International Journal of Psychophysiology 186 (2023) 1–9

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Momentary gustative-olfactory sensitivity and tonic heart rate variability are independently associated with motivational behavior

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ARTICLE INFO

Keywords:
Ageusia
Anhedonia
Anosmia
Ecological momentary assessment
Heart rate variability
Probabilistic Reward Task

ABSTRACT

Deficits in motivational functioning including impairments in reward learning or reward sensitivity are common in psychiatric disorders characterized by anhedonia. Recently, anhedonic symptoms have been exacerbated by the pandemic caused by the Coronavirus disease 2019 (COVID-19) in the general population. The present study examined the putative associations between loss of smell (anosmia) and taste (ageusia) sensitivity, irrespective of COVID-19 infection, and anhedonia, measured by a signal-detection task probing the ability to modify behavior as a function of rewards (Probabilistic Reward Task; PRT). Tonic heart rate variability (HRV) was included in the model, due to its association with both smell and taste sensitivity as well as motivational functioning. The sample included 114 healthy individuals (81 females; mean age 22.2 years), who underwent a laboratory session in which dispositional traits, resting HRV and PRT performance were assessed, followed by a 4-days ecological momentary assessment to obtain daily measures of anosmia and ageusia. Lower levels of tonic HRV and lower momentary levels of smell and taste sensitivity were associated with impaired reward responsiveness and ability to shape future behavioral choices based on prior reinforcement experiences. Overall, the current results provide initial correlational evidence that could be fruitfully used to inform future experimental investigations aimed at elucidating the disruptive worldwide mental health consequences triggered by the pandemic.

1. Introduction

Anhedonia, the reduced ability to experience pleasure in previously rewarding activities or stimuli, represents a critical symptom of several neuropsychiatric disorders, particularly major depressive disorder. In the past decades, anhedonia has been associated with changes within the brain reward system which are mirrored at the behavioral level by impaired reward-related sensitivity and learning (Pizzagalli, 2022). The Coronavirus disease 2019 (COVID-19) pandemic and the subsequent national lockdowns have had a massive impact on people's lives, leading to mental health deterioration worldwide, including exacerbation of anhedonic symptoms among the general population (Medda et al., 2022; Wieman et al., 2022). Beyond the physical symptoms caused by the viral infection, such as anosmia and ageusia (i.e., loss of olfactive and gustatory sensitivity, respectively), cough, fever, shortness of breath, hypoxia, and severe pneumonia (Giacomelli et al., 2020; Rothan and Byrareddy, 2020), short- or long-term psychological effects have been reported as consequences of SARS-CoV-2 infection (Taquet et al., 2021). A high prevalence of depression (14.9 %) and anxiety (14.8 %) emerged in the post-illness stage in both hospitalized and non-hospitalized patients (Rogers et al., 2020). In spite of these epidemiological data, the precise psychopathological mechanisms associated with increased risk for depressive symptoms in the context of the COVID-19 pandemic remain largely unexplored.

The current study aimed to investigate the associations among the most typical clinical manifestations of the viral infection, namely

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https://doi.org/10.1016/j.ijpsycho.2023.01.010
Received 5 November 2022; Received in revised form 24 January 2023; Accepted 26 January 2023
Available online 3 February 2023

anosmia and ageusia, on the motivational system, driven by the idea that these symptoms may have contributed to the mental health worsening associated with the pandemic. Importantly, the present study took a dimensional approach and assessed different degrees of anosmia/ageusia along a continuum in the general population, irrespective of actual infection.

A putative biomarker that prospectively predicted resilience versus susceptibility to mental health difficulties associated with COVID-19 stress is heart rate variability (HRV), a surrogate index of cardiac vagal modulation (Miller et al., 2021; Makovac et al., 2022; Wekenborg et al., 2022). A wealth of studies supports the view that higher levels of tonic (resting) HRV reflect the ability of the organism to flexibly adjust in the face of changing internal or external (i.e., environmental) demands (Thayer and Lane, 2000; Thayer and Lane, 2009), and this is possible since the vagus nerve is an integral part of the brain-heart bidirectional communication (e.g., Thayer et al., 2012). Not surprisingly, resting HRV has been found to predict psychopathological symptoms longitudinally, including anhedonia (e.g., Vazquez et al., 2016). Particularly relevant to the aim of the present investigation is the fact that the vagus nerve also contributes to gustatory and olfactory information, due to its connection with the epiglottis region and olfactory processing areas of the cortex (e.g., Heckmann et al., 2003; Horii et al., 2013). In fact, HRV changes have been found to be negatively correlated with perceived odor intensity and positively correlated with perceived odor pleasantness (e.g., Bensafi et al., 2002; Glass et al., 2014).

Given the putative role of HRV in both motivational functions and gustatory/olfactory perception, we hereby hypothesized that lower tonic HRV would be associated with reduced taste/smell sensitivity and enhanced anhedonic behavior, measured both subjectively by self-reports and objectively by the Probabilistic Reward Task (PRT) (Pizzagalli et al., 2005; Pizzagalli et al., 2008), a signal detection task recommended by the Research Domain Criteria as an objective probe of reward learning (NIMH, 2016). Surprisingly, in spite of the number of studies linking HRV to depressive symptoms, this is the first study to examine the association between HRV and performance on the PRT.

