Localization of Odors Can Be Learned

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Abstract

Chemicals selectively stimulating the olfactory nerve typically cannot be localized in a lateralization task. Purpose of this study was to investigate whether the ability of subjects to localize an olfactory stimulus delivered passively to 1 of the 2 nostrils would improve under training. Fifty-two young, normosmic women divided in 2 groups participated. One group performed olfactory lateralization training, whereas the other group performed cognitive tasks. Results showed that only subjects performing lateralization training significantly improved in their ability to lateralize olfactory stimuli compared with subjects who did not undergo such training.

Key words: directional smelling, lateralization, olfaction, olfactory training, smell, trigeminal system

Introduction

In vision and audition, the pair of receptor organs is crucial for spatial orientation and localization of stimuli in the 3-dimensional environment. Whether the pair of receptor organs in olfaction fulfils the same function of localizing odor sources is not yet clear. Von Békésy suggested this be the case when sniffing is involved and proposed internostril odor concentration and timing differences as possible explaining mechanisms (von Békésy 1964). Usage of stereo cues to localize odors in space has been demonstrated in rats (Rajan et al. 2006). It seems that the ability to localize odor sources in humans depends on whether the chemical is "pure" olfactory or mixed olfactory trigeminal. The odorant delivery method to the olfactory cleft (passive application of the chemical into the nostrils or active sniffing in the outer space) also appears to play a role. It is widely accepted that mixed trigeminal-olfactory chemicals can be accurately localized when applied passively to 1 of the nostrils (von Skramlik 1924; von Békésy 1964; Schneider and Schmidt 1967; Lambooij et al. 1999; Hummel et al. 2003; Wysocki et al. 2003; Frasnelli et al. 2011). Moreover, the degree of trigeminal stimulation of an odorant has been associated with the accuracy of odor localization (Frasnelli and Hummel 2005; Frasnelli et al. 2011). Relatively selective odorants seem hard or impossible to localize (von Skramlik 1924; Lambooij et al. 1999; Frasnelli et al. 2011) in a passive stimulation procedure. Actively sniffing relatively selective odorants, however, appears to improve the localization ability (Schneider and Schmidt 1967; de Kock et al. 2001; Wysocki et al. 2003; Porter et al. 2007). The authors related the findings to sniffing, which has been shown to enhance olfactory performance at different levels (Sobel et al. 1998; Sobel et al. 2000; Mainland and Sobel 2006).

Also olfactory training has been shown to influence olfactory function (e.g., olfactory thresholds (Hummel et al. 2009), odor intensity, olfactory event-related potentials (OERPs) (Livermore and Hummel 2004), scent tracking (Porter et al. 2007)), with different mechanisms being proposed to explain this influence, both at peripheral and central nervous levels. We followed the question whether training could improve the ability to localize an olfactory stimulus. Partially for technical

reasons we chose to first focus on odor localization independent of sniffing, which is following a passive application of the odorant to 1 of the nostrils. One study briefly addressed the question of the olfactory lateralization ability of passively applied olfactory stimuli after a short training paradigm directed to this purpose (Wysocki et al. 2003) without finding a significant improvement. In order to address some of the limitations of the previous study, we investigated a significant number of young women, tested 2 odorants (hydrogen sulfide, H_2S, and phenylethyl alcohol, PEA), added a control group, and developed an intensive training paradigm over a period of 10–20 days. H_2S, the smell of rotten eggs, is believed to be a highly selective olfactory chemical (Kobal G, 1998), whereas PEA has long been used as a chemical stimulating predominantly the olfactory nerve starting with the study of Doty et al. (1978) where only 1 in 15 anosmic subjects could detect it. Results of most of studies employing PEA in a lateralization task support this observation, in that subjects were not able to correctly identify the stimulated nostril or the direction of stimulation in an active task (Radil and Wysocki 1998; Wysocki et al. 2003; Frasnelli et al. 2009; Frasnelli et al. 2010). There are, however, reports stating the contrary (Kobal and Hummel 1992; Porter et al. 2005).

Overall the purpose of this study was to investigate whether the ability to localize a relatively selective olfactory stimulus delivered passively to 1 of the nostrils can be trained. We hypothesized that before training subjects would not be able to distinguish the stimulated nostril above chance level and that this would remain constant for the control group.

Material and methods

The study was performed according to the "Declaration of Helsinki on Biomedical Studies involving Human Subjects" and approved by the Ethics Committee of the University of Dresden Medical School (EK41022009).

