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Odor Localization and Sniffing

Johannes Frasnelli[1,2], Genevieve Charbonneau[2], Olivier Collignon[2] and Franco Lepore[1,2]

[1]Centre hospitalier universitaire Sainte-Justine and [2]Centre de Recherche en Neuropsychologie et Cognition, Université de Montréal, Montréal, Québec, Canada

Correspondence to be sent to: Johannes Frasnelli, Département de Psychologie, Université de Montréal, Salle F-475, Pavillon Marie-Victorin, 90, Avenue Vincent-d'Indy, Montréal, Québec, H2V 2S9, Canada. e-mail: frasnelli@yahoo.com

Abstract

For humans, the localization of an odorant seems only possible if the odorant also stimulates the trigeminal nerve. There is, however, some evidence that active sniffing may affect this ability and facilitate the localization of pure odorants. Therefore, we tested the ability of 40 subjects to localize a pure odorant and a mixed olfactory/trigeminal stimulus under 2 stimulation conditions: either odors were blown into the subjects' nostrils (passive) or subjects had to actively sniff the odors (active). Subjects could only reliably localize the mixed olfactory/trigeminal stimulus. However, we found a significant interaction between stimulation condition and nature of the odorant. So, the mixed olfactory/trigeminal stimulus was more localizable in the passive condition, whereas the pure odorant was better localized in the active condition. Interestingly, subjects had more correct answers after stimulation of the right nostril than of the left nostril (where subjects performed significantly below chance when stimulated with the pure odorant), suggesting possible laterality effects. These results suggest that active sniffing may affect our ability to localize odors. Other than mixed olfactory trigeminal stimuli, pure odorants are, however, not localizable even in active condition of sniffing.

Key words: directional smelling, lateralization, olfaction, trigeminal system

Introduction

Although the advantages and functions of bilaterality are obvious in vision and audition, its function in the human sense of smell is unclear. One possible function of bilaterality in the olfactory sense could be that it allows for localizing an odor source in space (i.e., directional smelling). Directional smelling describes the ability to localize an odor source in space by perceiving the differences of the odor's concentration—the concentration gradient—reaching both nostrils, with a higher odor concentration on the nostril closer to the odor source (Kobal et al. 1989). The highest concentration gradient can be reached by presenting an odor to only one nostril and odorless air to the other nostril (monorhinal presentation). Rats have been shown to be able to localize monorhinally presented odorants after a training period. This was true even for pure odorants (Rajan et al. 2006), that is, chemical substances that exclusively stimulate the olfactory nerve, as opposed to mixed olfactory/trigeminal stimuli which also stimulate the trigeminal nerve. Stimulation of the trigeminal nerve leads to sensations of burning, cooling, itching, or stinging (Laska et al. 1997). In fact, most odorants we encounter in our daily lives are mixed olfactory/trigeminal stimuli (Doty et al. 1978), and there is a strong consensus that humans can localize mixed olfactory/trigeminal stimuli with high accuracy (von Skramlik 1924; von Békésy 1964; Prah and Benignus 1984; Kobal et al. 1989; Hummel et al. 2003; Wysocki et al. 2003; Porter et al. 2005), where a stronger trigeminal activation leads to a better performance (Cometto-Muniz and Cain 1990; Hummel et al. 2003; Frasnelli and Hummel 2005). It is, however, still highly debated if humans are able to localize monorhinally presented pure odorants.

In principle, when testing odor localization, odorants can be presented in 2 different ways. If the odor is delivered within an air stream blown into the nostril, the subject does not have to sniff in order for the odor to reach the olfactory mucosa. This passive stimulation is opposed to active stimulation, where the odor reaches the olfactory mucosa during the active sniffing process only. When subjects were tested with a pure odorant under passive stimulation, they were consistently found to be unable to identify the stimulated nostril (Schneider and Schmidt 1967; Prah and Benignus 1984; Kobal et al. 1989; Radil and Wysocki 1998; Frasnelli et al. 2008). However, a slightly different picture emerges for active stimulation. Whereas in one study, subjects were unable to localize the pure odorant phenyl ethyl alcohol, even after extensive training and with feedback (Wysocki et al. 2003), other groups found that subjects were able to localize 1 of 2 pure odorants above chance (Schneider and Schmidt

1967; Porter et al. 2007). The authors of the latter explained this ability to localize odorants with the fact that subjects were able to sniff actively during odor presentation.

