Chem. Senses 34: 523–527, 2009 doi:10.1093/chemse/bjp029

Comparison between Odor Thresholds for Phenyl Ethyl Alcohol and Butanol

Ilona Croy, Kornelia Lange, Franziska Krone, Simona Negoias, Han-Seok Seo and Thomas Hummel

Department of Otorhinolaryngology, Smell and Taste Clinic, University of Dresden Medical School, Fetscherstrasse 74, 01307 Dresden, Germany

Correspondence to be sent to: Ilona Croy, Department of Otorhinolaryngology, Smell and Taste Clinic, University of Dresden Medical School ("Technische Universität Dresden"), Fetscherstrasse 74, 01307 Dresden, Germany. e-mail: ilona.croy@mailbox.tu-dresden.de

Abstract

Aim of the study was to compare results of odor threshold test using different numbers of dilution steps, separately for butanol and phenyl ethyl alcohol (PEA). Methods: A total of 116 subjects participated (29 patients with olfactory dysfunction and 87 normosmic subjects). The olfactory threshold for butanol and PEA was examined with 8 (wide step method) and 16 (narrow step method) dilutions. With a delay of about 1 week, all 4 tests were repeated. Results: Test time was shortened by approximately 2 min (25%) for patients when using the wide step method. Butanol and PEA thresholds were not significantly different; in addition, a significant correlation was found between thresholds for the 2 odors ($r = 0.60$, $P < 0.001$). Threshold test with both odorants as well as with wide or narrow step method provided satisfying reproducibility (test–retest reliability: $r = 0.80$–0.84, $P < 0.001$). Patients with olfactory dysfunction could be clearly separated from normosmic subjects using all 4 different tests. Discussion: The results indicate that threshold testing with PEA is an alternative to butanol. The wide step method provided similar results as the narrow step method but required less time.

Key words: olfactory testing, psychophysics, smell

Introduction

Olfactory function can be tested using psychophysiological, electrophysiological, or imaging techniques. In clinical praxis, the University of Pennsylvania Smell Identification test (Doty et al. 1984), the Conneticut Chemosensory Clinical Research Center test (Cain et al. 1988), and the "Sniffin' Sticks" test (Hummel et al. 1997) are the most commonly used psychophysiological tests for comprehensive assessment of olfactory function. The Sniffin' Sticks test consists of 3 subtests, measuring olfactory threshold, discrimination, and identification ability and is used by many clinicians all across Europe (Hüttenbrink 1997). Whereas the threshold test is assumed to reflect mainly peripheral olfactory processes, the discrimination and the identification tasks seem to be more related to higher order cognitive processing, largely involving various memory functions (Landis et al. 2005). This test proved to have a good reliability and a good validity for the detection of olfactory dysfunction (Hummel et al. 1997; Lötsch et al. 2008). The regular Sniffin' Sticks threshold test is based on 16 dilution steps of butanol and takes about 7–15 min.

In this study, we planned to compare the results of the odor threshold test using just 8 dilution steps with the idea to make the test less time consuming. This could be an advantage especially for clinical practice and in patients with concentration deficits. Additionally, we wanted to compare results for the threshold test for the regularly used butanol with those obtained for phenyl ethyl alcohol (PEA)(Doty et al. 1986). Because PEA is often used as a standard in electrophysiological olfactory testing (Hummel and Kobal 2001) and in olfactory-based functional magnetic resonance tomography (Boyle et al. 2007), it would be of advantage to use the same odorant during each of the different types of measurements.

Materials and methods

A total of 116 subjects participated. The sample was divided into 29 patients with olfactory dysfunction (21 women, 8 men, mean age 55.5 years, range 28–72 years) and 87 normosmic controls (46 women, 41 men, mean age 41.6 years, range 19–74 years). The groups differed significantly in age ($P < 0.001$) and in tendency in sex distribution ($P = 0.065$), with the patient group being older and including more women. Olfactory dysfunction was mainly caused by upper

respiratory tract infections or sinunasal disease. For details regarding the sample, see Table 1.

