Functional roles played by the sympathetic supply to lip blood vessels in the cat

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Izumi, Hiroshi. Functional roles played by the sympathetic supply to lip blood vessels in the cat. Am. J. Physiol. 277 (Regulatory Integrative Comp. Physiol. 46): R682–R689, 1999.—In the anesthetized cat we used laser-Doppler flowmetry to investigate the part played by cervical superior sympathetic trunk (CST) fibers in the control of blood vessels in an orofacial area (the lower lip). The blood flow increase (antidromic vasodilatation) elicited by inferior alveolar nerve (IAN) stimulation was not affected by ongoing repetitive CST stimulation over the frequency range examined (0.2–10 Hz), although reflex parasympathetic vasodilatation was attenuated. The vasoconstrictor responses elicited by IAN stimulation in some preparations were reduced in a frequency-dependent manner (at 0.2–1 Hz) during ongoing CST stimulation (and replaced by vasodilator responses). The vasoconstrictor response evoked directly by brief CST stimulation was attenuated, but not transformed to a vasodilator response, by ongoing CST stimulation. Thus in the cat lower lip 1) sympathetic stimulation attenuated one type of vasodilator response (parasympathetic-mediated vasodilatation), but not another (antidromic vasodilatation), and 2) ongoing sympathetic (CST) stimulation at low frequencies (<1 Hz) prevented further sympathetic-mediated vasoconstriction.

parasympathetic vasodilatation; antidromic vasodilatation; orofacial area; vasoresponse

IN THE OROFACIAL AREA, the blood vessels in the skin and exocrine glands, such as the salivary and lacrimal glands, are considered to be amply supplied with vasoconstrictor fibers of sympathetic origin in both animals and humans. One indication of this is that electrical stimulation of the peripheral cut end of the superior cervical sympathetic trunk (CST) fibers in the control of blood vessels in an orofacial area examined (see review by Izumi, Ref. 8). Even so, the functional significance of these sympathetic nerves is still unclear and, with respect to the orofacial area, the traditional view of a diffusely organized sympathetic system is no longer tenable. In fact, no sympathetically mediated vasoconstrictor responses have been found to occur reflexly in orofacial tissues in response to a variety of stimuli (such as trigeminal, gustatory, and visceral stimuli) (16), although parasympathetically mediated vasodilatation is evoked reflexly by the same stimuli (8). However, possible roles for the sympathetic supply to the orofacial area were suggested by reports that the sympathetic nerves to this area exert inhibitory effects on antidromic vasodilatation, muscle spindle afferent activity, and electromyographic activity, and that these inhibitory effects are not secondary to sympathetic vasoconstriction (5, 20, 26).

A lot of evidence has accumulated in recent years in favor of interactions between sympathetic nerves and sensory, parasympathetic, and other sympathetic nerves (6, 7, 10, 23–25, 29, 31–33). On the basis of these reports, a general conclusion about the role of the sympathetics could be that they exert inhibitory effects on vasodilatation regardless of whether it is of antidromic or parasympathetic origin.

In the present study, we began by examining whether sympathetic inhibitory effects within a particular orofacial vascular bed are or are not specific to one type of vasodilatation (viz., antidromic or parasympathetic). We also studied the modulating effect of ongoing sympathetic activation on the vasoconstrictor response elicited by brief stimulation of the CST and on that sometimes elicited by electrical stimulation of the peripheral end of the inferior alveolar nerve (IAN), and we compared these effects with the modulating effect of an adrenergic α-blocker. We did this to test the idea that reflex sympathetic vasoconstriction is not seen in the orofacial area because it is prevented in some way by the ongoing discharge in the sympathetic supply to these vascular beds. The vascular bed of the cat’s lower lip was selected for these experiments because 1) the blood vessels in orofacial tissues are innervated by cranial parasympathetic, superior cervical sympathetic, and trigeminal (sensory) fibers (see reviews by Gibbins, Ref. 3, and Izumi, Ref. 8) and 2) the blood flow responses evoked in this tissue by electrical stimulation of each of the above fiber types have been well studied (8).

