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# Comparison of lateralized and binasal olfactory thresholds*

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SUMMARY

*We investigated whether dirhinal olfactory thresholds differ from monorhinal ones. Experiments 1 and 2 investigated butanol, Experiment 3 phenylethylalcohol. In Experiments 2 and 3 pen-like odor dispensing devices were used, in Experiment 1 odors were presented in glass bottles. Participants were in excellent health (Experiment 1: 14 female [f], 15 m [m], mean age [ma] 24 years; Experiment 2: 12 f, 19 m, ma 24 years; Experiment 3: 19 f, 19 m, ma 32 years). Thresholds were assessed for left, right, and both nostrils. No significant difference was found between dirhinal results and results for the best of two nostrils. Apart from this, thresholds were found to improve with repeated testing. In conclusion, using two odorants with different techniques of administration in studies performed at different sites, the present results indicated that there is no major difference between odor detection thresholds obtained for the best and both nostrils.*

*Key words: olfaction, thresholds, spatial summation, learning*

## INTRODUCTION

As with other sensory systems, the sense of smell is essentially bilateral. Odorants entering the left or right nostril stimulate the olfactory epithelium on that side and then project ipsilaterally to the olfactory bulb and, predominantly, onto higher processing centers within the brain. Unlike the obvious advantages for other sensory systems, such as acoustic localization or binocular vision, the function of the separate sensory inputs for olfaction is unclear, although many hypotheses have been put forward. For example, it has been proposed that input from two nostrils may have functional significance in the discrimination of odor intensity, or odor quality (e.g., Sobel et al., 1999). On the other hand, Eccles (2001) has suggested a, possibly more important, non-sensory role of the two nostrils in defense against infection and other dangers due to exposition of the nasal mucosa to the environment.

When investigating odor thresholds a number of studies showed an advantage for one nostril over the other: the right nostril for left and right-handers with 1-butanol, isoamylbutyrate, and pyridine (Cain and Gent, 1991), the left nostril for left-handers with n-butanol (Youngentob et al., 1982) or the left nostril for right-handers and the right nostril for left handers using 2-butanone (Frye et al., 1992). In contrast, several other studies have reported the absence of significant differences in sensitivity between the two nostrils, or between monorhinal and dirhinal stimulation (Koelega and Köster, 1974; Hornung et al., 1990; Zatorre and Jones-Gotman, 1990; Zatorre and Jones-Gotman, 1991; Betchen and Doty, 1998; Klimek et al., 1998). For example, using sniff bottles and a two alternative forced choice staircase procedure, Betchen and Doty (1998) found no significant differences relating to side of nose or between the "best" (lowest threshold) nostril and the threshold for both nostrils. Klimek et al. (1998) used a triple forced choice threshold measure with n-butanol presented in pen-like odor dispensing devices (Hummel et al., 1997). Significant differences were found between stimuli presented to either nostril as compared to dirhinal presentation, however, similar to the findings reported by Hornung et al. (1990), these differences became non-significant when the best nostril was compared to both nostrils.

The aim of the series of experiments reported here was to investigate possible sources of variation that may have produced inconsistencies in previous research on the relative contribution of dirhinal and monorhinal stimulation to odor sensitivity. Specifically, the present study explored the influence of

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odor quality, method of testing, and individual differences in odor thresholds.

It has been suggested that, to some degree, the divergence in findings may be a result of odorant quality differences. Betchen and Doty (1998) noted that studies using odorants that more strongly stimulate the trigeminal nerve tend to produce lateralized differences in sensitivity. However, these authors also acknowledge that, at threshold levels, most odorants are unlikely to stimulate the trigeminal nerve (Hummel et al., 1992). They noted that studies using phenyl ethyl alcohol (PEA) which induces little trigeminal activity (von Skramlik, 1926; Doty et al., 1978; Kobal and Hummel 1992), tend not to show these lateralized differences (Zatorre and Jones-Gotman, 1990; Betchen and Doty, 1998). Thus, quality differences may be a potential source of variation and as such require more careful investigation. For this reason, in the current study both butanol and PEA were used. Measures of airflow and intranasal volume were taken to examine their possible influence on olfactory thresholds.