In a first session, all subjects were tested for olfactory identification and discrimination abilities using the Sniffin' Sticks test. Additionally, a detailed history was taken regarding general healthy and olfactory function. In the next session, olfactory threshold was examined 4 times in each subject for butanol and PEA with 8 (wide step method) and 16 (narrow step method) dilutions, covering the same range of concentrations. The sequence of testing the 4 conditions was randomized across all participants in a balanced order. For analyzing the test–retest reliability of the tests, the 4 olfactory threshold tests were repeated in a third session. The test–retest interval was an average of 7.2 days (standard deviation 5.1). In the retest, all the 87 normosmic controls and 16 of the patients participated.

The measurement of odor threshold was performed using the Sniffin' Sticks. The pens have a length of approximately 14 cm with an inner diameter of 1.3 cm. The pens tampon is filled with 4 ml of a 4% odor solution; solvent for PEA was propylene glycol, and solvent for butanol was water. Further dilutions were established with a dilution ratio of 1:2. As explained, for the narrow step method, the 16 dilutions were prepared in a geometric series starting from a solution with 4% butanol or PEA, respectively. For the wide step method, every second step of the narrow step method was left out, so that 8 different dilutions remained.

For odor presentation, the pen's cap is removed by the experimenter for about 3 s and the pen's tip is placed approximately 2 cm in front of both nostrils. Odor thresholds were assessed using a single-staircase, 3-alternative forced-choice procedure (Ehrenstein W and Ehrenstein A 1999). Three pens were presented in a randomized order, with 2 containing the solvent and the third the odorant. Subjects had to identify the odor-containing pen. Triplets were presented at intervals of approximately 20 s. Reversal of the staircase toward lower concentrations was triggered either when the odor was correctly identified in 2 successive trials or toward higher concentrations when the odor was not recognized in 1 trial. Total number of reversals was 7; threshold was defined as the mean of the last 4 staircase reversals. There was no absolute number of correct responses required.

For measuring the needed time to perform the tests, we stopped the time during the test and additionally counted the required triplets until the threshold was reached.

Table 1 Demographic data for patient and normosmic subjects

	Patients		Normosmic subjects	
	Mean (SD)	Number (%)	Mean (SD)	Number (%)
Sex				
Women		21 (72.4%)		46 (52.9%)
Men		8 (27.6%)		41 (47.1%)
Sex difference between groups: $P = 0.065$ (Chi-square test)				
Age in years	55.5 (12.2)		41.6 (19.0)	
Age difference between groups: $P < 0.001$ (t-test)				
Cause of olfactory loss				
Idiopathic		6 (20.7%)		
Viral infection of upper respiratory tract		16 (55.2%)		
Sinunasal disease		6 (20.7%)		
Trauma		1 (3.4%)		

SD, standard deviation.

Statistical analysis

For threshold results and for the required time and triplets, we analyzed pairwise comparisons of the odor threshold methods using Bonferroni-adjusted t-tests. For comparison between groups, the between-subjects contrast for the 4 threshold tests were examined. To make sure that the difference in age and sex between groups did not confound the results in the analysis of variance for repeated measures, age was added as a covariate and sex as a between-subject factor. For retest reliability, the coefficient of correlation was calculated for test and retest for each method. Additionally, we computed retest reliability separately for patients and normosmic controls. Due to the small number of subjects in the patient group, we then additionally calculated the intraclass correlation coefficient.

Results

In the comparison of the threshold results between the 4 odor threshold tests, we found no significant differences, either for patients or for controls ($P > 0.21$, see Figure 1 and Tables 2 and 3).

With each of the 4 different methods, it was reliably possible to distinguish patients from normosmic controls ($P < 0.001$). Furthermore, we found high correlations between the narrow and the wide step method for butanol as well as for PEA ($r = 0.88$–0.90, $P < 0.001$, see Figure 2). The correlation between the odorants PEA and butanol appeared to be moderately high for the wide step method as well as for the narrow step method ($r = 0.60$–0.64, $P < 0.001$, see Figure 2).

Analyzing test–retest correlations, we found satisfying retest reliability for all the 4 threshold tests for the whole sample ($r = 0.80$–0.84, see Table 4), separately for patients ($r = 0.74$–0.88) and normosmic controls ($r = 0.78$–0.84).

