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The importance of stimulus site and intensity in differences of pain-induced vascular reflexes in human orofacial regions

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Abstract

Studies in anaesthetized animals have indicated that noxious stimulation may produce marked blood flow changes in various orofacial structures, but the influence of painful stimulation on the blood flow regulation of the orofacial area of humans has been studied only to a limited extent. The purpose of this investigation was to study whether there are differences in temporal and spatial patterns of pain-induced vasoactive reflexes between various orofacial regions and hand in healthy human volunteers. Dynamic changes in blood flow in various orofacial regions elicited by painful stimulation of the tooth and finger were measured by means of Laser Doppler imaging (LDI) and computer-assisted infrared thermography (IRT). Blood flow of the finger was recorded by laser Doppler flowmetry (LDF) and plethysmography (PLET). During both stimulus paradigms there was a transient elevation in heart rate (HR) and blood pressure (BP). At the same time there was a significant blood flow decrease in the finger (LDF, PLET) and in the nose (LDI, IRT). In contrast to tooth stimulation, finger stimulation caused a more marked blood flow reduction in the finger. Only high intensity tooth stimulation, but not finger stimulation, caused a long-lasting vasodilatation both in lower and upper lip. The blood flow changes in the lips were not correlated with changes in systemic blood pressure or heart rate. In the cheek, there were no marked flow changes during either finger or tooth stimulation. These data indicate that painful tooth (regional) stimulation, but not finger (remote) stimulation, can induce a long-lasting vasodilatation in parts of orofacial tissues which cannot be explained by changes in central cardiovascular parameters. This tooth-stimulation-induced blood flow increase supports the hypothesis of a special vasodilator reflex mechanism in the orofacial area. Furthermore, tooth-stimulation-induced vasoconstriction in the nose and dilatation in the lips indicate that separate vasoactive reflex mechanisms may exist for different orofacial regions.

Keywords: Pain; Blood flow; Central autonomic reflex; Laser Doppler imaging; Thermography; Tooth pulp stimulation

1. Introduction

Several earlier findings in anesthetized animals have shown that different kinds of noxious stimulation cause blood flow changes in several orofacial structures (Olgart et al., 1991; Izumi and Karita, 1992; Sasano et al., 1994, 1995; Shoji, 1996). The influence of pain or painful stimulation on the blood flow regulation of the orofacial area of humans has been studied only to a limited extent. It is well documented that painful stimulation -induced blood flow changes in the skin of the hand and foot are a result of both centrally mediated generalized somato-autonomic vascular reflexes, and axon reflexes (cf. Wallin, 1990). Our earlier findings (Kemppainen et al., 1994; Magerl et al., 1994) have indicated that painful tooth stimulation inducing a vasoconstriction in the skin of the hand may generate a blood flow increase in the orofacial region. Recent human studies (Magerl et al., 1996) have demonstrated that pain-induced vasoconstrictor reflexes in the hand are somatotopically organized i.e. close (homotopic) stimulation is more effective than remote (heterotopic) stimulation. Moreover, these vascular reflexes in the hand seem to reflect the intensity and discrimination of painful stimuli (Magerl et al., 1990, 1996). Apart from some tentative suggestions (Kemppainen et al., 1994; Magerl et al., 1994) there have been no systematic investigations to clarify the possible importance of stimulus site and intensity for vascular reflex responses in the orofacial area. Thus, one aim of this investigation was to study whether there are differences in pain-induced vascular reflexes between the orofacial region and the hand in relation to stimulus site and intensity. On the other hand, it is reported that tooth-stimulation-induced vascular responses

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may differ within separate orofacial structures, varying from a long-lasting blood flow increase in the upper lip (Kemppainen et al., 1994) a transient blood flow elevation in the earlobes (Magerl et al., 1994), to no change of blood flow in the cheeks (Kemppainen et al., 1994). Therefore, the present study was also conducted to determine the spatial and temporal organization of pain-induced blood flow response patterns simultaneously in various orofacial regions. Different experiments were conducted with painful stimulation of the tooth pulp and finger at comparable magnitudes of pain sensations. Pain-induced blood flow responses were recorded simultaneously from various orofacial regions and from the skin of the finger. In the orofacial area, blood flow measurements were performed by Laser Doppler Imaging (Wårdell et al., 1993) and computer-assisted infrared thermograghy (Magerl et al., 1996). In contrast to our earlier studies with laser Doppler flowmetry (Kemppainen et al., 1994; Magerl et al., 1994), with these more sophisticated recording techniques it is possible to document the magnitude, time-course and spatial distribution of vasoactive reflex patterns from the separate orofacial regions simultaneously. The blood flow measurements from the skin of the hand were performed by using laser Doppler flowmetry and plethysmography. The possible contribution of central cardiovascular parameters to the blood flow alterations was investigated by determining the spatial extent of the blood flow change in the orofacial region, and by comparing the changes in blood flow in the orofacial area and in the hand with the changes in blood pressure and heart rate.