The hypothesis that anosmia and ageusia may have contributed to the mental health worsening associated with the pandemic is preliminarily supported by the studies conducted on individuals who contracted the COVID-19 infection. For example, Yom-Tov et al. (2021) analyzed posts by a large cohort of Reddit users within the /r/covid19positive subforum (n = 15,821) and found significant associations between mention of anosmia/ageusia and transition to a risk state of suicidal ideation or depression. The second study was conducted on a sample of 104 healthcare workers, supporting the association between experienced taste/olfactory loss and increased emotional distress and depression, persisting even after the recovery from the disease (Dudine et al., 2021).

These findings are not surprising considering that olfactory and gustatory disturbances (especially hyposensitivity) have been described in psychopathological conditions characterized by anhedonia (reviewed in Atanasova et al., 2008; Atanasova et al., 2010; Athanassi et al., 2021; Hur et al., 2018; Kohli et al., 2016; Naudin et al., 2012; Negoias et al., 2010; Schablitzky and Pause, 2014), to the point that the term "olfactory anhedonia" has been coined with reference to depression (Negoias et al., 2016; Rottstaedt et al., 2018). For example, a large population study conducted on 5275 adults has shown that individuals older than 40 years who reported alterations in smell and taste were more likely to meet the diagnostic criteria for major depressive disorder (Khil et al., 2016). Notably, reduced olfactory bulb volume is a putative biological vulnerability factor for the occurrence and/or maintenance of depression (Croy and Hummel, 2017; Sabiniewicz et al., 2022) and a predictor of therapeutic outcome, with non-responders having a smaller volume compared to responders (Pouliot et al., 2008). Moreover, impairments in olfactory sensitivity tend to be worse in recurrent compared to first-episode depression (Khil et al., 2016) and depressive symptoms worsen or improve in parallel with the course of primary olfactory dysfunctions (Atanasova et al., 2010; Naudin et al., 2012). Lastly, and particularly relevant to the aim of the current investigation, healthy individuals with self-reported anhedonic symptoms are also characterized by impaired olfactory sensitivity (Hur et al., 2018).

Overall, in light of the reviewed evidence, the current investigation hypothesized that reduced tonic HRV and olfactory and gustatory hyposensitivity would be significantly associated with anhedonic behavior. While acknowledging the correlational nature of the study, it was expected that probing these interrelations along a continuum in a healthy population may allow identifying potential early risk factors, to be further corroborated in subsequent experimental inquiries.

2. Materials and methods

2.1. Participants

Participants were recruited among university students and through word of mouth in the general population. They were invited to participate in a study on "Perception and motivational processes" and were told that they could win up to 20 euros for their participation. The data were collected from May 2021 to November 2021.

The protocol was approved by the Institutional Review Board (IRB) of the Department of Psychology, Sapienza University of Rome (Prot. N. 1170/2021). The final sample included 114 participants (33 males, 81 females), between the age of 20 and 30 (mean age 22.24 ± 2.93 years). Exclusionary criteria were: self-disclosed (a) history or presence of serious medical conditions; (b) formal diagnosis of psychiatric disorder or problematic substance use; (c) neurological disorders including traumatic brain injury, history of childhood neurological disorders; (d) use of drugs/medications; and (e) pregnancy or breast-feeding.

2.2. Procedure

After reading and signing the informed consent, participants were asked to complete online a set of questions assessing sociodemographic and lifestyle or medical information (e.g., age, weight, nicotine and alcohol consumption, medication intake, COVID-19 infection in the previous six months), followed by validated questionnaires to evaluate symptoms of depression, anxiety, and stress, and anhedonic symptoms, and a revised form of the Smell and Taste Check developed by the Global Consortium for Chemosensory Research (GCCR, 2020).

Subsequently, a laboratory appointment was scheduled, during which resting HRV was first assessed for 5 min; then, participants performed the PRT (Pizzagalli et al., 2005; Pizzagalli et al., 2008). Next, participants were instructed about the ecological momentary assessment (EMA) procedure and asked to fill out electronic diaries received via Qualtrics.com on their smartphones for four consecutive days. At the end of EMA, participants were debriefed and reminded that they would be compensated for participation with the money that they won during the task.

2.2.1. Questionnaires

2.2.1.1. Depression, Anxiety and Stress Assessment. The Italian version of the Depression Anxiety Stress Scales (DASS-21) (Bottesi et al., 2015) was used to assess trait depression, anxiety, and stress. The scale includes 21 items (7 for each subscale), and the answers are provided on a 4-point Likert scale (from 0 = Did not apply to me at all to 3 = Applied to me very much or most of the time). Examples of items are: "*I couldn't seem to experience any positive feeling at all*" (depression), "*I felt I was close to panic*" (anxiety), "*I found it hard to wind down*" (stress). Given the heterogeneity of the items of the scale, internal consistency was calculated by means of McDonald's omega. Internal consistency in the present study for the overall scale was ω = 0.929, while the specific coefficient

for DASS depression was ω = 0.887.

2.2.1.2. Self-reported anhedonia. The Italian version of the Temporal Experience of Pleasure Scale (TEPS) (Stratta et al., 2011) is an 18-item scale used to tap individual differences in anticipatory and consummatory experiences of pleasure. Examples of items are: "*When something exciting is coming up in my life, I really look forward to it*" (anticipatory), "*The smell of freshly cut grass is enjoyable to me*" (consummatory). Answers are provided on a 6-point Likert scale (from 1 = Very false for me to 6 = Very true for me). Internal consistency in the present study was ω = 0.720.