Fifty-two healthy, normosmic women participated in 6/7 sessions. A schematic representation of the setup can be found in Figure 1. Two groups were created: 27 subjects (mean age, 23.22 years; standard deviation [SD], 3.01 years) followed an olfactory lateralization training protocol (smell training group—ST), whereas 25 (mean age, 23.44 years; SD, 3.59 years) followed a "brain jogging" training paradigm (brain jogging group—BJ). Aims and potential risks of the study were thoroughly explained to all subjects before written informed consent was obtained. Medical history, nasal endoscopy, and olfactory performance tests were performed to ascertain normosmia and to ensure absence of medical and rhinological pathology that could interfere with olfactory function. Two evaluation sessions were performed before and after the training procedure. These sessions included a lateralization test with PEA (40% v/v concentration) and H_2S (4 p.p.m.) using an air dilution olfactometer (OM6b: Burghart). A total number of 20 stimuli of 250 ms duration were applied within a continuous air stream to each nostril. The interstimulus interval was 30 s on average. Testing was performed separately for PEA and H_2S, and the order of stimulation was randomized across subjects. Subjects were additionally asked to rate the pleasantness of the 4 stimuli at the beginning and at the end of the sessions. Intensity and lateralization ratings were collected after every stimulus using a continuous visual analogue scale (left-hand end: no smell/left nostril; right-hand end: extremely intensive/right nostril). Subjects were instructed to move the marker to the left or right end of the scale according to the perceived intensity of the stimulus and to their level of certainty on the stimulated nostril. For the consequent lateralization rating analysis, the interval from 0 to 40 was considered relevant for the "left side" stimulation, the interval between 60 and 100 as "right side" while the interval from 40 to 60 was considered "undecided." The range of the scale 50 ± 10 units was considered separately for statistical analyses in order to filter out responses where we assumed that the subjects were still not fully decided what to indicate. This was based on the clinical experience with visual analogue scales in the field of pain and the clinical interpretation of these ratings. In analogy to clinical studies where changes of 13% are considered significant (Todd et al. 1996; Gallagher et al. 2001; Gallagher et al. 2002), in this present investigation we regarded a change

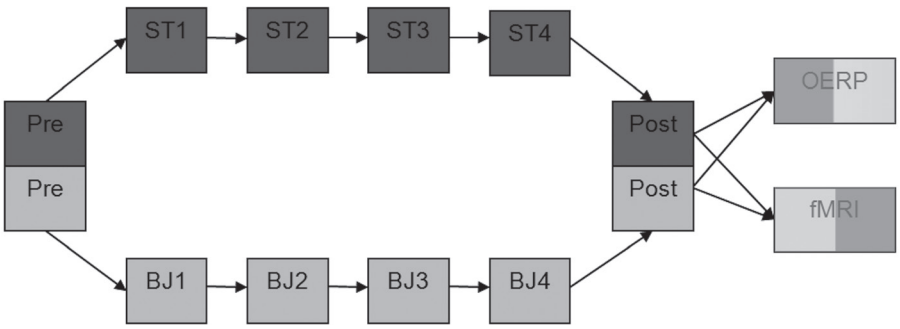

Figure 1 A schematic representation of the experimental setup: the ST and BJ groups are represented with dark and light gray, respectively; "pre" and "post" represent the pre- and post-training sessions, respectively; ST1-4 and BJ1-4 represent the 4 training sessions for the ST and BJ groups; the shaded final sessions (fMRI and OERP) are not subject of this present study.

of 10% of the entire scale from neutral as a meaningful difference. Lateralization scores were calculated for each category by summing up the number of correct, undecided, and incorrect answers, with a maximum score of 40. In order to assess whether subjects actually could lateralize the odorants, based on the chosen cutoff values of 40 and 60, we calculated the level of random performance or chance level (set at ca. 50% probability of a right answer), as well as the level when lateralization ability can be assumed, or certainty level (set at ca. 95% probability of a correct answer). Because equal probability of answers across the scale cannot be assumed, we first calculated the normal distribution of answers based on the pretraining ratings of all 52 subjects separately for PEA and H_2S. The probability of an answer between 40 and 60 was found to be 33% for PEA and 31.8% for H_2S, whereas the probability to give a correct answer (meaning either between 0 and 40 or between 60 and 100) was in average 33.5% for PEA and 34.1% for H_2S. Based on this, using binomial distribution, chance level was calculated at 13 points for both PEA (the probability to give a correct answer was 52% at this level) and H_2S (the probability to give a correct answer was 48.8% at this level). The same binominal distribution was used to calculate the number of right answers required for stating that the odor was detected with a certainty of ca. 95%. This was 18 points for both odorants, the probability for a correct answer being 95.3% for PEA and 94.5% for H_2S. At this cutoff level, lateralization ability can be assumed. Additional analysis was performed with the raw lateralization data (means of absolute ratings ranging from 0 to 100), as well as defining "left" with the interval 0–49, "undecided" with 50 uniquely, and "right" with the interval 51–100. All subjects completed an "olfactory interest questionnaire" (Croy et al. 2013) before and after the training.

