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Gender Differences in Chemosensory Perception and Event-related Potentials

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Abstract

The present study investigated chemosensory gender differences by means of ratings of total nasal chemosensory intensity, unpleasantness and sensory irritation and simultaneous recordings of chemosensory event-related potentials (CSERPs) for three concentrations of the olfactory/trigeminal stimulus pyridine in 19 women and 17 men, all young adults. Results show that, compared to men, women gave higher intensity and unpleasantness ratings, in particular for the highest stimulus concentration. The gender differences in perceived intensity are reflected in the signal-to-noise ratio of the individual CSERP averages, revealing more identifiable early components (P1, N1) in women than in men. The late positive component, labeled P2/P3, displayed larger amplitudes at all electrode sites and shorter latencies at Cz, in women compared to men. The effects of increased pyridine concentration on perception (larger in women) and CSERPs (similar across gender) imply that the two measures involve partially different neural processing. CSERP component identifiability is proposed here as a general means of assessing signal-to-noise ratio of the CSERPs.

Key words: intensity, irritation, olfaction, sex, trigeminal, unpleasantness

Introduction

Gender-related differences in odor perception were first reported at the end of the nineteenth century (Toulouse and Vaschide, 1899) in terms of lower detection thresholds for camphor in women than in men. During the 20th century, the question of gender differences in chemosensory perception has received increased interest (Brand and Millot, 2001). Some studies have demonstrated superior olfactory performance in women with respect to detection sensitivity (Schneider and Wolf, 1955; Koelega, 1970, 1994; Koelega and Köster, 1974), discrimination (Wallace, 1977; Schleidt *et al.*, 1981) and identification (Cain, 1982; Doty *et al.*, 1985; Ship *et al.*, 1996; Brämerson *et al.*, 2004). Notably, women display a higher prevalence than men in reporting odor-related environmental complains, such as sick-building syndrome and chemical intolerance (Fiedler and Kipen, 1997).

In comparison to detection, discrimination and identification of odorous substances, gender differences in perceived intensity and hedonics has received relatively little attention. One study on this topic, the National Geographic Smell Survey with 'scratch-and-sniff' items, revealed higher intensity ratings by women than by men for mercaptan, rose, isoamylacetate and eugenol (Wysocki and Gilbert, 1989). In a laboratory study, in which 10 pyridine concentrations were presented, women were found to report unpleasantness at lower concentrations (lower unpleasantness detection thresholds) than men and gave higher unpleasantness ratings for suprathreshold concentrations (Broman and Nordin, 2000).

Although the common chemical or chemesthetic sense (mediated in the mucosa of the face by the trigeminal nerve) has been less investigated than the olfactory sense, it does also seem to be more sensitive in women than in men, at least when the stimulus is presented nasally. Thus, Cometto-Muniz and Noriega (1985) demonstrated more intense perception of CO_2 pungency when employing both magnitude estimation and magnitude matching.

Recordings of chemosensory event-related potentials (CSERPs) have yielded higher amplitudes in women than in men in response to vanillin, H_2S and amyl acetate (Becker *et al.*, 1993; Evans *et al.*, 1995; Morgan *et al.*, 1997). However, some aspects of the relations between gender, chemosensory perception and CSERPs remain unresolved. One aim of the present study was therefore to further investigate gender differences in both chemosensory perception and CSERPs. A second aim was to approach the issue of how these measures in men and women are influenced by the olfactory/trigeminal properties of the stimulus.

The study was conducted by means of psychophysical assessment of perceived total nasal (chemosensory) intensity, unpleasantness and sensory irritation and by assessing CSERPs for three concentrations of the dual olfactory and trigeminal stimulant pyridine, suggested for use in odor tests in clinical settings and commercially used in a variety of products (Sutton, 1962; Sherman *et al.*, 1979). The three concentrations were expected to cover a wide perceptual spectrum from predominantly olfactory to predominantly trigeminal in activation.

