

Prevalence and correlates of parosmia and phantosmia among smell disorders

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22 Abstract

23 Among those many individuals who suffer from a reduced odor sensitivity (hyposmia/anosmia) some 24 individuals also experience disorders that lead to odor distortion, such as parosmia (i.e., distorted odor 25 with a known source), or odor phantoms (i.e., odor sensation without an odor source). We surveyed a 26 large population with at least one olfactory disorder (N = 2031) and found that odor distortions were 27 common (46%), with respondents reporting either parosmia (19%), phantosmia (11%), or both (16%). In comparison to respondents with hyposmia or anosmia, respondents with parosmia were more likely to be 28 29 female, young, and suffering from post-viral olfactory loss (p < 0.001), while respondents with 30 phantosmia were more likely to be middle-aged (p < 0.01) and experiencing symptoms caused by head trauma (p < 0.01). In addition, parosmia, compared to phantosmia or anosmia/hyposmia, was most 31 prevalent 3 months to a year after olfactory symptom onset (p < 0.001), which coincides with the timeline 32 33 of physiological recovery. Finally, we observed that the frequency and duration of distortions negatively 34 affects quality of life, with parosmia showing a higher range of severity than phantosmia (p < 0.001). Previous research often grouped these distortions together, but our results show that they have distinct 35 patterns of demographics, medical history, and loss in quality of life. 36

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39 Introduction

40 Olfactory dysfunction affects a quarter of the population, and with the advent of COVID-19 this number is likely to rise (Pellegrino, Cooper, et al., 2020). In addition to reduced odor sensitivity, some individuals 41 42 also experience odor distortion (Burges Watson et al., 2020; Keller & Malaspina, 2013; Leopold, 2002). 43 Reduced sensitivity has been well described in the literature leading to better diagnosis and treatment 44 (Hummel et al., 2017; Oleszkiewicz et al., 2019). Still, despite the differences between parosmia (i.e., 45 distorted odor with a known source) and phantosmia (i.e., odor sensation without an odor source) (Hummel et al., 2017) most studies do not separate them. This is partly due to the large variance in their 46 clinical presentation (Frasnelli et al., 2004) and because many patients report having both symptoms 47 48 (Sjölund et al., 2017).

49 In general, when patients with parosmia inhale odorants their perception does not match their 50 memory from before the distortion. In most cases of parosmia, the distorted odors are usually perceived as 51 unpleasant ("cacosmia"), but there have been cases in which the distortions were pleasant ("euosmia", 52 (Landis et al., 2006)). Additionally, recent evidence suggests that specific odors, such as coffee, meat, onion, and toothpaste, are more likely to trigger parosmia than others (Parker, Kelly, Smith, et al., 2021). 53 54 Phantosmia, on the other hand, describes the perception of an odor in the absence of a source – there is only the illusion of a smell. Parosmia has been reported among 10% to 60% of olfactory dysfunction 55 56 patients (Nordin et al., 1996; Parma et al., 2020; Reden et al., 2007) while the range is much smaller (3 – 57 16 %) for phantosmia (Bainbridge et al., 2018; Nordin et al., 1996; Ohayon, 2000; Rawal et al., 2016; 58 Reden et al., 2007; Sjölund et al., 2017). These numbers indicate that incidences of parosmias and 59 phantosmias are not rare, but the variance indicates that the reported frequency depends on the definition 60 of parosmia or phantosmia.

Most parosmia appears to co-occur with olfactory loss due to viral infection, with the majority of
cases resolving within a year (Liu et al., 2020; Nordin et al., 1996; Quint et al., 2001; Reden et al., 2007).
Patients suffering from parosmia also had smaller olfactory bulbs compared to those with reduced

sensitivity and no distortion (Mueller et al., 2005; Rombaux et al., 2009). In addition, parosmia was
eliminated by preventing odors from entering the olfactory cleft in a case study (Liu et al., 2020). This
supports a peripheral etiology and is consistent with the theory that parosmia results from mistargeting
that occurs when olfactory sensory neurons regrow axons to the olfactory bulb during recovery (Holbrook
et al., 2005; Hong et al., 2012a).