2.2.1.3. Smell and Taste Sensitivity Assessment. An adapted form of the Smell and Taste Check, developed by the GCCR (2020), was used (see S1 in the online Supplementary Material). The scale consists of an experiential test to assess olfactory and gustatory sensitivity, and it involves 17 items, inquiring about individuals' general perception of their smell and taste sensitivity, the level of nasal occlusion, and smell and taste sensitivity in response to specific elements. Responses are given on a series of Visual Analogue Scales (VAS), from 0 = Absence of smell/taste to 10 = Excellent smell/taste. The olfactory rating is based on smell sensitivity to alcohol and to elements chosen among cosmetics, spices, fruit and vegetables, and food. Gustative rating is based on taste sensitivity to vinegar/lemon, sugar, salt, and coffee/tea. The survey used in the present study differs from the original for the reduced number of elements included in each category (i.e., $n = 5$ in the Cosmetics and Detergents; $n = 6$ in the Spices and Food ingredients; $n = 5$ in the Fruit and Vegetables; $n = 5$ in the Other categories), the absence of questions about nasal and gustatory sensations (e.g., cold sensitivity), and the absence of a question on the difference between actual and previous smell and taste sensitivity. Internal consistency of the overall item set in the present study was ω = 0.801.

2.2.2. Physiological assessment

Heart rate variability refers to the variability in timing between consecutive heartbeats (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). In the current study, tonic (i.e., resting) HRV was recorded for 5 min with the Bodyguard 2 (Firstbeat) HR monitor, with participants sitting alone in a comfortable position while they leafed through a gardening magazine (i.e., "vanilla baseline"; Jennings et al., 1992). The Bodyguard 2 only allows to record inter-beat intervals (IBIs); however, validation studies have supported its validity against the electrocardiogram, particularly for time domain HRV measures (e.g., Bogdány et al., 2016).

HRV was therefore assessed by computing the root mean square of successive beat-to-beat interval differences (rMSSD), which reflects vagal regulation of HR and is less susceptible to respiratory influences (Penttilä et al., 2001). High-Frequency HRV (HF-HRV) was also assessed as a convergent frequency-domain measure of vagally-mediated HRV. HRV analyses, as well as outlier and artifact detection, were performed using the software Kubios HRV Standard (v. 3.4.3) (Tarvainen et al., 2014). This software uses an advanced detrending method based on smoothness prior formulation in which the filtering effect is attenuated in the beginning and the end of the data, thus avoiding the distortion of data end points (Tarvainen et al., 2002). The IBIs were first visually inspected, and when needed, a correction option was used in which artifacts were detected from a time series consisting of differences between successive RR intervals; overall, $n = 40$ (0.54 %) beats were corrected, and the "Very low correction" option was always used.

2.2.3. Probabilistic Reward Task

The PRT is a well-validated signal-detection task developed to provide an objective measure of participants' ability to modify behavior as a function of reward (Pizzagalli et al., 2005), which yields measures of reward responsiveness and reward learning. The task was administered in the laboratory via E-Prime (version 3.0) and consisted of 300 trials, divided into 3 blocks of 100 trials, separated by a 30-second break. Trials started with a fixation cross for 1000–1400 ms in the middle of the screen. The cross was replaced for 500 ms by a mouthless cartoon face. After 500 ms, a short mouth (10.00 mm) or a long mouth (11.00 mm) was presented for 100 ms. After 100 ms, the mouthless face returned and remained on the screen for additional 1500 ms. Importantly, the difference in stimulus length was small (1 mm), making the discrimination between a short or long mouth difficult (Pizzagalli et al., 2005). Participants were instructed to identify which stimulus (long or short) was presented by pressing two keys ("v" or "m") on the keyboard (counterbalanced across subjects) and were told that not all correct responses would be rewarded. Within each block, the short and long stimuli were presented equally often in a pseudorandomized sequence with the constraint that no more than three instances of the same stimulus were presented consecutively. For each block (100 trials), reward feedback ("Correct!! You won 20 cents") was presented after 40 correct trials presented for 1500 ms after the correct response and was followed by a blank screen for 250 ms (Bogdan and Pizzagalli, 2006). Importantly, one stimulus (labelled as the "rich stimulus") was disproportionately rewarded compared to the other (labelled as the "lean stimulus") for correct responses with a ratio of 3 to 1. Thus, during each block, participants received 30 reward feedbacks for correct identifications of the rich stimulus and only 10 reward feedbacks for correct identifications of the lean stimulus. A controlled reinforcer procedure was used so that reward feedback was given according to a pseudorandom schedule that determined which specific trials were to be rewarded for correct identifications (Johnstone and Alsop, 2000). If a participant failed to make a correct response for a trial in which feedback was scheduled, reward feedback was delayed until the next correct identification of the same stimulus type (rich or lean). If feedback was not given (i.e., the subject was inaccurate or accurate, but no feedback was scheduled), a blank screen was displayed for 1750 ms. The total duration of the task was about 24 min.