Some data from this study have been briefly reported in abstract form (Kemppainen et al., 1999).

2. Material and methods

2.1. Subjects

Eight healthy human volunteers (seven males, one female, mean age 27.5 years, range 21–41 years) participated in three experiments after they had given their informed consent. The ethics committee of the medical faculty of the University of Erlangen-Nürnberg approved the experiments, and before the experiments the volunteers gave their informed consent in accordance with the Helsinki Declaration of 1975. If the subject was not familiar with the kind and intensity of stimuli and other experimental situations, they first participated in a training session to familiarize them with the experimental procedures. Subjects were tested while seated in a comfortable position in a dental chair. All the experiments were carried out in an air-conditioned room in which the temperature was kept between 21 and 23°C.

2.2. Stimulation techniques

The dental stimulation was generated with a constant-current tooth stimulator as has been described before (Kemppainen et al., 1985). The cathode of the stimulator was glued onto an intact upper incisor. The anode was attached to the arm of the subject. The cathode was covered with resistance material to prevent a connection between the cathode and extrapulpal tissues. The stimulator had a built-in circuit for measuring the electrode resistance. The resistances of the tested teeth were monitored throughout the experiment in monopolar coupling and they were between 1.5 and 3.5 MΩ. The test current consisted of constant current pulses of 10 ms duration at a frequency of 5 Hz, which should activate pulpal A-delta fibers at liminal perceptual intensities (Närhi et al., 1982; Närhi, 1985; Virtanen, 1985; Virtanen et al., 1987). When testing dental sensitivity, we determined detection and pain thresholds by slowly increasing the current until the subject felt the first sensation (= detection threshold), and then the stimulation current was increased until the pain threshold was achieved. Dental pain thresholds were always determined preceding the experiments and they ranged from 10 to 18 μA. During the different experimental sessions, electrical stimulation of the right upper incisor was performed at intensities of 1.5 and 3 times the individual threshold.

In the hand, pain was induced by repetitive mechanical impact stimuli to the dorsal aspect of the right finger. The technique used for this has been described in detail elsewhere (Kohllöffel et al., 1991). Briefly, a hollow plastic bullet (0.49 g, 6 mm diameter) guided in a barrel was shot (repetition rate 1 Hz) perpendicularly against the dorsal skin of the right index finger. In the preliminary tests, the individual pain threshold for mechanical stimulation was first determined for each subject. During the experiment, the intensity of finger stimulation was three times the pain threshold.

2.3. Blood flow measurements

In the orofacial region, pain-induced blood flow changes in various structures were mapped by a laser Doppler perfusion imager (LDI) and computer-assisted infrared thermography (IRT). The former provides the relative information about the movement of red cells in the superficial tissue structures. IRT, on the other hand, is a measure for local tissue temperature changes related mainly to blood flow in deeper subcutaneous tissues (Forster et al., 1995).

In the LDI technique (cf. Wårdell et al., 1993), a low power He-Ne laser beam (wavelength 632 nm) was directed through a computer-controlled optical scanner at the orofacial tissues, which were scanned by moving the laser beam step by step in a rectangular pattern over the selected regions. With this technique, median sampling depth is about 0.2 mm. In the presence of moving blood cells, a fraction of the light is Doppler-shifted, detected and converted into an electrical signal for further processing. The output signal of the processor relates linearly to tissue perfusion. This output signal was then sampled and stored

by a personal computer. From the captured perfusion values a color-coded image was generated and presented on a monitor. Further image processing and data analysis was made on the displayed image. A scanning time of 90 s was used during which the images from the areas of interest (upper and lower lips, nose, and cheeks) could be documented. The blood flow measurements were performed bilaterally for the lips and cheeks (Fig. 1).