69 With phantosmia, peripheral origins of distortion may be maintained through abnormally active 70 olfactory sensory neurons, loss of inhibitory neurons, or microbial infection creating a malodor (D. 71 Leopold, 2002). The removal of the olfactory epithelium or even briefly occluding a nostril (irrelevant of 72 side) has been shown to eliminate the olfactory illusions for some patients (Leopold et al., 1991, 2002). Many phantosmia patients have a history of head trauma (Leopold, 2002; Sjölund et al., 2017), 73 74 psychiatric disorders (Croy et al., 2013; Frasnelli et al., 2004), temporal lobe epilepsy, and phantosmic 75 episodes in the form of auras (Aiello & Hirsch, 2013; Leopold, 2002), suggesting a central etiology from 76 overactive neurons.

77 Patients with symptoms of olfactory distortion may suffer to a larger extent than those with a reduced sensitivity, as they are continually reminded of their problem. In fact, individuals with reduced 78 79 perception of odors are often not even aware of their disorder (Oleszkiewicz et al., 2020; Oleszkiewicz & 80 Hummel, 2019). However, most reports on odor distortions have not used a quantitative approach to compare them with anosmia and hyposmia-instead reporting anecdotal patient experiences. Here we 81 compared them directly using a survey designed to gather information about parosmia and phantosmia. 82 83 This quantitative approach allowed us to provide diagnostic criteria and reveal patterns of the disorder. 84 Using this method, we saw several distinct differences among the disorders and created a severity metric 85 for clinical use.

86

87 Materials and Methods

Participants

89	A total of 2246 individuals filled out an online questionnaire survey that was distributed globally in			
90	English with English speaking countries (UK and USA) representing the largest proportions of			
91	respondents. The survey was launched in parallel with a new informational website about smell loss			
92	(www.abscent.org) which had two parts: an area with information that could be accessed by anyone, and			
93	a "member area" with a closed forum, access to the Sniff Smell Training app, and other more premium			
94	features. Access to the member area was given to anyone who completed the survey. Primary areas of			
95	recruitment were the AbScent website and social media posts to AbScent's Facebook and Twitter			
96	accounts. Survey data was collected between May of 2019 and October of 2020. This procedure was			
97	conducted according to the Declaration of Helsinki for studies on human subjects and approved by the			
98	University of Tennessee IRB review for research involving human subjects (IRB # 19-05253-XM).			
99	Procedure			
100	The Sense of Smell Questionnaire was created from prior research surveys (Frasnelli et al., 2004; Keller			
101	& Malaspina, 2013; Landis et al., 2010) and patient observations by the authors. It was designed to			
102	specifically address features of odor distortion (Supp. Appendix I). Two binary response (yes or no)			
103	questions accompanied by a descriptive caption were used to create four groups of smell impairment:			
104	A. Parosmia - the experience of distorted smells which have an obvious source:			
105	Do you have parosmia (distorted sense of smell)?			
106	B. Phantosmia - the experience of smells that have no obvious origin:			
107	Do you experience smells that are not present (phantosmia)?			
108	Participants who only chose A or B were classified as Parosmic and Phantosmic respectively while those			
109	choosing both were considered both Parosmic/Phantosmic. All other smell impaired participants were			

110	considered Anosmic/Hyposmic. The questionnaire used a branching design such that questions specific to		
111	each disorder were only presented to those who responded with "Yes" to the quality disorder.		
112	Statistical Analysis		
113	We used a unimodal analysis to look at differences across groups. We used chi-square analysis for		
114	categorical responses and analysis of variance (ANOVA) for continuous responses. Responses were		
115	bootstrapped to provide confidence intervals using the boot package (Davison & Hinkley, 1997). Here,		
116	we resampled (with replacement) the responses 1000 times to estimate error in all comparisons and		
117	visualizations.		
118	To determine degree of severity, three questions were considered - each were asked within each odor		
119	distortion question block (answering "Yes" to Parosmia or Phantosmia) and had the same options. Below		
120	is an example of the questions for Phantosmia/Parosmia.		
121	A. How often do you experience smells that are not present (for phantosmia) or how often do		
122	you experience parosmia (distorted sense of smell)? (daily, once every week, once every		
123	month)		
124	B. How long does a Phantosmia/Parosmia episode last? (seconds, minutes, hours, days)		
125	C. How would you describe your Phantosmia/Parosmia? (mild, strong)		
126	These questions together had a low intercorrelation coefficient (0.55). Questions A and C loaded onto the		
127	same principal component with question C explaining less variance (89% compared to 77%). Therefore,		
128	question C was dropped and A and B were summed to create a severity score of the disorder. Analysis		
129	was done with the psych package in R (Revelle, 2017).		
130	Two open-ended text questions describing distortions of parosmia or phantosmia underwent text analysis.		
131	Sentences were cleaned and words were spell checked with hunspell using a large English dictionary		
132	(Ooms, 2020). Sentimental analysis, using the scentimentr package (Rinker, 2019), was done at the		