It is worth noting that sniffing plays a major part in the formation of the olfactory percept (Sobel et al. 1999; Bensafi et al. 2003; Zelano et al. 2005; Mainland and Sobel 2006). More specifically, it has been argued that sniffing facilitates odorant detection (Sobel et al. 2000) as well as odor discrimination (Laing 1986). It could therefore be speculated that sniffing enables humans to detect differences in the input from both nostrils which in turn would allow us to discriminate between the stimulated and the unstimulated nostril, that is, to localize pure odorants.

Although Schneider and Schmidt (1967) presented 3 odors (ammonia, *n*-butane, coffee) with different degree of trigeminal stimulation to their subjects in both passive and active smelling conditions, both conditions were not directly compared with one another, probably due to substantial methodological differences. In the passive condition, where the odors were blown in one nostril and odorless air delivered to the other, subjects could only localize ammonia. In the active condition, where the odors were delivered to 3 spots in front of the subjects' noses, subjects could this time localize both ammonia and *n*-butane but not coffee. Although the 2 conditions were too different to be directly compared with each other, the results suggest that active sniffing may facilitate localization (Schneider and Schmidt 1967), which is in line with the notion of sniffing affecting olfactory perception (Sobel et al. 1999; Porter et al. 2005; Mainland and Sobel 2006).

In summary, there is evidence that odor localization may be easier under active sniffing conditions than when presented passively. However, no study has attempted to compare the 2 conditions systematically, which consequently became one of the primary aims of the present experiment.

In this study, we investigated the effect of active and passive stimulation on the localization of a pure odorant (phenyl ethyl alcohol) and a mixed olfactory/trigeminal stimulus (eucalyptol). We hypothesized that eucalyptol would be easier to localize than phenyl ethyl alcohol due to its trigeminal stimulation properties. According to earlier reports (Schneider and Schmidt 1967; Frasnelli et al. 2008), we expected subjects to perform below chance when tested with the pure odorant under passive stimulation. In line with other studies (Schneider and Schmidt 1967; Porter et al. 2005), we hypothesized that active stimulation would facilitate the localization of the pure odorant. We also hypothesized that a mixed olfactory/trigeminal stimulus should be easily localizable in both conditions (Kobal et al. 1989; Hummel et al. 2003; Frasnelli et al. 2008).

Material and methods

The study was conducted according to the Declaration of Helsinki and was approved by the ethics board of the Université de Montréal. Forty subjects (20 women) between 18 and 36 years of age (mean age 25 years) participated in the study. Exclusion criteria were a history of olfactory dysfunction, traumatic brain injury, or any other neurological and psychiatric disease known to cause olfactory dysfunction. A quick 8-item odor identification test was used to screen subjects for olfactory dysfunction.

We investigated subjects' ability to localize 2 commonly used odorants. Phenyl ethyl alcohol, a rose odor, is considered to be a pure odorant (Doty et al. 1978), whereas eucalyptol also evokes a cooling sensation and is therefore considered a mixed olfactory/trigeminal stimulus. We compared odor localization in 2 paradigms: active sniffing versus passive stimulation. Passive stimulation was achieved with an experimental design as previously described (Kobal et al. 1989). In short, we assessed the ability to localize odorants by presenting them to either one nostril in a high density polyethylene squeeze bottle (total volume 250 ml) filled with 15 ml of a 50% odorant solution where propylene glycol served as a solvent; at the same time, an identical bottle filled with 15 ml of odorless propylene glycol was presented to the contralateral nostril. The bottles have a pop-up spout that was placed into either nostril. A puff of approximately 15 ml of air was delivered by pressing the 2 bottles at the same time by means of a handheld squeezing device (Hummel et al. 2003). Subjects were blindfolded. They held onto the spouts to prevent any incidental movements that could have occurred during the squeezing of the bottles, which in turn might have produced mechanical irritation interfering with the subject's ability to localize the odor. Per odor and stimulation condition, a total of 40 stimuli were presented to the subjects at an interstimulus interval of approximately 30 s, resulting in a testing time of 20 min; stimulation of the left or right nostril followed a pseudorandomized sequence; each nostril was stimulated 20 times. After each stimulus, subjects made a 2-alternative (left/right) forced-choice judgment on the localization of the odorant. They responded by raising the corresponding hand and were not constrained in time.