METHODS

Preparation of animals. Thirty-four adult cats, unselected as to sex and of 2.8–4.1 kg body wt (approximate age 2–4 years), were initially sedated with ketamine hydrochloride (30 mg/kg im) and then anesthetized with a mixture of α-chloralose (50 mg/kg iv) and urethan (100 mg/kg iv). These anesthetics were supplemented if and when necessary throughout the experiment. The anesthetized animals were intubated, paralyzed by intravenous injection of pancuronium bromide (Mioblock; Organon, Teknika, Netherlands; 0.4 mg/kg initially, supplemented with 0.2 mg/kg every hour or so after testing the level of anesthesia; see below), and artificially ventilated via the tracheal cannula with a mixture of 50% air-50% O2. The ventilator (model SN-480–6; Shinano, Tokyo, Japan) was set to deliver a tidal volume of 10–12 cm3/kg at a rate of 20 breaths/min, and the end-tidal concentration of CO2 was determined by means of an infrared analyzer (Capnomac Ultima; Datex, Helsinki, Finland) as reported previously (10). Blood pH, arterial Po2, and arterial PCO2 data were obtained at intervals of 90 min using a blood
gas analyzer (model 148; Ciba-Corning, Medfield, MA), and ventilation was adjusted to keep these parameters within normal limits. Ringer solution was continuously infused at a rate of ~8 ml/h, and 8.4% NaHCO₃ solution was added if necessary (both solutions from Otsuka Pharmaceutical, Tokyo, Japan). Rectal temperature was maintained at 37–38°C with the use of a heating pad.

The criteria for maintenance of an adequate depth of anesthesia were the persistence of miotic pupils and the absence of a reflex elevation of heart rate and arterial blood pressure during stimulation of the central end of the lingual nerve. If the depth of anesthesia was considered inadequate, additional α-chloralose and urethane (i.e., intermittent doses of 5 and 10 mg/kg iv, respectively) were administered. Once an adequate depth of anesthesia had been attained, supplementary doses of pancuronium were given approximately every 60 min to maintain immobilization during periods of stimulation.

In all experiments, the vagi and superior CSTs were cut bilaterally in the neck before any stimulation. All cats were killed at the end of the experiment by an overdose (~150 mg) of pentobarbital sodium.

The experimental protocols were reviewed by the Committee on the Ethics of Animal Experiments of Tohoku University School of Medicine, and they were carried out in accordance with both the Guidelines for Animal Experiments issued by Tohoku University School of Medicine and The Law (No. 105) and Notification (No. 6) issued by the Japanese Government. All animals were cared for and used in accordance with the recommendations in the current National Research Council guide.

Electrical stimulation of the superior CST, IAN, and lingual nerve. The present experiments involved electrical stimulation of the peripheral cut end of the IAN (Fig. 1A), the central cut end of the lingual nerve (LN; Fig. 1B), or the peripheral cut end of the CST (Fig. 1C). When the LN was to be stimulated, the IAN was not sectioned. In this study, all nerves were sectioned and stimulated unilaterally under a binocular microscope. A bipolar silver electrode attached to a NIHON Kohden model SEN-7103 Stimulator was used for stimulation. For "ongoing" sympathetic stimulation, the CST was stimulated for periods of 7 min each using a supramaximal voltage (10 V) and pulses of 2 ms duration at various frequencies (0.2–10 Hz, Figs. 2–6). The IAN was dissected free from the mandibular canal on the side on which lip blood flow (LBF) was to be measured and was stimulated [for 20 s using supramaximal voltage (30 V) at 10 Hz with pulses of 2 ms duration] either alone or during ongoing CST stimulation. In some experiments, with the vagi and sympathetic trunks both cut in the neck, the IAN was stimulated alone or some 5–7 min after an intravenous injection of phentolamine (1 mg/kg via the femoral vein). The LN was stimulated [for 20 s using a supramaximal voltage (30 V) at 20 Hz with pulses of 2 ms duration] either alone or during ongoing CST stimulation. In some experiments, the CST was stimulated briefly (for 20 s at 10 Hz) during ongoing CST stimulation at 0.2–10 Hz. The two types of CST stimulation were delivered via the same set of electrodes, the ongoing stimulation being interrupted for the 20 s needed to deliver the brief CST test stimulation. Electrical stimulation of the IAN, LN, or CST was begun some 3–4 min after the start of a period of repetitive ongoing sympathetic stimulation, unless otherwise noted.