sentence-level across participants that provided sentences longer than the 1st quartile length of all

sentences (>7 words) and density plots were used to provide a visual representation. Average sentiment

and negative emotion count of each sentence were then used as predictors for degree of severity.

- 136 Furthermore, sentences were broken down into one word nouns with SpacyR (Benoit & Matsuo, 2018).
- 137 Summary tables of counts were constructed and visually represented in wordclouds with the size
- 138 representing the frequency using ggwordcloud (Pennec & Slowikowski, 2018).
- All analysis were done in R (version 4.3) and the code along with data can be found here:

140 https://osf.io/5ebjt/

141 Results

142 Only participants reporting an olfactory disorder, 18 years of age or over, and not born with the smell 143 problem (congenital) were considered in the analysis (N = 2031). From this large population with an olfactory disorder, we report that odor distortions are common to smell impairment (46%) with 144 145 individuals reporting either parosmia (19%), phantosmia (11%), or both (16%) (Figure 1a). Exploratory 146 analysis revealed individuals reporting "both" types of odor distortion did not represent parosmia and phantosmia evenly (Supp Fig. 1). Due to this heterogeneity, we excluded this population from the rest of 147 148 the analysis leaving three groups – Anosmic/Hyposmic, Parosmic, and Phantosmic. Parosmia and 149 phantosmia showed distinct patterns, both from each other as well as from those with reduced sensitivity, 150 in demographics, medical history, and impacts to quality of life. Using two questions, we were able to 151 derive a severity score that influences many of these patterns.

152 Demographics and Medical History

- 153 Our sample was predominantly female (72%) with an age range from 21 to over 71 (see Supp Table 1).
- 154 Respondents with parosmia were more likely to be female and younger than phantosmic ($\chi^2 = 5.84$, p =
- 155 0.047 and $\chi^2 = 4.79$, p < 0.001 respectively) or anosmic/hyposmic individuals ($\chi^2 = 14.12$, p < 0.001 and
- 156 $\chi^2 = 4.62, p < 0.001$ respectively) (Figure 1B). In contrast, phantosmia prevalence peaked for 41-50 year

157 old ($\chi^2 = 2.82, p = 0.01$) and anosmia/hyposmia was more prominent in older individuals (61 and over; χ^2 158 = 5.18, p < 0.001). There were no differences in gender between phantosmic vs. anosmic/hyposmic 159 populations ($\chi^2 = 0.08, p = 0.78$).

160 The three most common etiologies resulting in an olfactory disorder are viral (70%), sinonasal disease

161 (10%) and traumatic impact (8%) (Figure 1C). Among those with post-viral disorders, parosmia was the

162 most common disorder ($\chi^2 = 8.58$, p < 0.001) and among those who suffered traumatic impact,

163 phantosmia was the most common disorder ($\chi^2 = 3.69, p = 0.006$).

164 Compared to phantosmic and anosmic/hyposmic individuals, parosmia occurred suddenly ($\chi^2 = 3.61, p < 1.61$

165 0.001) with less nasal blockage ($\chi^2 = 4.56$, p < 0.001) (Figure 1F, G). Parosmia, compared to other

166 olfactory conditions, was less likely to last more than two years ($\chi^2 = 8.36$, p < 0.001) and more likely to

appear during recovery from the initial olfactory impairment (3 - 12 months) ($\chi^2 = 13.35$, p < 0.001)

168 (Figure 1D). Similarly, parosmic individuals were more likely to say their condition was improving ($\chi^2 =$

169 10.02, p < 0.001) and less likely to report their condition as unchanged ($\chi^2 = 2.68, p = 0.02$). Phantosmia,

170 on the other hand, was more stable, with no change in improvement across time in comparison to the

anosmic/hyposmic group ($\chi^2 = 1.59$, p = 0.33) (Figure 1E). Overall, parosmic individuals showed the

172 most deviation from the other olfactory disorders (phantosmia and anosmia/hyposmia).