In the comparison of the time needed to perform the tests, we found significant differences between the wide and the narrow step method. The wide step method required less triplets until getting the threshold and therefore was significantly less time consuming than the narrow step method (P

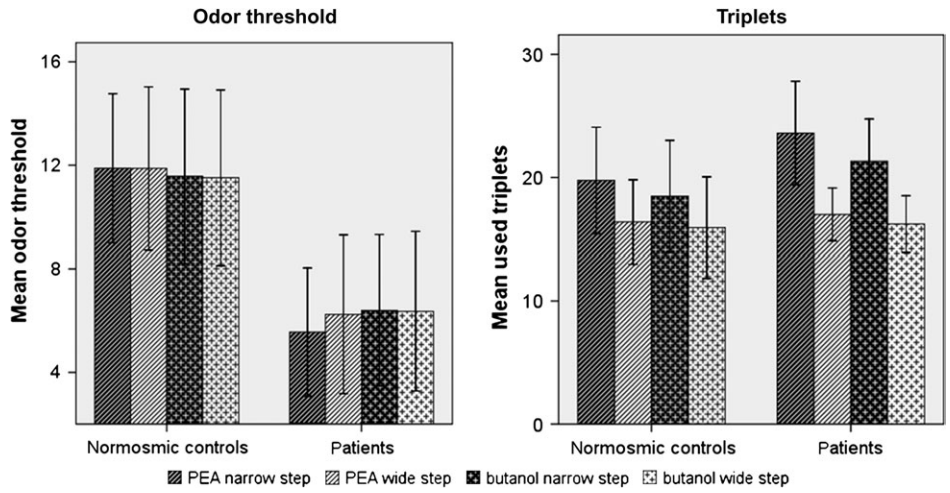

Figure 1 Comparison of the 4 tests according to odor threshold results and required triplets. Mean and standard deviations (error bars) are shown. Data are presented separately for patients (N = 29) and normosmic subjects (N = 87).

Table 2 Results, required triplets, and time of the threshold tests in normosmic subjects and patients

	Normosmic Subjects Mean (SD)	Patients Mean (SD)	Between-group comparison
Threshold results			
PEA narrow step	11.88 (2.88)	5.56 (2.48)	$P < 0.001$; $F = 89.96$**
PEA wide step	11.87 (3.16)	6.24 (3.07)	$P < 0.001$; $F = 47.98$**
Butanol narrow step	11.57 (3.37)	6.40 (2.93)	$P < 0.001$; $F = 39.27$**
Butanol wide step	11.52 (3.40)	6.36 (3.08)	$P < 0.001$; $F = 35.61$**
Required triplets			
PEA narrow step	19.76 (4.32)	23.61 (4.21)	$P < 0.001$; $F = 13.75$**
PEA wide step	16.39 (3.42)	17.00 (2.14)	NS
Butanol narrow step	18.47 (4.54)	21.32 (3.43)	$P = 0.025$; $F = 5.17$*
Butanol wide step	15.93 (4.12)	16.21 (2.30)	NS
Required time (in min)			
PEA narrow step	7.71 (1.77)	9.13 (1.77)	$P = 0.002$; $F = 10.57$**
PEA wide step	6.24 (1.52)	6.40 (1.14)	NS
Butanol narrow step	7.32 (2.50)	8.11 (1.46)	NS
Butanol wide step	6.03 (1.52)	6.12 (1.17)	NS

SD, standard deviation; NS, not significant.
*$P < 0.05$.
**$P < 0.01$.

< 0.001). Especially for patients, there was a clear time advantage in the wide step method (see Figure 1). Depending on the odor used, time savings ranged between 24.5% and 30% in patients and 16.4% and 18.1% in normosmic subjects (see Table 2). Measurements with butanol required less triplets than those for PEA for the narrow step method (P = 0.005), but not for the wide step method (P = 0.13).

Discussion

Both dilution step methods lead to similar and reproducible results in patients and controls, but the wide step method was significantly less time consuming. Thus, in this respect, the wide step method provides an advantage for olfactory threshold testing in patients, especially for patients with concentration deficits (e.g., mild cognitive impairment; Murphy et al. 1998) where time of investigation should be kept as short as possible.