The P1, N1 and P2/P3 CSERP components were chosen for evaluation, defining P2/P3 as the largest positive component after N1. The olfactory P1 and N1 have been reported to correlate with detection sensitivity (Tateyama *et al.*, 1998), thus reflecting primary sensory processing. The present study was designed to elicit a P3 component (cf. Polich *et al.*, 1994; Cass and Polich, 1997). However, the P2/P3 denotion is chosen here partly due to the P2 often being completely overlapped by the P3 component (Pause *et al.*, 1996), partly due to a lack of consensus in the chemosensory research community on the labeling of these components in the late positive complex. The olfactory P3 occurs when the stimulus is unexpected but actively attended (Geisler and Murphy, 2000) and reflects cognitive 'context updating' of the external environment (Donchin and Coles, 1988). The olfactory P3 amplitude has been related to novelty and significance of the stimulus and its latency related to the time required for cognitive evaluation of the stimulus (Pause *et al.*, 1996; Pause and Krauel, 2000; for a neuropsychological investigation of the olfactory P3, see also Geisler *et al.*, 1999).

Gender differences in CSERPs were studied with respect to mean amplitudes and latencies, but also with respect to component identifiability, which provides information complementary to the former, traditional type of comparison. In participants or experimental conditions where the signal-to-noise ratio is low, the task of selecting components from the background noise is difficult. Surprisingly, the identifiability of CSERP components has so far with only a few exceptions been used as an indication of signal-to-noise ratio (Sakuma *et al.*, 1996; see also Peters *et al.*, 2003). Traditionally, the researcher presupposes that the components are present and selects them routinely in accordance with (i) the morphology of the averaged waveform, (ii) established criteria, such as latency intervals based on normative data or group averages and (iii) corresponding components recorded at other electrode sites. A risk taken when using only these three criteria is that noise is selected to represent stimulus-generated brain activity. Hence, a more strict procedure than often is used to select components, provided by a identifiability heuristics in the present study, is to additionally include the criterion that (iv) the component should be clearly distinguishable from the background noise, either by its height or by its width.

Materials and methods

Participants

The participants were 17 men (mean age = 25.6, SD = 1.5 years) and 19 women (mean age = 27.2, SD = 3.1 years), who were recruited by placarding, mainly in the campus area and paid for participation. All participants were right-handed except for two men and one woman and all were non-smokers, except for one man. They were screened for colds, allergies and breathing problems based on self-reports (Nordin *et al.*, 2003). The study was carried out in accordance with the Helsinki Declaration and approved by the Ethics Committee at Umeå University. A signed informed consent form was obtained from each participant.

Stimuli

Three pyridine concentrations of vapor dilutions by flow were used: 13% (1.014 l/min of saturated pyridine vapor mixed with 6.786 l/min of pure air), 15% (1.170 l/min pyridine mixed with 6.630 l/min air) and 19% (1.482 l/min pyridine mixed with 6.318 l/min air) v/v. These were obtained after careful pilot testing, aiming at obtaining three clearly suprathreshold concentrations with different perceptual profiles: predominantly odorous (13%), a balanced mixture of odor and irritation (15%) and predominantly irritating (19%). The pilot testing was conducted by instructing each of three young women and three young men to select three pyridine concentrations (from within a range of concentrations that were strong enough to generate stable CSERPs, yet not very unpleasant in intensity) with the aimed perceptual profiles. The pilot participants did subsequently reach a concensus that the three suggested concentrations from the pilot testing had the three perceptual profiles. Each concentration was presented 20 times to the participant. In order to reveal possible effects of concentration on the CSERPs (Kobal, 1981), the 60 stimuli were presented in one out of four randomized sequences. All stimuli had a 200 ms duration and were generated by a dynamic olfactometer (OM2S; Burghart Instruments, Germany) that does not alter the mechanical or thermal conditions of the mucosa (Kobal and Hummel, 1988). The olfactometer produces two gaseous streams of clean and odorized air, which are switched by a mechanism of vacuum-controlled valves. During stimulation, odorized air reaches the nasal cavity and during interstimulus intervals (ISI) clean air reaches the cavity. Stimuli were applied nonsynchronously to breathing. The nasopharyngeal closure breathing technique was used to restrict breathing to the mouth, which results in higher CSERP amplitudes compared to normal breathing (Thesen and Murphy, 2001). The stimuli were presented in a constantly flowing air stream of 7.8 l/min with controlled temperature and humidity (39°C, 80% RH) with a 30 s ISI to the right or left nostril. Stimulated nostril side was balanced between groups.

