Chemosensory Alterations and Impact on Quality of Life in Persistent Alcohol Drinkers

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Abstract

Background: Heavy alcohol consumption-associated chemosensory dysfunction is understudied, and early detection can help predict disease-associated comorbidities, especially those related to four quality of life (QOL) domains (physical, psychological, social, and environment). We examined self-reports of chemosensory ability of individuals with different alcohol drinking behaviors and their association with changes in QOL domains.

Methods: Participants (n = 466) were recruited between June 2020 and September 2021 into the NIAAA COVID-19 Pandemic Impact on Alcohol study. Group-based trajectory modeling was used to categorize participants without any known COVID-19 infection into three groups (non-drinkers, moderate drinkers and heavy drinkers) based on their Alcohol Use Disorders Identification Test consumption scores at four different time points (at enrollment, week 4, week 6 and week 12). Linear mixed models were used to examine chemosensory differences between these groups. The associations between chemosensory abilities and QOL were determined in each group.

Results: We observed significant impairment in self-reported smell ability of heavy drinking individuals compared to non-drinkers. In contrast, taste ability showed marginal impairment between these groups. There were no significant differences in smell and taste abilities between the moderate and non-drinking groups. Heavy drinkers’ impairment in smell and taste abilities was significantly associated with deterioration in their physical, psychological, social and environmental QOL.

Conclusion: Persistent heavy drinking was associated with lower chemosensory ability. Heavy drinkers’ reduced smell and taste function and association with poorer QOL indicate that early assessment of chemosensory changes may be crucial in identifying poorer well-being outcomes in heavy drinkers at risk for alcohol use disorder.

INTRODUCTION

Alcohol use disorder (AUD), the most prevalent substance use disorder, leads to 3.3 million global deaths each year (WHO, 2018). To date, heavy alcohol consumption is linked with malnutrition (Santolaria et al., 2003) and mental health conditions like depression and anxiety (Almeida-Filho et al., 2007). Heavy drinkers exhibit alterations in their chemosensory percepts, particularly disturbances in taste (gustation) and smell (olfaction) (Maurage et al., 2014; Silva et al., 2016). Moreover, individuals with AUD (vs. healthy controls) were shown to have taste deficits and impaired olfactory discrimination but preserved threshold detection (Brion et al., 2015). Chemosensory alteration is dependent on alcohol consumption patterns, such that heavy drinkers exhibit increased smell and taste dysfunction, whereas light-to-moderate drinkers show a lower prevalence of smell dysfunction (Liu et al., 2016). Researchers have examined the relationship between chemosensation and alcohol consumption (Peeples, 1962; Hayes et al., 2011; Beckett et al., 2017; Rawal et al., 2021); however, it is unclear if variation in chemosensory function is a determinant or a consequence of alcohol consumption, or possibly a causal bidirectional relationship.

Clinical and preclinical findings reveal that females exhibit enhanced sensitivity to odors (Kobal et al., 2001; Baum and Keverne, 2002) as well as better discrimination and identification abilities (Doty et al., 1985) than males. A recent NHANES 2011–2014 study found that young women with self-reported odor deficit tend to feel the burning effects of alcohol more and lose pleasure in consuming alcohol compared to men who report odor impairment (Rawal et al., 2021). The first reports on sex differences in odor perception appeared at the end of the 19th century (Toulouse and Vaschide, 1899), in which women (vs. men) reportedly showed lower detection thresholds in their trigeminal functioning tested using camphor. In general, women have outperformed men in their smell (Sorokowski et al., 2019) and taste (Wang et al., 2020) abilities. It is important to understand the difference in chemosensory functioning between men and women alcohol drinkers.
Both heavy alcohol consumption (Castillo-Carniglia et al., 2019) and chemosensory dysfunction (Chen et al., 2021) are known contributors to psychological disturbances (e.g. cognitive dysfunction, anxiety and depression). Persistent olfactory or gustatory dysfunction is associated with a significant reduction in a person’s QOL (Croy et al., 2014; Erskine and Philpott, 2020), including increased depressive symptoms (Hur et al., 2018), anxiety (Nordin et al., 2011) and nutritional issues (Toussaint et al., 2015). However, it is unclear if chemosensory dysfunction in heavy drinkers is associated with changes in their QOL.