For IRT, an infrared camera was used (Thermo-Vision 870, Agema, Sweden) and recordings were transferred to a personal computer via interface (IR-SAVE, Gesotec, Germany). The operating range of the sensor was 2-5 μm wavelength. Thermal resolution of the system was less than 0.1°C. The areas of interest for IRT were: upper and lower lips, nose, cheeks and forehead. Thermogram-images were taken continuously at 15 second intervals and analyzed off-line by densitometry.

Blood flow measurements were performed on the skin of the right index finger and ring finger by laser Doppler flowmetry (LDF; Periflux Pf2B, Perimed AB, Stockholm, Sweden) and plethysmography (PLET). These non-invasive techniques do not give absolute values, but permit comparable measurements of relative changes in the skin blood flow (Johnsson et al., 1984). All the LDF and PLET data were digitized and stored in a conventional PC.

2.4. Course of the experiments

This investigation consisted of three separate experiments in which painful tooth pulp stimulation of the upper right incisor (1.5 and 3× pain threshold) and right middle finger (3× pain threshold) were performed in eight human volunteers. All eight subjects participated in each three experimental sessions. To avoid dependencies of the values and responses between different measurements the three experimental sessions (three different stimulations) were performed on separate days. During the experiments the subject sat comfortably in a dental chair. Each stimulation period lasted 90 s. The subjective pain levels evoked by dental or finger stimulation were evaluated by a visual analogue scale, VAS (0 = no pain, 100 = the worst imaginable pain intensity). Simultaneous blood flow assessments from the orofacial region (LDI, IRT) and hand (LDF, PLET) were done in the same way before, during and after the painful stimuli in each experimental session. During all experiments, mean arterial blood pressure (MAP) and heart rate (HR) responses were monitored continuously from the left middle finger using a noninvasive cuff method (Finapress, Ohmeda, Zürich, Switzerland). With the help of an external trigger, the start of IRT, LDF, PLET, MAP and HR recordings were synchronized with the beginning of the first LDI scanning. Nine LDI scans (duration 90 s) were taken, and painful stimuli were always presented during the third scan. Trigger pulses indicated the start and the end of the stimuli. IRT, LDF, PLET, HR and PB responses were obtained for at least 5 min before the painful stimuli commenced, the last 1 min prior to stimulation being used for baseline in statistical analysis.

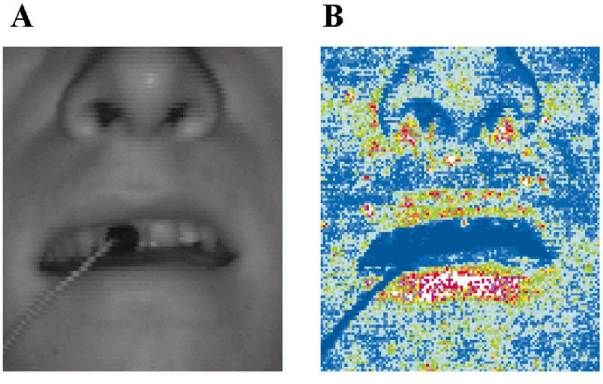

Fig. 1. A partial photo of the face (A) and a corresponding image of the orofacial blood flow (B) measured by laser Doppler imaging (LDI) during electrical tooth stimulation.

2.5. Data analysis

All data, orofacial blood flow (LDI, IRT), skin blood flow of the finger (LDF and PLET) and systemic cardiovascular (MAP and HR) responses, was computed as a percent change of baseline for each experiment. In the analysis of orofacial LDI data, the mean values calculated from the first two LDI scans (= pre-stimulation scans) for each areas of interest were first averaged from which the relative values were then calculated for each of the nine LDI scans. For the analysis of LDI and IRT data the positions of the areas of interest were corrected if movements of the subject could be detected between different images. To count the IRT, LDF, PLET, HR, MAP responses for painful stimulation, the data was reduced to six sections: one for baseline (= 60 s before the start of the stimulation), three during stimulation (0–15, 30–60, and 60–90 s after stimulation start), two post stimulation (0–1 and 2–3 min after the end of the stimulation). In the analysis of the IRT data, there were two more additional values after the end of stimulation to record the long-lasting responses that can be seen in IRT.

2.6. Statistics

The statistical significance of the results was investigated by analysis of variance (ANOVA) with the factor stimulus type (tooth stimulation at 1.5 times pain threshold, tooth stimulation at three times pain threshold, and finger stimulation at three times pain threshold) and one or two repeated measure factors: (1st) ipsi vs. contralateral, which was available only for the LDI data, and (2nd) time. A Sheffé post-hoc test was performed on significant factors. Changes to baseline were tested using a modified Student's *t*-test. The statistical package used was 'Statistica for Windows', Statsoft™, Tulsa, OK, USA. A probability value (P) of less than 0.05 was considered to represent a significant difference. All values are given as mean ± SEM, unless stated otherwise.