Ratings of chemosensory perception

At each stimulus presentation the participant focused on an eye-fixation point on the center of a computer screen. After each stimulus presentation, this image shifted to a Borg CR-100 scale (ranging from 0 to 100; Borg and Borg, 2002) with which the perceived intensity of the stimulus was rated, reflecting the combined olfactory and trigeminal sensations (i.e. total nasal chemosensory intensity). The CR-100 has descriptive adjectives that correspond to specific numbers on the scale (nothing at all, 0; minimum, 1.5; extremely weak, 2.5; very weak, 6; weak, 12; moderate, 25; strong, 45; very strong, 70; extremely strong, 90; maximum, 100). The participant was told to always read the descriptive words before choosing any number between 0 and 100 corresponding to the sensation. By using descriptors, the scale has been assumed to have ratio-scale properties (Borg, 1982).

After rating the intensity, the screen image shifted to a CR-10 scale (ranging from 0 to 10; Borg, 1998). The participant was first to judge whether the stimulus was pleasant or unpleasant and then to rate how pleasant or unpleasant it was. Principally similar to the CR-100, the descriptive adjectives of the CR-10 correspond to specific numbers on the scale (nothing at all, 0; extremely weak, 0.5; very weak, 1; weak, 2; moderate, 3; strong, 5; very strong, 7; extremely strong, 10).

Finally, the image shifted to a four-point scale with the endpont descriptors 'no irritation' (at scale point 0) and 'strong irritation' (at 3). After reporting irritation, the eye-fixation point was again shown until the next stimulus was presented. Prior to the session, the participant was carefully instructed that sensory irritation refers to a stinging, smarting, pungent or dry sensation in the nose (Berglund and Shams Esfandabad, 1993), dissociable from a pure odor sensation. The use of three different scales served to keep the participant from routinely assigning a number based on their previous rating.

CSERP recordings

EEG records of 2048 ms including a 512 ms prestimulus period (constituting baseline) were obtained with silver electrodes from the sites of Fz, Cz and Pz of the International 10-20 system, referenced to linked earlobes (A1 + A2) and grounded on the forehead. Eye-blink artifacts were monitored from Fp2/A1 + A2 and single recordings with artifacts >50 μV were discarded. The records were amplified (20 000 times), filtered (0.02–30 Hz band-pass filter; an additional low-pass filter, 18 Hz, for off-line analyses), digitized (250 Hz), stored on disk and averaged off-line separately for each concentration and each electrode site. As a control condition, EEG records in response to 20 clean-air presentations (5 s ISI) were recorded after the 60 pyridine stimuli. In this condition the flow rate for the odorized air was reduced to zero and the dilution flow was increased to accomplish a constrant flow in the nasal cavity that was the same as during the ISI. Thus, the valve-switching conditions were identical during pyridine presentation and the control condition. The participant was told to relax and to avoid movements and eye blinks when perceiving a stimulus. The CSERP recordings took in total ~32 min.

For identification, apart from considering (i) the morphology of the averaged waveform, (ii) established criteria and (iii) corresponding components recorded at other electrode sites, a component had to be clearly distinguishable from the background noise, either by its height (amplitude) or by its width (base).