Another potential source of variation is the method used for testing. To establish that there genuinely is, or is not, bilateral interaction, it is necessary to show that the effects obtained are stable, or at least consistent. For example, Frye et al. (1992) and Youngentob (1982) used olfactometry whereas Klimek et al. (1998) used "Sniffin' Sticks" (Kobal et al., 1996), and Betchen and Doty (1998) used sniff bottles. In the present research all three experiments have similar designs with the exception that in Experiment 1 sniff bottles were used for stimulation, whereas "Sniffin' Sticks" were employed in the two other experiments.

## MATERIALS AND METHODS

The study was divided in three parts. In experiments 1 and 2 butanol odor detection thresholds were tested; in experiment 3 phenyl ethyl alcohol (PEA) thresholds were assessed. In experiments 2 and 3 pen-like odor dispensing devices were used for odor presentation ("Sniffin' Sticks"), in experiment 1 odor presentation was performed using glass bottles. Experiments 1 and 2 were conducted at the Smell and Taste Center at the Department of Otorhinolaryngology of the University of Pennsylvania, Philadelphia, PA, USA. Experiment 3 was performed at the Department of Otorhinolaryngology at the University of Dresden Medical School, Dresden, Germany. All participating subjects were in excellent health with no indication of any major nasal or health problems; most of the subjects participating in experiment 1 also participated in experiment 2 (for details of the study population see Table 1). Investigations were performed according to the Declaration of Helsinki on biomedical studies involving human subjects (Summerset West amendment). All subjects gave written consent.

Subjects were instructed not to drink anything other than water nor eat or smoke one hour before commencement of testing. The session started with a thorough medical history recorded in all subjects. Handedness was determined using the Briggs and Nebes Inventory (Briggs and Nebes, 1975) which is based on 12 questions related to handedness. Lefthanders scored between -24 and -9 points, righthanders between +9 and +24 points. Then, for experiments 1 and 2 of the experiment normal olfactory function was ascertained by means of the "University of Pennsylvania Smell Identification Test" (UPSIT) comprised of 40 odors that have to be identified by means of a multiple forced choice task from a list of 4 items (Doty et al., 1984). For experiment 3 olfactory functioning was assessed using the odor identification test as it is established in the "Sniffin' Sticks" test battery (Hummel et al., 1997; Kobal et al., 2000). In addition, using "Sniffin' Sticks" in experiment 3 additional threshold testing was performed for PEA prior to the experimental session. For technical reasons, however, not all of the subjects investigated in this part of the study received this pre-test with the same PEA concentrations as they had been used for the following mono- and dirhinal testing.

In experiments 1 and 2, testing of the patency of nasal passages was determined using acoustic rhinometry (Eccovision®, Hood Laboratories Inc., Pembroke, MA, USA). Lateralized measurements established both the minimal cross-sectional area (MCSA) of the nasal cavity and the volume of the nasal cavity over a length of 3.6 cm (Roithmann et al., 1994; Min and Jang, 1995; Porter et al., 1996). In experiment 3 nasal airflow was determined using anterior rhinomanometry (Neurootometrie, Hortmann, Germany). Inspiratory air-flow was analyzed in a lateralized fashion at 150 mPa (McCaffrey, 1991). Both, acoustic rhinometry and rhinomanometry, were performed immediately before assessment of olfactory thresholds.

Thresholds were assessed for the left, the right, and both nostrils. Each of the threshold measurements took 10-15 min, with a 3-5 min interval between these measurements. The order of threshold testing was randomized across all participating subjects. For assessment of thresholds subjects wore goggles that prevented visual identification of the stimuli. Odor detection thresholds were assessed by the initially ascending single staircase method (see below) (Doty, 1991). Odorants were presented in two different ways:

1) in experiments 2 and 3 of the study subjects were tested using pen-like odor-dispensing devices termed "Sniffin' Sticks" (Kobal et al., 1996; Hummel et al., 1997).