3. Results

The average intensities of the tooth pulp stimulation at 1.5 and 3 times pain threshold were 22.8 ± 1.6 and 47 ± 2.2 μA, respectively. The respective average pain magnitude estimates on VAS scores were 35 ± 2.2 and 74.4 ± 3.8. The average pain magnitude estimate for painful finger stimulation (three times pain threshold) was 76.8 ± 1.8. Thus, the average pain estimates for high intensity finger and tooth stimulation were of comparable magnitude.

3.1. Effect of painful stimuli on cardiovascular parameters and finger blood flow

Fig. 2 shows the relative MAP, HR, and blood flow responses (LDF) in the skin of the finger during different painful stimuli. High intensity finger and tooth stimulation induced a comparable increase in MAP which rapidly recovered after the end of stimulation (Fig. 2A). Stimulus intensity had a significant effect on MAP responses (ANOVA, 1.5 vs. 3 times tooth pain threshold, $F = 2.33$, $P < 0.05$). During the first 15 s of each painful stimulation, there was a short-lasting elevation in HR which recovered to baseline level during the continuance of the stimulation (Fig. 2B). The HR responses were not significantly affected by the stimulation type (ANOVA, F (stimulus type) $= 0.26$, $P = 0.77$).

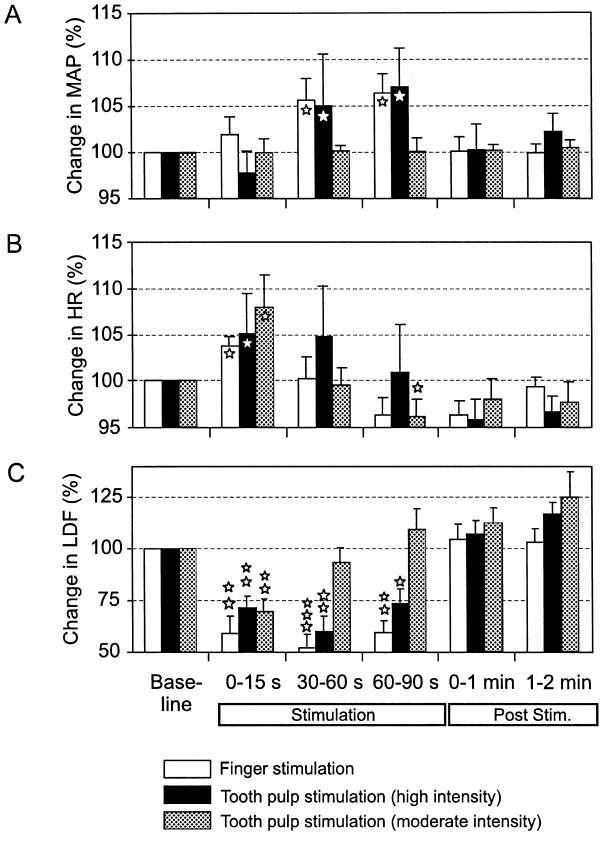

Fig. 2. The effect of different painful stimuli (A) on mean arterial pressure (MAP), (B) on average heart rate (HR) and (C) on blood flow response (LDF) in the skin of the finger. Results are expressed as relative changes to baseline. Data are mean ± SEM, $n = 8$ for all measurements. The stimulation period lasted 90 s. The changes during the first 15 s of stimulation express the arousal reaction. In the graphs, the significant differences between the accompanying value and baseline are marked by asterisks: $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$, t-test.

Each of the painful stimuli elicited a blood flow reduction in the skin of the finger (Fig. 2C). There was a significant intensity-dependent increase in LDF responses (ANOVA, 1.5 vs. 3× tooth pain threshold, $F = 4.6$, $P < 0.001$). During moderate tooth stimulation, the blood flow reduction was seen only for the first 15 s, whereas with high the intensity stimuli the blood flow responses were higher and remained significantly reduced during the whole stimulation period of 90 s. In comparison to other stimulation paradigms, high intensity finger stimulation tended to induce the most marked blood flow reduction in the finger. In each case, the blood flow of the finger returned to the baseline level rapidly after the end of the painful stimuli. Both LDF and PLET results showed similar pain-evoked blood flow decrease in the finger. In the figure, only LDF data is presented.