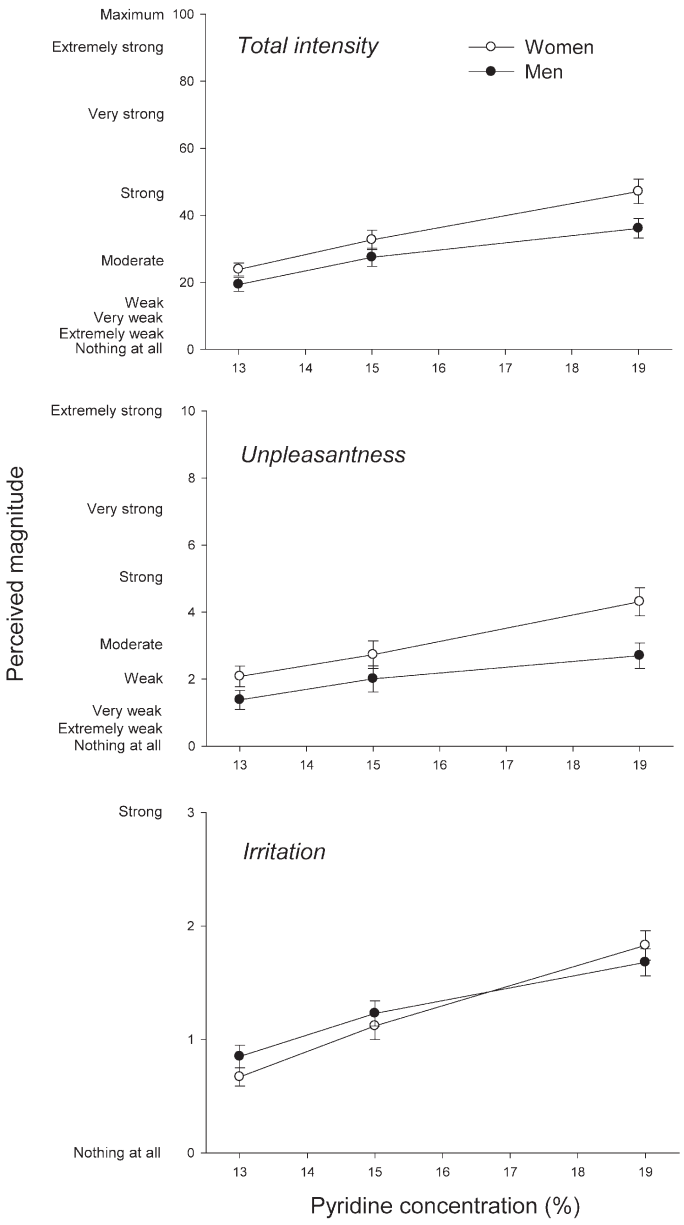

Figure 1 Mean (±SE) perceptual ratings of total intensity, unpleasantness (all stimuli were rated by all participants as unpleasant) and sensory irritation as a function of pyridine concentration.

Results

Chemosensory perception

Mean ratings of total perceived intensity, unpleasantness (all stimuli were rated by all participants as unpleasant) and sensory irritation are presented in Figure 1. Two-way, group by stimulus concentration analyses of variance (ANOVAs) with repeated measures across concentrations with Greenhouse–Geisser correction, showed a tendency of higher intensity ratings in women than in men [$F(1,102) = 3.68$, $P = 0.07$], a main effect of concentration on intensity ratings [$F(2,34) = 104.97$, $P < 0.001$] and a tendency of a group-by-concentration interaction for perceived intensity [$F(2,102) = 3.32$, $P = 0.06$]. The same pattern was observed for unpleasantness, with significantly higher ratings by women [$F(1,102) = 4.20$, $P < 0.05$], a main effect of concentration [$F(2,34) = 69.63$, $P < 0.001$] and a group-by-concentration interaction [$F(2,102) = 5.76$, $P < 0.01$]. For sensory irritation, there was no main effect of gender [$F(1,102) = 0.07$, n.s.], but a main effect of concentration [$F(2,34) = 116.86$, $P < 0.001$] and a group-by-concentration interaction [$F(2,102) = 3.76$, $P < 0.05$]. Because both a main effect of group ($P = 0.07$) and a group-by-concentration interaction ($P = 0.06$) almost reached statistical significance ($P < 0.05$) for total intensity, post-hoc one-way ANOVAs were conducted also for this perceptual dimension. This yielded significant gender differences for intensity [$F(1,34) = 5.37$, $P < 0.05$] and unpleasantness [$F(1,34) = 7.92$, $P < 0.01$] at the strongest stimulus concentration, but not for the remaining seven combinations of concentration and perceptual dimension [$F(1,34) < 2.80$, $P > 0.10$].