Four training sessions were performed between the 2 evaluation sessions with an interval of 2 to a maximum of 4 days in between (ST, 1–4; BJ, 1–4; see Figure 1). Each session of the olfactory lateralization training protocol (ST, 1–4) comprised of 3 parts: in the first part, 10 PEA and 10 H_2S stimuli were presented to the subjects to the left and right nostril in a randomized order with subjects knowing the side of the stimulation. In the second part, a series of 6 stimuli per odorant was presented to each nostril in a randomized order without knowing the stimulated side. Subjects were then asked to decide upon the stimulated side (left or right) and received immediate feedback from the experimenter on the correctness of their evaluation. The third part consisted of a 2-choice evaluation test (left or right) with 10 stimuli of both odorants conceived to assess changes in the lateralization performance (number of correct-side identifications) during the 4 training sessions. The brain jogging protocol consisted of 2 tasks for each training session (BJ, 1–4): a calculation task evaluating the time in seconds necessary to perform 100 calculations (Nintendo) and a number binding test evaluating the time in seconds necessary to bind a series of randomly positioned numbers from 0 to 25 on a sheet of paper (Reitan 1958; Reitan and Wolfson 1993).

Within the setup of the final evaluation session, OERPs were recorded for 12 subjects of the olfactory training group and 13 subjects of the BJ group. The rest of the subjects from each group took part 2–4 days later to an functional magnetic resonance imaging (fMRI) session. Results of the electrophysiological and the fMRI sessions will be discussed elsewhere.

A series of control measures were designed to ensure that subjects used only olfactory cues to localize odors along the sessions. The left and right outputs of the olfactometer were interchanged across subjects within a session and from session to session for the same subject to level potential intensity or odor quality difference between the 2 lines of the olfactometer. The valve switching sounds from one side to the other during the evaluation sessions were masked by white noise applied through head phones.

Statistics

Data were analyzed using SPSS 15.0 software (SPSS Inc.). Independent sample *t*-tests were performed to assess the group differences in terms of age or olfactory interest score. Analyses of variance (ANOVAs) were performed to assess the performance level across the 4 training sessions (BJ, 1–4 and ST, 1–4) for the calculation or the number of binding task and for the lateralization score for BJ and ST subjects, respectively. Separate ANOVAs for PEA and H2S were performed for the intensity and hedonic ratings with "group" (BJ/ST) as between-subjects factor and "side" (left/right), "session" (pre-/post-training), and "session time" (begin/end), respectively, as within-subject factors. Further on lateralization scores were submitted to ANOVAS, adopting "training session" (pre-and post-training) and "answer" (correct/undecided/incorrect) as within-subject factors and "group" (ST/BJ) as between-subjects factor. Degrees of freedom were adjusted according to Greenhouse-Geisser. Significant main effects and interactions are indicated. The *t*-tests for independent samples with Bonferroni correction were used for additional comparisons between groups. Further on 1 sample *t*-test was used to compare the correct lateralization score to chance level. The level of significance was set at 0.05.

Results

Group description

The 2 groups were not different in terms of age ($T = 0.23$, $P = 0.81$) or olfactory interest score ($T = 0.05$, $P = 0.97$) as derived from the "olfactory interest questionnaire" (Croy et al. 2013). The time interval between the single training sessions did not differ between the 2 groups.

Lateralization ratings

An ANOVA 2*2*3 with "odor" (H_2S and PEA), "training session" (pre- and post-training), "answer" (correct, undecided, and incorrect) as within-subject factors and "training group" (BJ and ST) as between-subjects factor was conducted. The analysis revealed a significant effect of "answer" ($F[2;100] = 5.5$, $P < 0.05$) and an interaction "odor*answer" ($F[2;100] = 5.7$, $P < 0.01$), "answer*training session" ($F[2;100] = 8.0$, $P = 0.001$), and "answer*training session*group" ($F[2;100] = 9.1$, $P < 0.001$). The main effect of group missed statistical significance ($F = 4.0$; $P = 0.052$).

Additional paired *t*-tests with Bonferroni corrections showed no significant difference between the 2 sessions for either of the answers for the BJ group. For the ST group, significant differences between the training sessions were found for both odorants: the number of correct answers increased in the post-training session (PEA: $T_{26} = -3.0$, $P < 0.05$; H_2S: $T_{26} = -4.0$, $P < 0.001$, see Table 1), whereas the number of undecided answers decreased (PEA: $T_{26} = 4.27$, $P < 0.001$; H_2S: $T_{26} = 4.02$, $P < 0.001$). Thus, unlike the BJ subjects, ST subjects showed a significant improvement of their correct lateralization scores after training. Significant differences in terms of answers between the 2 groups were found in a one-way ANOVA with Bonferroni corrections only for the post-training session and only for the correct (PEA: $F[1,50] = 11.7$, $P = 0.001$; H_2S: $F[1,50] = 13.4$, $P = 0.001$; see Figure 2) and undecided answers (PEA: $F[1,50] = 13.9$, $P < 0.001$, H_2S: $F[1,50] = 5.6$, $P < 0.05$). Subjects that performed ST were significantly better in correctly identifying the stimulated side for both odorants compared with subjects who performed BJ.