Measurement of lower LBF and systemic arterial blood pressure. Changes in blood flow in the lower lip adjacent to the canine tooth were monitored on one side using a laser-Doppler flowmeter (LDF; ALF21R, Advance, Tokyo, Japan) as described before (10, 11, 13, 16). The probe was placed against the lower lip without exerting any pressure on the tissue. The LDF values obtained in this way represent the blood flow in superficial vessels. Previous studies have indicated a significant correlation between blood flow recordings from oral tissues obtained by laser-Doppler flowmetry and by other well-established methods (2, 22). The analog output of the equipment does not give absolute values but shows relative changes in blood flow (for technical details and evaluation of the LDF method, see Stern et al., Ref. 34). Electrical calibration for zero blood flow was performed for all recordings. Several gains were selectable and the maximum output of a given gain level (defined electrically) was taken as 100%. At the settings used in this study, the ratio between the magnitude of the LBF increases and the amplitude of the baseline fluctuations ("signal-to-noise ratio") was 8–10 when either the IAN or LN was stimulated with a supramaximal voltage. The output from the various devices was continuously displayed on an eight-channel chart recorder (model W5000; Graphtec, Tokyo, Japan) at a speed of 30 mm/min. The magnitude of the blood flow changes elicited by nerve stimulation or intravenous phentolamine and the amplitude of the basal LBF level were assessed by making measurements in millimeters on the chart record. In Figs. 3 and 5, flow levels are expressed in arbitrary units.

Systemic arterial blood pressure was recorded from the femoral catheter via a Statham pressure transducer. A tachograph (model AT-610G; NIHON Kohden, Tokyo, Japan) triggered by the arterial pulse was used to monitor heart rate.
Types of tests performed. The main tests carried out in this study were as follows: 1) effects on LBF induced by electrical stimulation of CST, the peripheral cut end of IAN, and the central cut end of LN and 2) effects of ongoing electrical stimulation of CST on the various changes in LBF (increases, decreases, and biphasic changes) evoked by IAN and LN stimulation.

Statistical analysis. All numerical data are given as the mean ± SE. The significance of changes in the test responses was assessed using a paired Student's t-test, Welch's t-test, or an ANOVA followed by a contrast test. Differences were considered significant at the level P < 0.05. Data were analyzed using a Macintosh computer with StatView 4.5 and Super ANOVA.

RESULTS

Effects of CST stimulation and phentolamine on LBF and systemic arterial blood pressure. Figure 2 shows the effects of ongoing CST stimulation and intravenous phentolamine on the basal LBF level (Fig. 2A) and on systemic arterial blood pressure (Fig. 2B) with the ipsilateral IAN intact or sectioned. Such CST stimulation reduced the basal LBF level [F(4,28) = 53.32, P < 0.001, n = 8 in each group] in a frequency-dependent manner (for intact IAN, r = 0.715, n = 5 in each group, P < 0.0001; for sectioned IAN, r = 0.839, n = 5 in each group, P < 0.0001) (Fig. 2A). Slight increases in arterial blood pressure were elicited by CST stimulation regardless of whether the IAN was cut (for cats with intact IAN, F(4,36) = 4.321, n = 10 in each group, P < 0.01; for IAN-sectioned cats, F(4,28) = 2.831, n = 8 in each group, P < 0.05). However, a statistically significant blood pressure increase was elicited by CST stimulation only at 2 Hz in both IAN-intact and -sectioned cats. In terms of the changes in these two variables evoked by CST stimulation, no significant difference was observed between the intact and IAN-sectioned cats (NS, ANOVA). On the other hand, intravenous infusion of phentolamine (1 mg/kg) elicited a marked decrease in systemic arterial blood pressure (by 29.9 ± 5.1 mmHg, n = 10, P < 0.01), but it had no statistically significant effect on the basal LBF level (NS, Welch's t-test; n = 13).