CSERP component identifiability

The procedure for identifying CSERP components revealed a general pattern in that the women's CSERPs, compared to the men's, were more easily identified. In total, 96.3% of the women's components were identified according to the used heuristics, whereas only 80.4% of the men's components were identified. Table 1 shows the identifiability of the components for different stimulus concentrations and electrode sites. Men had fewer identifiable P1 and N1 components than did women. For the P2/P3 component, the identification was either 100% or close to 100% for both men and women.

The signal-to-noise ratio of the CSERPs depends partly on the number of artifact-free recordings included in the individual averages. The average (SD) number of such recordings included in an averaged CSERP for women and men were 13.0 (3.0) and 14.5 (2.6) for 13%, 12.8 (3.2) and 12.4 (2.6) for 15% and 11.8 (2.9) and 12.1 (2.8) for 19% pyridine, respectively. A two-way, group by stimulus concentration ANOVAs with repeated measures across concentration showed a main effect of concentration on number of included single recordings [$F(2,54) = 8.73$, $P < 0.001$], but no main effect of gender [$F(1,27) = 0.01$, n.s.] and no group-by-concentration interaction [$F(2,54) = 1.80$, n.s.]. Thus, the number of artifact-free, single recordings cannot account for the obtained differences in component identifiability. Due to the, in general, small number of identifiable P1 components, only N1 and P2/P3 were considered for further analysis.

CSERP amplitudes and latencies

Figure 2 presents mean amplitudes and latencies for N1 and P2/P3 recorded at Cz. Results from mixed-model ANOVAs

Table 1 Percentage of identifiable P1, N1 and P2/P3 components for three pyridine concentrations at Fz, Cz and Pz

	Fz		Cz		Pz	
	Women	Men	Women	Men	Women	Men
13%						
P1	84.2	64.7	93.3	64.7	94.4	47.1
N1	100	82.4	100	82.4	100	76.5
P2/P3	100	94.1	100	100	100	100
15%						
P1	94.4	52.9	88.9	47.1	83.3	47.1
N1	94.4	76.5	100	88.2	100	88.2
P2/P3	94.4	100	100	100	100	100
19%						
P1	93.3	66.7	86.7	60	93.3	60.0
N1	100	86.7	100	100	100	86.7
P2/P3	100	100	100	100	100	100

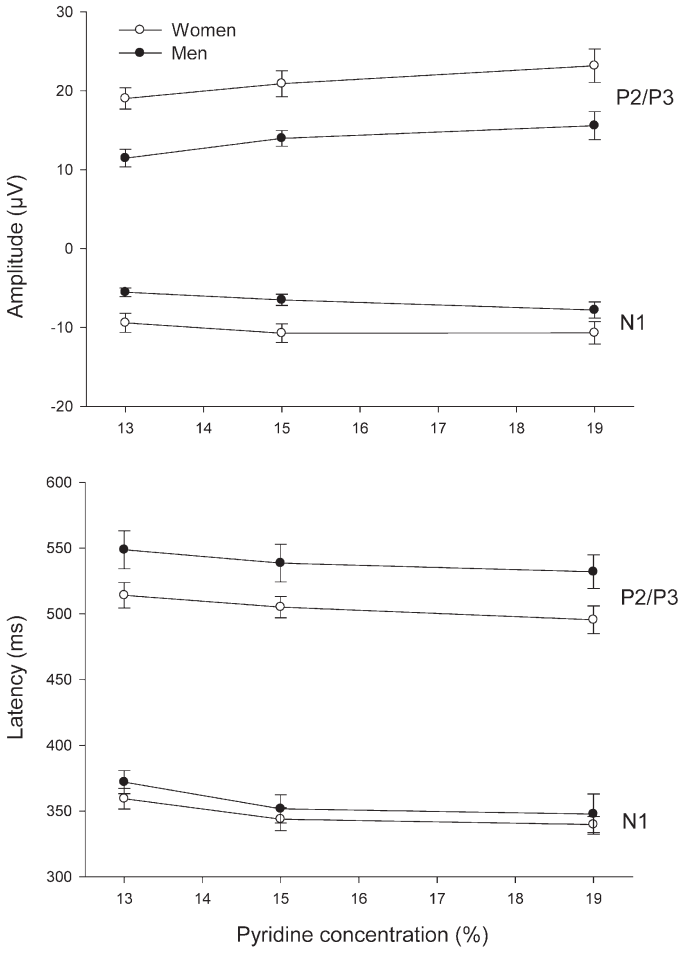

Figure 2 Mean (±SE) base-to-peak amplitudes and peak latencies of event-related potentials recorded at Cz as a function of pyridine concentration.