No significant difference in performance level between the 2 nostrils was found for either of the 2 sessions. We tested also whether scores from each session differed from chance level. The correct lateralization scores of the "pretraining session" did not differ significantly from chance level for both H_2S (mean score for all 52 subjects = 14.57; SD = 6.56, $T_{51} = 1.73$, $P > 0.05$) and PEA (mean score = 13.38, SD = 5.47, $T_{51} = 0.5$, $P > 0.05$), meaning that subjects could not correctly identify the stimulated nostril. The correct lateralization scores from the "post-training session" were analyzed separately for the 2 groups (see Table 1). The BJ group scores for both odorants remained statistically not different from chance level. On the other hand, the scores for ST group were found to be significantly higher than chance level. Scores for both PEA and H_2S were higher than 18, the calculated certainty level, so that it can be assumed that subjects, in average, could correctly lateralize the odorants. Moreover, the mean score for H_2S was even significantly higher than certainty level ($T_{26} = 4.14$, $P < 0.05$)

Intensity and hedonic ratings

Neither a significant main effect nor an interaction was found for intensity ratings between the 2 groups or between sessions, neither for H_2S nor for PEA (see Figure 3). In terms of hedonic ratings, only an interaction session*group in case of H_2S was found to be significant ($F = 11.8$, $P = 0.001$). Post hoc analysis revealed that ST subjects rated H_2S significantly more pleasant in the post-training session, whereas BJ subjects rated H_2S as more unpleasant (see Figure 4).

No difference between the 2 groups was seen after training in terms of "olfactory interest score."

Training protocol (ST 1–4 and BJ 1–4)

For the BJ group, the results for both tests showed a significant improvement in performance level across the 4 training sessions (calculation task: $F[3;72] = 11.1$,

Table 1 Correct lateralization scores and SD values for PEA and H_2S for the pre- and post-training sessions for each group (BJ: $N = 25$; ST: $N = 27$)

Odor	Group	Session	Lateralization score	SD	One sample *t*-test (test value = 13)		Paired *t*-test	
					T	*P*	*T*	*P*
PEA	BJ	Pre	12.68	3.56		ns		ns
		Post	13.04	5.30		ns		
	ST	Pre	14.04	6.80		ns	−3	<0.05
		Post	18.59	6.30	4.62	<0.001		
H_2S	BJ	Pre	15.40	6.28		ns		ns
		Post	13.96	7.34		ns		
	ST	Pre	13.81	6.86		ns	−4	<0.001
		Post	21.37	7.25	6	<0.001		

Results of 1 sample *t*-test for comparisons with chance level (test value = 13, only significant results are shown); results of paired *t*-tests with Bonferroni corrections between pre- and post-training sessions for each groups and odorant (only significant results are shown).
ns, not significant.

