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

Vidyulata Kamath1, Victor A. Del Bene2,3, Christopher Collette2, Alexandra Jacob4, Pariya L. Fazeli3,5, David E. Vance5

Received: 5 October 2022 / Accepted: 31 October 2022 / Published online: 10 November 2022
© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022

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.
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 ≥ 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 ≥ 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.
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 bilaterally, 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 \( \leq 33 \) 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”). Responses were summed to yield a composite score that ranges from 0 to 57. Higher scores indicate higher levels of satisfaction with quality of life.

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

|                         | Overall MLWH (\(n = 51\)) | Black MLWH (\(n = 34\)) | White MLWH (\(n = 17\)) | \(t\)-value | \(\chi^2\) | \(p\) 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
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).

Sensitivity = %TP = TP/(TP + FN)
Specificity = %TN = TN/(TN + FP)
PPV = TP/(TP + FP)
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%).
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 2: Prevalence of psychophysical and self-rated olfactory impairment in Black and White men living with HIV

|                         | White participants (n = 17) | Black participants (n = 34) | Total sample (n = 51) |
|-------------------------|----------------------------|-----------------------------|-----------------------|
| Psychophysical smell lossa | 6 (35.3%)                  | 25 (73.5%)                  | 31 (60.8%)            |
| Self-rated smell lossb   | 4 (23.5%)                  | 14 (41.2%)                  | 18 (35.3%)            |

aUniversity of Pennsylvania Identification Test (UPSIT) score ≤ 33; bfor 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.

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).
**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 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, quality 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). Collectively, 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 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.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12078-022-09305-x.

Acknowledgements We would like to thank all the participants who volunteered for this study.

Author Contribution Concept and design: VK, VAD, and DEV; manuscript writing: VK, VAD, CC, AJ, and DEV; data collection: PLF and DEV; data analysis: VK; data interpretation: VK, VAD, and DEV; manuscript revisions and approval: all.

Funding This study was supported by a NIH/NIA P30-award (Deep South Resource Center for Minority Aging Research (RCMAR); P30 AG031054), NIH/NIMH R01-award (1R01MH106366-01A1), and by a NIH/NIA P30-award (Edward R. Roybal Center for Translational Research in Aging and Mobility; P30 AG022838). Dr. Kamath receives support from R01AG064093 and R01NS108452.

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.

References

Adams DR, Wroblewski KE, Kern DW, Kozloski MJ, Dale W, McClintock MK, Pinto JM (2017) Factors associated with inaccurate self-reporting of olfactory dysfunction in older us adults. Chem Senses 42:223–231