with repeated measures across stimulus concentrations and with Greenhouse–Geisser correction are given in Table 2 for peak amplitudes and latencies. The results show consistently larger P2/P3 amplitudes and a tendency of larger N1 amplitudes at Cz in women compared to men. The P2/P3 latencies at Cz were signficantly shorter in women. Typically, the amplitudes increased and latencies decreased with an increase in stimulus concentration. There were no group-by-concentration interactions. The scalp distribution of P2/P3 changes with increased concentration from a centro-parietal maximum at the lowest concentration, to a central maximum at the highest concentration: For the 13% pyridine concentration, the P2/P3 mean amplitudes at the Fz, Cz and Pz sites were 11.3, 15.5 and 15.6 μV, respectively. For the 15% concentration, corresponding amplitudes were 12.9, 17.5 and 17.2 μV and for the 19% concentration, the amplitudes were 13.7, 19.4 and 18.5 μV, respectively.

Grand averages of the CSERPs across participants recorded at the three electrode sites in response to the three pyridine concentrations and clean air are presented in Figure 3. The averaged responses provide further evidence for larger amplitudes and a general tendency of shorter latencies in women compared to men. The responses to clean air suggest that the ERPs are not induced by mechanical or thermal stimulation.

Discussion

The present investigation used a mixed olfactory/trigeminal stimulus to study gender-related differences in chemosensory function, both psychophysically (perceptual ratings) and electrophysiologically (CSERP recordings) and to study effects of stimulus concentration on these measures. The results suggest that women perceive pyridine as more intense than men. Interestingly, the chemosensory stimuli were also found to be rated as more unpleasant by women than by men. Whether this effect is a direct consequence of the enhanced perceived intensity and the increased magnitude given by women to irritation at the highest concentration, or whether it, independent of intensity, reflects a difference in hedonic interpretation is yet an open question.

The findings of Cometto-Muniz and Noriega (1985), suggesting that women are more sensitive than men to pungent properties of a chemosensory stimulus is supported by the present group-by-concentration interaction for sensory irritation, although there was no main effect of gender on sensory irritation. Thus, whereas women rated the weakest pyridine concentration (assumed to be predominantly odorous) as, in average, less irritating than men did, they rated the strongest concentration (predominantly trigeminal) as more irritating. Further support for this conclusion is found in the significant gender differences for intensity and unpleasantness at the strongest pyridine concentration. It is well documented that for most chemical substances the perception of odor dominates at relatively low concentrations and at high concentrations sensory irritation does not only dominate, but does also suppress odor intensity (e.g. Cain and Murphy, 1980; Cometto-Muniz and Hernadez, 1990). It is quite likely that the strong trigeminal impact of the stimulus is underlying these gender differences in intensity and unpleasantness. An objective validation of the pilot testing (after which the pilot participants subsequently reached a concensus regarding the three perceptual profiles) to find a stimulus range from predominantly odorous to predominantly trigeminal in activation is found in the CSERP scalp topography. Thus, the topography changed from a centro-parietal maximum to a central maximum as a result of increased stimulus concentration. The two topographies have consistently been demonstrated to be characteristic of olfactory and trigeminal stimuli, respectively (Hummel *et al.*, 1992; Hummel and Kobal, 1992; Kobal *et al.*, 1992; Livermore *et al.*, 1992) and are likely to reflect different cortical ERP generators (Kettenmann *et al.*, 1996). At a first glance, the present results oppose those of Hummel *et al.* (2003). In applying a