In the active sniffing condition, the exact same bottles, odorants, concentrations, solvent, interstimulus intervals, and number of stimulations were applied as in the passive smelling condition. This time, however, the subjects themselves moved the 2 bottles close to their nostrils so that the caps sealed the nostrils. They took one sniff, so the air from the headspace of the left and right bottle reached into the left and right nostril, respectively (Wysocki et al. 2003). Again, after each stimulus, subjects were asked to raise their hand to indicate which nostril the odorant had been presented to.

We tested all subjects in the following paradigm in which odors and stimulation conditions were counterbalanced to avoid habituation: run 1: odor 1 under stimulation condition 1; run 2: odor 2 under stimulation condition 2; run 3: odor 1 under stimulation condition 2; and run 4: odor 2 under

stimulation condition 1. After the second run, subjects took a break of at least 10 min.

Task performance was calculated simply by adding up the number of correct localizations following the presentation of an odorant to either the left or right nostril (von Skramlik 1924; von Békésy 1964; Kobal et al. 1989; Hummel et al. 2003; Wysocki et al. 2003; Frasnelli et al. 2008). Data were analyzed using a $2\times (2 \times 2 \times 2)$ repeated measures analysis of variance with sex as a between subject factor as well as odor (phenyl ethyl alcohol, eucalyptol), stimulation condition (active, passive), and stimulated side (left, right) as within subject factors. When relevant, post hoc analyses were computed using *t*-tests. In addition, we also examined if mean results for a given odorant and condition were different from chance level using 1-sample *t*-tests. Statistical analyses were performed by SPSS 16.0 for Windows (SPSS Inc., Chicago, IL).

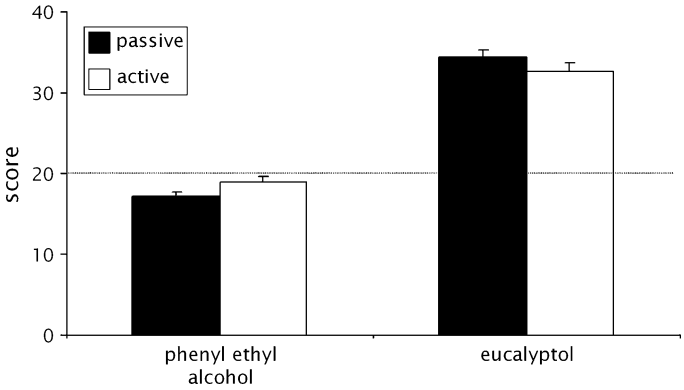

Figure 1 Subjects mean localization scores (error bars indicate standard error of the mean) for phenyl ethyl alcohol (left) and eucalyptol (right). Black bars indicate scores when subjects were passively stimulated, white bars indicate scores when subjects were actively sniffing. The dashed line indicates chance performance (score of 20).

Results

When subjects tried to localize eucalyptol, they reached, on average, a score of 34.4 [standard error of the mean: 0.9]/40 (corresponding to 86%) in the passive stimulation condition and 32.6 (1.1)/40 (82%) in the active sniffing condition. When localizing phenyl ethyl alcohol, they reached a score of 17.2 (0.5)/40 (43%) in the passive stimulation condition and 19.0 [0.7]/40 (48%) in the active sniffing condition. Mean results are presented in Figure 1.