3.2. Reflex vasodilatation in the lips and vasoconstriction in the nose evoked by painful stimuli

Fig. 3 shows the average blood flow responses to painful stimuli measured by LDI from different orofacial regions. Only high intensity tooth stimulation induced a reflex vasodilatation in the upper and lower lip, which lasted several minutes after the end of stimulation (Fig. 3A,B). The blood flow responses were significantly affected by the stimulus site and intensity similarly in the upper (ANOVA: tooth vs. finger stimulation = 16.6, $P < 0.001$; 1.5 vs. 3× tooth pain threshold $F = 3.9$, $P < 0.001$) and lower lip (ANOVA: tooth vs. finger stimulation = 12.7, $P < 0.004$; 1.5 vs. 3× tooth pain threshold $F = 6.6$, $P < 0.005$). The reflex vasodilatation during high intensity tooth stimulation was typically seen bilaterally in the lips. The ipsilateral responses tended to be slightly higher but these differences were not significant (ANOVA: upper lip, ipsilateral vs. contralateral, $F = 0.65$, $P = 0.68$; lower lip, ipsilateral vs. contralateral, $= 0.54$, $P = 0.47$). The maximal average ipsilateral/contralateral deflections above the baseline in the upper and lower lips were 23 ± 5/18 ± 4 and 32 ± 7/23 ± 8%, respectively. In the figure, the blood flow changes of the upper (Fig. 3A) and lower lip (Fig. 3B) are presented as the average of the ipsilateral and contralateral responses.

As shown in Fig. 3C, the blood flow in the skin of the nose was reduced during each painful stimuli. These blood flow reductions varied significantly depending on the stimulus intensity (ANOVA: 1.5 vs. 3× tooth pain tooth pain threshold, $F = 4.4$, $P < 0.03$). In comparison to other stimulation paradigms, high intensity tooth stimulation tended to induce the most marked blood flow decrease in the nose. The blood flow of the nose returned to the baseline level rapidly after the end of the painful stimuli.

Only high intensity tooth stimulation caused a slight and

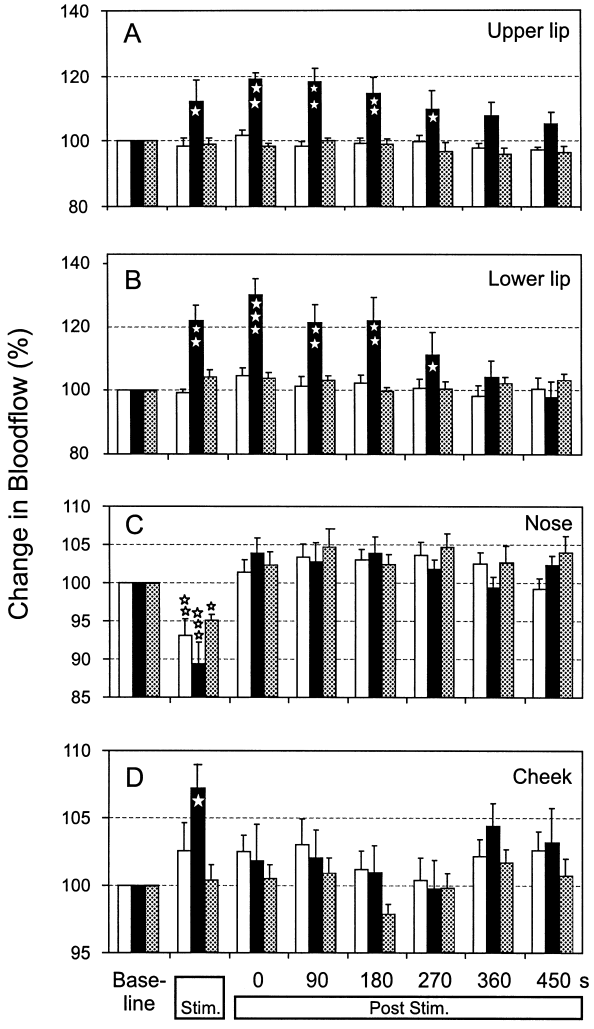

Fig. 3. Average ($n = 8$) blood flow response in the upper lip (A), lower lip (B), nose (C) and cheek (D) during the different painful stimuli as revealed by laser Doppler imaging (LDI). Scanning time for each image was 90 s. The time scale denotes the start of each scan. The stimulation period lasted 90 s (one LDI scan). Each bar represents the mean blood flow changes as compared to baseline in the according regions of interest. The error bars represent ±SEM. The significant differences from the baseline are marked by asterisks: $*P < 0.05$, $**P < 0.01$, $***P < 0.001$, t-test.