To lend insight into these questions, we used data from an ongoing longitudinal study to investigate the association between self-reported chemosensory dysfunction and drinking behavior and related outcomes of participants across four time points [at enrollment, weeks 4 (week04), 8 (week08) and 12 (week12)]. The associations between self-reported chemosensory dysfunction and QOL in heavy drinking individuals were also examined. We hypothesized that heavier drinking patterns across the study period would be associated with greater chemosensory dysfunction and worse QOL. The taste and smell data were collected as part of a survey study initiated during the COVID-19 pandemic and were self-reported measures. As discussed recently by various groups using the Global Consortium on Chemosensory Research (GCCR) survey in COVID-19 patients, self-report is a useful tool for clinicians and scientists to determine the ongoing chemosensory dysfunction (Parma et al., 2020; Cecchetto et al., 2021). The specificity of smell loss in predicting COVID-19 positive status reached 75% using the GCCR survey, which demonstrates the potential of this self-report-based instrument in capturing smell dysfunction in the absence of in-person interaction with the subjects (Gerkin et al., 2021). The results obtained in this study address a research gap in alcohol and chemosensory dysfunction and shed light on the importance of early assessment of chemosensory health in chronic alcohol drinking individuals.

METHODS

Participants
The COVID-19 Pandemic Impact (C19-PIA) study was initiated in the NIAAA Intramural Clinical Research Program in June 2020. This study was approved by the NIH Intramural Institutional Review Board (IRB) and is registered in clinicaltrials.gov (NCT04391816). The overall goal of this study was to examine the impact of the COVID-19 pandemic on alcohol use and consequences in individuals across the spectrum of alcohol use. The details on the study design and the primary results are reported elsewhere (Luk Jeremy et al., 2022; Revision et al., 2022). While the C-19 PIA study was initiated due to the pandemic, the current analysis was designed to examine, as a secondary outcome, changes in chemosensation and relationship to alcohol drinking in this sample. Four hundred and sixty-six participants were enrolled between June 2020 and November 2021 into the NIAAA C19-PIA on Alcohol study conducted online and/or by phone. Most participants (83.7%) were residing in the Greater Washington DC area, specifically in Maryland (53.2%), Washington DC (17.6%) and Virginia (12.9%). The present study used repeated measurements [at enrollment, weeks 4 (week04), 8 (week08) and 12 (week12)] from this ongoing longitudinal study with a focus on drinking patterns, chemosensory functioning and QOL. We excluded participants with COVID-19 positive status (n = 17) as taste and smell impairments are vital symptoms of COVID-19 (Parma et al., 2020) and could be a confounding factor. In addition, since chemosensory functioning diminishes with age (Boyce and Shone, 2006), participants who were older than 70 years of age (n = 9) were also excluded, yielding a final analysis sample of n = 440. The NIH Intramural IRB approved the present ongoing study and is registered in clinicaltrials.gov (NCT04391816).

Alcohol consumption
The Alcohol Use Disorders Identification Test-consumption (AUDIT_C) subscale, a three-item screening questionnaire on alcohol consumption, can be used as a screener for heavy drinking or alcohol use disorder (Synofzik et al., 1993). We used AUDIT-C as a measure of alcohol consumption rather than the total AUDIT score or other AUDIT subscales (AUDIT-harmful or AUDIT-dependence), which include the assessment of the negative consequences of drinking. The participants were administered the AUDIT at all four study time points [at enrollment, week04, week08 and week12] in the C19 PIA study.

Smoking status
Smoking history was assessed using the Fagerström Test for Nicotine Dependence to characterize the participant’s lifetime smoking status. The smoking status obtained was utilized as a control variable in analyses of taste and smell to account for impairment that is not linked to alcohol consumption (Schneller et al., 2018).

Primary outcome measure
Taste and smell
The smell and taste questionnaires were modified survey questions initially designed by GCCR (Parma et al., 2020). Participants were asked to complete an online questionnaire to ‘Rate your ability to smell CURRENTLY’ and ‘Rate your ability to taste CURRENTLY’ at all four time points. The smell and taste abilities were scored based on self-rating on a visual analog scale (0–100), with higher scores indicating a better sense of taste/smell.

Secondary outcome measures
Flu-like, cough and cold symptoms
Participants were asked if they were experiencing any of the following symptoms: fever/feeling feverish, cough, sore throat, runny or stuffy nose, fatigue, difficulty breathing, diarrhea or stomach upset. The participants were to respond ‘yes’ or ‘no’ for the presence or absence of each symptom at each time point.