Eucalyptol was far more localizable then phenyl ethyl alcohol (odor: $F[1,38] = 371$, $P < 0.001$). There was no main effect of stimulation. However, there was an interaction between these 2 factors (odor × stimulation: $F[1,38] = 5.78$, $P = 0.021$), indicating the differential effect of active sniffing on both types of odorants. Subjects achieved higher scores in the active condition for localized phenyl ethyl alcohol, whereas the active procedure led to lower scores for eucalyptol.

In addition, there was an effect of side ($F[1,38] = 15.6$; $P < 0.001$), indicating that subjects detected a right nostril stimulation better than a left one. In fact, in all conditions, subjects had more correct answers when they were stimulated on the right side than when they were stimulated on the left side; the difference was significant for all conditions (every $P < 0.022$) with the exception of eucalyptol in the passive stimulation condition.

We then tested if scores for each nostril were significantly different from chance (chance score: 10). All 4 scores were significantly above chance for eucalyptol (every $P < 0.001$). For phenyl ethyl alcohol, the scores for the right nostril were both not different from chance. The scores for the left nostrils, however, were both significantly below chance (passive stimulation condition: 7.2 [0.6], $P < 0.001$; active stimulation condition: 8.5 [0.5], $P = 0.007$; see Figure 2). We used binomial statistics to determine the number of subjects that performed significantly below chance (score ≤ 6/20, $P = 0.036$). When tested with phenyl ethyl alcohol on the left

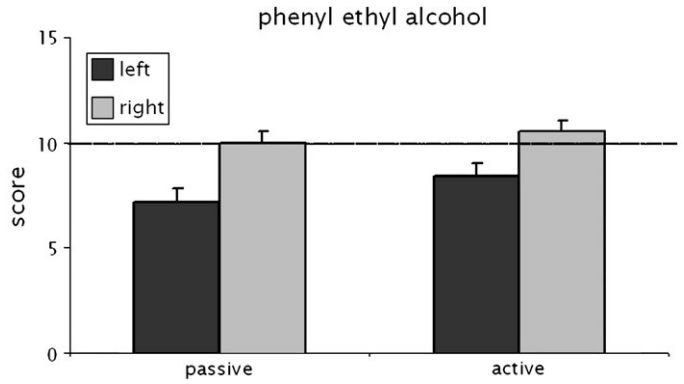

Figure 2 Subjects mean localization scores (error bars indicate standard error of the mean) for phenyl ethyl alcohol broken down for left (dark gray) and right (light gray) sided stimulation. The dashed line indicates chance performance (score of 10).

nostril, 17 subjects had such a score of 6 or worse in the passive condition and 14 did in the active condition. When tested on the right nostril, 5 and 4 subjects performed significantly below chance in the passive and active condition, respectively. This underperformance was not due to outliers because scores in all conditions followed a normal distribution (Kolmogorov–Smirnov test). Furthermore, in the passive stimulation condition, this underperformance after left-sided stimulation led to an aggregate score for phenyl ethyl alcohol below chance (chance score: 20; $P < 0.001$), whereas the score for localizing phenyl ethyl alcohol while actively sniffing was not significantly different from chance. In order to investigate whether or not there was a tendency for the subjects to say right when they were not sure, we calculated the criterion *c* as suggested by Macmillan and Creelman (2005). In fact, in all conditions, there was a slight rightward tendency with *c*'s between –0.05 and –0.21 (*c* can range from –1 to +1. A *c* of 0 denotes no tendency; negative

values signify a tendency to the right, positive values signify a tendency to the left).

Finally, no significant differences were found between women and men.

Discussion

The current study had the primary purpose of addressing the effect of active sniffing on odor localization as compared with the same ability when passively smelling odorants. In doing so, we came across several interesting findings. We feel that 3 of these findings deserve to be discussed in further detail.

