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Perception of olfactory and intranasal trigeminal stimuli following cutaneous electrical stimulation

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Abstract. Based on previous research it may be hypothesized that the perception of odorants is modified by an axon reflex emanating from trigeminal afferents activated via the skin and/or the intranasal respiratory epithelium. The present experiment investigated the effects of trigeminal cutaneous stimulation on intensity estimates of intranasal chemical stimuli. While the left nostril was stimulated chemically with olfactory and trigeminal stimulants, four regions of the face were stimulated electrically. Intensity estimates of the chemical stimuli tended to increase after cutaneous electrical stimulation which may be interpreted in terms of response priming. The effect of electrical stimulation did not differ at the 4 stimulation sites. The results argue against the hypothesis that the processing of intranasal chemical stimuli is modified peripherally by cutaneous trigeminal excitation.
Key words. Olfaction; olfactory nerve; trigeminal nerve; somatosensory system; interaction; electrical stimulation.

The sense of smell is composed of sensations predominantly mediated by the olfactory and the trigeminal systems. Few chemical stimuli produce exclusively trigeminal (e.g., stinging) or olfactory sensations[1,2]. Mutual interactions have been demonstrated between the trigeminal and the olfactory system. While Cain and Murphy[3] presented evidence that these interactions take place centrally, research has been accumulating which indicates that they may also occur at the peripheral level. A possible mechanism is suggested by the presence of peptidergic trigeminal fibers within the olfactory epithelium[4]. Several studies indicate that olfactory receptor responses to chemical stimuli can be modified by activation of the trigeminal nerve, and that this modification may occur through the release of peptides[5]. The trigeminal system may also modulate the resting activity of the olfactory bulb[6]. Bouvet et al.[7] found that electrical stimulation of chemosensitive afferents from the frog's respiratory epithelium resulted in increased spontaneous receptor firing, modified mass neuronal activity in the mucosa, and reduced amplitude of both the electro-olfactogram and single unit responses to the odorant isoamylacetate. Thus, it appears that stimulants of the trigeminal nerve may be able to modify olfactory perception at a peripheral level.

Similar to the neurogenic inflammatory response in somatosensory afferents this interaction may take place via an axon reflex[4,5] which in turn might be activated via afferents from the skin and/or the intranasal respiratory epithelium. Thus, the hypothesis in question was that human olfactory perception may be modified by peripheral stimulation of the trigeminal nerve. As a first step towards its verification or falsification, the present experiments investigated the effects of electrical stimulation of trigeminal afferents from the facial skin on intensity estimates of intranasal chemical stimuli.

Four regions of the face, corresponding to the left or right maxillary and mandibular branches of the trigeminal nerve, were stimulated electrically. For chemical stimulation of the nasal mucosa, the two odorants H_2S and vanillin and the trigeminal stimulant CO_2 were used. The chemical stimulants were always presented to the left nostril. Given that the hypothesis under investigation was true, 1) stimulation of the maxillary branch ipsilateral to the site of chemical stimulation could be expected to have a greater influence on chemosensory perception, and 2) stimulation of the mandibular branch would affect the perception of chemical stimulants to a lesser degree than would activation of the maxillary branch.

Materials and methods

13 healthy volunteers (7 male, 6 female) between the ages of 18 and 34 years participated in the study. The investigation was performed in accordance with the Declaration of Helsinki/Hong Kong. Ethics approval was obtained prior to the commencement of the study.

Chemical stimuli. Chemical stimuli were chosen so as to stimulate either the olfactory (H_2S: 0.78 ppm; vanillin: 2.06 ppm) or trigeminal (CO_2: 40% v/v) nerves. Stimulus duration was 200 ms, the interstimulus interval was approx. 40 s. Chemical stimuli were always presented to the left nostril.

Electrical stimulation. For each subject, thresholds for electrical stimulation were established by presenting stimuli of ascending intensity (duration 2 ms, interval approx. 2 s; constant current rectangular pulses; Digitimer DS7, UK). The subject indicated the intensity at which a sensation first became apparent. An average threshold was computed from three trials. During experiments trains of 10 rectangular electrical shocks (duration 2 ms, interval 2 ms) were delivered at thrice threshold level. The chemical stimulus was administered 1 s after the electrical stimulation. Within the 4 sessions the stimulating electrode was placed on the left and right jaw below the mouth in the line of the cheek bone, and slightly lateral to the left and right cheek bones.