Performance was analyzed with respect to response bias (*logb*), which is an empirically derived measure of systematic preference to choose the most frequently rewarded stimulus calculated as:

$$logb = \frac{1}{2} log\left[\frac{(RICHcorrect + 0.5) \times (LEANincorrect + 0.5)}{(RICHincorrect + 0.5) \times (LEANcorrect + 0.5)}\right],$$

Discriminability (*logd*) was also computed as a control measure of participants' ability to discriminate between the two stimuli reflecting task difficulty. Discriminability was calculated as:

$$logd = \frac{1}{2} lod\left[\frac{(RICHcorrect + 0.5) \times (LEANcorrect + 0.5)}{(RICHincorrect + 0.5) \times (LEANincorrect + 0.5)}\right],$$

0.5 was added to each variable to make the calculation of the response bias and discriminability possible in cases in which one of the raw cells was equal to 0.

To examine general task performance, secondary analyses considered accuracy and reaction times (RT) (Pizzagalli et al., 2005). Before the analyses, trials with RTs <150 ms or longer than 2500 ms were excluded to remove outliers; then, trials with RTs (following natural log transformation) falling outside the mean 3 ± SD were considered as additional outliers and excluded.

2.2.4. Ecological momentary assessment (EMA)

The research protocol ended with the EMA, involving repeated sampling of individuals' current behaviors and experiences in real-time, aiming to minimize recall bias and maximize external validity (Shiffman et al., 2008). Pre-programmed e-mails containing links to the electronic diary were delivered by Qualtrics.com in a semi-random way about every 2 h during waking hours for 4 consecutive days (always from Wednesday to Saturday). The distribution of diaries was scheduled

according to participants' wake-up/bedtimes and meal schedules. Importantly, participants were also instructed to fill out the diary whenever they had a meal outside of the schedule. Following the initial notification, these EMA questions were available to the participants only for 25 min.

The assessment involved questions about smell ("*How much are you perceiving the smell of what you are eating?*") and taste ("*How much are you perceiving the taste (bitter, sweet, sour, salty) of what you are eating?*") perception of the current meal. Each diary took 1–2 min to be filled out and answers were provided by the participants on VAS from 0 = Not at all to 10 = Very much. Intraclass correlation coefficients of type 1 ($ICCs_{(1)}$) were respectively, 0.46 for taste and 0.51 for smell, suggesting that approximately half of the variability of EMA responses in these two items coalesce into stable individual differences across time points of assessment. Intraclass correlation coefficients of type 2 ($ICCs_{(2)}$) were respectively, 0.92 for taste and 0.91 for smell, attesting the high reliability of their person-level means at the between level. Moreover, the between-level correlations between EMA-based smell and taste scores with smell and taste sensitivity assessed at the baseline were, respectively, 0.346 ($p < .001$) and 0.358 ($p < .001$), in line with recent calls for multiple intensive repeated assessments to obtain proper individual average estimates in the constructs of interest by disentangling between- and within-person sources of variability (Mielniczuk, 2023).

The assessment comprised also a few questions on daily social interactions (occurrence, duration, and valence) that go beyond the objective of the present investigation and therefore will not be described here.

2.3. Data analysis

Preliminary evaluations were conducted to ensure no violation of the assumptions of normality, linearity, homogeneity of variances, and sphericity. Given the high correlation between the convergent measures of HRV, i.e., rMSSD and HF-HRV ($r = 0.83$; $p < .0001$), all subsequent analyses were performed on rMSSD only.

Independent sample *t*-tests, and correlation analyses were performed in SPSS (v. 27) to control for the influence of potential confounders. Specifically, *t*-test were implemented to test for differences between i) males and females on levels of tonic rMSSD; ii) those with nasal occlusion versus those without, iii) those with allergies versus those without; and iv) smokers versus non-smokers on smell and taste perception. Pearson's correlations were performed on body mass index, age, and rMSSD.

Two General Linear Models (GLMs) with Block (Block 1, Block 2, Block 3) as within-subject variable were computed separately on response bias and discriminability. For accuracy and RT, the GLM also included the within-subjects Trial Type (lean, rich). Taking into account previous studies reporting significant effects of nicotine craving on response bias (Peechatka et al., 2015), all analyses included smoking status as a covariate. ΔResponse Bias was then computed as Response Bias during Block 3 minus Response Bias during Block 1, as in previous studies (e.g., Bogdan and Pizzagalli, 2006).

Partial correlations were performed to test for associations of dispositional variables (i.e., scores on the DASS-21, TEPS, adapted form of the Smell and Taste Check, tonic rMSSD) and ΔResponse Bias, controlling for potential confounders.

In line with previous studies (Bakker et al., 2017) and given our focus on the between-subjects level of analysis (see below), subjects with <30 % of valid EMA assessments were discarded for final analyses. Multilevel models described below were all carried out with the Mplus 8.7 software (Muthén and Muthén, 1998-2017) by using robust maximum likelihood estimators with a full information maximum likelihood approach under the missing-at-random assumptions to handle missing data. Specifically, a multilevel model was tested and examined (henceforth, EMA Model), in which PRT was considered as the dependent variable at the between-subjects level, while the stable components (between-subjects) of taste and smell perceptions emerging from the EMA assessments were modeled as indicators of a single latent variable capturing their shared variance. This latent variable, along with RMSSD, were specified as determinants of ΔResponse Bias while at the within-subjects level the unstructured covariance between taste and smell sensitivities was specified.

3. Results

Table 1 reports frequencies, mean and standard deviations for socio-odemographic, dispositional, physiological, and laboratory olfactory/gustatory variables. No effects of potential confounders (i.e., body mass index, age, and sex on HRV; nasal occlusion, allergies and smoking on smell and taste perception) emerged from preliminary analyses.