The wide step method is not only an advantage for the subject or patient, on an individual level, but also in terms of the organization of the clinical routine. In our Smell and Taste Clinic, for example, we assess olfactory function in about 8 patients on a regular working day. A time saving of about 2.5 min in the butanol threshold test adds up to approximately 20–30 min a day. Thus, use of the wide instead of the narrow step method in patients can help to enhance subjects' and patients' compliance and to reduce costs for the clinic, without significant loss of information. On the other hand, the narrow step method provides the better resolution. This may be interesting for research or clinical matters, like detect subtle dysfunction or variations in olfactory sensitivity.

Both odorants produced reliable threshold results and were equally good to distinguish between patients and normosmic subjects such that the threshold test with butanol could be exchanged with tests for PEA. This is important because many electrophysiological and imaging studies on the sense of smell often use the pleasant, rose-like smell of PEA (e.g., Boyle et al. 2007; Lombion et al. 2009). Because of the only moderately high correlation between thresholds for the 2 odorants, on an individual level still results for 1 of the 2 odors should be used.

In summary, we have shown that alternatives to the often used olfactory Sniffin' Sticks threshold test can save time and

Table 3 Comparison between the methods

	PEA	Butanol
Threshold results		
Normosmic subjects	No significant difference between the 4 methods (pairwise comparison between the methods)	
Patients	No significant difference between the 4 methods (pairwise comparison between the methods)	
Savings between wide and narrow step method		
Required triplets		
Normosmic Subjects	17.1%, $P < 0.001$**	15.7%, $P < 0.001$**
Patients	28%, $P < 0.001$**	24.1%, $P < 0.001$**
Required time (in min)		
Normosmic Subjects	18.1%, $P < 0.001$**	16.4%, $P < 0.001$**
Patients	30%, $P < 0.001$**	24.5%, $P < 0.001$**