Table 1. Characteristics of the 3 experiments.

| | Experiment 1 | Experiment 2 | Experiment 3 |
|---|---|---|---|
| Odorant tested | Butanol | Butanol | Phenyl ethyl alcohol |
| Odor presentation system | Glass bottles | Odor pens ("Sniffin' Sticks") | Odor pens ("Sniffin' Sticks") |
| Means to assess nasal patency | Acoustic rhinometry | Acoustic rhinometry | Rhinomanometry |
| Location of testing | Philadelphia, PA, USA | Philadelphia, PA, USA | Dresden, Germany |
| Number of Participating subjects | 29 | 31 | 38 |
| Number of female subjects | 14 | 12 | 19 |
| Number of male subjects | 15 | 19 | 19 |
| Age range [years] | 18-40 | 18-40 | 18-68 |
| Mean age [years] | 24.0 | 24.4 | 32.2 |

2) in experiment 1 with so-called sniff bottles (Doty et al., 1995) (volume 125 ml, height 10.5 cm, diameter of opening 4 cm; screw-on caps with teflon lids).

Thus, in experiments 2 and 3 of the study subjects were tested by means of the same technique but different odors, while in experiments 1 and 2 they were tested with the same odorant but different techniques. In case the same subjects were tested with the two techniques, odor pens and bottles, testing sessions were separated by an interval of one to seven days.

In the single staircase method, subjects are required, on a given trial, to report which of three stimuli, the odorant plus 2 blanks, is different. Sixteen dilutions were prepared in a geometric series starting from 4% butanol dissolved in distilled water, or 4% phenyl ethyl alcohol dissolved in propylene glycol, respectively. Three pens were presented in a randomized order, with two containing the solvent and the third the odorant at a certain dilution. The subject's task was to identify the odor-containing pen. Triplets were presented at intervals of 20 s. Testing started out at the lowest concentration available. Concentrations were increased until correct detection occurred on two consecutive trials. If an incorrect response was given on any trial, the staircase was moved upward one concentration step. If a correct response was given, the staircase was reversed and subsequently moved downward. Threshold was defined as the mean of the last four out of seven staircase reversal points. The subjects' scores range between 0 and 16. Throughout testing subjects received no feedback as to the accuracy of their responses.

*Statistical analyses*

Results were analyzed by means of SPSS 10.0 for Windows using MANOVAs (multivariate analyses of variance, repeated measurements design; between-subject factor "experiment", within-subject factors "side tested"; Greenhouse-Geisser correction of degrees of freedom; post hoc testing using Bonferroni-tests) and t-tests for paired samples. In addition, correlations (Pearson) were computed between the variables of interest. The alpha level was set at 0.05. To avoid inflation of the alpha level for correlational analyses it was lowered to 0.01.

## RESULTS

Descriptive statistics of results obtained for threshold testing are presented in Table 2.

*Best nostril vs. both nostrils:*

When comparing results obtained for dirhinal odor presentation to results obtained for the best of the two nostrils, no significant difference was found (factor "side tested": $F[1,95] = 0.27$, $p = 0.60$) (Figure 1). While different thresholds resulted from the use of the different techniques (factor "experiment": $F[2,95] = 4.13$, $p = 0.019$) there was no significant interaction between factors "experiment" and "side tested" ($F[2,95] = 0.71$, $p = 0.50$). Coefficients of correlations between best and both nostrils ranged between 0.57 and 0.91 (Experiment 1: $r = 0.70$, $p<0.001$; Experiment 2: $r = 0.57$, $p = 0.001$; Experiment 3: $r = 0.91$, $p<0.001$).

Table 2. Descriptive statistics (M: means, SD: standard deviation) of the results obtained in the 3 experiments.

| | | Experiment 1 | Experiment 2 | Experiment 3 |
|---|---|---|---|---|
| | odorant | Butanol | Butanol | PEA |
| | technique | bottles | odor pens | odor pens |
| Left nostril | M | 9.37 | 7.62 | 8.38 |
| | SD | 2.48 | 2.04 | 2.86 |
| Right nostril | M | 9.35 | 7.55 | 8.38 |
| | SD | 2.73 | 1.98 | 3.28 |
| Both nostrils | M | 10.35 | 8.70 | 9.42 |
| | SD | 2.90 | 1.69 | 3.00 |
| Best nostril | M | 10.55 | 8.53 | 9.11 |
| | SD | 2.83 | 1.99 | 3.04 |

*Left vs. right nostril:*

No difference was found between left and right nostrils (factor "side tested": $F[1,95] = 0.01$, $p = 0.91$). Again, different thresholds resulted from the use of the different techniques (factor "experiment": $F[2,95] = 4.40$, $p = 0.015$) (Figure 2). However, there was no significant interaction between factors "experiment" and "side tested" ($F[2,95] = 0.01$, $p = 0.99$). The correlation coefficients between results obtained for the left and right nostrils ranged between 0.23 and 0.81 (Experiment 1: $r = 0.27$, $p = 0.14$; Experiment 2: $r = 0.23$, $p = 0.21$; Experiment 3: $r = 0.81$, $p<0.001$).