3.1. PRT performance

All participants passed the quality check. Following outlier removal, 1.76 % of trials were excluded. The GLM with response bias as the dependent variable revealed a main effect of Block, $F(2,224) = 9.45$, $p < .001$, $\eta_p^2 = 0.078$. Pairwise comparisons showed an increase in response bias from the first block to the following blocks, where Block 1 was characterized by a significantly lower response bias (0.06 ± 0.25) compared to Block 2 (0.12 ± 0.30) ($d = 0.22$; $p = .02$) and Block 3 (0.14 ± 0.28) ($d = 0.31$; $p = .001$), with no statistical differences between Block 2 and Block 3 ($d = 0.08$; $p = .395$) (Fig. 1A). A significant Block by Smoking Status interaction also emerged, $F(2,224) = 4.22$, $p = .016$, $\eta_p^2 = 0.036$ with non-smokers showing the same pattern described above (Block 1 vs Block 2: $d = 0.45$; $p = .002$; Block 1 vs Block 3: $d = 0.52$; $p < .001$; Block 2 vs Block 3: $d = 0.01$; $p = .91$) and smokers failing to show any difference between blocks (Block 1 = 0.07 ± 0.25; Block 2 = 0.05 ± 0.26; Block 3 = 0.09 ± 0.29; all *p*s > 0.28).

Analyses on discriminability yielded no significant main effect of Block or Block by Smoking Status interaction (Fig. 1B).

Accuracy showed significant main effect of Trial Type, $F(1, 112) =$

Table 1
Participants' characteristics at baseline.

Variable	N; M ± SD
Sex	33 M, 81 F
Age (years)	22.24 (±2.93)
BMI (Kg/m^2)	22.01 (±3.54)
Smoke	65 No, 49 Yes*
Alcohol	39 No, 55 Low, 20 Moderate
COVID-19	6 Yes, 108 No
Respiratory Disease	19 Yes, 95 No
Nasal Occlusion	45 No, 55 Low, 14 Moderate
DASS-D	13.28 ± 9.35
DASS-A	9.26 ± 8.48
DASS-S	17.07 ± 8.71
TEPS-ANT	4.37 ± 0.66
TEPS-CON	4.74 ± 0.70
Taste sensitivity	8.32 ± 1.27
Smell sensitivity	7.94 ± 1.45
HR (bpm)	79.86 ± 19.44
RMSSD (ms)	64.96 ± 98.02
HF-HRV	1063.92 ± 1048.99

Notes: *1–2 cigarettes/day ($n = 16$); 3–6 cigarettes/day ($n = 19$); 6–10 cigarettes/day ($n = 10$); >10 cigarettes/day ($n = 4$). M = Males; F = Females; BMI = Body Mass Index; COVID-19 = Coronavirus disease 2019 infection in the previous 6 months; DASS-D = depression subscale of the Depression Anxiety Stress Scale-21 – Depression; DASS-A = anxiety subscale of the Depression Anxiety Stress Scale-21; DASS-S = stress subscale of the Depression Anxiety Stress Scale-21; TEPS-ANT = Temporal Experience of Pleasure Scale – Anticipatory; TEPS-CON = Temporal Experience of Pleasure Scale – Consummatory; Smell and taste sensitivity are derived from the adapted Smell and Taste Check; HR = Heart Rate; RMSSD = root mean square of successive beat-to-beat interval differences; HF-HRV = high frequency heart rate variability.

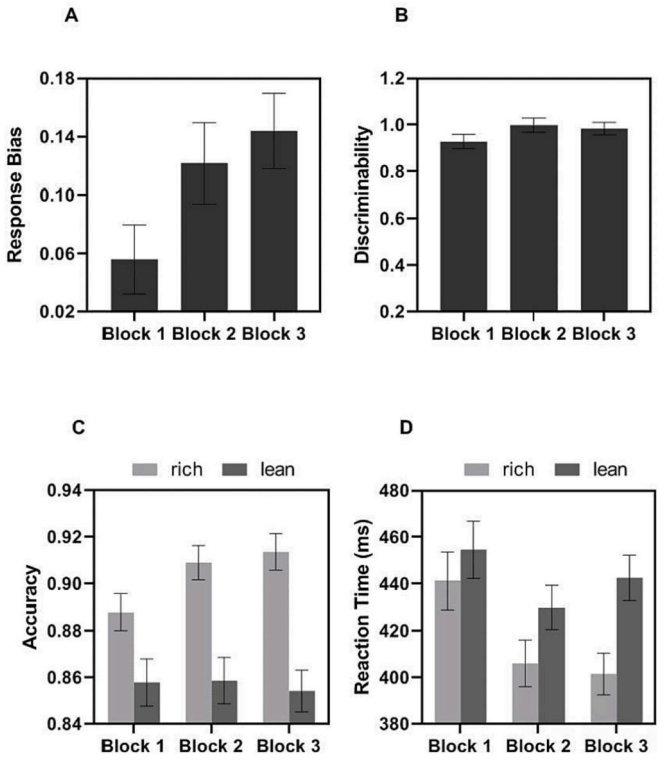

Fig. 1. (A) Response Bias and (B) discriminability across Blocks during the Probabilistic Reward Task. (C) Accuracy and (D) reaction time for the rich and lean stimuli across Blocks.
Note. Error bars: 95 % Confidence Interval.