First, we found that the type of stimulation (active sniffing vs. passive stimulation) differentially affected the ability to localize odorants depending on the nature of the odorant. On average, a mixed trigeminal–olfactory stimulus could be localized better under a passive sniffing condition, although the difference between the 2 stimulation conditions was not significant. A pure odorant, however, was better localized under the active sniffing condition. These results clearly demonstrate that sniffing affects olfactory perception, thus supporting the claims of Mainland and Sobel (2006). The sniff is an important contributor to the formation of the olfactory percept (Sobel et al. 1999; Bensafi et al. 2004), possibly because sniffing increases olfactory performance (Porter et al. 2005) by increasing olfactory attention (Zelano et al. 2005). Our data do not support this claim in a straightforward manner but rather suggest that sniffing is another factor in the complex interplay leading to the perception of chemosensory stimuli. It would seem that sniffing affects perception differently depending on the nature of the odorant and, under certain conditions, can lead to weaker performances as it was the case for eucalyptol in the current study.

However, we did not find any evidence that phenyl ethyl alcohol is localizable, even under active stimulation conditions. Phenyl ethyl alcohol is commonly used in olfactory research. It is considered to be a pure odorant because only 1 of 15 anosmic subjects could detect phenyl ethyl alcohol (Doty et al. 1978). It has, therefore, repeatedly been used to assess subjects' ability to localize pure odorants. In most of these studies, subjects were unable to localize phenyl ethyl alcohol (Radil and Wysocki 1998; Wysocki et al. 2003; Frasnelli et al. 2008). In one report, however, the authors claimed that subjects were able to localize phenyl ethyl alcohol (Porter et al. 2005). Although the authors mention a series of control experiments, they unfortunately fail to describe their methodology in detail, which makes comparisons between studies somewhat difficult and speculative. Apparently, they stimulated their subjects with each of 4 odorants (one of them being phenyl ethyl alcohol) 13–14 times in a localization task. Stimulus duration was 3 s. They tested 16 subjects; 5 of them were able to localize phenyl ethyl alcohol above chance. Eugenol, the other stimulus authors considered to be a pure odorant used in this study, was also localized by 5 out of 16 subjects. The authors do not report mean scores for the different odors they used. However, the *t*-test revealed that subjects' mean score was above chance for phenyl ethyl alcohol but not for eugenol (Porter et al. 2005). Based on this, the authors claimed that even pure odorants can be localized. However, alternative explanations are also possible. Although it is typically described as a pure odorant, phenyl ethyl alcohol may also cause some trigeminal activation, especially with long stimulus durations. In fact, Doty et al. (1978) had found 1 of 15 anosmic subjects to be able to detect phenyl ethyl alcohol (and eugenol, too). In both studies, stimulus duration was approximately 3 s. Therefore, under certain conditions, phenyl ethyl alcohol may also have some weak trigeminal properties. As a matter of fact, Kobal and Hummel (1992) argue that pure phenyl ethyl alcohol activates the trigeminal nerve, at least to some degree. Furthermore, there is another issue to consider with regards to the study of Porter et al. (2005). When stimuli are repeated 13 times, a score of 7 represents the 50% chance of the forced-choice localization task. Assuming binomial distribution, a significant score above chance is reached with a score of 10 ($P = 0.035$). In other words, just 3 hits separate a performance at chance from a performance significantly above chance. This highlights the importance of performing a large number of repetitions when doing a localization task. Taken together, a very weak trigeminal stimulation by phenyl ethyl alcohol may have been enough to raise the average score above the threshold of significance. In our study, we used diluted phenyl ethyl alcohol, tested a larger sample of subjects, and performed more repetitions. We did not find any evidence that subjects were able to localize phenyl ethyl alcohol. We therefore suggest that if an odorant can be localized, it is an indication that it also stimulates the trigeminal nerve, which is in line with earlier reports (e.g., Prah and Benignus 1984; Kobal and Hummel 1992; Cometto-Muniz and Cain 1998; Wysocki et al. 2003). Therefore, reports showing humans as being able to localize phenyl ethyl alcohol (Porter et al. 2005), lavender (von Békésy 1964), or *n*-butane (Schneider and Schmidt 1967) should perhaps not be seen as supporting the claim that humans can localize pure odorants but rather seen as an indication that in certain concentrations and conditions, these odorants may also activate the trigeminal nerve and should therefore not be considered as pure odorants. In addition, some words have to be said about eugenol, which has often been considered as being a pure odorant. However, there are some elements that need to be considered. First, it is known that eugenol activates trigeminal chemoreceptors, such as TRPV1 (Yang et al. 2003). Second, when sniffing eugenol, one can clearly perceive a burning sensation. Finally, eugenol has a long history of use as an anesthetic agent in dentistry. Therefore, it may be argued that the lack of localizability of eugenol is not due to the fact that eugenol is a pure odorant but rather because eugenol anesthetizes trigeminal fibers rendering the stimulus nonlocalizable over time. Therefore, eugenol may be not the optimal choice when looking for a stimulus in a localization task.