Effects of IAN and LN stimulation on LBF. In the 34 animals in which IAN and LN stimulation was performed, stimulation of the peripheral cut end of the IAN sometimes evoked a simple rise in LBF (in 22 animals), sometimes a simple fall (in 5 animals), and sometimes a biphasic response (a fall followed by a rise; in 7 animals). By contrast, stimulation of the central cut end of the LN always evoked a simple rise in LBF.

Effects of ongoing CST stimulation on the LBF increase evoked by IAN and LN stimulation. During ongoing CST stimulation at frequencies of 0.2–10 Hz, blood flow responses were evoked in the lower lip by stimulating the IAN in a peripheral direction or the LN in a central direction. Typical examples of evoked LBF increases are shown in Fig. 3, A and B, and mean data are shown in Fig. 4. There was no statistically significant difference in the blood flow increase elicited by IAN stimulation whether the IAN was stimulated without (control) or during CST stimulation (over the frequency range examined) (NS, ANOVA, n = 8 in each group; Figs. 3A and 4). On the other hand, the LBF response to LN stimulation was reduced in a frequency-dependent manner by CST stimulation [F(6,60) = 40.62, n = 8 in each group, P < 0.0001 (Figs. 3B and 4)], an effect previously reported by us (10).

Effects of ongoing CST stimulation and phentolamine on the falls and biphasic changes in LBF evoked by IAN stimulation. Figure 5 shows typical examples of the effects of electrical stimulation of the CST at various frequencies (0–2 Hz; Fig. 5, A and B) and of phentolamine administration (Fig. 5D) on blood flow responses (biphasic responses or simple falls in LBF) in the lower lip elicited by electrical stimulation of the peripheral cut end of the IAN. Mean data are shown in Fig. 6, A and C, for the biphasic responses and in Fig. 6, B and D, for similar experiments in which IAN stimulation evoked a simple fall in LBF. The falls in LBF elicited by IAN stimulation (whether or not they were followed by a rise) were reduced in a frequency-dependent manner during concurrent CST stimulation at 0.2–1 Hz [F(4,16) = 13.58, n = 5 in each group, P < 0.001 in Fig. 6A; F(4,12) = 35.06, n = 4 in each group, P < 0.001 in Fig. 6B], and they were completely abolished at 2 Hz CST stimulation (Figs. 5, A and B, and 6, A and B). By contrast, the magnitude of the increases in LBF that formed part of the biphasic responses was almost unchanged by concurrent CST stimulation at any of the frequencies examined [F(4,16) = 2.16, n = 5 in each group, P = 0.16].
In experiments in which only a fall in LBF was elicited by IAN stimulation without CST stimulation, a rise in LBF appeared during ongoing CST stimulation at all frequencies examined (Fig. 5B). In such experiments, there was no statistically significant difference in the magnitude of the LBF increases whatever the frequency of CST stimulation (0.2–2 Hz; NS, ANOVA, n = 4; Fig. 6B).

The falls in LBF elicited by IAN stimulation, regardless of whether they were (Fig. 6C) or were not (Fig. 6D) followed by increases, disappeared completely on administration of phentolamine (1 mg/kg iv; Fig. 5D). The magnitude of the rise in LBF that formed part of the biphasic response was unaffected by phentolamine administration (Fig. 6C; NS, paired t-test; n = 5). When a simple fall in LBF was elicited by IAN stimulation, this was replaced by an increase after phentolamine administration (Fig. 6D).

![Fig. 3. Typical examples of effects of ongoing sympathetic stimulation on vasodilator responses. Effects on lower LBF evoked by electrical stimulation of the peripheral cut end of IAN (A) and of central cut end of lingual nerve (LN; B). Above stimuli were delivered either alone (control) or during ongoing repetitive CST stimulation (both in vagosympathectomized cats). IAN and LN were stimulated where indicated (○) for 20 s at a supramaximal voltage (30 V) at 10 Hz with pulses of 2 ms duration. Frequencies (0.2–10 Hz) of CST stimulation (10 V) are shown at top. au, Arbitrary units.](image)