174 Figure 1. Parosmia and Phantosmia are distinct disorders. (A) The number of study participants reporting having 175 either parosmia, phantosmia or both. The two disorders were distinct in demographics (B), etiology (C), the time 176 course of disease (D-F), and amount of congestion (G). Colors and icons represent olfactory disorders: green with a 177 distorted grid icon represents individuals with parosmia, orange with an outlined cigarette icon represents 178 individuals with phantosmia, as cigarette smell was a common phantom smell reported in our sample pool, and 179 purple with a nose deny icon represents individuals with no parosmia nor phantosmia, but who reported an issue 180 with smell (hyposmia/anosmia). Normalized prevalence represents the frequency difference between 181 anosmia/hyposmia (baseline) and the other two olfactory disorders (parosmia or phantosmia). Error bars represent 182 bootstrapped standard errors. Mo., Months; Y, Year 183 Parosmia is defined as distortion with an odor source, but the triggers for phantosmia are unknown. We 184 report that all but one parosmic patient had specific sources that were distorted (99.7%, Figure 2A) while only a few phantosmic individuals had situations that triggered a distorted episode (17.0%). Sentences (N 185 186 = 547) used to describe distortions for parosmia mostly had a negative sentiment, but there were

187 positively described distortions (e.g., "my smell disorders are actually pleasant, flatulence smell like extra

virgin olive oil and sometimes bubble gum") (Figure 2B). Disgust was the highest emotion (Figure 2C, F(3) = 107.63, p < 0.001). Compiling words that trigger a distorted episode, parosmic individuals frequently reported foods that are roasted (coffee, meat) or contain sulfur (onion, egg, garlic). Phantosmic individuals instead reported places (room, house) or temporal events (e.g., time, week) while some referred to specific sensory (loud tv, cigarette smoke) or cognitive events (stress, memory).





3 Quality of Life

All olfactory disorders affect overall quality of life, but each in different ways. Smell impaired individuals are concerned with failing to detect a hazard (> 50%) such as spoiled food (82.2%) followed by fire (72.8%) and gas (72.3%) (Figure 3A). Phantosmic and anosmic/hyposmic individuals showed a higher concern for failing to detect fire and gas than parosmic individuals.

Other changes to quality of life include increased anxiety about being alone (25.2%), being in social settings (19.1%), cleanliness (50.4%), and cooking (40.2%) followed by a reported decrease in socializing (29.0%) 213 and motivation to eat (42.1%) (Figure 3B). Among olfactory disorders, there was a higher anxiety for 214 cleanliness among those with phantosmia and those with parosmia had a lower motivation to eat, cook and socialize. Both olfactory disorders reported more social anxiety than anosmic/hyposmic. Parosmic 215 216 individuals also found it difficult to adjust to their disorder ($\chi^2 = 3.76$, p < 0.001) which might be a result 217 of its acute nature during recovery. Phantosmics reported changes in their weight, with some gaining and others losing weight since the onset of the disorder ($\chi^2 = 5.27$, p < 0.001) (Figure 4C). Intimacy was 218 altered among 24% of respondents, but there were no differences across olfactory disorders ($\chi^2 = 5.40$, p 219 220 = 0.24).



221

Figure 3. Impacts on quality of life. Percentage of respondents (A) concerned about failing to detect common
 hazards and (B) reporting changes in common behaviors. Error bars represent bootstrapped standard errors.

224 <u>Developing a Severity Score</u>

A single scale of severity from structured questions has proven to be a clinically useful measure for parosmia, and here, we extend this idea to phantosmia (Landis et al., 2010). We combined the frequency and duration of distortion episodes to develop a severity score for both phantosmia and parosmia. Increases in the overall severity of the disorder affects the quality of life of individuals suffering from these disorders. Those with parosmia show a higher severity score than those with phantosmia (B = 1.96, t = 11.66, p < 0.001); Figure 4A), and an increased severity score was inversely correlated with overall quality of life for both disorders (B = -0.39, t = 4.16, p < 0.001; Figure 4B). More specifically, BMI

- trended towards a significant correlation with severity score for those with phantosmia (b = 0.05, t = 1.79,
- 233 p = 0.07; Figure 4C). As determined by the sentiment analysis, there was no relationship between severity
- score and negative emotions (B = -1.35, SE = 2.45, t = 0.55, p = 0.58), the type of emotion (F(3) = 0.02, p
- 235 = .99), or overall sentiment (B = -0.53, SE = 0.49, t = 1.09, p = 0.28).