Test procedure. All subjects were familiar with both the stimulants used and the experimental procedure prior to testing. In addition, they were acquainted with a breathing technique (velopharyngeal closure[2]) whereby respiratory flow inside the nasal cavity is avoided during stimulation. Chemical stimulation was performed as described previously[8,9]. Subjects were comfortably seated in a ventilated chamber. White noise of approximately 50 dB SPL (ERA stimulator, Tönnies) prevented them from hearing the switching process. Each subject completed 4 test sessions, each of which was divided into 2 blocks separated by a 10 min recovery period. Within each block the 3 chemical stimulants were randomly presented 12 times; 6 occurred following electrical stimulation and 6 with no prior stimulation. 'Shock' and 'no shock' trials were randomly distributed throughout both blocks. The order of electrode placement for electrical stimulation, i.e., left or right cheek or jaw, was randomised for each subject.

Psychophysical measurements. Following each presentation subjects estimated the intensity of the sensation produced by the chemical stimulus, i.e., they rated the overall intensity of the different stimuli[10] in comparison to the overall intensity of the first chemical stimulus presented, H_2S, which therefore served as a standard (100 estimation units). Ratings were made by moving a joystick to adjust the length of a bar on a visual analogue scale displayed on a computer screen in front of the subject. In addition, on 6 random occasions subjects were prompted to estimate the intensity of the electrical stimulus by adjusting a pointer superimposed on another visual analogue scale. The left end of the scale indicated no sensation, and the right an extremely strong sensation.

Tracking performance. In order to detect changes in the state of vigilance (and/or motoric coordination), during the intervals between the stimuli subjects were requested to perform a tracking task on the video screen[11]. They were required to keep a small square, which could be controlled by a joystick, inside a larger one, which moved around unpredictably. The performance was checked by counting how often, and by measuring for how long, the subjects had lost track of the independently moving square (range from 0 to 100% success in tracking). The data were averaged for each session.

Statistical analysis. The data were evaluated by means of analyses of variance (ANOVA; program SPSS/PC+) with a repeated measures factorial design. Intensity estimates of chemical stimuli were evaluated via a 3-way ANOVA with 'chemical stimulant' (CO_2, H_2S, vanillin), 'site of electrical stimulation' (left and right chin, left and right cheek), and 'shock condition' (with and without shock) as factors. Intensity estimates of electrical stimuli and tracking performance scores were analysed using a 1-way ANOVA with 'site of electrical stimulation' as a factor.

Results

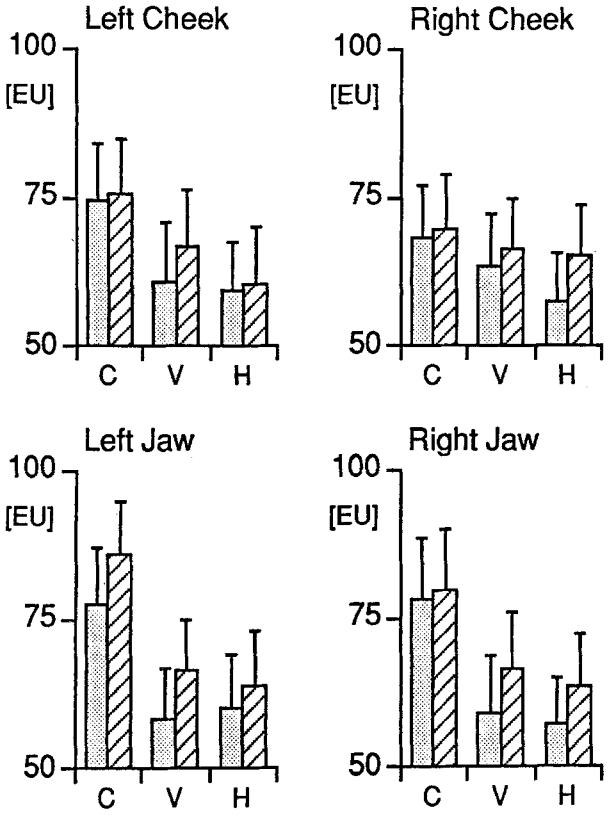
Electrical stimulation. No significant differences were observed between the intensity estimates of electrical stimuli ($df = 36/3$, $F = 0.32$, n.s.) across the four test sessions (intensity estimates in estimation units; mean = M, standard deviation = SD; left cheek: $M = 44.2$, $SD = 22.0$; right cheek: $M = 48.8$, $SD = 22.7$; left jaw: $M = 46.6$, $SD = 23.8$; right jaw: $M = 46.4$, $SD = 28.5$). Thus, it can be concluded that the electrical shocks at the 4 stimulation sites were of the same perceived intensity.