![Fig. 4. Mean data (±SE) for effects of ongoing sympathetic stimulation on vasodilator responses. Effects on lower LBF evoked by electrical stimulation of peripheral cut end of IAN (○; n = 8) and of central cut end of LN (●; n = 8) (both in vagosympathectomized cats). Above stimuli were delivered either alone (control) or during ongoing repetitive CST stimulation (at 0.2–10 Hz). Ordinate shows IAN- and LN-stimulated increases in LBF during CST stimulation (expressed as a percentage of response to IAN and LN stimulation in the absence of CST stimulation; “control”). Statistical significance was assessed by means of ANOVA followed by a contrast test. *P < 0.05, **P < 0.01, ***P < 0.001 vs. control.](image)

![Fig. 5. Typical examples of effects of ongoing sympathetic stimulation or phentolamine on biphasic and vasoconstrictor blood flow responses to electrical stimulation of IAN and CST. Effects on blood flow responses elicited by stimulation of the peripheral cut end of IAN induced by ongoing repetitive CST stimulation (biphasic, A; vasoconstrictor, B) and by intravenous administration of phentolamine at 1 mg/kg (D) and effects of ongoing CST stimulation on the vasoconstrictor response evoked by brief CST stimulation (C). Traces show lower LBF and systemic arterial blood pressure (ABP). IAN and CST stimuli were delivered ipsilaterally [in A and B, either alone (control) or during ongoing repetitive CST stimulation; in D, before or after phentolamine; all in vagosympathectomized cats]. IAN and CST were stimulated where indicated (○ and ●, respectively) IAN for 20 s at a supramaximal voltage (30 V) at 10 Hz with pulses of 2 ms duration and CST for 20 s at a supramaximal voltage (10 V) at 10 Hz with pulses of 2 ms duration. Frequencies (0.2–10 Hz) of ongoing CST stimulation (10 V) are shown below the stimulus marker.](image)
Effect of ongoing CST stimulation on the fall in LBF evoked by brief CST stimulation. The amplitude of the fall in LBF evoked by brief (20 s) CST stimulation was attenuated by ongoing CST stimulation in a frequency-dependent manner (Fig. 5C). However, this response was not transformed to a rise in LBF by ongoing CST stimulation (Fig. 5C), a result in accordance with our previous findings (19).

DISCUSSION

The blood flow changes elicited in this study by stimulation of the IAN, LN, or CST were either too large or in the wrong direction to have been the passive result of any evoked blood pressure changes (which were anyway quite small). Thus we feel justified in referring to them as “vasoconstriction” or “vasodilatation,” as appropriate.

Vascular responses to IAN stimulation. We previously reported that electrical stimulation of the peripheral cut end of the IAN elicits one of three different patterns of vascular response in the cat gingiva and lower lip: vasodilatation, vasoconstriction, or a biphasic response (vasoconstriction followed by vasodilatation) (12, 17). These vasodilator and vasoconstrictor responses or components were considered to be due to activation of sensory fibers and sympathetic α-adrenergic fibers, respectively, because they were abolished by prior treatment with capsaicin, the pungent agent of the hot pepper, and phentolamine, an adrenergic α-receptor blocker, respectively. At this time, we cannot be sure why parasympathetically mediated vasodilatation does not occur in the lower lip on electrical stimulation of the peripheral cut end of the IAN, although we found evidence for parasympathetic vasodilator fibers in the IAN originating from the otic ganglion in our previous studies (15, 16).

Sympathetic supply to the lower lip. The sympathetic fibers that run from the superior cervical ganglion to innervate structures in the head are known to travel both along branches of the carotid artery and via cranial nerves such as the facial and trigeminal nerves (e.g., Kandel et al., Ref. 18). The presence of sympathetic vasoconstrictor fibers in the IAN has previously been reported by a number of investigators (17, 27, 30). In the present study, frequency-dependent basal blood flow decreases were observed in the lower lip after electrical stimulation of the peripheral cut end of the CST regardless of whether the IAN was or was not cut (Fig. 2B). This indicates that some sympathetic vasoconstrictor fibers travel to the lower lip without joining the IAN (see Fig. 1), a conclusion consistent both with the observation of Matthews and Robinson (27) that section of this nerve did not abolish the vasoconstriction in the lower lip produced by stimulation of the CST in the cat and with the finding of Kerezoudis et al. (21) that section of the IAN failed to modify the dopamine level in the gingiva of the rat.