Figure 4 Degree of severity for parosmia and phantosmia. (A) Distribution of severity scores among parosmic and phantosmic groups. (B) The severity score correlates with the reported impact of the olfactory disorder on their quality of life. Error bands represent 95% confidence intervals. (C) Differences in frequency of weight fluctuation. Error bars represent bootstrapped standard errors. (D) Relationship between degree of severity score and body mass index. Error bands represent 95% confidence intervals.

Discussion

To date, little attention has been given to parosmia and phantosmia– with studies often combining them rather than studying them separately. Our study reveals some distinct differences between parosmia and phantosmia, as well as from hyposmia/anosmia. They are common olfactory impairments, with half of the participants with smell dysfunction reporting these disorders. Both parosmia and phantosmia vary in severity and are distinct in terms of demographics, medical history, and quality of life issues. Our survey also suggests that parosmia and phantosmia have distinct underlying mechanisms.



Parosmia represents a distortion of smell when an odorous source is present. Instead of smells becoming weaker, as described in hyposmia/anosmia, they change in quality such that perceived smells are not the same as patients remember from before the onset of parosmia. In our survey, there is a distinct demographic that more commonly experiences parosmia – individuals who are younger, female, and recovering from a virus.

266 In general, there is a negative correlation between age and recovery from smell loss, such that losing smell at an older age results in slower recovery. One possibility is that parosmia is a symptom of 267 268 recovery, and those who are older have a smaller chance of developing parosmia (Cavazzana et al., 2018; 269 Hummel & Lötsch, 2010; London et al., 2008; Ogawa et al., 2020; Reden et al., 2006). Supporting this 270 idea, individuals in the early stages of recovery from smell loss who report parosmia also reported more 271 improvement over time than those with either phantosmia or a simple reduction in smell. Others have 272 reported this co-occurrence of parosmia through times of recovery (Liu T. et al., 2020; Nordin et al., 273 1996; Quint et al., 2001; Reden et al., 2007). The presence of parosmia has indicated faster return to the sense of smell in some studies (Liu T. et al., 2020; Reden et al., 2007), but not others (Hummel & Lötsch, 274 275 2010). This discrepancy may be due to patient age, since older patients have reduced olfactory regenerative capacity (Mobley et al., 2014). 276

Past research has reported parosmia commonly occurs with olfactory loss due to viral infection 277 278 and frequently resolves within a year of the incident, with only 26% of an initial parosmic patient sample 279 (N = 112) having parosmia after 14 months (Liu et al., 2020; Nordin et al., 1996; Quint et al., 2001; 280 Reden et al., 2007). Similarly, in a study by Damm and coworkers (2014), 26% from a group of 47 281 initially parosmic patients reported no parosmia after an observation period of 4 months (Damm et al., 282 2014). Parosmia was the most prevalent outcome among post-viral disorders in our sample (nearly 90 % of parosmics) while parosmia had the lowest prevalence among those suffering from head trauma or 283 284 conductive loss etiologies (e.g. polyps). As mentioned, patients with parosmia also showed higher

prevalence of the disorder after the initial incident (> 3 months - 1 year), not during, and did not show issues with nasal patency.

Leading theories for parosmia suggest a peripheral origin of the disorder. Although these patients 287 288 do show differences in neural activation (Iannilli et al., 2019), this might be a downstream effect. In fact, 289 in hyposmic patients with parosmia, olfactory bulb volumes have been shown to be smaller compared to 290 hyposmic patients without parosmia (Mueller et al., 2005; Rombaux et al., 2009). In neurogenesis, the 291 axons of newly born sensory neurons must find the correct targets in the olfactory bulb. Abnormalities 292 may occur during the process (Murai et al., 2016; Schwob et al., 2017), such that a sensory neuron tuned 293 to one odor mistakenly stimulates an area of the bulb that signals the presence of a different odor. Axons reach the bulb approximately 1-3 months after injury, which matches the timing of parosmia in this 294 295 survey. Taken together, our data support a peripheral cause of distortion that may result from a variety of 296 mechanisms related to recovery such as differences across olfactory sensory neurons in time to recover or 297 a mismatch in rewiring in the olfactory bulb. This is supported by animal models where olfactory maps significantly change after regeneration of ablated neurons, leading animals to have to relearn the correct 298 299 odor match (Yee & Costanzo, 1998) and this is most likely due to mistargeting by a receptor-defined 300 subset of peripheral neurons (Christensen et al., 2001; Holbrook et al., 2005).