21.34, $p < .001$, $\eta_p^2 = 0.160$ and Trial Type by Block interaction, $F(2, 224) = 5.51$, $p = .005$, $\eta_p^2 = 0.047$. Pairwise comparisons showed that rich (vs lean) trials were characterized by higher accuracy, and this was particularly true for Blocks 2 (0.91 ± 0.08 vs 0.86 ± 0.11; $d = 0.40$; $p < .0001$) and 3 (0.91 ± 0.08 vs 0.85 ± 0.10; $d = 0.49$; $p < .0001$) compared to Block 1 (0.89 ± 0.08 vs 0.86 ± 0.11; $d = 0.26$; $p = .005$) (Fig. 1C).

As to RT, the model yielded main effects of Trial Type, $F(1, 112) = 24.72$, $p < .001$, $\eta_p^2 = 0.181$ and Block, $F(2, 224) = 10.41$, $p < .0001$, $\eta_p^2 = 0.085$, as well as a significant Trial Type by Block interaction, $F(2, 224) = 12.832$, $p < .0001$, $\eta_p^2 = 0.103$. Pairwise comparisons showed that rich (vs lean) trials were characterized by shorter RTs, and this was particularly true for Blocks 2 (406.07 ± 106.93 vs 430.01 ± 100.18; $d = 0.23$; $p < .0001$) and 3 (401.51 ± 95.38 vs 442.55 ± 104.29; $d = 0.41$; $p < .0001$) compared to Block 1 (441.34 ± 131.18 vs 454.60 ± 131.52; $d = 0.10$; $p = .01$) (Fig. 1D).

Collectively, these findings suggest that the PRT elicited the intended effects: a robust response bias toward the more frequently rewarded stimulus, which was also associated with more accurate and shorter RT relative to the lean stimulus. Nicotine use significantly influenced results, with the response bias mostly developed by non-smokers.

Partial correlations controlling for smoking severity yielded a significant and positive association of tonic HRV and ΔResponse Bias ($r = 0.35$; $p < .001$). Scores on the DASS-21, TEPS, and adapted form of the Smell and Taste Check were not significantly associated with ΔResponse Bias.

3.2. EMA model

Since eight subjects reported a very large proportion of missing data points on EMA variables (>70 % of the total), they were excluded from the final analyses. Final average proportion of valid assessments in the EMA measures was 59.34 % (SD = 15.04). Thus, the final sample for testing the EMA models comprised 106 subjects. Excluded subjects did not evidence any significant difference in study variables with respect to other subjects.

Descriptive statistics related to the EMA Model are supplied as Supplementary Materials (Table S3 and Fig. S4 for the scatterplots). The model showed a substantial fit to the data: Satorra-Bentler $\chi^2(df = 4) = 3.73$, $p = .44$. Additional fit indices and completely standardized estimates of the model are displayed in Fig. 2. As shown in Fig. 2, ΔResponse Bias scores were also controlled for the smoking status (0 = non-smokers vs. 1 = smokers): this effect revealed a negative significant association between smoking status and the outcome variable (*standardized* β coefficient = −0.18, $p < .05$), indicating reduced reward responsiveness and reward-based learning in smokers. RMSSD resulted significantly associated to ΔResponse Bias (*standardized* β coefficient = 0.26, $p < .01$), and so did the between-subjects latent variable capturing the shared variance between taste and smell (*standardized* $\beta = 0.23$, $p < .05$). In other words, a lower parasympathetic control of the heart at rest and an impaired gustatory and olfactory sensitivity were independently associated with a weakened ability to modify behavior as a function of rewards. Statistical significance of all substantive effects was also ascertained after the Bonferroni step-down (Holm) correction of estimated p values. Moreover, all exogenous and endogenous variables at the between-level were controlled for depression (scores on the DASS) measured at the baseline, which did not exert any statistically significant effect. Overall, these two determinants explained 16.2 % of the ΔResponse Bias total variance.

Although the two models are not statistically comparable, it has to be mentioned, that when we have re-estimated the model depicted in Fig. 2 by substituting RMSSD with HF-HRV, the standardized effect of HF-HRV on Delta Response Bias was not statistically significant ($p > .05$). This pattern of divergent results is not unusual even in cases of high correlations between the two indices and might be due to the fact that RMSSD is less influenced by respiratory frequency and shifts in respiration rate and volume can markedly change HRV indices without affecting vagal tone.

4. Discussion

The present study combined a laboratory session and an ecological momentary assessment with the overarching goal to evaluate whether tonic HRV, taste and smell sensitivity and reward responsiveness could be significantly interrelated, hypothesizing to find positive associations among all the examined variables. The hypothesis of a positive correlation between tonic vagally-mediated HRV and gustatory and olfactory sensitivity on one hand and reward responsiveness on the other was driven by anatomic knowledge on the involvement of the vagus nerve.