Effects of sympathetic activation on vasodilator responses. There is now considerable evidence that activation of sympathetic nerves exerts an inhibitory influence on afferent nerve-induced (antidromic) vasodilatation in both body skin (6, 7, 29) and dental pulp (20, 31). This inhibition is thought to result from an attenuation of the release of the vasodilator agents via an activation of presynaptic α-adrenoceptors on the sensory nerve terminals. Whatever the mechanism actually is, these data suggest that sympathetic vasoconstrictor activity can effectively override the vasodilator effect induced...
by antidromic stimulation of nociceptive C fibers in some tissues (body skin and dental pulp). However, the present results suggest that the situation is different in the lower lip. Indeed, as shown in Figs. 3 and 4, the LBF increase we elicited by electrical stimulation of the peripheral cut end of the IAN was not significantly affected by concurrent stimulation of the cervical superior sympathetic trunk at frequencies within the range 0.2–10 Hz. The above results suggest that inhibition of vasodilatation by ongoing CST stimulation (when it occurs) is not due to a simple additive effect at the smooth muscle level and that sympathetic vasoconstriction does not necessarily override a vasodilator response. At present, we know of no data to explain the apparent tissue-specific nature of the interaction between sympathetic vasoconstrictor activity and antidromic vasodilatation.

Nearly 50% of the neurons in the rat superior cervical ganglion project to blood vessels, judged by neurochemical and retrograde tracing studies (4, 35), and tonically active vasoconstrictor neurons have been reported to be present in the superior cervical ganglion of both rat (28) and cat (27). On this basis, a major role of the superior cervical sympathetic neurons supplying orofacial areas would seem likely to be the production of vasoconstriction. However, we found recently in cats that no sympathetically mediated vasoconstrictor responses occurred reflexly in orofacial tissues in response to a variety of stimuli (such as trigeminal, gustatory, and visceral stimulation) even though parasympathetic-mediated reflex vasodilatation was evoked by these same stimuli (see review by Izumi, Ref. 8). This result was surprising because electrical stimulation of the peripheral cut end of the superior CST consistently evokes a vasoconstrictor response in all the orofacial tissues examined so far (9, 12, 14, 17). In a previous study, we found that CST stimulation reduced parasympathetic-mediated blood flow increases in certain orofacial areas (such as the lower lip and palate) (10). This modulatory effect was also seen in the present study (Fig. 3B). This modulation was not simply the result of an additive effect between vasoconstriction and vasodilatation and it did not occur in the tongue or submandibular gland (10). We suggested a possible modulatory action of superior cervical sympathetic vasomotor neurons within certain vascular beds in the orofacial area (10). This idea is consistent with other data that have accumulated in recent years suggesting a physiological role for sympathetic neurons in the orofacial area that is unrelated to vasoconstriction (5, 20, 26). Nevertheless, it must be admitted that the functional role of the superior cervical sympathetic neurons supplying the orofacial area is still not entirely clear.

Effects of sympathetic activation on vasoconstrictor responses. There are now a lot of data confirming the importance of norepinephrine (NE) as a neurotransmitter and neuromodulator at the vascular neuroeffector junction (see review by Wilson and Dunn, Ref. 36). It is unlikely that the reductions in the IAN-evoked vasoconstrictor responses induced by ongoing CST stimulation and phentolamine were secondary to effects on circulatory parameters such as blood pressure or the basal LBF level. In fact, phentolamine (1 mg/kg iv) had much the same effect on the vasoconstrictor responses as CST stimulation at 1–2 Hz, although its effect on blood pressure and basal LBF was quite different (quantitatively and/or qualitatively; see Fig. 2). It remains to be determined whether the interaction between ongoing CST activity and IAN-induced vasodilatation results from an inhibition of neurotransmitter release from sympathetic nerve terminals (inactivation of sympathetic vasoconstrictor fibers) or from a blockade of adrenergic α-receptors on vascular smooth muscle by unknown substance(s) released from sympathetic nerve terminals during CST stimulation (see Perspectives and Fig. 7).