Table 2 Results from two-way ANOVAs of event-related potentials

	Base-to-peak amplitude		Peak latency	
	N1	P2/P3	N1	P2/P3
Fz				
Group (G)	$F = 1.5^{ns}$	$F = 14.8^{***}$	$F = 0.2^{ns}$	$F = 1.4^{ns}$
	df = 1,19	df = 1,25	df = 1,19	df = 1,25
Concentration (C)	$F = 3.5^{*}$	$F = 8.9^{**}$	$F = 2.4^{ns}$	$F = 4.0^{*}$
	df = 2,38	df = 2,50	df = 2,38	df = 2,50
G × C	$F = 0.1^{ns}$	$F = 0.1^{ns}$	$F = 0.1^{ns}$	$F = 0.3^{ns}$
	df = 2,38	df = 2,50	df = 2,38	df = 2,50
Cz				
Group (G)	$F = 3.7^{ns}$	$F = 10.4^{**}$	$F = 0.7^{ns}$	$F = 4.5^{*}$
	df = 1,23	df = 1,27	df = 1,23	df = 1.27
Concentration (C)	$F = 3.0^{ns}$	$F = 11.1^{***}$	$F = 12.6^{***}$	$F = 5.6^{**}$
	df = 2,46	df = 2,54	df = 2,46	df = 2,54
G × C	$F = 0.1^{ns}$	$F = 0.5^{ns}$	$F = 2.5^{ns}$	$F = 0.6^{ns}$
	df = 2,46	df = 2,54	df = 2,46	df = 2,54
Pz				
Group (G)	$F = 1.1^{ns}$	$F = 12.1^{**}$	$F = 0.1^{ns}$	$F = 2.7^{ns}$
	df = 1,22	df = 1,27	df = 1,22	df = 1,27
Concentration (C)	$F = 3.9^{*}$	$F = 6.7^{**}$	$F = 7.0^{**}$	$F = 5.5^{**}$
	df = 1,44	df = 1,54	df = 1,44	df = 1,54
G × C	$F = 1.8^{ns}$	$F = 1.2^{ns}$	$F = 0.7^{ns}$	$F = 0.3^{ns}$
	df = 1,44	df = 1,54	df = 1,44	df = 1,54

$^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$; ^{ns}non-significant.

test paradigm based on the well-known ability to localize stimulated nostril side when trigeminal (but not olfactory) sensations are evoked, no gender differences were found in localization ability for benzaldehyde and eucalyptol, implying no gender difference in trigeminal sensitivity. A posible explanation for this discrepancy is that the gender-related difference in perceived irritation is predomiantly influenced by cognitve factors, rather than by peripheral sensitivity as reflected by the ability to localize stimulated nostril side.

The present CSERPs data for women and men agree to a considerable extent with the perceptual data. This is supported by the higher identifiability of P1 and N1 components in women than in men, indicating a higher signal-to-noise ratio in women. The proposed heuristic for identifying CSERP components appears to be useful as a complementary means of communicating the quality of the obtained CSERP data. However, further steps can be taken in future research for developing a heuristic that may include quantitative criteria. It should be noted that the component identifiability also is dependent on the number of artifact-free, single recordings that are included in the averaged CSERP. Common generators of artifacts are eye blinks. Thus, nasal irritation is known to elicit motor responses in the zone around the eye (Jalowayski *et al.*, 2001). In accordance with this, the number of recorded single recordings included in an averaged CSERP declined as the stimulus concentration increased and thus the trigeminal impact, whereas no gender differences were observed.

Further support for an agreement between CSERP and perceptual data is that despite the fact that a higher percentage of CSERPs with low signal-to-noise ratios for men than for women were excluded from the group means, the men displayed lower mean P2/P3 amplitudes, confirming past results (e.g. Evans *et al.*, 1995; Morgan *et al.*, 1997). Importantly, the present results do also show shorter P2/P3 latency in women than in men, which to our knowledge has not previously been demonstrated. However, this difference does only reach statistical significance at the Cz site and should be interpreted with certain caution.