**$P < 0.01$.

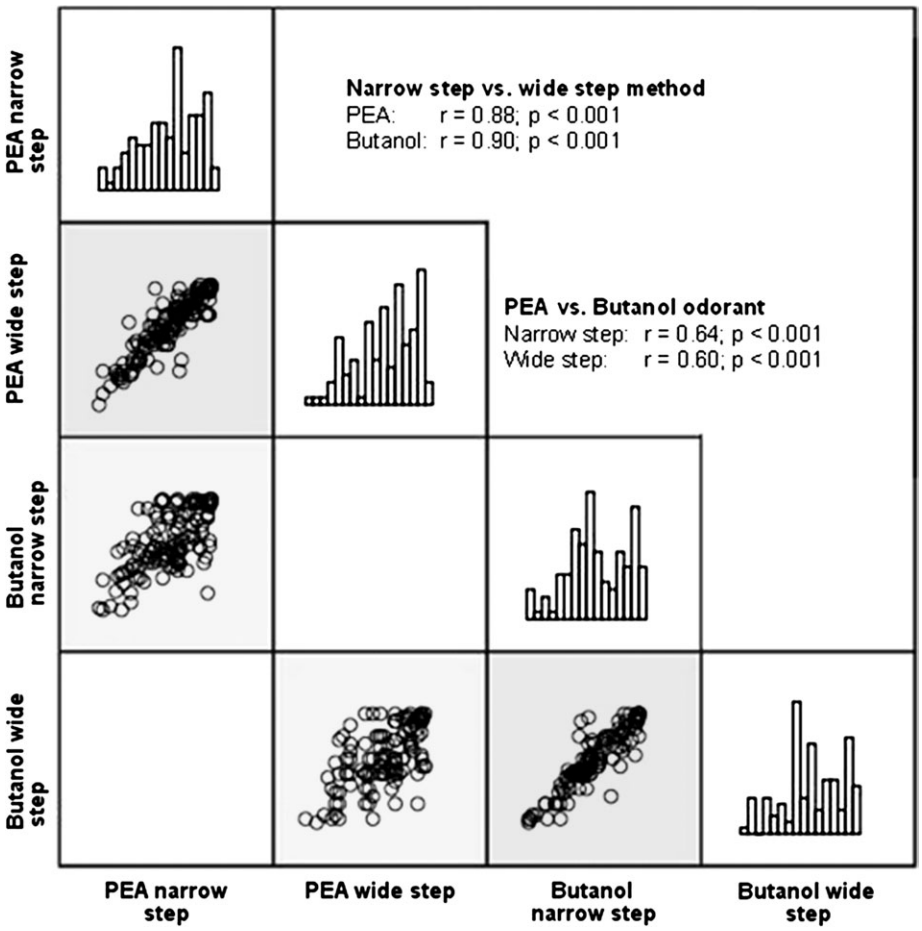

Figure 2 Coherence matrix for threshold results between narrow and wide step method and between PEA and butanol odorant. Shown are scatterplots for the threshold results as well as distribution histograms for the 4 threshold results ($N = 103$).

Table 4 Retest reliability of the odor threshold methods

	Sample (N = 103)[a]	Patients (N = 16)[b]	Normosmic controls (N = 87)[b]
PEA narrow step	0.823	0.793	0.826
PEA wide step	0.836	0.737	0.849
Butanol narrow step	0.818	0.868	0.833
Butanol wide step	0.801	0.880	0.824

[a]Test–retest correlation.
[b]Intraclass correlation coefficient.

may be better suited for patients by reducing the number of dilution steps or for certain projects by using PEA instead of butanol.

Acknowledgements

We would like to thank Dr Johannes Frasnelli, Dr Jens Reden, and Monika Roesner for their contribution to collection of the data.

References

Boyle JA, Frasnelli J, Gerber J, Heinke M, Hummel T. 2007. Cross-modal integration of intranasal stimuli: a functional magnetic resonance imaging study. Neuroscience. 149(1):223–231.

Cain WS, Gent JF, Goodspeed RB, Leonard G. 1988. Evaluation of olfactory dysfunction in the Connecticut Chemosensory Clinical Research Center. Laryngoscope. 98(1):83–88.

Doty RL, Gregor TP, Settle RG. 1986. Influence of intertrial interval and sniff-bottle volume on phenyl ethyl alcohol odor detection thresholds. Chem Senses. 11(2):259–264.

Doty RL, Shaman P, Dann M. 1984. Development of the University of Pennsylvania Smell Identification test: a standardized microencapsulated test of olfactory function. Physiol Behav. 32(3):489–502.

Ehrenstein W, Ehrenstein A. 1999. Psychophysical methods. In: Windhorst U, Johansson H, editors. Modern techniques in neuroscience research. Berlin (Germany): Springer. p. 1211–1241.

Hummel T, Kobal G. 2001. Olfactory event-related potentials. In: Simon S, Mal N, editors. Methods and frontiers in chemosensory research. Boca Raton (FL): CRC press. p. 429–464.

Hummel T, Sekinger B, Wolf S, Pauli E, Kobal G. 1997. 'Sniffin' Sticks': olfactory performance assessed by the combined testing of odor identification, odor discrimination and olfactory threshold. Chem Senses. 22:39–52.

Hüttenbrink KB. 1997. Disorders of smell and taste. Standard and recent methods in diagnosis and therapy. Laryngorhinootologie. 76: 506–514.

Landis BN, Hummel T, Lacroix JS. 2005. Basic and clinical aspects of olfaction. Adv Tech Stand Neurosurg. 30:70–105.

Lombion S, Comte A, Tatu L, Brand G, Moulin T, Millot JL. 2009. Patterns of cerebral activation during olfactory and trigeminal stimulations. Hum Brain Mapp. 30(3):821–828.

Lötsch J, Reichmann H, Hummel T. 2008. Different odor tests contribute differently to the evaluation of olfactory loss. Chem Senses. 33(1):17–21.

Murphy C, Bacon AW, Bondi MW, Salmon DP. 1998. Apolipoprotein E status is associated with odor identification deficits in nondemented older persons. Ann N Y Acad Sci. 855:744–750.

Accepted May 5, 2009