![Diagram showing mechanisms of sympathetic and parasympathetic nervous system interactions](image-url)
Conversion of vasoconstriction to vasodilation. The inability of ongoing CST stimulation to transform CST-induced vasoconstriction to vasodilatation (Fig. 5C) is in marked contrast to its effect on the vasoconstrictor response sometimes evoked by IAN stimulation (Fig. 5, A and B). The simplest explanation for this difference is as follows. The IAN is a mixed nerve, and so its stimulation activates vasodilator as well as vasoconstrictor fibers (see Fig. 7). An abolition of the vasoconstrictor effect mediated by sympathetic fibers running in the IAN could unmask a previously hidden (Fig. 5B) or partially hidden (Fig. 5A) vasodilator response. Thus a transformation of a vasoconstrictor response to a vasodilator response by ongoing CST stimulation would be expected to occur only when the test response was evoked by stimulation of a mixed nerve (such as IAN). This explanation implies that no vasodilator fibers to the lower lip are activated when the test response is evoked by brief CST stimulation.

Effect of spontaneous sympathetic discharge on orofacial vasoconstrictor responses. Our previous findings (10) and data reported by other investigators (1) suggest that under the present experimental conditions, the spontaneous discharge in the fibers of the CST innervating the vascular beds supplied by the common carotid artery or the salivary glands (probably constituting the vasoconstrictor population) has a frequency of ~0.5–1 Hz. Ongoing CST stimulation at these frequencies was sufficient to abolish (or almost abolish) the vasoconstrictor effect of IAN stimulation (Fig. 6). This may mean that IAN-evoked vasoconstriction would not occur under physiological conditions, because it would presumably be suppressed by the spontaneous sympathetic discharge in the CST. It may also indicate that the spontaneous rate of discharge in the sympathetic supply to the lower lip (and possibly other orofacial areas) in some way prevents a significant vasoconstriction being elicited by a higher level of sympathetic discharge. This is consistent with the repeated finding (see introduction) that reflex sympathetic vasoconstriction cannot normally be demonstrated in orofacial tissues (including the lower lip) under resting conditions, although these areas receive a sympathetic vasoconstrictor supply (10).

To conclude, the main findings of this study are 1) that sympathetic vasoconstrictor stimulation does not necessarily override a vasodilator response (because, in the cat’s lower lip, ongoing CST stimulation reduced parasympathetically mediated vasodilatation but not antidiromically mediated vasodilatation) and 2) that active preconstriction of blood vessels by ongoing CST stimulation at low frequencies, presumed to be within the physiological range for spontaneous sympathetic discharge in the CST, attenuated or abolished the vasoconstriction elicited by stimulation of the sympathetic vasoconstrictor fibers running in the IAN.

Perspectives

At present, we can only speculate on the mechanisms underlying the modulatory effects we have observed. As indicated in Fig. 7, two possible explanations for the modulatory effect of ongoing CST activity on IAN-evoked vasoconstriction are that unknown substance(s) released from sympathetic nerve terminals during CST stimulation could cause 1) an inhibition of neurotransmitter release from sympathetic nerve terminals (inactivation of sympathetic vasoconstrictor fibers) or 2) a blockade of postjunctional adrenergic α-receptors. The latter effect would come into operation if, for example, adrenergic α-receptors on vascular smooth muscle could not be activated because they were already occupied by NE released from sympathetic nerve terminals by the ongoing CST stimulation. Either effect (1 or 2) could also explain the attenuation of brief CST-induced vasoconstriction by ongoing CST stimulation and the unmasking of a vasodilator response evoked when a mixed nerve (such as IAN) is stimulated. As also indicated in Fig. 7, unidentified substance(s) released from CST nerve terminals may act in an inhibitory way on parasympathetic nerve terminals in the IAN or on postjunctional vasoactive intestinal peptide receptors (to attenuate parasympathetic-mediated vasodilatation), but not on the terminals or postjunctional receptors involved in antidiromic vasodilatation. Each of these ideas will require specific investigation. Our observation that sympathetic vasoconstrictor responses (whether evoked by brief CST stimulation or by IAN stimulation) are abolished or nearly abolished by ongoing CST activation at frequencies around the spontaneous discharge level may explain why reflex sympathetic vasoconstrictor responses cannot normally be evoked in orofacial tissues under physiological conditions.

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FUNCTIONAL ROLES OF SYMPATHETIC NEURONS