transient blood flow increase in the cheek. (Fig. 3D). The blood flow responses in the cheek were not significantly affected by any of the stimulus type (ANOVA: $F = 1.8$, $P = 0.18$). The blood flow responses were similar between ipsilateral and contralateral cheek (ANOVA, ipsilateral vs. contralateral, $F = 0.62$, $P = 0.72$). In the figure, the blood flow changes are presented as the average of the ipsilateral and contralateral responses.

3.3. Temperature elevation in the lower lip and reduction in the nose induced by painful stimuli

Fig. 4 shows the average pain-induced temperature responses measured by IRT from different orofacial areas. Only high intensity tooth stimulation elicited a long lasting temperature elevation in the lower lip 1–2 min after end of stimulation (Fig. 4A). The time courses of the IRT responses varied significantly during different stimulation conditions (ANOVA, $F = 2.2$, $P < 0.04$). In the figure, the relative temperature elevations are presented from the lower lip bilaterally. The average baseline temperatures of the lower lip were 33.32 ± 0.34, 33.33 ± 0.32, and 33,40 ± 0.59°C during high intensity finger stimulation, high intensity tooth stimulation and moderate tooth stimulation, respectively.

As shown in Fig. 4B, each of the painful stimuli induced a reduction in temperature of the nose skin. These temperature reductions were significantly different between the two stimulation intensities (ANOVA, 1.5 vs. 3× tooth pain threshold, $F = 4.4$, $P < 0.03$). The average baseline temperatures of the nose were 33.40 ± 0.37, 34.31 ± 0.22, and 33.37 ± 0.29°C during high intensity finger stimulation, high intensity tooth stimulation and moderate tooth stimulation, respectively.

None of the painful stimuli caused any changes on the temperatures measured from either ipsilateral or contralateral cheek (data not shown).

4. Discussion

The current results show that only high intensity tooth stimulation, but not finger stimulation at comparable intensities or moderately painful tooth stimulation, was effective in eliciting a long-lasting reflex vasodilatation in the upper and lower lips. Tooth stimulation was associated with an intensity-dependent vasoconstrictor response in the skin of the nose and finger. Moreover, these pain-induced vasocon-

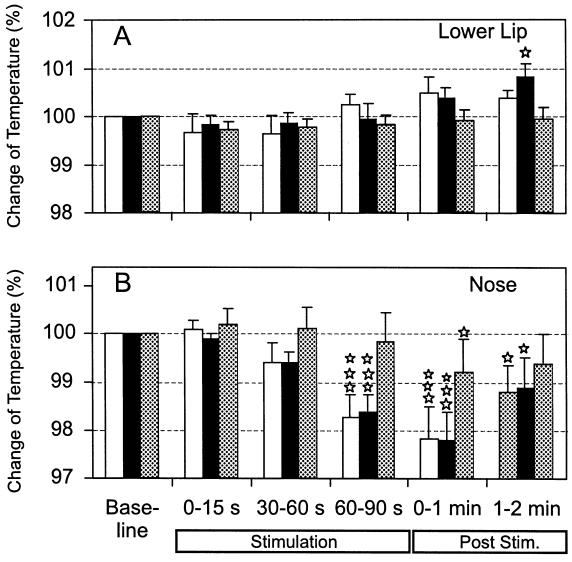

Fig. 4. Average ($n = 8$) temperature changes in the lower lip (A) and in the nose (B) as measured by thermography during the different painful stimuli. Data are expressed as relative changes to baseline. The error bars represent ±SEM. The significant differences from the baseline are marked by asterisks: $*P < 0.05$, $**P < 0.01$, $***P < 0.001$, t-test.

strictor responses showed somatotopic organization, i.e. finger stimulation had more marked effects in the hand than in the facial area when compared to responses evoked by tooth stimulation in the same tissues. None of the stimuli caused any marked blood flow changes in the skin of the cheeks. These results indicate that pain may importantly contribute to the local trigeminal blood flow regulation in humans, and that separate vasoactive reflex mechanisms may exist for different orofacial tissues.