To the best of our knowledge, this is the first study showing a specific association between resting HRV and the ability to modify behavior as a function of rewards (i.e., performance on the PRT). This is surprising, considering that reduced tonic HRV has been proposed as a putative biomarker for depressive symptoms, including anhedonia (Kemp et al., 2010; Koch et al., 2019 for meta-analyses; Thayer and Lane, 2009), with animal models precisely linking decreased HRV with stressor-induced behavioral indicators of anhedonia (Grippo et al., 2006, 2008; Moffitt et al., 2008). Indeed, studies examining the role of HRV in motivated behavior in humans are sparse and limited by the focus on phasic HRV. Overall, increased parasympathetic modulation of the heart (measured by HF-HRV) was found in individuals with substance use disorders in response to substance-related cues (Erblich et al., 2011; Garland et al., 2012; Ingjaldsson et al., 2003; Wang et al., 2018), whereas increases in sympathovagal balance (assessed by Low Frequency/HF-HRV) have been reported as an index of approach-motivated behavior and attractiveness (Ikisawa et al., 2020; Schettino et al., 2022). The only exception is the study by Wu and colleagues, who examined tonic HRV and found it to be inversely correlated with (food) craving in adolescents, after controlling for sex and age (Wu et al., 2020). This is coherent with

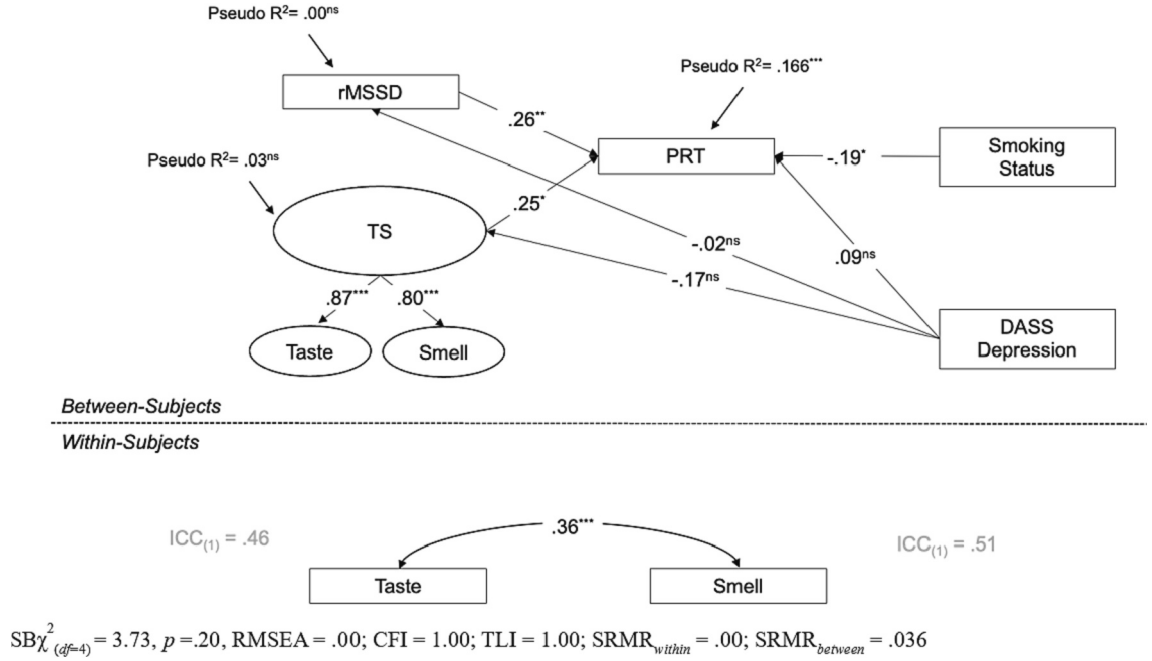

Fig. 2. Standardized model estimates from ecological momentary assessment (EMA) model.
Note. DASS Depression = Depression subscale of the Depression Anxiety Stress Scales; RMSSD = root mean square of successive differences between normal heartbeats; PRT = ΔResponse Bias computed as Response Bias during Block 3 minus Response Bias during Block 1; TS = taste and smell sensitivity between-subjects latent variable; Smoke Status = non-smokers (0) vs. smokers (1); $SB\chi^2$ = Satorra-Bentler chi-square test statistic; RMSEA = root mean square error of approximation; CFI = comparative fit indices; TLI = Tucker-Lewis fit index; SRMR = squared root mean residual. $^{ns} = p > .05$, $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$.

current finding of a reduced reward responsiveness in individuals with lower levels of tonic HRV.

Notably, the reported association with tonic HRV did not emerge when the subjective measure of anhedonia was considered and this was unexpected, considering that previous endeavors were mostly based on questionnaires (e.g., Vazquez et al., 2016). The lack of association of scores on the TEPS with resting HRV and performance on the PRT may be due to the fact that our sample was composed of healthy individuals, thus limiting the range of scores on the lower end.

Contrary to our hypotheses, resting HRV was not associated with smell and taste sensitivity. With this regard, it has to be noted that previous evidence only supports an influence of smell and taste sensitivity on phasic HRV (e.g., Bensafi et al., 2002; Glass et al., 2014); therefore, it is plausible that tonic HRV is not linked with gustatory and olfactory sensitivity.

The hypothesis of an association between ageusia and anosmia with dysregulation in motivated behavior was driven by existing evidence of i) impaired smell and taste sensitivity in psychopathological conditions characterized by anhedonia (Atanasova et al., 2008); ii) anhedonic symptoms in neurological conditions characterized by loss of smell and taste (Kohli et al., 2016; Keller and Malaspina, 2013); and iii) the consequences of the experimental manipulation of smell/taste sensitivity on psychological symptoms, such the emergence of depressive-like behavior after induction of transient anosmia (Ahn et al., 2018) or olfactory bulbectomy (Morales-Medina et al., 2017) in animal models. Particularly relevant to the aim of the current study is the work of Cieslak et al. (2015) who found that smell identification was differentially related to the symptoms, with better performance being associated with less anhedonia. To the best of our knowledge, only one study found the opposite pattern, with elevated social anhedonia predicting better olfaction recognition after 3 years in a large community sample (Cohen et al., 2012).