Brandt J, Benedict R (2001) Hopkins verbal learning test-revised: professional manual. Psychological Assessment Resources
Doty RL, Deems DA, Stellar S (1988) Olfactory dysfunction in par vestibular disorders and quality of life: an updated review. Chem Senses 39:185–194
Dastgheyb RM, Buchholz AS, Fitzgerald KC, Xu Y, Williams DW, Springer G, Anastos K, Gustafson DR, Spence AB, Adimora AA, Waldrop D, Vance DE, Milam J, Bolivar H, Weber KM, Haughey NJ, Maki PM, Rubin LH (2021) Patterns and predictors of cognitive function among virally suppressed women with HIV. Front Neurol 12:604984
Desiato VM, Levy BM, Byun YJ, Nguyen SA, Soler ZM, Schlosser C (2014) Olfactory disorders and quality of life: a systematic review and meta-analysis. Am J Psychiatry 157:1399–1405
Devanand DP, Michaels-Marston KS, Liu X, Pelton GH, Padilla M, Desiato VM, Levy DA, Byun YJ, Nguyen SA, Soler ZM, Schlosser C, Nordin S, Hummel T (2018) Brain volume changes in hyposmic patients and without olfactory disorders. J Laryngol Otol 126:692–697
Dornand DP, Michaels-Marston KS, Liu X, Pelton GH, Padilla M, Mader K, Bell K, Stern Y, Mayeux R (2000) Olfactory deficits in patients with mild cognitive impairment predict Alzheimer’s disease at follow-up. Am J Psychiatry 157:1399–1405
Doty RL, Deems DA, Staller S (1988) Olfactory dysfunction in parkinsonism: a general deficit unrelated to neurologic signs, disease stage, or disease duration. Neurology 38:1237–1244
Doty RL, Frye RE, Agrawal U (1989) Internal consistency reliability of the fractionated and whole university of pennsylvania smell identification test. Percept Psychophys 45:381–384
Doty RL, Shaman P, Dann M (1984) Development of the University of Pennsylvania Smell Identification Test: a standardized microencapsulated test of olfactory function. Physiol Behav 32:489–502
Fasunla AJ, Daniel A, Nwanwko U, Kuti KM, Nwaorgu OG, Akindinya OO (2016) Evaluation of olfactory and gustatory function of HIV infected women. AIDS RES Treat 2016:2045383
Fjaeldstad AW, Smith B (2022) The effects of olfactory loss and parosmia on food and cooking habits, sensory awareness, and quality of life - a possible avenue for regaining enjoyment of food. Foods 11(12):1686
Gellrich J, Han P, Mennes C, Betz A, Junghanns A, Raue C, Schriever VA, Hummel T (2018) Brain volume changes in hypoxic patients before and after olfactory training. Laryngoscope 128:1531–1536
Hannum ME, Ramirez VA, Lipson SJ, Herriman RD, Toskala AK, Lin C, Joseph PV, Reed DR (2020) Objective sensory testing methods reveal a higher prevalence of olfactory loss in COVID-19-positive patients compared to subjective methods: a systematic review and meta-analysis. Chem Senses 45:865–874
Haxel BR, Bertz-Duffly S, Fruth K, Letzel S, Mann JW, Muttray A (2012) Comparison of subjective olfaction ratings in patients with and without olfactory disorders. J Laryngol Otol 126:692–697
Hornung DE, Kurtz DB, Bradshaw CB, Seipel DM, Kent PF, Blair DC, Emko P (1998) The olfactory loss that accompanies an HIV infection. Physiol Behav 15:549–556
Hyde M, Wiggins RD, Higgs P, Blane DB (2003) A measure of quality of life in early old age: the theory, development and properties of a needs satisfaction model (casp-19). Aging Ment Health 7:186–194
Jang SS, Choi JS, Kim JH, Kim N, Ference EH (2022) Discordance between subjective and objective measures of smell and taste in us adults. Otolaryngol Head Neck Surg 166:572–579
Knaapila A, Raittola A, Sandell M, Yang B (2017) Self-ratings of olfactory performance and odor annoyance are associated with the affective impact of odor, but not with smell test results. Perception 46:352–365
Knaapila A, Tuorila H, Kyviv KO, Wright MJ, Keskitalo K, Hansen J, Kaprio J, Perola M, Silventoinen K (2008) Self-ratings of olfactory function reflect odor annoyance rather than olfactory acuity. Laryngoscope 118:2212–2217
Knobel H, Alonso J, Casado JL, Collazos J, Gonzalez J, Ruiz I, Kindelman JM, Carmona A, Juega J, Ocampo A, Group GS (2002) Validation of a simplified medication adherence questionnaire in a large cohort of HIV-infected patients: the GEEMA study. AIDS 16:605–613
Lechien JR, Calbaraz K, Chesa-Estomba CM, Khalife M, Hans S, Calvo-Henriquez C, Martiny D, Journe F, Soverey L, Sausez S (2020) Objective olfactory evaluation of self-reported loss of smell in a case series of 86 COVID-19 patients. Head Neck 42:1583–1590