Quality of life
The World Health Organization Quality of Life—Brief scale was administered at all time points to evaluate several aspects of QOL, including physical health, psychological, social relationships and environment (WHO, 1998). These outcomes provide information related to individuals’ energy level for everyday activities, ability to focus and feel lively, feeling of satisfaction in relationships and peer support, as well as satisfaction level regarding their current living situations and access to health services. QOL measures can provide vital information about the overall health outcomes due to chemosensory changes in individuals associated with alcohol
use. Responses for the 24 items utilized to calculate the four domain subscales were rated on a scale from 1 to 5, coded as: 1 = very poor, 2 = poor, 3 = neither poor nor good, 4 = good and 5 = very good. Raw scores for each domain are calculated by summing the items within each domain, and these scores are then transformed to a 0–100 scale. Higher scores indicated a better QOL.

Statistical analyses

Group-based trajectory modeling (GBTM) is a finite mixed modeling method employed in developmental and clinical research to capture behavior heterogeneity over time (Nagin and Odgers, 2010). Using the traj command in STATA, we utilized GBTM to identify alcohol drinking groups using the heterogeneous alcohol consumption data of the study participants derived from longitudinal data across four study time points. This is an appropriate method for our research question as it effectively captures group differences in the longitudinal pattern of alcohol consumption over time; it also allows for using a zero-inflated Poisson model to account for the positive skewness and zero-inflation in the alcohol consumption data (Nagin and Odgers, 2010). Missing data were handled using Full Information Maximum Likelihood (Supplementary Table S1). GBTM analysis on alcohol consumption scores at the four study time points categorized the participants into three drinking groups (Table 1). We chose the three-group model (Fig. 1) as the optimal model due to significant decreases in the absolute values of the log-likelihood and information criteria from 2 to 3 groups, a reasonably high entropy and interpretable trajectory with reasonable model fit. Next, we provided the ‘beta estimates (β); 95% CI; P-value’ to report between group differences.

Sensitivity analyses

We did three sets of sensitivity analyses. First, we evaluated the impact of missing data on the chemosensory measures and compared the demographic characteristics (age, gender, smoking and AUD history) of participants with follow-up missing and non-missing datasets. Second, we examined LMM for our outcome measures (smell and taste) in dataset with no missing data values. Third, to further investigate the possibility that age or any self-report of existing cold/flu symptoms was a substantial confounder, two separate LMMs were tested between the alcohol drinking groups (heavy drinkers vs. non-drinkers) excluding participants’ data: (a) above 60 years of age and (b) with any self-report on existing fever, runny nose, stuffed nose, diarrhea, cold or flu symptoms. STATA 16 (StataCorp, 2019, College Station, TX) and SPSS 28.0 (IBM, New York, USA) were used for all statistical analyses.

RESULTS

Demographic and clinical variables of the alcohol drinking groups

Characteristics of our study sample are summarized in Table 1. Significant sex differences were observed between the non-drinking and heavy drinking groups. Heavy drinkers comprised a higher percentage of men (66.9%) than women (33.1%). The percentage of men was significantly lower in
non-drinking (49.6%) than in the heavy drinking group (66.9%, \( P = 0.01 \)). Notably, the heavy drinking group comprised a higher percentage of smokers (41.9%) than non-drinkers (21.7%, \( P = 0.002 \)). The heavy drinking group consisted of a higher percentage of participants (78%) with a previous history of AUD diagnosis than moderate (29%) and non-drinkers (31%). This finding supports the alcohol group categorization in our study. The percentage of the white population was higher in the heavy drinking group (61.3%) than in the non-drinking group (42.6%, \( P = 0.03 \)). The AUDIT_C scores of heavy drinkers were significantly different from the non-drinkers across study time points (Table 1).

### Smell and taste differences between the alcohol consumption groups

The adjusted model for age and smoking status revealed significant group \( F_{1,217} = 5.1; P = 0.03 \) and time \( F_{3,156} = 8.5; P < 0.001 \) effects on smell ability, and a trend-level group \( F_{1,200} = 3.5; P = 0.06 \) and significant time effect \( F_{3,165} = 8.5; P < 0.001 \; \text{Table 2} \) on taste of non-drinkers versus heavy drinkers. Specifically, heavy drinkers exhibited significantly lower smell (\( \beta = -4.4 \; [95\% \; CI \; 8.21 \; to \; -0.55]; \; P = 0.03 \)) ability than non-drinkers. No differences in smell and taste abilities were seen between moderate and non-drinkers (Fig. 2A and B; Table 2; Supplementary Table S2).