In the present investigation, LDI and IRT techniques were applied for the first time to record pain-evoked vasoactive reflexes in the orofacial area. Although being indirect measures, both LDI (Wårdell et al., 1993) and IRT (Magerl et al., 1996) have proved earlier to be reliable and successful methods for documentation of blood flow changes in the skin of the hand. When compared to LDF (Izumi and Karita, 1992; Kemppainen et al., 1994; Shoji, 1996) and plethysmography (Drummond, 1992; 1995a,b), which have both been widely used to measure orofacial blood flow regulation, LDI and IRT have the advantage of giving information on the spatial distribution of the vasoactive changes simultaneously from separate tissues. The current findings that tooth stimulation activated simultaneously a long-lasting vasodilatation in the lips, a transient vasoconstriction in the nose and no response in the cheeks, emphasize the usefulness and validity of LDI and IRT techniques in clarifying spatial and temporal features of pain-induced vasoactive reflex responses and mechanisms in the orofacial region.

This reflex vasodilatation in the lips elicited by high intensity tooth stimulation could be mediated via a number of neural mechanisms. Several studies have shown that antidromic activation of primary afferent fibers (Blumberg and Wallin, 1987; Magerl et al., 1987; Jänig and Lisney, 1989; Ochoa et al., 1993) result in similar pattern of peripheral vasodilatation as during painful tooth stimulation in the present study. In this study, stimulation of the upper central incisor (innervated by the second branch of the trigeminal nerve) led to similar blood flow increase both in upper (innervated by the second branch of the trigeminal nerve) and lower lips (innervated by the third branch of the trigeminal nerve) bilaterally. These findings, in the anatomical point of view, are difficult to explain by an axon reflex mechanism only. However, we cannot exclude the possibility that antidromic impulses in small-diameter afferents are partly contributing to reflex vasodilatation induced by tooth pulp stimulation in the present study.

The present reflex vasodilatation in the lips elicited by tooth stimulation could well be based on a centrally mediated parasympathetic vasodilator mechanism. There are several reports showing that in various animals organs like tongue, lip and submandibular glands (Lundberg et al., 1989; Nilsson et al., 1985; Kaji et al., 1988; Izumi and Karita, 1992) and arteries supplying skin of the face (Zhu et al., 1997) are innervated by parasympathetic fibers releasing vasodilator transmitters such as vasoactive intestinal peptide (VIP), a vasodilator substance with a long half-life (Goadsby and Macdonald, 1985). Noxious stimulation of the orofacial structures has been shown to induce active somato-parasympathetic vasodilatation on the cat face (Izumi and Karita, 1992; Sasano et al., 1994, 1995; Shoji, 1996). Finally, recent studies with patients have demonstrated that unilaterally compromised parasympathetic outflow prevented normal stimulation-induced vasodilatation (Drummond, 1995a,b) in the affected side of the forehead skin.

The third possible neuronal mechanism for the facial blood flow increase in the present study is a sympathetic vasodilatory reflex. The existence of specific sympathetic vasodilator fibers has been reported both in animals (Bell et al., 1985) and in humans (Lundberg et al., 1989; Wallin, 1990). In the skin of the human foot, active sympathetic vasodilatation has also been described under some conditions (Lundberg et al., 1989). Microneurographic studies in human face have shown that activation of sympathetic nerve fibers in the supraorbital nerve by arousal stimuli or body heating coincided with blood flow increase in the forehead (Nordin, 1990). There is no doubt that high intensity tooth stimulation in the present study caused arousal which could have activated the hypothetical sympathetic vasodilatation reflex, possibly also contributing to the present blood flow increase in the lips. More recent studies in patients (Drummond, 1992, 1995a,b), however, have suggested that sympathetic activity merely contributes to stimulation-evoked sudomotor activity whereas an intact parasympathetic innervation may be important for stimulation-evoked vasodilatation in orofacial region.

It is common knowledge that pain is able to produce central cardiovascular changes, which may contribute to the blood flow changes in various peripheral structures. In the present study, high intensity tooth and finger stimuli induced an identical transient elevation in HR and BP, whereas blood flow elevation in the lips was found only during tooth stimulation. Moreover, in contrast to transient cardiovascular changes, tooth stimulation elicited a long-lasting blood flow increase in the lips. Thus, the changes in systemic HR and PB were not likely to have mediated the currently found blood flow increases in the lips.