301 Parosmic patients showed higher disturbances to their social life, leading to an avoidance of 302 social and eating activities. In comparison to hyposmia/anosmia, this did not lead to any associated 303 behavioral outcomes that we measured, such as weight fluctuation, but more rigorous assessments are 304 warranted (Mattes & Cowart, 1994). For instance, we clearly show that individuals with parosmia are 305 reminded of their disorder regularly, which has been hypothesized as a reason for greater disruption in 306 daily life (Croy et al., 2013; Frasnelli & Hummel, 2005; Hong et al., 2012b). These patients also report 307 more difficulty adjusting to their disorder, which may explain a recent report showing higher depression 308 and anxiety symptoms in this patient group (Giguere et al., 2020).

309 The distortions experienced describe a common thread of sources (e.g. coffee) that has been 310 reported in the literature and there is little doubt that the terms used to describe these distortions generally have a negative valence associated with them (dirty, sewage, unpleasant, rotting, disgusting, sickly sweet 311 and vomit-inducing) (Burges Watson et al., 2020; Keller & Malaspina, 2013; Parker, Kelly, Smith, et al., 312 313 2021). Some explanations for this negative valance towards distorted odors has been the low familiarity to 314 odors activating unlearned neuronal mapping or the fact that many unpleasant odorants within an odor 315 mixture have low detection thresholds. Although our question about distortions had a negative phrasing, 316 "Which odors do you find particularly unpleasant and distorted? (Describe in as much detail as possible)", 317 individuals still reported some positive changes. Looking at the positive and negative sentimental sentences, there seems to be a valence shift in which odors commonly perceived as positive are described 318 319 negatively, but a few, usually related to body odors, shift from negative to positive. For instance, fecal 320 smells may turn pleasant whereas coffee becomes unpleasant. One explanation for this shift from negative 321 to positive is that some of the key aroma compounds responsible for the strong and usually repulsive 322 smell of feces were not perceived at all by those with parosmia (Parker, Kelly, & Gane, 2021). In the absence of these potent odors, other pleasant compounds may dominate perception of the mixture. 323

324 <u>Phantosmia</u>

Phantosmia is an olfactory experience when there is no odor source present. These phantom odors may be 325 326 high or low in intensity and may be familiar or unfamiliar odors and cannot be perceived by others 327 nearby. Unlike previous reports done at a population level (Bainbridge et al., 2018; Sjölund et al., 2017), 328 in our sample females were not more prone to phantosmia (p = 0.78). This difference in findings may be 329 due to previous studies categorizing parosmia and phantosmia together. For instance, a population level 330 study found females to be almost twice as likely to have phantosmia than men, but the group under study 331 also reported they were 6 times more likely to have parosmia thus representing a heterogeneous group 332 (Sjölund et al., 2017). However, our results do agree with previous findings regarding age, in which

individuals between 40 and 60 years of age were more likely to have phantosmia than older individuals (>
60 years) (Bainbridge et al., 2018).

335 Phantosmia was the most common olfactory disorder among those who suffered a head trauma. Phantosmic patients have previously been reported to have a history of head trauma (Leopold, 2002; 336 337 Sjölund et al., 2017), as well as psychiatric disorders (Croy et al., 2013; Frasnelli et al., 2004), temporal 338 lobe epilepsy and phantosmic episodes commonly preceding seizures, and migraines in the form of auras (Aiello & Hirsch, 2013; Leopold, 2002). Additionally, we show that phantosmic patients had more 339 340 sinonasal diseases (e.g. polyps) and more blockage than those suffering from parosmia. This suggests that 341 at least some of these phantom odors do not come from an odorous source, as airflow is needed to carry 342 volatiles.