Further, the adjusted model for age and smoking status revealed both significant sex \( F_{1,112} = 4.3; \; P = 0.04 \) and time \( F_{3,80} = 3.5; \; P = 0.02 \) effects on smell ability of men versus women heavy drinkers. Men reported greater smell impairment than women (\( \beta = -6.7 \; [95\% \; CI \; -13.14 \; to \; -0.32]; \; P = 0.04 \)). No sex difference in the taste ability of heavy drinking participants was seen (Table 2; Supplementary Table S2).

### QOL differences between the alcohol consumption groups

The adjusted model for age and smoking status revealed significant group and time effects on all QOL domains, except for social relationships compared between non-drinkers versus heavy drinkers. A significant difference in the social
Table 2. Effects of alcohol drinking groups, sex (heavy drinkers), and time on smell, and taste ability, adjusted for age and smoking status

|                     | Smell |                      | Taste |                      |
|---------------------|-------|----------------------|-------|----------------------|
|                     | Sample size | Group effect | Time effect | Sample size | Group effect | Time effect |
| Non-drinkers vs. moderate drinkers | 837 | $F_{1,289} = 2.7; P = 0.11$ | $F_{1,246} = 6.6; P < 0.001$ | 836 | $F_{1,284} = 2.3; P = 0.13$ | $F_{1,264} = 9.3; P < 0.001$ |
| Non-drinkers vs. heavy drinkers | 604 | $F_{1,217} = 5.1; P = 0.03$ | $F_{3,156} = 8.5; P < 0.001$ | 603 | $F_{1,200} = 3.5; P = 0.06$ | $F_{3,163} = 11.9; P < 0.001$ |
| Male vs. female heavy drinkers | 316 | $F_{1,112} = 4.3; P = 0.04$ | $F_{3,80} = 3.5; P = 0.02$ | 315 | $F_{1,101} = 1.9; P = 0.16$ | $F_{3,86} = 6.1; P < 0.001$ |

Note: 114/114 participants at enrollment responded to smell/taste questions, 67/67 at week04, 58/58 at week08 and 63/64 at week12 in the non-drinking group; 200/200 at enrollment, 143/146 at week04, 115/115 at week08 and 112/113 at week12 in moderate drinking group, while 122/123 at enrollment, 71/71 at week04, 64/65 at week08 and 62/63 at week12 in heavy drinking group.

Fig. 2. Bar plots illustrating smell (A) and taste (B) reports across study time of 12 weeks in alcohol consumption groups: non-drinkers, moderate drinkers and heavy drinker.

Flu-like, cough and cold symptoms
The presence of flu-like, cough and cold symptoms was reported by less than 5% of participants at enrollment, with a similar percentage at week04, and a reduction to less than 3% of the participants at weeks 8 and 12. The prevalence of these symptoms remained similar across drinking groups (Supplementary Table S3).

Association of QOL domains with chemosensory alterations by alcohol consumption groups
Moderate and heavy drinkers revealed significant positive associations between their smell and taste abilities and all QOL domains. In non-drinkers, a significant positive association between smell ability and physical health was seen, while no other significant associations between smell and taste ability and other QOL domains were observed (Table 3; Supplementary Table S5).

Our sensitivity analyses revealed no significant difference in demographic characteristics (age, gender, smoking and AUD history) of the two datasets (follow-up missing and the non-missing datasets). Furthermore, the findings were unchanged when excluding participants with age >60 years ($n = 63$) as well as analyzing the datasets with no missing data values at any of the study time points. Repeating analyses with exclusion of participants with cold/flu symptoms revealed marginal significance for outcome measures; however, we noted similar effect sizes to those seen in our primary analyses (Supplementary Table S6).

DISCUSSION
In this study, we observed a notable impairment in self-reported smell and taste abilities of heavy alcohol drinkers compared to non-drinkers, indicating negative impact of continued chronic alcohol consumption on chemosensation. These results held after controlling for confounders like age and smoking status, which are known to influence taste and smell perceptions (Boyce and Shone, 2006; Vennemann et al., 2008) significantly. Further, less than 5% of these participants reported cold or flu symptoms (Supplementary Table S3), making those effects unlikely to have a substantial contribution to these results.