*Effects of repeated testing:*

When comparing results of repeated testing of both nostrils in experiment 3, sensitivity was found to be increased during the second test (1st test: $M = 8.15$, $SEM = 0.60$; 2nd test: $M = 9.24$, $SEM = 0.59$; $t = 3.12$, $df = 29$, $p = 0.004$).

*Correlations between lateralized thresholds and measures of nasal patency:*

No significant correlations were obtained between lateralized threshold measures and parameters of acoustic rhinometry (MCSA: $r<0.15$, $p>0.43$; volume of the anterior nasal cavity: $r<0.38$, $p>0.03$) or anterior rhinomanometry ($r<0.32$, $p>0.06$), respectively. This is not unexpected as, clinically, the correlation between olfactory function and nasal patency is low.

## DISCUSSION

The major finding of this study was that the relative contribution of each nostril to dirhinal detection thresholds does not differ significantly regardless of the method of stimulation ("Sniffin' Sticks" or sniff bottles) or the odorant used (PEA or n-butanol). Mean thresholds for both nostrils together did not differ from that of the more sensitive nostril, i.e., no summation was observed. In addition, there were no significant differences between the left and right nostrils. These findings support previous studies such as the one by Betchen and Doty (1998) who

compared PEA thresholds using sniff bottles. Similarly, Klimek et al. (1998) investigated detection thresholds for n-butanol in 63 patients suffering from chronic sinusitis; they also saw no significant differences between the dirhinal results and the results obtained for the better nostril. However, the present results are in contrast with some previous work (Youngentob et al., 1982; Cain and Gent, 1991; Frye et al., 1992).

Lateralized effects are known for suprathreshold measures of olfactory performance: Bromley and Doty (1995) and Cain (1977) found considerable bilateral additivity of intensity, i.e., perceived intensity was greater dirhinally than for either side of the nose. Similarly, von Skramlik (1926) described an effect of summation for different odorants, finding that an odorant administered to both nostrils seemed to be stronger than when it was administrated to only one side. Odor recognition memory has been shown to be facilitated by presenting odors to both nostrils suggesting central summative integration (Bromley and Doty, 1995). While these results indicate a benefit of birhinal stimulation for suprathreshold stimuli, they also involve a greater degree of cortical involvement than, relatively simple, threshold judgements and hence more linguistic mediation and higher level perceptual and cognitive processing (which itself may be lateralised). In addition, suprathreshold stimulation may lead to the involvement of the trigeminal system (Hummel et al., 1992) which exhibits strong bilateral additivity itself (Medina and Cain, 1982). Thus, it is difficult to compare suprathreshold results with those of this study.

No significant correlation could be found between threshold testing and measurements of the nasal patency. This fact might be explained by the findings of Sobel et al. (2000) who explored the relation between nasal patency, nasal airflow, and odor detection threshold. When examining thresholds for the nostril with the lower flow-rate, subjects sniffed significantly longer and obtained similar thresholds compared to measurements of the high flow-rate nostril. When sniff duration was restricted to the same value for both nostrils the high air flow-rate nostril showed a significant advantage in threshold measurement compared to the low flow-rate nostril. Thus, it appears to be difficult to address the effect of airflow on the olfactory detection threshold without the simultaneous measurement of airflow and threshold (compare Youngentob et al., 1986).