In the present study, our aim was to compare orofacial blood flow responses to noxious inputs, which arrive either from spinal or trigeminal pathways. For this activation of C-fibers is needed which in the skin can be achieved using a repetitive mechanical stimulus (Koltzenburg and Handwerker, 1994) while at the tooth pulp an electrical stimulation is a more effective and non-invasive method (Virtanen, 1985; Virtanen et al., 1987). Only high intensity tooth stimulation (average current strength: 47 μA) induced an increased blood flow in the lips. This stimulus intensity activates not only pulpal A-δ fibers but also C afferent fibers (Närhi, 1985; Virtanen, 1985). On the other hand, moderately painful tooth stimulation with the average stimulus strength of 22.8 μA, which is in the A-δ fiber activation range (cf.

Närhi, 1985; Virtanen, 1985), did not produce any marked blood flow increase in the lips. These findings suggest that activation of nociceptive C fibers may be important in provoking long-lasting blood flow increases in the orofacial region. Interestingly, in comparison to tooth stimulation the high intensity finger stimulation at the same average magnitude and activating C-afferent fibers (Koltzenburg and Handwerker, 1994) and causing comparable arousal, as indicated by cardiovascular responses and by peripheral vasoconstriction, did not cause any marked blood flow changes in the lips. Thus, the differences in vascular responses during high intensity stimulation of the finger and tooth pulp are not due to different classes of afferent fibers activated by the two stimuli. These results indicate that, whatever the mechanism, a vasodilator reflex in the lips cannot be induced by nociceptor input from the hand but only from the trigeminal region – at least under the conditions of our experiment.

In the current study, painful stimuli of the finger and tooth induced a short lasting and an intensity-dependent blood flow decrease in the skin of the finger and nose. These blood flow decreases occurred simultaneously to the pain-induced HR and BP elevation. Previously it has been shown that various stimuli causing arousal, mental stress and pain produce an increase in sympathetic nerve traffic and are associated with transient reflex vasoconstriction in the human skin (Oberle et al., 1988; Lundberg et al., 1989; Wallin, 1990). On the other hand, body cooling has been shown to produce the same pattern of decrease in skin temperatures in finger and nose, which suggests the existence of a similar functional vasoconstrictor innervation in these areas (Blair et al., 1961). Thus, the most plausible explanation for the present pain-induced blood flow decrease in the skin of the finger and nose is a sympathetic vasoconstrictor reflex. These vasoconstrictor reflexes showed clear intensity and pain estimate -dependence: high intensity tooth stimulation associated with higher subjective pain reports induced a more marked blood flow reduction than the moderately painful tooth stimulation. Consistent with this are recent studies, which have shown that activation of nociceptive fibers in forearm by noxious chemicals led to a sustained vasoconstrictor reflex in the skin of the hand, which was clearly correlated to the magnitude of the sensation (Magerl et al., 1996). Only high intensity finger and tooth stimulation induced to tonic vasoconstriction in the skin of the finger. During moderately painful tooth stimulation, the blood flow reduction was seen only for the first 15 s, which rapidly adapted to the baseline level during the continuance of the stimulation. These results are in line with previous studies (Magerl et al., 1996) which showed that sustained sympathetic reflexes can be efficiently induced by stimulation of nociceptive C afferent fibers, whereas mildly painful stimuli causing arousal-like autonomic responses habituated easily (Bromm and Treede, 1980).

In addition to earlier findings on vasodilatation reflexes, the current LDI and IRT data demonstrate that tooth stimulation can simultaneously elicit reflex vasodilatation in one and vasoconstriction in another orofacial tissue. These results indicate that separate vasoactive regulation mechanisms may exist for different orofacial regions. In the present investigation, tooth stimulation-induced reflex vasodilatation in the lip was bilateral, although there was a tendency to a more marked ipsilateral component of this reflex. The contralateral component of reflex vasodilatation could be due to crossed pathways in the brainstem (Lambert et al., 1984).

In conclusion, this study demonstrates that high intensity tooth pulp stimulation, but not finger stimulation, can induce long-lasting trigeminal blood flow elevations. Both tooth and finger stimuli were associated with a transient blood flow decrease in the hand and nose skin. These pain-induced blood flow reductions were most likely mediated by a sympathetic vasoconstriction response. Although this sympathetic vasoconstrictor reflex shows some segmental organization, it is more generalized than the vasodilator reflex. A plausible explanation for the pain-evoked orofacial blood flow increase is a special trigeminal vasodilator, possibly parasympathetic, reflex.

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