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Research report

Disinhibition of olfaction: Human olfactory performance improves following low levels of alcohol

Yaara Endevelt-Shapira [a,*], Sagit Shushan [a,b], Yehudah Roth [b], Noam Sobel [a]

[a] Department of Neurobiology, Weizmann Institute of Science, Rehovot 76100, Israel
[b] Department of Otolaryngology-Head and Neck Surgery, Edith Wolfson Medical Center, Holon 58100, Israel

HIGHLIGHTS

- We test olfactory performance after ingestion of alcohol.
- We find that low levels of alcohol improve olfactory performance.
- We hypothesize that true human olfactory abilities are obscured by cortical inhibition.

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ABSTRACT

We hypothesize that true human olfactory abilities are obscured by cortical inhibition. Alcohol reduces inhibition. We therefore tested the hypothesis that olfactory abilities will improve following alcohol consumption. We measured olfaction in 85 subjects, 45 in a between-subjects design, and 40 in a repeated-measures within-subjects design before and after consumption of alcoholic or non-alcoholic beverages. Subjects were also assessed using neurocognitive measures of inhibition. Following alcohol consumption, blood alcohol levels ranged from 0.005% to 0.11%. Across subjects, before any consumption of alcohol, we found that individuals who were less inhibited had lower (better) olfactory detection thresholds ($r = 0.68$, $p < 0.005$). Moreover, after alcohol consumption, subjects with low alcohol levels could make olfactory discriminations that subjects with 0% alcohol could not make (chance = 33%, alcohol = 51.3 ± 22.7%, control = 34.7 ± 31.6%, $t(43) = 2.03$, $p < 0.05$). Within subjects, we found correlations between levels of alcohol and olfactory detection ($r = 0.63$, $p < 0.005$) and discrimination ($r = -0.50$, $p < 0.05$), such that performance was improved at low levels of alcohol (significantly better than baseline for detection) and deteriorated at higher levels of alcohol. Finally, levels of alcohol-induced improved olfactory discrimination were correlated with levels of alcohol-induced cognitive disinhibition ($r = 0.48$, $p < 0.05$). Although we cannot rule out alternative non-inhibitory alcohol-induced routes of influence, we conclude that improved olfaction at low levels of alcohol supports the notion of an inhibitory mechanism obscuring true olfactory abilities.

1. Introduction

Although humans direct only limited attention to olfaction [1,2], human olfactory abilities are high [3–6]. Consistent with this dissociation, humans are very poor at assessing their own olfactory abilities [7,8]. Moreover, these abilities can improve with practice. For example, through aversive conditioning humans can learn to discriminate previously indiscriminable odors [9], through practice humans can learn to track a scent trail [10], and repeated exposure to an odorant can lower (improve) its detection threshold [11], in some cases driving a shift from complete lack of detection to clear detectability [12,13]. Whereas these examples entail gradual changes in olfactory abilities, there are other examples of instantaneous improvements in olfaction. Many of these cases are anecdotal. For example, in his story "The Dog Beneath The Skin" [14]. Oliver Sacks describes a medical student whose sense of smell became extremely sensitive after a discrete instance of recreational drug use. This is not the only report of rapid-onset hyper-olfaction. In a separate case, following stroke, a 65 year-old man shifted to olfactory exploration as his primary mode of object investigation, and tended toward better spontaneous odor naming in comparison to healthy controls [15]. Whereas the influence of training and

* Corresponding author. Tel.: +972 8 934 6273; fax: +972 8 934 6254.
E-mail address: yaara.endevelt@gmail.com (Y. Endevelt-Shapira).

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conditioning may be attributable to plasticity anywhere in the olfactory system [16], and the influence of drugs may reflect peripheral mechanisms such as cannabinoid effects on CB1-receptors in the olfactory bulb [17,18], rapid-onset hyper-olfaction following stroke implies the unveiling of olfactory capabilities that were previously masked or inhibited. With this in mind, the working hypothesis of this study is that human olfaction is under constant inhibition.

The ventral temporal brain structures that contain primary olfactory cortex [19] are under inhibitory influence of the prefrontal cortex (PFC) [20,21]. One path toward reducing this inhibition is alcohol consumption [22,23]. Alcohol consumption drives behavioral effects similar to those seen following PFC lesions, including deficits in planning, information processing, attention, and inhibitory control [24–27], the latter evident even after only moderate doses of alcohol alone [24,28].

Previous studies examining the effects of alcohol consumption on olfaction came to mixed conclusions. In agreement with our hypothesis, one early study found that moderate doses of alcohol increased sensitivity to the odorant guaiacol (a smoky odor) [29]. This, however, was a between-subjects design, susceptible to non-alcohol related group differences. In contrast, other studies using within subject designs reported either declined [30–32], or unchanged [31] olfactory performance following alcohol consumption. Here we set out to test the hypothesis that alcohol may improve olfactory performance in three separate experimental designs. In Experiments 1 and 2 we used a within-subjects repeated experimental design in a highly controlled laboratory setting where we measured olfactory performance as well as non-olfactory measures of inhibition on separate days before and after consumption of a beverage that was either with or without alcohol. Experiment 3 was a field-experiment where we measured olfactory performance and levels of alcohol amongst pub-goers. These experiments converged to imply that whereas high doses of alcohol impair olfactory performance, low doses of alcohol lead to improvements in olfactory performance above the no-alcohol baseline. These improvements are consistent with our hypothesis regarding inhibition in human olfaction.