The low number of left handers (handedness scores<-9: n=2) prevented an analysis of the influence of handedness on threshold data, but also lead to them having a small impact on the data. Some studies show different results, however. Frye et al. (1992) described that in 75 subjects the left nostril exhibited a slightly lower average threshold for n-butanone than the right. Left handed females were more sensitive than right handers in the left nostril, the opposite relationship occurred for males. Cain and Gent (1991) found in 33 subjects a 25% lower threshold for the right nostril than the left for four different odors, independently from the handedness of the subject. Youngentob et al. (1982) found that, while left handers had greater sensitivity in the left side of the nose, right handers showed a weak tendency toward greater sensitivity of the right nostril. In contrast, other studies have shown no significant influence of handedness at threshold level (Hummel et al., 1998).

The absence of a difference between the threshold of the "best" nostril and that of both nostrils suggests an interaction between the two sides of the nose in the form of suppression of the less sensitive side, as has been proposed by Cain (1977) following suprathreshold measurements. In fact, 10% of cells in the rat piriform cortex appear to respond only to bilateral stimulation, indicating that neural interaction does occur

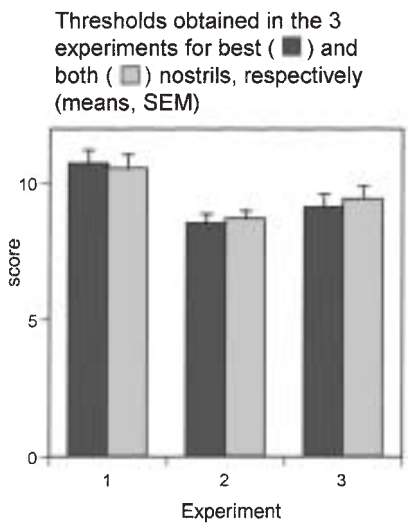


Figure 1. Comparison between threshold scores (means, SEM) of both nostrils (dirhinal testing) and best nostril (monorhinal testing). No significant differences were found.

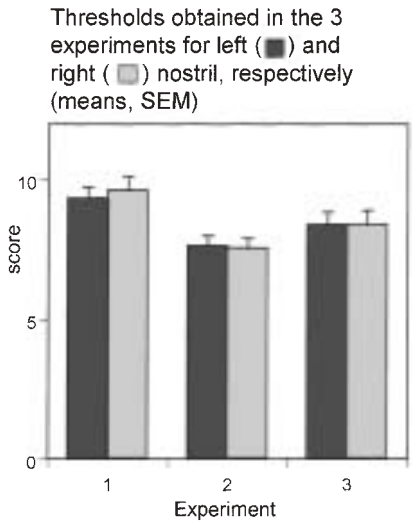


Figure 2. Comparison between monorhinal threshold scores (means, SEM), for left and right nostril. No significant differences were found.

(Wilson, 1997). Suppression may enhance the efficiency of processing by reducing or eliminating interference from the input of competing information, as has been suggested to occur between the cerebral hemispheres, for example, where right hemisphere output may be suppressed during linguistic tasks (e.g., Springer and Deutsch, 1998).

The similarity of the results obtained for the two presently used odors suggests that it is possible to generalize these results to a wider range of odor stimuli. It also seems to confirm that trigeminal activity observed at suprathreshold concentrations does not facilitate stimulus additivity or differences in nostril sensitivity at odor threshold levels. This was not unexpected as trigeminal thresholds have been shown to be above those for odor (Hummel et al., 1992).

In experiment 3 dirhinal threshold measurements were taken twice, making it possible to look at the influence of training. As shown previously (e.g., Engen and Bosack, 1969; Cain and Gent, 1991), retesting resulted in a significant improvement in test scores. In fact, Shimomura and Motokizawa (1995) found that both thresholds and the degree of lateralization decreased and became less variable with time. Cain and colleagues suggested that this is a learning effect, that transfers to other odors not used for testing, resulting from enhanced perceptual discrimination of features indicating the presence of an odor (Rabin and Cain, 1986; Cain and Gent, 1991). This effect needs to be carefully considered in cases where repetitive determination of thresholds is required, e.g., when investigating drug effects on olfactory sensitivity (Hummel and Kobal, 1992; Lötsch et al., 2001). These situations may require either use of experienced participants, or the training of inexperienced participants.

In conclusion, using two odorants with two different techniques of administration in studies performed at different sites, the present results indicated that there is no major difference between odor detection thresholds obtained for the best and both nostrils.

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