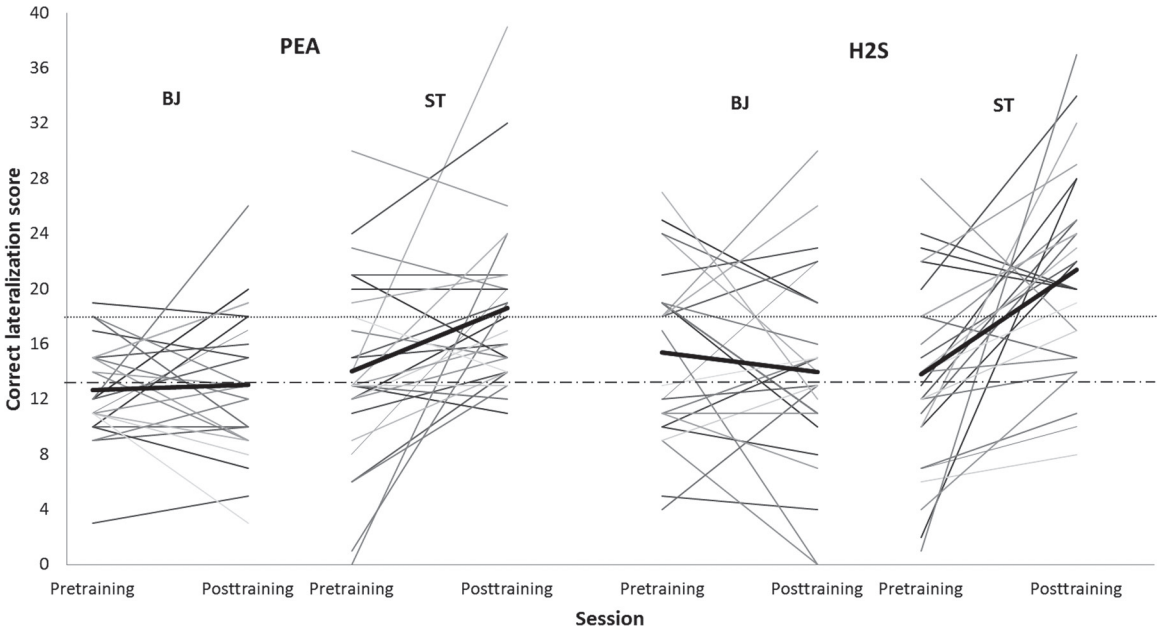

Figure 2 Individual correct lateralization scores of the entire set of subjects (thin gray level lines) under the 2 types of training (BJ and ST), as well as averaged responses (thick black lines) before and after training for both odorants (PEA—left and H_2S—right); chance level is marked at 13 through the mixed interrupted line, whereas certainty level is marked at 18 through the fine interrupted line.

$P < 0.001$ from 265.9 ± 85.4 s to 203.4 ± 62.5 s; number binding test: $F[3;72] = 35.7$, $P < 0.001$ from 36.4 ± 11.0 s to 22.8 ± 6.4 s).

Also for the ST group, the number of correct-side identifications increased across the 4 sessions (PEA: from 4.89 ± 1.58 to 6.06 ± 2.14; H_2S: from 6.41 ± 1.46 to 7.71 ± 1.69). An ANOVA with "odorant" (PEA, H_2S) and "sessions" (1–4) revealed a significant effect of sessions ($F[3;48] = 3.3$; $P < 0.05$) and of odor ($F[1;16] = 11.8$; $P < 0.01$).

Lateralization ratings—additional analysis

An alternative way of analyzing the lateralization results is by looking at the raw data (see Table 2). The mean responses range from 44.12 ± 12.1 to 52.34 ± 9.77 for the pretraining session and from 41.43 ± 14.14 to 59.17 ± 13.8 for the posttraining session. The *t*-tests were performed against a 0 hypothesis of a response of 50. Before training, a significant difference was seen only for the ST group for PEA left. After training, no significant difference was seen for the BJ group.

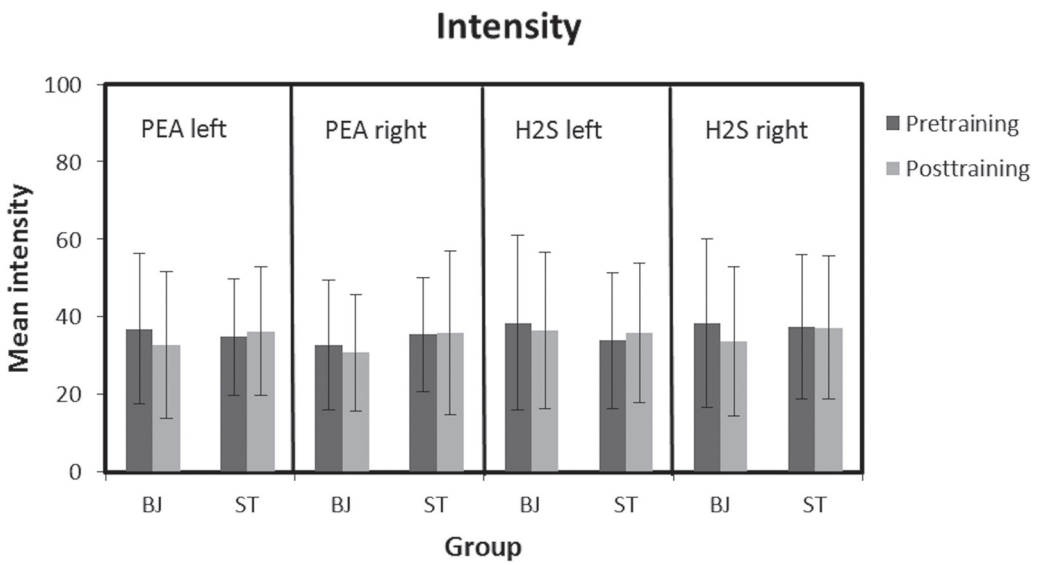

Figure 3 Intensity ratings with SD bars for PEA and H_2S for both groups and sessions.