The main strength of the present study is the implementation of an EMA design to assess taste and smell sensitivity, which adds external validity, as olfactory and gustatory sensitivity were assessed outside the laboratory setting, in everyday contexts. This is important considering the absence of associations between the one-shot laboratory assessment of taste and smell sensitivity by the Smell and Taste Check, developed by the GCCR, and performance on the PRT. On the contrary, lower momentary assessment of gustatory and olfactory sensitivity during daily meals over 4 consecutive weeks and weekend days was significantly associated with reduced reward learning. Smell and taste sensitivity can play a critical role for survival (e.g., helping us to avoid rotten food) but also guide motivated behavior, such as the drive to pursue food. Indeed, the olfactory tubercle is involved in motivated behavior (Da Cunha et al., 2012) and functional and structural overlaps between olfactory, limbic and reward systems have been reported (Soudry et al., 2011).

Importantly, momentary taste and smell sensitivity were associated with our objective measure of anhedonic behavior but not with scores on the TEPS (Table S2). Again, our findings point to the need to implement multiple assessment techniques (e.g., subjective, physiological, behavioral) when investigating complex psychological matters, in line with the Research Domain Criteria framework.

The main limitation of the study regards the correlational design. Only the effects of experimental manipulation of our putative predictors (HRV and smell/taste sensitivity) on our outcome variable (performance on the PRT as a proxy for anhedonic behavior) will allow drawing causal inferences. As a second limitation, the sample was mostly composed of females (71.1 %). Although no differences emerged for the key variables of the study between males and females, previous findings on sex differences in HRV, self-reported levels of anhedonia, and smell and taste sensitivity suggest that this may have biased the results (Koenig and Thayer, 2016; Sorokowski et al., 2019; Crockett et al., 2020). As previously noted, the lack of significant findings for subjective measures could be possibly explained by the sample being "too healthy". Accordingly, future studies may want to stratify sampling in order to cover the full range of symptom severity. In line with previous studies (Peechatka et al., 2015), smoking status appeared to have strong effects on the development of response bias. In this regard, another limitation of

the current study is the lack of assessment of nicotine craving, which is likely to play a role in the lack of reward responsivity shown by smokers (Cohen et al., 2012). Critically, however, all findings remained when accounting for smoking status, although a reduction in smell and taste sensitivity in smokers is known (e.g., Berube et al., 2021) and this is likely due to the fact that several smokers in the current sample only smoked a few cigarettes per day. Together with the relatively young age of participants, this may also explain the high percentage of smokers in the sample (~43 %). Lastly, given that our aim implied modelling anhedonic behavior as the outcome variable, it would have been methodologically more appropriate to implement the EMA before administering the PRT. We opted for not doing so to take advantage of the face-to-face laboratory session to i) interview participants on their meals habitual timing and ii) adequately instruct them on how to fill out the electronic diaries.

Limitations notwithstanding, our data provide important new insight into the associations between gustatory and olfactory sensitivity with anhedonic behavior, relying on multiple assessments and on both objective and subjective measurements of the outcome variable. HRV independently contributed to the anhedonic behavior in the opposite direction, above and beyond taste and smell sensitivity.

In sum, the present study focused selectively on two factors involved in mental health consequences triggered by the pandemic since HRV appeared to be a predictor of resilience during the COVID-19 pandemic (Miller et al., 2021; Makovac et al., 2022; Wekenborg et al., 2022) and that ageusia and anosmia are among the most frequent COVID-19 symptoms. Although correlational, current findings highlight that daily levels of smell and taste sensitivity and reduced parasympathetic modulation of the heart at rest are independently associated with anhedonic behavior along a continuum that goes from healthy to more pathological behavior. If substantiated by causal approaches, the present preliminary evidence points to the need to assess these variables in prevention and early detection programs targeting anhedonia.

Funding

This study was supported by Sapienza University of Rome (RM12117A8A578DB4).

Declaration of competing interest

Over the past 3 years, Dr. Pizzagalli has received consulting fees from Albright Stonebridge Group, Boehringer Ingelheim, Compass Pathways, Engrail Therapeutics, Neumora Therapeutics (formerly BlackThorn Therapeutics), Neurocrine Biosciences, Neuroscience Software, Otsuka, Sunovion, and Takeda; he has received honoraria from the Psychonomic Society and American Psychological Association (for editorial work) and from Alkermes; he has received research funding from the Brain and Behavior Research Foundation, the Dana Foundation, Millennium Pharmaceuticals, Wellcome Leap MCPsych, and NIMH; he has received stock options from Compass Pathways, Engrail Therapeutics, Neumora Therapeutics, and Neuroscience Software; he has a financial interest in Neumora Therapeutics, which has licensed the copyright to the Probabilistic Reward Task through Harvard University. No funding from these entities was used to support the current work, and all views expressed are solely those of the authors. All other authors have no conflicts of interest or relevant disclosures.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijpsycho.2023.01.010.

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