2. Methods

2.1. Subjects

Experiment 1: 20 subjects, 10 women, mean age = 24.7 ± 2.3 years.

Experiment 2: 20 subjects, 10 women, mean age = 25.4 ± 2.0 years.

Experiment 3: 45 subjects, 20 women, mean age = 27.2 ± 5.1 years.

Experiments 1–2: Subjects were screened for general health, no use of medication, no history of nasal insult or repair, and reported normal olfaction. All subjects participated after providing written informed consent to procedures approved by the Helsinki committee of the Wolfson Hospital in Holon, Israel.

2.2. Olfactory tasks

2.2.1. Experiment 1: Lab olfactory threshold test

We used a triple-forced-choice ascending staircase paradigm with reversals to measure olfactory detection thresholds for the odor phenyl ethyl alcohol (PEA, CAS no. 60-12-8, a rose-like odor). A geometric series of PEA dilutions was prepared in mineral oil. On each trial, a subject was presented with three opaque jars, one containing a PEA dilution, and two containing mineral oil alone. The subject was asked to indicate which jar contained the odorant. There was a ~40 s inter-trial-interval. An experiment started at a −7 log concentration step. If the subject was incorrect—the next trial contained the next higher concentration. This increase in concentration continued until a point of three consecutive correct detections of a given concentration, after which the following trial shifted to a lower concentration (reversal). Whereas incorrect detection then led to concentration re-increase (reversal), two additional consecutive correct detections led to an additional concentration decrease. The average of the last four staircase reversal points out of a total of seven reversals was used as the threshold estimate. These threshold tests have been estimated as highly reliable [33].

2.2.2. Experiment 2: Lab olfactory discrimination test

We used a three-alternative forced choice discrimination task. In each of 18 trials three opaque jars were presented to the subject in a randomized order. Two jars contained identical odors and the third contained a different odor (all equated for perceived intensity). Subjects were allowed to take one 2-second long sniff at each odor presentation, and were then asked to pick out the jar that contained the dissimilar odor. Matching inhalation to a concurrent tone controlled sniff duration. Three types of odor triplet were used. Two of the triplets entailed discrimination between odorant mixtures (mixture sets A and B), and one triplet entailed discrimination between enantiomers. In the mixture discriminations, two jars contained identical odorant mixtures of 5 or 6 components and the third contained a similar mixture with just one of the components replaced. The enantiomers used were (1*R*,2*S*,5*R*)-(−)-menthol (CAS no. 2216-51-5) and (1*S*,2*R*,5*S*)-(+)-menthol (CAS no. 15356-60-2). The monomolecules used for the mixtures were isoamyl acetate (CAS no. 123-92-2), isopropylbenzene (CAS no. 98-82-8), 1-pentanol (CAS no. 71-41-0), 1,7-octadiene (CAS no. 3710-30-3), 2-heptanone (CAS no. 110-43-0), heptanal (CAS no. 111-71-7), 3-methyl-2-buten-1-ol (CAS no. 556-82-1), propyl butyrate (CAS no. 105-66-8).

2.2.3. Experiment 2: Lab olfactory intensity and pleasantness rating

Five different odorants that span the hedonic scale [hydroxycitronellal (CAS no. 107-75-5), propyl butyrate (CAS no. 105-66-8), guaicol (CAS no.+90-05-1), hexanoic-acid (CAS no. 142-62-1), skatole (CAS no. 83-34-1)] were rated on a visual analogue scale (VAS, 20 cm long) for their pleasantness and intensity. Each rating repeated 3 times. The odors were presented for 2 s, and the subjects were allowed to take one sniff at each odor presentation. The rating results were normalized for each subject based on individual maximum and minimum rating across conditions: $x_{norm} = (x - x_{min})/(x_{max} - x_{min})$.

2.2.4. Experiment 3: Field olfactory discrimination task

We used a three-alternative forced choice discrimination task. In each of five trials, subjects activated three scratch-and-sniff micro-encapsulated odorant stickers (1 square inch), two containing an identical mixture of 20 components, and one containing a different yet perceptually similar mixture of 20 components (these odorant mixtures were different versions of *olfactory white* as in Ref. [34]). Order of odorants was counter-balanced. On each trial, subjects were asked to indicate which sticker (a/b/c) contained the different odor.

2.3. Non-olfactory tasks and measures in Experiments 1 and 2

2.3.1. BIS/BAS

A 20-item self-administered questionnaire that measures two dimensions of motivation [35]: BAS, which regulates responses to