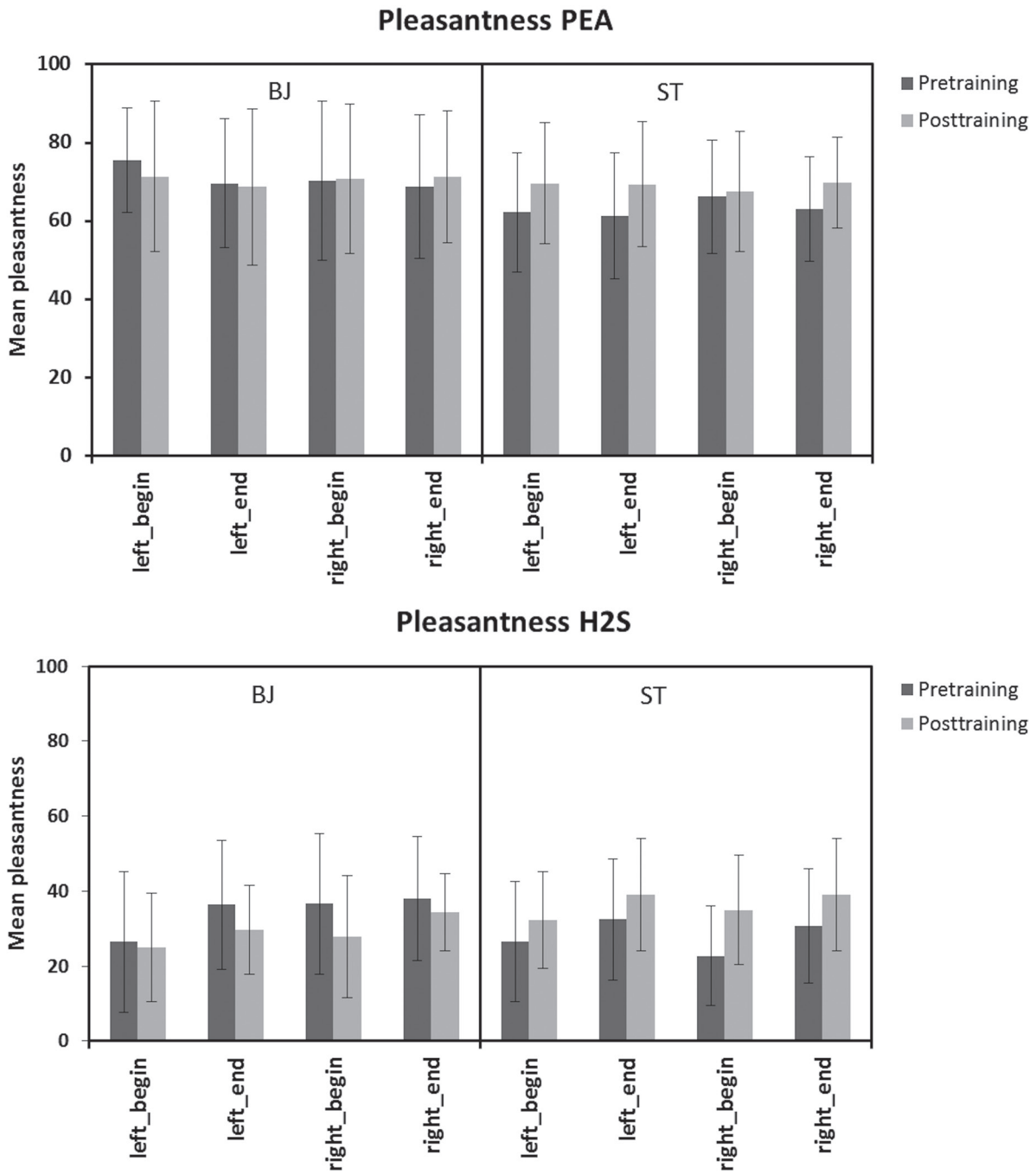

Figure 4 Pleasantness ratings with SD bars for PEA and H_2S for both groups for each session (pre- and post-training) before and after each session.

The ST group showed significant differences for H_2S for both sides, meaning significantly below 50 for the left side and above 50 for the right side. In the case of PEA, only a tendency for an improvement for the right-sided stimulation was shown. Further on, a one-way ANOVA for the lateralization scores of each odor and each side showed no significant differences between groups neither for the pre- or the post-training sessions. Paired *t*-tests were used to investigate the difference between sessions. No significant results were seen for the BJ group; for the ST group, only a significant difference was seen for H_2S left ($T_{27} = 2.56$, $P = 0.016$), and for H_2S right ($T_{27} = -1.96$, $P = 0.6$) and PEA right ($T_{27} = -1.79$, $P = 0.86$), only a trend toward lateralization was found. When applying Bonferroni corrections, no significant differences were found.

We also conducted an analysis where the interval 0–49 was considered correct for left side identification, 51–100 for the right side and 50 as undecided. A separate ANOVA with "session" (pre- and post-training), "answer" (correct, undecided, incorrect) as within-subject factors and "group" (smell training and brain jogging) as between-subjects factor

Table 2 Lateralization score as calculated with the raw data and SD values for PEA and H_2S for each nostril separately for the pre- and post-training sessions for each group

