higher sensitivity (79%) and lower specificity (45%) for self-reported olfactory abilities, suggesting low accuracy of self-report for determining psychophysical olfactory status (Schmidt et al. 2020). With respect to the predictive value of self-ratings, we found high PPV (88.9%), as most participants who self-rated olfactory dysfunction demonstrated actual psychophysical olfactory dysfunction. In contrast, the NPV of self-rated olfactory function was low (54.6%); about half of the participants who reported intact olfaction had psychophysical olfactory dysfunction. The higher rates of false negatives (unaware of olfactory dysfunction) in our sample are more consistent with prior literature investigating TBI and PD (Callahan and Hinkebein 2002; Leonhardt et al. 2019; Nordin et al. 1995; White et al. 2016; Yoo et al. 2019). Conversely, healthy older adults have shown low PPV (45.8%) and higher NPV (81.4%), indicating higher unawareness of intact olfaction (Adams et al. 2017). Similar results of more significant false positives were measured in positive COVID-19 and advanced cancer cohorts (Lechien et al. 2020; McGettigan et al. 2019). Altogether, our findings support previous work documenting that olfactory self-ratings may not be sensitive enough to detect psychophysical olfactory dysfunction and extend these findings to a sample of MLWH.

Unawareness of olfactory functioning has been associated with various demographic and clinical factors. For example, older age (i.e., ≥ 65 years) is associated with under-reporting of olfactory dysfunction, while persistent cold symptoms is associated with over-reporting smell impairment (Adams et al. 2017; Jang et al. 2022). The sudden vs. gradual onset of olfactory loss may also contribute to differences in the degree of unawareness, as gradual worsening of olfactory loss may be more subtle and lead to unawareness (Welge-Luessen et al. 2005). Unawareness may also differ across ethnoracial groups, with higher rates of unawareness observed in Black as compared to White cohorts (Adams et al. 2017). The present study found no associations between unawareness of olfactory functioning and age, race, education, smoking status, BMI, and HIV-related disease characteristics. As few studies have explored the associations between unawareness of olfactory functioning and other factors, such as depression symptoms, qualify of life (QOL), or smell habits, we attempted to fill this gap in the literature. We found no relationship between unawareness and depression symptoms or QOL. These findings are consistent with work by Oleszkiewicz et al. (2020) in a German rural sample, in which the authors found that individuals unbothered by their smell loss did not report experiencing major disruptions in their social functioning or well-being.

Interestingly, the TP group reported higher smell habits than the FN group, indicating greater use of scented products (i.e., cologne/perfume) in daily life. Regular exposure to scented products may influence self-report of olfactory function or awareness of psychophysical olfactory function. Perhaps increased exposure to multiple odors enriches one's olfactory environment leading to improved overall olfactory function (Vance and Burrage 2006). Although our study did not assess long-term smell habits, our findings appear to be in line with this hypothesis, suggesting that higher exposure to different scents may be more sensitive to declines in olfactory function. Our findings also cohere with prior work demonstrating an association between olfactory self-ratings and factors such as odor annoyance and the affective impact of odors rather than odor acuity (Knaapila et al. 2017, 2008).

Cognitive impairment is another factor that may drive unawareness of olfaction functioning. Associations between unawareness of olfactory dysfunction and poorer cognitive outcomes have been demonstrated in longitudinal studies, with unawareness linked to an increased likelihood of developing dementia (Adams et al. 2017; Devanand et al. 2000; Yoo et al. 2019). Wehling et al. (2011) found that individuals who were unaware of their olfactory dysfunction performed worse on a measure of attention/processing speed compared to individuals with intact awareness of olfactory function. In contrast, Leonhardt et al. (2019) compared FN and TP subgroups of PD patients on the same measure of visual set-shifting as administered in the current study with no significant differences observed between the groups. The present study found no significant differences in delayed recall between groups, which aligns with previous research in PD but conflicts with a study in healthy adults (Leonhardt et al. 2019; Wehling et al. 2011). In our sample, the FN group had faster speed of processing than the TP group, which was no longer significant after removal of three outliers with exceedingly slow scores on the test (e.g., >350 s). Collectivity, our findings do not support a link between cognitive dysfunction and unawareness of olfactory abilities in MLWH

but future studies with comprehensive cognitive testing will help clarify these associations further.