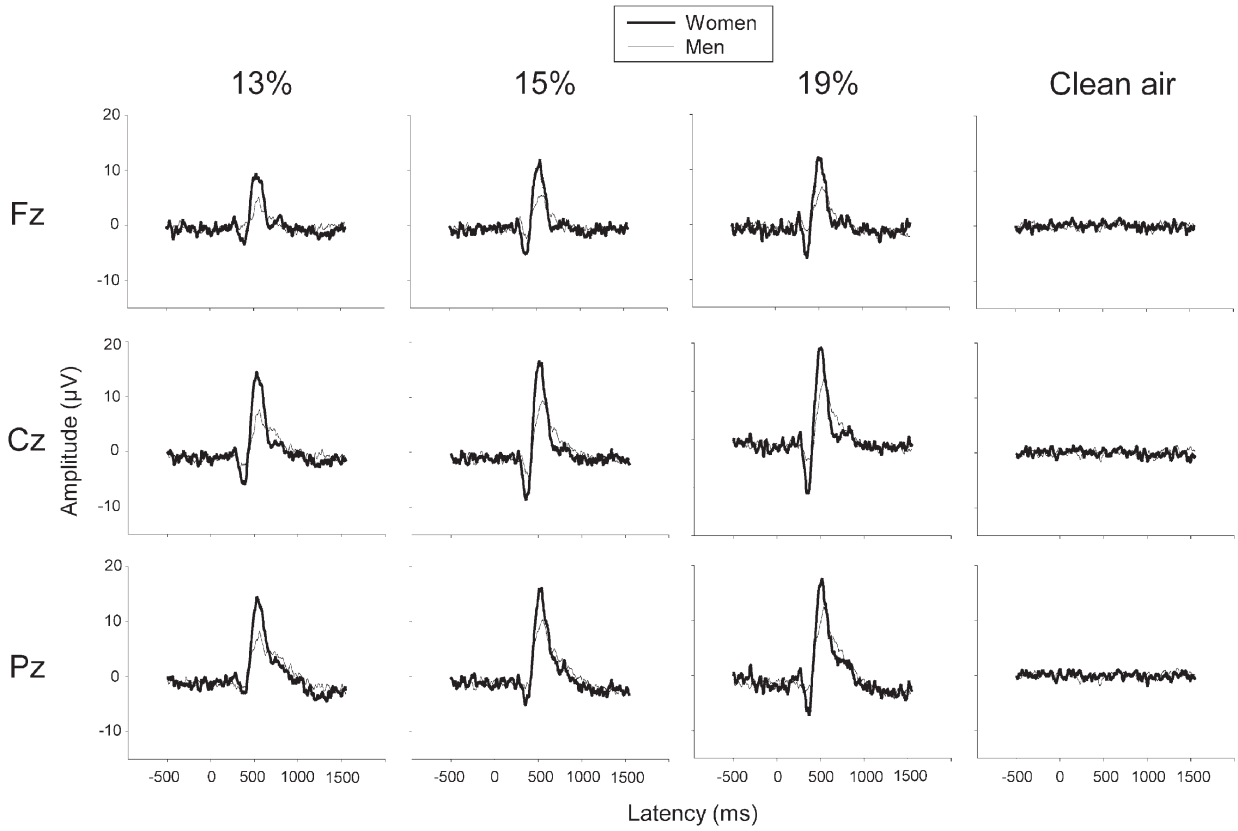

Figure 3 Grand averages of event-related potentials recorded at Fz, Cz and Pz in response to 13, 15 and 19% pyridine and clean air.

The finding of an increase in CSERP amplitude and a decrease in latency with an increase in stimulus concentration is also in accordance with the literature (e.g. Kobal and Hummel, 1988; Kobal, 2003). However, when interpreting these results one should bear in mind that the present study differs from these other studies in that the increase in concentration was intended to generate a clear shift in emphasis from olfactory to trigeminal activation.

The CSERP and perceptual data do also disagree in an important aspect. Thus, the effect of increased pyridine concentration on perception being larger in women than in men, in contrast to the concentration effect on CSERPs being similar across gender, imply that the two measures involve partially different neural processing. Further speculation regarding processing differences in these measures is provided by an attempt to give a general, modality-independent, statement on gender differences in chemoreception. The finding that women, compared to men, generated larger amplitudes and shorter latencies for the relatively exogenous P2/P3 component suggests that the observed perceptual gender differences predominantly have their origin at a relatively high level of neural processing. It is also quite likely that a considerable proportion of the perceptual differences between women and men can be referred to higher cognitive and neural levels than those reflected by the P2/P3 component.

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