Tracking performance. Results of the ANOVA ($df = 36/3$, $F = 1.81$, n.s.) indicated that tracking performance was stable across the four sessions (tracking performance in %; mean = M, standard deviation = SD; left cheek: $M = 84.5$, $SD = 8.0$; right cheek: $M = 84.5$, $SD = 8.8$; left jaw: $M = 83.3$, $SD = 8.7$; right jaw: $M = 86.5$, $SD = 28.5$).

Intensity estimates of chemical stimuli. CO_2 was perceived as having a higher intensity than H_2S and vanillin (fig.). This was confirmed by a significant effect of the factor 'stimulant' ($df = 24/2$, $F = 6.55$, $p < 0.01$). In comparison with the 'no-shock' condition, electrical stimulation tended to produce increased intensity estimates for all three stimulants at all stimulation sites (df 12/1, $F = 2.95$, $p < 0.1$). No significant differences were observed between electrical sites (df 36/3, $F = 0.32$, n.s.).

Discussion

The specific research hypothesis consisted of two parts: 1) stimulation of the maxillary branch of the trigeminal nerve ipsilateral to the site of chemical stimulation would have a greater influence on olfactory perception than contralateral stimulation, and 2) stimulation of the mandibular branch would affect the perception of odorants to a lesser degree than activation of the maxillary branch. However, the analysis of the intensity estimates did not reveal a significant difference between the 4 sites of electrical stimulation indicating that the processing of olfactory and trigeminal stimuli is not modified at the



Estimates of the overall intensity of chemical stimuli (means, standard error of means, n = 13; estimates in estimation units = EU). Hatched bars indicate intensity estimates of intranasal chemical stimuli following cutaneous electrical stimulation, dotted bars indicate ratings of stimuli without preceeding electrical stimuli. C, carbon dioxide, V, vanillin, H, hydrogen sulphide.
Within the 4 sessions electrical stimuli were applied to the left or right cheek or jaw, while chemical stimuli were always administered to the left nostril. Carbon dioxide was perceived as having a significantly higher intensity than hydrogen sulphide and vanillin. Throughout all experimental conditions electrical stimulation produced slightly increased intensity for all three stimulants ($p < 0.1$). A significant effect of the four stimulation sites could not be observed.

peripheral level by cutaneous trigeminal input. Although these data cannot exclude the existence of an effect of trigeminal cutaneous activation on olfactory perception which was too small to show up in the psychophysics investigated in this study, the present results let it appear unlikely that cutaneous stimulation induces an axon reflex which in turn might affect the perception of odorants.

Preliminary data provided by Bouvet et al.[7] indicated that electrical stimulation of the ophthalmic branch of the trigeminal nerve reduced the amplitude of the peripheral olfactory response to the chemosensory stimulant isoamylacetate in frogs. Given that a decreased amplitude of the electro-olfactogram corresponds to decreasing intensity estimates in humans[12], the current experiment supports the assumption that the effect observed by Bouvet et al. is not due to the trigeminal input from cutaneous afferents but rather relates to fibers originating from the respiratory epithelium.

At all four sites of electrical stimulation, there was a tendency for intensity estimates of the 3 chemical stimulants to increase after electrical stimulation of the skin, regardless whether the trigeminal nerve or the olfactory nerve had been stimulated. Although this effect was not statistically significant, these results may be interpreted in terms of the response priming by the electrical stimulus which preceeded chemical stimulation. That is, by focusing the subjects' attention[8] this cue may have enhanced intensity estimates of chemical stimuli by 'preparing' the central nervous system for their arrival. Thus, more research is required in order to ascertain the way in which trigeminal stimulation may modify olfactory processing at a peripheral level in humans. In order to accurately assess the influence of trigeminal stimulation on the olfactory receptors it may be necessary to directly measure responses from the epithelium by means of a technique such as the electro-olfactogram[12]. Although difficult to record, this technique would provide a highly sensitive measure with which to explore the meaning of trigeminal modifications of olfactory receptor responses.

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