Session	Odor	Side	Group	*N*	Lateralization score	SD	One sample *t*-test (test value = 50)	
							T	*P*
Pre	PEA	Left	BJ	25	48.04	11.85	ns	ns
			ST	27	44.12	12.10	–2.54	0.018
		Right	BJ	25	47.87	11.91	ns	ns
			ST	27	49.45	13.09	ns	ns
	H_2S	Left	BJ	25	45.64	11.76	ns	ns
			ST	27	50.10	12.44	ns	ns
		Right	BJ	24	52.18	12.54	ns	ns
			ST	27	52.34	9.77	ns	ns
Post	PEA	Left	BJ	24	49.49	12.65	ns	ns
			ST	27	47.46	15.16	ns	ns
		Right	BJ	24	49.42	13.81	ns	ns
			ST	27	55.36	13.73	2.03	0.53
	H_2S	Left	BJ	22	46.57	18.54	ns	ns
			ST	27	41.43	14.14	–3.14	0.004
		Right	BJ	22	54.12	15.38	ns	ns
			ST	27	59.17	13.80	3.45	0.002

Results of 1 sample *t*-test for comparisons with a test value of 50.
ns, not significant.

was conducted for the 2 odorants. No hypothesized effects or interactions were found with this approach.

Discussion

The main findings of this study were 1) olfactory stimuli delivered passively to 1 of the nostrils cannot be correctly lateralized by most of untrained subjects; 2) the ability to correctly identify the stimulated nostril can be trained.

The findings of the pretraining session are in line with previous studies showing that an olfactory stimulus delivered passively to 1 of the nostrils cannot be correctly lateralized. In line with the concept that a lateralization task can help to identify the chemicals that stimulate the trigeminal nerve, the results of the pretraining session may be interpreted as proof that PEA and H_2S, under the concentration, stimulus duration and volume used (Cometto-Muniz and Cain 1998; Frasnelli et al. 2011), are relatively selective olfactory stimulants. Importantly, in the final session the lateralization scores remained constant for the BJ subjects. This was also an important premise for the purpose of this present study, that is, to test the influence of training on the lateralization ability of pure olfactory stimuli applied passively to the nose.

A training effect was found for both odorants, more pronounced for H_2S. That is, subjects who performed a lateralization training showed a significantly better ability to lateralize passively applied intranasal olfactory stimuli, and this could be reproduced for 2 different olfactory chemicals. The duration of this effect or the transfer to the lateralization of other than the trained odors remains to be investigated in further studies. This finding seems to be supported by previous reports. Short, regular exposure to an odorant has already been shown to increase the olfactory sensitivity in healthy subjects (Dalton et al. 2002) and in patients with olfactory loss (Gitcho et al. 2009). In addition, scent tracking has been shown to improve after training (Porter et al. 2007). Moreover, odor localization benefits substantially from the simultaneous bilateral input of the 2 nostrils that seem to sample distinct non-overlapping spatial regions (Porter et al. 2005; Rajan et al. 2006).

Contrasting data come from Wysocki et al. (2003) who showed no significant effect of lateralization training. A lateralization task with PEA was performed in 10 subjects in the same session before and after a lateralization training involving 50 trials with foreknowledge of the side of stimulation. Subjects failed to identify the correct side after training. In a second experiment in 5 subjects, no learning effect was shown along a course of 100 lateralization trials without foreknowledge of the stimulated side but with immediate feedback concerning the correct response. Authors concluded that

the ability to lateralize olfactory stimuli cannot be trained. However, some differences between this and the present study need to be discussed. First, a much larger number of subjects took part in this present study. Because sex differences in response to repeated odor exposure have been previously described (Dalton et al. 2002), we only included women. Further on, an intensive training over a period of 10–20 days, with 2–4 days interval between the single training sessions, was employed in this present study. Both training methods (with foreknowledge and without foreknowledge but with feedback) were used in each training session and a short evaluation trial consisting of 10 odor presentations to assess the performance across the training. Subjects got better in identifying the stimulated nostril across the training sessions, and this was reflected also in the post-training lateralization task. Duration of training seems, therefore, to play an important role in the development of odor lateralization ability. In addition, the rating technique also could account for the noted differences. In our study, the lateralization of odors was graded using the visual analogue scale indicating the side of stimulation, whereas in the study of Wysocki et al. (2003), a dual-forced-choice paradigm was used. We could observe consistent dynamics of decision making for both odorants in that the number of correct-side identifications increased while the answers marked as "undecided" decreased for the ST subjects, whereas for BJ subjects no difference in terms of answer was registered between the 2 sessions. The number of incorrect answers remained the same between the 2 sessions for both groups. It could be argued that training led to shifting the undecided group of subjects toward making a decision. But the shift of decision making was directed toward the correct-side identification and not randomly distributed toward either of the 2 side choices. Therefore, we interpret this as a proof of a better ability to localize the odor stimuli acquired after the performed training.