Heavy drinking could affect measures of olfactory function either via true sensory changes (for threshold, intensity, etc.) or via altered cognition/memory function (for odor identification). The impact of heavy alcohol consumption on olfactory and taste dysfunction has been demonstrated using both subjective and objective measures (Brion et al., 2015; Hoffman et al., 2016; Liu et al., 2016). According to National Health and Nutrition Examination Survey 2013–2014 data, age, gender, ethnicity, educational attainment, family income, light-to-moderate alcohol consumption, cardiovascular disease (CVD) and history of asthma or cancer were reported as potential risk factors for smell dysfunction, while ethnicity, heavy alcohol consumption and CVD were associated with a higher prevalence of taste dysfunction (Liu et al., 2016).
Olfactory dysfunction [tested both objectively (UPST) and subjectively] was also reported in heavy alcohol drinking individuals (Hoffman et al., 2016). The quality and intensity of olfactory perception depend on the functional state of the nasal epithelium and the central and peripheral nervous systems. The damage caused to the olfactory epithelium presumably pertains to the disrupted immune system caused by chronic alcohol consumption (Pasala et al., 2015). It has long been posited that heavy alcohol consumption leads to impairment of the cognitive component of olfactory function as tested by olfactory identification (Maurage et al., 2011b). The connection of the olfactory system with emotional (amygdala) and cognitive (orbitofrontal cortex, OFC) brain regions is well known (Price, 1987), and olfactory judgements knowingly rely mainly on OFC (a crucial area involved in emotional, executive and olfactory processing) (Rolls, 2008). In many neurodegenerative disorders (schizophrenia, autism, depression and anorexia nervosa), olfactory testing is used to understand cognitive impairments (Roessner et al., 2005; Wiggins et al., 2009; Clepece et al., 2010; Velayudhan et al., 2013) and is even stated to possibly constitute as a cognitive marker in psychiatry (Atanasova et al., 2008). Specifically, AUD was associated with both impaired odor identification and source memory (on confabulation task), with a strong association between olfaction and source memory performances in the same individuals, which indicates the role of OFC in olfaction functioning in AUD individuals (Schnider et al., 1996). Notably, Maurage et al. used electrophysiological recordings to reveal that olfactory impairments in individuals with AUD are solely a consequence of cognitive impairment (abnormal latency and amplitudes of N1 and P2 waveforms) and not a consequence of general impairment that also impacts trigeminal functioning (Maurage et al., 2011a).

The present study was not focused on understanding the underlying mechanism behind the decreased smell functioning in heavy drinking individuals. It has been known that olfactory receptor neurons (OSNs) continually regenerate, approximately every 30–90 days, in the olfactory epithelium in response to normal turnover (Grazidei and Grazidei, 1979). The regeneration often accelerates following loss/damage due to drug (alcohol/tobacco), pathogen, or toxicant exposure through both inhalatory and non-inhalatory routes (Grazidei and Grazidei, 1979; Bergman et al., 2002). However, continuous alcohol consumption might inhibit the regeneration of OSNs in heavy drinkers, potentially similar to what is seen in other disease processes like chronic rhinosinusitis (Turner et al., 2010). Although we could hypothesize the potential involvement of the above noted mechanisms in smell dysfunction seen in heavy drinking individuals, this investigation needs to be extended in future studies to understand the causal effect of heavy drinking on the olfactory system. A significant decrease in smell perception of continuous heavy drinkers over the study period of 12 weeks was seen, even after adjusting for the demographic characteristics of patients. Given the stability in the drinking trajectories, it is possible that worsening of smell perception was not only driven by alcohol consumption observed during the 12-week study period but also reflected a more substantial drinking history prior to the study. Since our primary results remained unchanged after controlling for all possible confounders (including age, smoking status) and even our sensitivity analysis excluding individuals age >60 years and with any cold/flu symptoms did not change our primary results, we demonstrated that the smell deficits reported by heavy drinkers were uniquely explained by their chronic alcohol consumption. Furthermore, in our study, we noticed significant impairment in the smell ability of heavy drinking men compared to heavy drinking women. This