The strengths of this study include the well-characterized sample of MLWH, gold-standard 40-item assessment of psychophysical olfactory functioning, and the use of a continuous self-rating item for olfactory abilities. Prior studies have employed brief screenings of psychophysical olfactory functioning (e.g., 12-item Brief Smell Identification Test, 5-item Sniffin' Sticks) or binary (yes/no) self-ratings of olfactory functioning, which can affect concordance rates of self-rated and psychophysical measures (Haxel et al. 2012). Our study also had several limitations, including the absence of WLWH and a demographically matched HIV-uninfected group. Due to limited funding and study resources and to preserve power, WLWH were not included in the parent study. Sex differences have been reported with respect to olfactory abilities, cognitive functioning, psychiatric symptom reporting, and HIV-related characteristics (e.g., viral load, CD4 + T cell count) (Dastgheyb et al. 2021; Maki et al. 2018; Sorokowski et al. 2019). Though our findings were consistent with a similar study in WLWH (Fasunla et al. 2016), it will be important to extend and compare findings on unawareness of olfactory dysfunction to samples that include WLWH and HIV-uninfected cohorts. Finally, many olfactory studies like ours exclude participants diagnosed with sinonasal conditions that are likely to be more aware of their olfactory dysfunction (Haxel et al. 2012). How these factors influence sensitivity, specificity, PPV, and NPV in PLWH will be important to consider in future work. Finally, the Smell Habits Questionnaire is a novel measure developed for use in this pilot study, which has yet to be psychometrically validated. As such, the current results linking awareness of smell loss to higher smell habits in daily life are preliminary until validation of the measure and replication in larger cohorts can be completed.

Conclusions

Olfactory loss is a growing public health concern, as consequences of olfactory dysfunction can include poor quality of life, inadequate nutritional intake, and increased risk of depression (Croy et al. 2014, Fjaeldstad and Smith 2022). In PLWH, olfactory assessment has potential utility in differentiating individuals with amnestic MCI from individuals with HIV-associated neurocognitive disorder (HAND) (Sundermann et al. 2021). Self-report assessment of olfactory abilities appears to inadequately capture the full range of a person's olfactory status (Lötsch and Hummel 2019). Conversely, psychophysical olfactory testing can capture the magnitude of olfactory dysfunction, establish the validity of a patient's reported difficulties, and quantitatively track an individual's olfactory status over time. Improved self-assessment measures are critical to the clinical evaluation of patients, as persons with olfactory dysfunction may not pursue medical intervention without awareness. Moreover, unawareness of olfactory dysfunction may be a bellwether for poor cognitive outcomes, furthering the need for formal assessment (Adams et al. 2017; Devanand et al. 2000; Yoo et al. 2019). Along these lines, there is limited but emerging evidence that olfactory training can help improve cognition and reverse gray matter volumetric changes (Gellrich et al. 2018; Oleszkiewicz et al. 2021). Despite the convenience of self-report ratings, these assessments may not identify many MLWH who are unaware of psychophysical olfactory dysfunction. Psychophysical tests of olfactory functioning (e.g., UPSIT, Sniffin' Sticks) avoid the potential biases of self-report ratings and should be considered in the neuropsychological assessment and standard clinical care of PLWH.

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Data Availability Data are available upon approval by David Vance and UAB.

Declarations

Ethical Approval This study was approved by the UAB Institutional Review Board.

Informed Consent All participants provided informed consent for their study involvement.

Consent for Publication Not Applicable.

Conflict of Interest The authors declare no competing interests.

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