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Gender-specific Olfactory Sensitization: Hormonal and Cognitive Influences

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In one reported instance of induced olfactory sensitivity, men and women who were initially unable to smell androstenone (5-α-androst-16-en-3-one) developed that ability after repeated exposures (Wysocki *et al.*, 1989). This phenomenon has been believed to occur only for odorants to which participants have specific anosmia and possibly specific to the particular stimulus used in that experiment. Here, we demonstrate that induced olfactory sensitivity is both a more general and more restricted effect, with only women of reproductive age showing marked sensitization to multiple odorants after repeated threshold testing. These findings may offer an explanation for anecdotal claims of females' olfactory acuity.

Although gender differences have been observed within several different olfactory processes, these tend to be tasks that require higher cognitive processing such as memory for odors, odor identification and hedonic ratings (Cain, 1982; Doty *et al.*, 1985; Gilbert *et al.*, 1997). Studies looking at olfactory sensitivity have failed to show such gender differences. However, such studies have relied on single session evaluations, whereas the present studies demonstrate that repeated exposure is an important factor in inducing sensitivity (cf. Cain and Schmidt, 2002). Although males and females may begin a study with comparably similar olfactory detection thresholds, under some conditions, females of reproductive age will sensitize to odor stimuli by up to 11 orders of magnitude, while their male counterparts will not.

The phenomenon presented here was first encountered while repeatedly measuring taste and olfactory thresholds. Males and females between the ages of 20 and 32 were exposed repeatedly to benzaldehyde via a modified staircase method with a five-reversal criterion (Wetherill and Levitt, 1965). Oral saccharin thresholds were taken separately, each for a total of 30 sessions. Females' thresholds increased significantly, while males' did not (Figure 1). A two-way ANOVA with gender as a between-group factor showed that benzaldehyde thresholds decreased among females but not among males [$F(29,116) = 3.84$; $P = 0.007$]. This effect was seen among women in as few as six sessions [$F(1,5) = 4.20$; $P = 0.02$]. Oral saccharin thresholds remained unchanged over 30 sessions among both males and females, indicating that this phenomenon is specific to the olfactory modality.

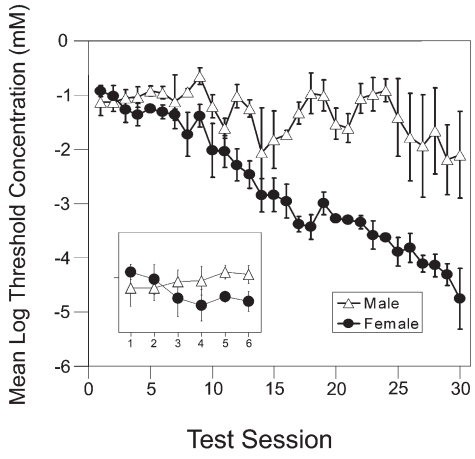

Figure 1 Gender effects of repeated test exposures on odor sensitivity among males and females aged 20–32 years. Mean thresholds (± SEM) are expressed as log millimolar concentration of benzaldehyde. Reproduced with permission from the Nature Publishing Group.

An additional study was completed with control odorants to evaluate whether participants' sensitization to benzaldehyde would generalize to other odorants in the absence of extended exposures to those odorants. Six trained participants from the previous experiment as well as six naïve participants took part in the experiment. Benzaldehyde, 5-methylfurfural (perceptually similar to benzaldehyde) and isoamylacetate (perceptually dissimilar to benzaldehyde) thresholds were collected as a baseline. In nine subsequent sessions benzaldehdye thresholds were collected. In the final sessions, 5-methlyfurfural and isoamylacetate thresholds were again measured. Sensitization again occurred only among the female participants [i.e. between the first five benzaldehyde thresholds and the last five benzaldehyde thresholds ($P = 0.01$)] where sensitivity increased by an average of five orders of magnitude. Females slightly increased in their sensitivity to a similar berry odor (5-methylfurfural) but not to amyl acetate (banana).

The phenomenon is not specific to benzaldehyde or cherry/almond odors. In repeated threshold testing to citralva, rather than benzaldehyde, females became more senstive to citralva while males did not ($P < 0.007$). No change in benzaldehyde thresholds (the control odorant) were seen in either group.

To explore the possible mediating effects of sex hormones on gender-specific olfactory sensitization, we tested two additional groups whose levels of estrogen were known to be lower than that of our original study population. The next experiments explored the role of sex hormones on the induction of olfactory sensitivity among post-menopausal females and age-matched males, as well as prepubescent boys and girls. In the first group, eight volunteers (four male, four female, ranging in age from 49 to 61 years) were repeatedly exposed to benzaldehyde. None of the females in this group were undergoing hormone replacement therapy. The prepubescent group consisted of eight volunteers (four males, four females aged 9–10 years). Baseline thresholds for both benzaldehyde and the control odorant, citralva, were measured. Participants were repeatedly tested for sensitivity to benzaldehyde for seven subsequent sessions and at the final session, detection thresholds were measured for the control odor. No significant increases in sensitivity were observed for either odorant among post-menopausal females or age-matched males. Neither were significant increases in sensitivity observed among prepubescent girls or boys.

The ability of women to show dramatic increases in olfactory sensitivity following repeated test exposures can explain many real-world phenomena in which females appear to be more sensitive and reactive than males (e.g. chemical intolerance syndromes) in the presence of low-level odors. However, the dramatic sensitivity changes seen, do not seem to be yoked to normal hormonal cycles since

females show only small fluctuations in threshold sensitivity across the menstrual cycle.

Interestingly, despite daily exposure to peri-threshold odorants common in the environment, females generally do not exhibit greater sensitivity to these odors on an initial threshold evaluation, suggesting the interplay of activational hormonal and cognitive factors (i.e. focused attention). The potential for vast improvements in odor sensitivity through attentional learning and with repeated exposure, during the reproductive years, may be advantageous for enhancing specific olfactory-mediated behaviors, such as mother–infant bonding.

To explore additional parameters of the phenomenon of gender-specific sensitization, further studies were conducted to evaluate (i) the role of focused attention, (ii) the effect of suprathreshold versus perithreshold concentrations and (iii) whether sensitization allows women to identify odorants at very low concentrations. Findings from these studies indicate that focused attention appears to be a necessary condition for sensitization to occur, that sensitization does not occur following repeated testing with suprathreshold concentrations and perhaps surprisingly, sensitization does not appear to confer an enhanced ability to identify the odorants at these very weak concentrations. Future studies will explore the apparent dissociation between threshold and suprathreshold responses.

Acknowledgements

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