



REPLY TO CROY AND HUMMEL:

Stereo smelling without involvement of nasal trigeminal function

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Many odorants stimulate the trigeminal nerve at high, but not low, concentrations, and trigeminal stimulation produces hot, cold, itching, tingling, or electric feelings that are spatially localizable. What has been under debate is whether internostril differences yield directionality in human olfaction without involving the trigeminal system. To address this issue, we employed two odorants that are well accepted as nontrigeminal—phenylethyl alcohol and vanillin—and demonstrated that an intermediate internostril difference in odor intensity produces a reliable spatial cue that subconsciously guides navigation (1). We thank Croy and Hummel (2) for their response to our work, where they raise a concern that the findings could result from trigeminal stimulation. The argument, however, appears to be based on a misinterpretation of our data and is not backed up by the existing literature, including some of their own studies. Moreover, if the heading perception biases observed in our study were induced by trigeminal cues, the largest effect should have been obtained under high, rather than intermediate, binaral concentration disparity.

Phenylethyl alcohol does not elicit a reliable trigeminal electrophysiological response in rats at vapor saturation (3); cannot be detected by 28 out of 29 anosmic individuals in neat form, the remaining one explainable by chance (4, 5); and cannot be lateralized when presented in neat form to one of the two nostrils in a large-sample study with normosmics (6). The concentrations of phenylethyl alcohol in our study were no greater than 5% vol/vol (1). Across all participants

tested, lateralization was at chance even under high binaral disparity (i.e., unilateral odor presentation), Bayes factor in favor of H_1 over H_0 (BF_{10}) = 0.20, which represents substantial evidence for the null hypothesis (7). We have since tested an additional 24 normosmic individuals who underwent prolonged exposures (5 min to 6 min per trial) to 4% or 0.8% vol/vol phenylethyl alcohol in one nostril and 1% or 0.2% vol/vol in the other, that is, concentration disparities that biased heading perception in our study. Their lateralization accuracies were again at chance, BF_{10} = 0.22 (Fig. 1).

Croy and Hummel (2) acknowledge that vanillin is a selective olfactory stimulant. There is no *in vivo* evidence that vanillin induces any trigeminal response. Pure vanillin activates only the olfactory cortex and no area associated with trigeminal processing (8), and cannot be detected by anosmic individuals (5). Vanillin has a solubility of ~11 mg/mL in water (9). The highest concentration we used was 10 mg/mL (1% g/mL or 1% m/v) (1). Across all participants tested, lateralization was also at chance when vanillin was presented unilaterally, BF_{10} = 0.18.

With regard to the anterior olfactory nucleus, the structure has been clearly shown to receive inputs from the ipsilateral and the contralateral olfactory bulbs in adult mice and macaque monkeys (10, 11). We conclude by restating that humans have a stereo sense of smell that does not require involvement of the trigeminal system.

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The authors declare no competing interest.

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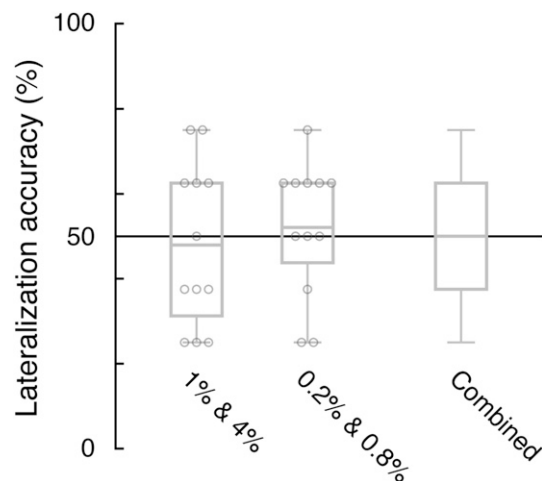


Fig. 1. Lateralization accuracies after prolonged exposures to phenylethyl alcohol in 24 normosmic individuals (17 females, mean age \pm SD = 25.0 \pm 2.8 y). In each trial, they were dichorhinally presented with two concentrations of phenylethyl alcohol that formed a 4:1 disparity, and instructed to continuously inhale through the nose and exhale through the mouth until a timer prompted them to stop (for a duration of 5 min to 6 min), at which point they were asked to verbally report which nostril smelled a higher concentration or a stronger odor. Half of them were exposed to 4% vol/vol phenylethyl alcohol in one nostril and 1% vol/vol in the other; the other half were exposed to 0.8% vol/vol in one nostril and 0.2% vol/vol in the other. Each completed eight trials, with a 2-min break in between two trials. In each box and whisker plot, the central line denotes the mean, and the bottom and top edges of the box indicate the 25th and 75th percentiles. The ends of the whiskers represent 90% CI. Each circle represents an individual.

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