Leonhardt B, Tahmasebi R, Jagsch R, Pirker W, Lehrner J (2019) Awareness of olfactory dysfunction in Parkinson’s disease. Neuropsychology 33:633–641
Lötsch J, Hummel T (2019) Clinical usefulness of self-rated olfactory performance - a data science-based assessment of 6000 patients. Chem Senses 44:357–364
Loudghi A, Alotaibi M, Lessard-Beaudoin M, Gris D, Busch K (2019) Unawareness of olfactory dysfunction in older adults. Int J Neurol Neurother 6:086
Maki PM, Rubin LH, Springer G, Seaberg EC, Sacktor N, Miller EN, Valcour V, Young MA, Becker JT, Martin EM, Neuropsychology Working Groups of the Women’s Interagency HIV Study (2018) Differences in cognitive function between women and men with HIV. J Acquir Immune Defic Syndr 79:101–107
McGettigan N, Dhubhirh PU, Barrett M, Sui J, Balding L, Higgins S, O’Leary N, Kennedy A, Walsh D (2019) Subjective and objective assessment of taste and smell sensation in advanced cancer. Am J Hosp Palliat Care 36:688–696
Monaghan TF, Rahman SN, Agudelo CW, Wein AJ, Lazar JM, Everaert K, Dmochowski RR (2021) Foundational statistical principles in medical research: sensitivity, specificity, positive predictive value, and negative predictive value. Medicina 57(5):503. https://doi.org/10.3390/medicina57050503
Mueller C, Temmel AF, Quint C, Rieger A, Hummel T (2002) Olfactory function in HIV-positive subjects. Acta Otolaryngol 122:67–71
Murphy C, Schubert CR, Cruickshanks KJ, Klein BE, Klein R, Nondahl DM (2002) Prevalence of olfactory impairment in older adults. JAMA 288:2307–2312
Nordin S, Monsch AU, Murphy C (1995) Unawareness of smell loss in normal aging and Alzheimer’s disease: discrepancy between self-reported and diagnosed smell sensitivity. J Gerontol B Psychol Sci Soc Sci 50:P187-192
Oleszkiewicz A, Abriat A, Doelz G, Azema E, Hummel T (2021) Beyond olfaction: beneficial effects of olfactory training extend to aging-related cognitive decline. Behav Neurosci 135:732–740
Oleszkiewicz A, Kunkel F, Larsson M, Hummel T (2020) Consequences of undetected olfactory loss for human chemosensory communication and well-being. Philos Trans R Soc Lond B Biol Sci 375:20190265
Radloff LS (1977) The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1:385–401
Razani J, Murphy C, Davidson TM, Grant I, McCutchan A (1996) Odor sensitivity is impaired in HIV-positive cognitively impaired patients. Physiol Behav 59:877–881
Reitan R, Wolfson D (1985) The halstead-reitan neuropsychological test battery. Neuropsychology Press, Tucson
Reitan RM (1955) The relation of the Trail Making Test to organic brain damage. J Consult Psychol 19:393–394
Schmidt N, Paschen L, Witt K (2020) Invalid self-assessment of olfactory functioning in Parkinson’s disease patients may mislead the neurologist. Parkinsons Dis 2020:7548394
Sorokowski P, Karwowski M, Misiak M, Marczak MK, Dziekan M, Hummel T, Sorokowska A (2019) Sex differences in human olfaction: a meta-analysis. Front Psychol 10:242
Sundermann EE, Fields A, Saloner R, Gouaux B, Bharti A, Murphy C, Moore DJ (2021) The utility of olfactory function in distinguishing early-stage Alzheimer’s disease from HIV-associated neurocognitive disorders. AIDS 35:429–437
Vance D, Burrage J (2006) Chemosensory declines in older adults with HIV: identifying interventions. J Gerontol Nurs 32:42–48
Vance DE, Cody SL, Nicholson WC, Cheatwood J, Morrison S, Fazeli PL (2019) The association between olfactory function and cognition in aging African American and Caucasian men with HIV: a pilot study. J Assoc Nurses AIDS Care 30:e144–e155
Wehling E, Nordin S, Espeseth T, Reinvang I, Lundervold AJ (2011) Unawareness of olfactory dysfunction and its association with cognitive functioning in middle aged and old adults. Arch Clin Neuropsychol 26:260–269
Welge-Luessen A, Hummel T, Stojan T, Wolfensberger M (2005) What is the correlation between ratings and measures of olfactory function in patients with olfactory loss? Am J Rhino 19:567–571
White TL, Kurtz DB (2003) The relationship between metacognitive awareness of olfactory ability and age in people reporting chemosensory disturbances. Am J Psychol 116:99–110
White TL, Sadikot AF, Djordjevic J (2016) Metacognitive knowledge of olfactory dysfunction in Parkinson’s disease. Brain Cog 104:1–6
Yoo HS, Chung SJ, Lee YH, Ye BS, Sohn YH, Lee PH (2019) Olfactory anosognosia is a predictor of cognitive decline and dementia conversion in Parkinson’s disease. J Neurol 266:1601–1610

Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.