The mechanisms of phantosmia are largely unknown. Hallucinations in other senses can be due to overactive neurons, either peripheral or in the brain. Olfactory sensations can also result from temporal lobe seizure or direct stimulation of the olfactory bulb (Bérard et al., 2021; Kumar et al., 2012a; R.N.DeJ., 1954). Debilitating cases of phantosmia have been treated by the removal of the olfactory bulb (Kaufman et al., 1988; Markert et al., 1993), removal of the olfactory epithelium (Leopold et al., 1991, 2002), or unilateral blockage of the olfactory cleft (Liu et al., 2020). The central or peripheral origin of phantosmia is unclear, and may be heterogeneous across cases (Leopold, 2002).

350 Phantosmic patients, compared to parosmics, reported worries about not being able to detect hazards (fire, gas) that might be noticed through smell. As previously discussed, phantosmics showed 351 352 increased blockage and sinonasal diseases and this might decrease odor sensitivity to all odors, including hazards. Only a few (~20%) had recurring situations that triggered a phantom episode, describing these 353 354 triggers as place, temporal, or cognitive events. Additionally, phantosmic patients reported more changes 355 in weight, with individuals experiencing more severe phantoms having an increase in weight (measured 356 by BMI). Fluctuation in appetite with olfactory dysfunction occurs due its involvement in metabolic 357 status (Guzmán-Ruiz et al., 2021), which could lead to changes in food preference (Pellegrino, et al.,

2020) and weight (Kershaw & Mattes, 2018). However, it is difficult to say whether phantoms are causal.
For example insulin-dependent diabetics, who often have a comorbidity of being overweight, were twice
as likely to experience phantom odors (Chan et al., 2018). This may warrant additional studies to replicate
our findings and delve into specific dietary changes and whether adiposity is related to a higher rate of
smell phantoms.

363 <u>Study Limitations</u>

364 Our study is based on cross-sectional data from a survey, therefore, direction of associations among variables with time cannot be established and this may undermine our causal inference in recovery for 365 366 parosmia patients. Longitudinal studies with this patient group should be done to confirm our results. 367 There is also an issue of subjective reporting for olfactory disorder types. We provided clear definitions of 368 each type of distorted disorder, but it is difficult to exclude the possibility that some participants did not 369 understand the meaning of parosmia and phantosmia. Indeed, we have a large category of respondents 370 reporting both parosmia and phantosmia that were not included in the analysis as it did not fall into a 371 separate group and were difficult to interpret. The group who reported both parosmia and phantosmia could be either those who experience distortions from both known and unknown sources, or those with a 372 hybrid scenario where they recognize the source of their distortions, but for whom the distorted smell 373 persists for hours or days after the stimulus has disappeared. Patients have reported this before as a "smell 374 375 lock" and clinicians have referred to it as olfactory perseveration (Parker et al. 2021a). Lastly, we sampled 376 from a smell loss group that has interest in their disorder (actively joining an interest group / charity) that 377 might have prioritized severe cases relative to mild ones. There was also an overlap in our sampling times 378 with the COVID-19 pandemic. Post-viral loss was the most prominent etiology in our sample – this might 379 be due to our sampling times overlapping with the COVID-19 pandemic, where smell loss is a prominent 380 symptom of the disease. This overshadowed other important etiologies from our analysis including smell 381 disorders induced by chemotherapy, neurotoxicity, and neurodegenerative diseases. Thus, our results may

not represent the typical patient population at large. We report half the smell loss patients to experienceodor distortion and this should be considered a liberal estimate.

384 Conclusion

Two common symptoms of olfactory dysfunction, parosmia and phantosmia, represent distinct conditions 385 386 that, along with hyposmia and anosmia, have characteristic patterns of medical history, demographics and 387 how they affect quality of life. They are not rare, with almost half our sample reporting symptoms, and 388 cause additional distress typically after an initial olfactory dysfunction starts to resolve. The mechanisms 389 for distinct features of these smell distortions should undergo consideration in the clinic and research 390 setting. If parosmia relates to neurogenesis, what does the character of distortion tell us about the 391 underlying population of recovered neurons? Similarly, if phantosmia is centrally caused what does this 392 tell us about our perception of reality? Distortions among olfactory disorders may provide answers to 393 interesting research questions.

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