### Table 3. Association between chemosensory ability and QOL domains by alcohol drinking group

|                  | Physical QOL | Psychological QOL | Social QOL | Environment QOL |
|------------------|-------------|------------------|-----------|-----------------|
| **Non-drinkers** |             |                  |           |                 |
| Smell: Sample size (n) | 270 | 268 | 269 | 271 |
| Smell effect | $F_{1,219} = 4.2; P = 0.04$ | $F_{1,224} = 2.0; P = 0.16$ | $F_{1,211} = 0.06; P = 0.80$ | $F_{1,215} = 0.09; P = 0.76$ |
| Time effect | $F_{1,184} = 7.3; P < 0.001$ | $F_{1,186} = 7.6; P < 0.001$ | $F_{1,185} = 0.51; P = 0.67$ | $F_{1,187} = 5.0; P = 0.002$ |
| **Taste: Sample size (n)** | 269 | 267 | 268 | 270 |
| Taste effect | $F_{1,228} = 2.1; P = 0.15$ | $F_{1,242} = 3.9; P = 0.05$ | $F_{1,226} = 0.03; P = 0.86$ | $F_{1,224} = 0.53; P = 0.47$ |
| Time effect | $F_{1,182} = 6.7; P < 0.001$ | $F_{1,186} = 7.8; P < 0.001$ | $F_{1,184} = 0.56; P = 0.64$ | $F_{1,186} = 5.2; P = 0.002$ |
| **Moderate drinkers** | 518 | 518 | 520 | 520 |
| Smell: Sample size (n) | 518 | 518 | 520 | 520 |
| Smell effect | $F_{1,496} = 4.1; P = 0.04$ | $F_{1,508} = 9.4; P = 0.002$ | $F_{1,506} = 4.9; P = 0.03$ | $F_{1,503} = 12.3; P < 0.001$ |
| Time effect | $F_{1,358} = 29.4; P < 0.001$ | $F_{3,360} = 22.5; P < 0.001$ | $F_{3,357} = 4.3; P = 0.01$ | $F_{3,358} = 22.3; P < 0.001$ |
| **Heavy drinkers** | 516 | 516 | 518 | 518 |
| Smell: Sample size (n) | 516 | 516 | 518 | 518 |
| Smell effect | $F_{1,485} = 6.2; P = 0.01$ | $F_{1,491} = 5.1; P = 0.03$ | $F_{1,491} = 7.2; P = 0.01$ | $F_{1,487} = 3.6; P = 0.06$ |
| Time effect | $F_{1,356} = 28.9; P < 0.001$ | $F_{3,356} = 20.8; P < 0.001$ | $F_{3,355} = 4.2; P = 0.01$ | $F_{3,355} = 20.4; P < 0.001$ |
| **Taste: Sample size (n)** | 279 | 276 | 279 | 278 |
| Smell effect | $F_{1,237} = 12.9; P < 0.001$ | $F_{1,229} = 16.2; P < 0.001$ | $F_{1,239} = 15.8; P < 0.001$ | $F_{1,213} = 21.5; P < 0.001$ |
| Time effect | $F_{1,188} = 4.3; P = 0.01$ | $F_{1,187} = 6.3; P < 0.001$ | $F_{1,190} = 1.5; P = 0.21$ | $F_{1,185} = 3.4; P = 0.02$ |
| **Taste: Sample size (n)** | 279 | 276 | 279 | 278 |
| Smell effect | $F_{1,216} = 11.5; P < 0.001$ | $F_{1,210} = 11.6; P < 0.001$ | $F_{1,218} = 28.2; P < 0.001$ | $F_{1,216} = 24.8; P < 0.001$ |
| Time effect | $F_{1,187} = 4.5; P = 0.01$ | $F_{1,186} = 6.2; P < 0.001$ | $F_{1,189} = 1.6; P = 0.19$ | $F_{1,187} = 3.7; P = 0.01$ |
finding may pertain to overall higher alcohol consumption in men than women (Bratberg et al., 2016). We note in our study that the percentage of men heavy drinkers was significantly higher than women heavy drinkers. However, a significant sex difference in taste reports was not evident. We also noticed a marginal self-reported taste dysfunction in heavy drinking group (vs. non-drinkers); some possible mechanisms implicated in this alteration of taste function in chronic drinkers include genetic variations (Bachmanov et al., 2002), changes in gene expression, epigenetic modifications of taste receptors (Xiao et al., 2021) and morphological changes in the salivary gland ranging from extremely dilated ducts with desquamated cells and stasis of content to epithelial atrophy (Ferraris et al., 2000). Due to taste deficiencies, negative food choices and intake ultimately disrupt nutritional health and impair immune function (Mattes and Cowart, 1994).