The exact mechanism behind a better lateralization ability acquired with training remains to be clarified. A previously described increase in sensitivity after repeated exposure to an olfactory stimulus (Frasnelli et al. 2002; Shimomura and Motokizawa 1995) with animal studies providing data for an increased responsiveness at the level of the olfactory epithelium (Youngentob and Kent 1995; Hudson and Distel 1998) could be an explanation for the better odor lateralization found in this present study. One study showed that the repeated measurement of odor thresholds leads not only to an increase of sensitivity but also, over time, to a stabilization of the internostril threshold difference (Shimomura and Motokizawa 1995). Although thresholds have not been measured in this present study, it could be speculated that repeated exposure to the same olfactory stimuli leads to an increase in sensitivity and a decrease in variability of the internostril threshold difference. Consequently, this would allow subjects to focus on other perceptual cues indicating the presence of an odor. A follow-up study has already been designed to address this question.

It is known that almost all chemicals produce a trigeminal activation (Doty et al. 1978), at least from a certain concentration. If we accept that the internostril localization ability of the chemical reflects its trigeminality in untrained subjects, we could say that the lateralization threshold approximates the trigeminal threshold of that chemical (Wysocki et al. 2003). Knowing the interaction between the trigeminal and the olfactory systems, with the olfactory threshold of a chemical typically being lower than the trigeminal one (Livermore and Hummel 2004), it might be that lateralization training actually lowered the trigeminal threshold of the chemical possibly as a consequence of a specific increase in trigeminal sensitivity (compare Dalton and Hummel 2000).

Mainland et al. (2002) showed that training 1 nostril to detect androstenone results in both nostrils recognizing the odorant with comparable performances. Central olfactory learning processes were implied possibly related to pattern recognition at the level of the primary olfactory cortex (that receives information from both nostrils; Mainland et al. 2002). Nostril-specific responses at the level of the primary olfactory cortex and at the level of superior temporal gyrus were described using fMRI in a recent study (Porter et al. 2005). Results from animal studies show that repeatedly reinforced odor presentations enhance the representation of that odorant in a stable EEG amplitude pattern emerging over the surface of the olfactory bulb (Grajski and Freeman 1989). Concerning the results of this present study, one could speculate that the training-induced reinforcement of the nostril-specific activation patterns is responsible for the better stimulus localization ability.

No significant difference in performance level between the 2 nostrils was found. A predominance of the right nostril in olfaction has been described in previous studies, for example, in odor discrimination performance (Zatorre and Jones-Gotman 1990, 1991) or intensity ratings (Thuerauf et al. 2008). This idea seems to be supported by fMRI studies showing larger ipsilateral activations in the right hemisphere (Savic et al. 2000). Even a right-sided supremacy in lateralization ability was demonstrated, findings being related to the right hemisphere specialization of processing spatial information (Mesulam 2000) that seems to lead to a right-sided response bias, well described in other sensory systems (see de Kock et al. 2001). It has to be kept in mind that a continuous analogue scale was used in our study for the lateralization ratings. Therefore, subjects were free to assess their level of certainty as opposed to a forced choice procedure. This might account for the lack of the previously described tendency for a rightward lateralization.

Chance-level performances were registered in the pre-training session and consistently for the BJ group in the post-training session. Previous studies described subjects performing even below chance level for relatively selective odorants (Schneider and Schmidt 1967; Lambooij et al. 1999) and particularly for PEA (de Kock et al. 2001). We could not reproduce this in this present study although this

phenomenon has also been repeatedly reported in our laboratory. It should be noted that comparisons to chance level for results of individual nostrils could not be performed due to the complexity of the design by using a visual analogue scale. The reason for a below chance-level performance in lateralizing certain relatively selective odorants remains unclear. Only the correct lateralization scores of the ST group after training were significantly higher than chance level. Moreover, they were higher than the calculated certainty level, with H_2S scores being even significantly higher. This would mean that not only did the ST group improve but actually subjects could lateralize the odorants.

Odor intensity was not significantly different between the 2 odors, sides of stimulation, or between training sessions for either of the 2 odorants. Consequently, the results of previous studies stating a right-sided lateralization of olfactory sensitivity could not be reproduced in this study; neither could be shown that intensity is a sensitive parameter in odor lateralization, as previously implied (Thuerauf et al. 2008). Also the hedonic ratings were the same for the left and right nostrils for both odorants. Therefore, neither of hedonic properties seems to have an impact on odor lateralization. This finding is in agreement with previous studies (Thuerauf et al. 2008). Other studies report the right nostril to be more sensitive for pleasant odorants (Herz et al. 1999; Dijksterhuis et al. 2002).

Exposure to the intensive olfactory training over a period of 2–3 weeks does not seem to have an impact on the reported importance of odors in the daily life. One possible explanation might be that the impact of odors on daily life is not defined through the frequency of exposure, but that other factors play a role. Among those the individual verbal and memory abilities could influence the level of impact of odors on daily life through the integrative processing of smell, speech, and memory in temporo-limbical brain areas (Westervelt et al. 2005).

In summary, our results confirm that olfactory stimuli cannot be localized when passively applied to 1 of the nostrils. The main finding of this study was that the ability to localize intranasally applied olfactory stimuli can be trained, as a further proof of the plasticity of the olfactory system.

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