The second topic of particular interest relates to the findings regarding the pure odorant. Under active stimulation subjects performed below chance. Moreover, they performed even worse under passive stimulation leading to a performance that was significantly below chance. In addition, when looking at the results from each nostril separately, it can be seen that subjects performed below chance in both the passive and active condition but only for the left nostril. Taken together, our results confirm those a recent report in which subjects' performance in a localization task was found to be significantly below chance for eugenol and phenyl ethyl alcohol (Frasnelli et al. 2008). Another report also described some subjects as performing below chance when localizing pure odorants (Schneider and Schmidt 1967). In both studies, however, the authors did not report the results for both nostrils separately. The reason for our "laterality" finding is unclear. Our data show that this effect is driven by the results obtained in the left nostril. In both stimulation conditions, although subjects performed at chance when the odor was delivered to their right nostril, they performed significantly below chance after left-sided stimulation. In other words, subjects gave, on average, as many times the answer right as the answer left when the right nostril had been stimulated; however, when the left nostril was stimulated they answered significantly more often right than left.

The third main result of this study was that subjects showed a tendency to localize stimuli presented to the right nostril better than those presented to the left nostril. In our study, the results for the right nostril were significantly superior to those of the left for the 3 most difficult conditions of localizations but not for the easiest one (eucalyptol in the passive condition). This rightward tendency was independent from subjects' handedness (4 of our subjects were left-handers). For all 4 conditions, the left-handers also had more correct answers on the right than on the left side, although the difference was not significant due to the small sample size.

Most studies showed no difference between odor thresholds obtained from both nostrils (e.g., Koelega and Köster 1974; Hornung et al. 1990; Zatorre and Jones-Gotman 1990, 1991; Betchen and Doty 1998; Frasnelli et al. 2002, but see Youngentob et al. 1982; Cain and Gent 1991); however, there appears to be a nostril difference favoring the right nostril in some higher order tasks such as in odor discrimination (Zatorre and Jones-Gotman 1990, 1991) and odor intensity (Thuerauf et al. 2008). The latter result is of particular interest because, in the paradigm we used, the intensity of a stimulus is probably the main cue when asked to localize an odor. It has also been reported that olfactory stimulation of the right nostril evokes higher activations in olfactory regions than stimulation of the left nostril. In one such study, right-sided stimulation led to larger activations in the right orbitofrontal cortex (Savic and Gulyas 2000), which is in line with the fact that olfactory input is mainly processed ipsilaterally (Hummel et al. 1995), at least until the primary olfactory cortex (Gottfried 2006). With regard to these parameters, data from olfaction are highly consistent with other sensory domains (Royet and Plailly 2004). Therefore, odor localization may be quite similar to spatial localization in other sensory modalities. In fact, a rightward response bias is also known to exist in other sensory systems, such as in auditory localization (Lewald et al. 2002; Lewald 2004; Dufour et al. 2007). Similarly, in the visual domain, subjects generally lateralize to the left the vertical center when bisecting horizontal lines, as if there was a rightward shift in the perceived location of this central point (Bowers and Heilman 1980; Bradshaw et al. 1983, 1985). One common explanation for the rightward bias in these sensory systems is that it reflects a structural specialization of the right cerebral hemisphere for the allocation and control of spatial attention (Mesulam 2000), inducing a tendency to localize uncertain spatial targets to the right (weak) hemifield. Such hypotheses of hemispheric asymmetries in the spatial processing of olfactory stimuli (and its relation with other sensory modalities) remain, however, to be more thoroughly investigated in future research.

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