Finally, the smell and taste dysfunction seen with increased alcohol consumption was associated with deterioration in the overall life quality of both moderate and heavy drinkers, within all four domains, namely, physical health, psychological, social relationships, and environment. However, the effect was more significant in heavy drinkers. Smell and taste deterioration, in general, are associated with a reduced appetite, which can lead to malnourishment (Malaty and Malaty, 2013). Similarly, chemosensory dysfunction can impair one’s ability to maintain personal hygiene, which can reduce social life, affect mental stability, and deplete the overall life quality (Hummel et al., 2011). The observed impairment in chemosensory ability with increased alcohol consumption and association of smell and taste dysfunction with reduced life quality highlight the importance of early detection of any change in these sensory variables as a crucial step towards reducing the likelihood for the occurrence of comorbid health conditions, including malnutrition, obesity, anxiety, or depression in individuals at risk for AUD.

Limitations

The findings are based on subjective (self-report) evaluation of taste and smell functions since the study was conducted during the COVID-19 pandemic. We acknowledge that the results may be influenced by reporting bias. Although in our analysis we excluded any participant with a positive COVID-19 diagnosis, we could not completely rule out the possibility of reporting biases by the participants. Because of limited access to reliable SARS-CoV2 testing options, the number of positive cases was likely underestimated. Furthermore, we could not collect objective chemosensory measures; however, once safety guidelines surrounding the pandemic allow for the safe collection of objective measures in a clinical setting, we plan to incorporate these measures into this ongoing study. Chemosensory dysfunction, a third chemosensory modality, which is of high relevance to the burning effects of alcohol, has not been explored in the present study due to the lack of descriptive variables on the type of alcoholic beverage consumed. Fourthly, it is difficult to interpret the participants’ rating of taste and smell, which may often be influenced by the loss of flavor perception through retronasal olfaction. Retronasal olfaction critically determines the appreciation of flavor in both foods and beverages and in the absence of adequate explanation participants fail to distinguish between taste and flavor. Therefore, data from the present study should be taken cautiously. Data on any pre-existing pathological conditions, head trauma or concussion, that could impact chemosensation were not assessed and should be considered as potential confounders for consideration in future studies. Lastly, the findings obtained support our hypothesis suggesting that it is alcohol consumption that has led to chemosensory function changes in heavy drinking individuals but given this is an observational study, we cannot determine the direction of effects, and future experimental studies are needed to address this question.

CONCLUSION

Our study documents the effects of consistent alcohol consumption over the study period of 12 weeks on chemosensory perception. Although studies have reported an association between alcohol consumption and chemosensory alterations, the present study reports the effect of continuous alcohol consumption on chemosensation across the spectrum of alcohol use. Our results help address a critical literature gap and provide evidence supporting the inclusion of chemosensory assessments as indicators of heavy alcohol consumption indices. Understanding symptom severity can help improve the overall physical and psychological health of heavy drinkers. Early investigation in smell and taste changes may help design more effective treatments to delay the progression and complications of olfactory and taste alterations. Improvement in assessment of chemosensory disturbances may help inform and improve patient counseling, particularly regarding safety issues, and for determination of disability and monitoring the overall life quality of these individuals.

ABBREVIATIONS

QOL, quality of life; AUD, alcohol use disorder; GCCR, Global Consortium on Chemosensory Research; AUDIT_C, Alcohol Use Disorders Identification Test-consumption; GBTM, group-based trajectory modeling; LMMs, linear mixed models; OSNs, olfactory sensory neurons

SUPPLEMENTARY MATERIAL

Supplementary material is available at Alcohol and Alcoholism online.

AUTHOR CONTRIBUTIONS

Conceptualization: K.A., P.V.J., N.D. and V.A.R. Writing—original draft: K.A. Data curation: M.L.S., J.W.L. and B.L.S. Data analysis and interpretation: K.A., J.W.L. and P.M. Reviewing and editing: K.A., J.W.L., P.V.J., P.M., V.A.R., N.D., D.G., C.M., L.T., R.B.J-L. and R.M. Supervision: P.V.J. and V.A.R.

DISCLOSURE

The content is solely the authors’ responsibility and does not necessarily represent the official views of the NIH.

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**CONFLICT OF INTEREST STATEMENT**

The authors declare no competing interests.

**DATA AVAILABILITY**

Data described in the manuscript will be made available by contacting the corresponding author (P.V.J.).

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