Vasodilator system for the face

GUILLERMO GONZALEZ, M.D., BURTON M. ONOFRIO, M.D., AND FREDERICK W. L. KERR, M.D.

Section of Neurological Surgery, Mayo Clinic and Medical School, Rochester, Minnesota

The authors describe investigations in cats to delineate a vasodilator system to the face, which they undertook after a previous study showed that radiofrequency coagulation of the trigeminal ganglion produced a pronounced flush in the skin of the corresponding division. Results demonstrate a vasodilator system emerging from the brain stem with the facial nerve which, by way of the greater superficial petrosal nerve, reaches the trigeminal ganglion. There the fibers are distributed to each of the divisions of the fifth nerve; in addition, a moderate number of vasodilator fibers also appear to leave the brain stem directly with the trigeminal nerve. Vasodilator effects were elicited by stereotaxic stimulation of the facial and trigeminal nuclei in the brain stem. There is, therefore, a dual vasomotor control of the facial cutaneous vascular bed; the classical sympathetic vasoconstrictor system of the face is complemented by a vasodilator system capable of producing changes of equal but opposite amplitude in vessel caliber.

Key Words • autonomic control • facial vasodilatation • brain stem • trigeminal nerve • facial nerve • greater superficial petrosal nerve

Vasoconstrictor fibers from the cervical sympathetic chain have long been known to control the caliber of cutaneous vessels of the face; on the other hand, no vasodilator component is known to exist. The general belief is that vasodilatation in this area results from inhibition of the sympathetic vasoconstrictor tone.

Two clinical observations suggest the presence of an active vasodilator mechanism. The first, made independently by one of the authors and by Sweet and Wepsic, was that when the trigeminal ganglion in patients with tic douloureux was destroyed by high frequency electrocoagulation, a marked flush developed in the area of the corresponding division. The other phenomenon is emotional flush or blushing, which occurs with equal intensity in patients in whom the cervical sympathetic nerve has been removed. This investigation was undertaken in order to elucidate the pathways and mechanisms responsible for these phenomena.

Material and Methods

Adult cats weighing between 6 and 9 lb were used. All procedures were carried out under pentobarbital anesthesia. Prior to stimulation, gallamine triethiodide was administered intravenously and artificial respiration was maintained with a Harvard respirator.

Vasodilator system for the face

The trigeminal ganglia and their divisions were exposed bilaterally by an extensive craniectomy and excision of the brain rostral to the colliculi. When required, the facial nerve was exposed from its origin at the brain stem as far as the middle ear; the greater superficial petrosal nerve was also exposed in selected experiments from the geniculate ganglion as far as the third division of the trigeminal nerve. Stimulation at various levels of these nerves was delivered through a Grass stimulus isolation unit by means of a fine steel electrode led against an indifferent lead placed in the cervical or temporal muscle. Stimulus parameters ranged from 9 to 12 V, and pulse duration 1 msec at 100 Hz maintained for 2 to 3 min; the frequency was higher than necessary for maximal response, but was used because of technical factors related to thermistor amplification circuits.

Stereotaxic stimulation of the brain stem followed a posterior fossa craniectomy and excision of the cerebellum. A steel microelectrode, insulated except for the distal 7 to 10 μ, was advanced into the medulla in 0.5-mm increments at successive mediolateral and caudorostral planes by means of a micromanipulator. The obex was used as zero for the coronal plane; the floor of the fourth ventricle constituted zero for the vertical plane. Stimulus parameters were similar to those used in stimulation of the peripheral structures. A small electrolytic lesion was made at sites from which maximal vasomotor responses were elicited. The medulla was embedded in paraffin and serial sections were made and stained with luxol fast blue to identify the electrode tip positions.

The chronic rhizotomies of the facial and trigeminal nerves were done via a unilateral occipital craniectomy; testing of vasomotor responses was always delayed from 1 to 2½ weeks postoperatively. Vasomotor responses were determined indirectly by means of three thermistors placed on the supraorbital ridge, and the upper and lower lip, respectively. Preliminary amplification was obtained with thermal analog amplifiers; the output from these was led to a Minneapolis Honeywell 1508 Visicorder and recorded on light-sensitive paper.

Results

Vasomotor responses were studied in relation to stimulation of the:

1. trigeminal divisions
2. cervical sympathetic chain
3. trigeminal divisions after acute and chronic trigeminal posterior rhizotomy
4. facial nerve and the greater superficial petrosal nerve
5. trigeminal divisions after chronic section of the facial nerve
6. brain stem.

The results are described as follows.

1. Stimulation of the Trigeminal Divisions

Stimulation of each division of the trigeminal nerve produced an increase in cutaneous temperature of as much as 3°C in the case of the third division, up to 2.2°C for the second, and up to 1.0°C for the first division. With minor variations this pattern was consistently observed; the third division was usually the most responsive and the first the least so. The response began after a latency of 5 to 8 sec and lasted for approximately 6 to 8 min following stimulation for 2 to 3 min. These responses are illustrated in Fig. 1.

Stimulation of one division near the ganglion resulted in a rise in temperature in its cutaneous distribution with a moderate increase in cutaneous temperature in the adjacent division; this overlap was due to current spread, since it was not seen when the divisions were stimulated more distally following foraminotomy.

2. Cervical Sympathectomy

Temperature rises elicited by stimulation of the first division of the fifth nerve were of small amplitude and frequently could not be obtained. However, when cervical sympathectomy was performed 1 week prior to testing, the same clear-cut rise in temperature occurred in the first division distribution as seen
FIG. 1. Vasomotor responses of the face in the normal animal. Upper: Second division stimulation. Lower: Third division stimulation. In this and subsequent illustrations each trace corresponds to the temperature recorded from the skin of the supraorbital area (I Div), the upper lip (II Div), and lower lip (III Div). Onset and end of stimulation are indicated by the bar, and stimulus parameters are shown beneath it. The temperature prior to stimulation at the site of each thermistor is indicated by the figure on the coordinate at left.

FIG. 2. Stimulation of the ipsilateral cervical sympathetic chain; a gradual fall and prolonged delay in recovery of temperature in the territory of each of the trigeminal divisions is seen, the response being weakest in the first division. See Fig. 1 legend for key.

in the territory of the second and third trigeminal divisions. The only difference between the normal and sympathectomized side was that in the latter the first division responses were consistently of greater amplitude. Conversely, when the normal sympathetic chain was stimulated, a drop in temperature of the skin in all three divisions occurred, as expected. Comparing this response to the vasodilator response demonstrates that sympathetic vasoconstriction develops more slowly but persists considerably longer after the end of stimulation. It is interesting to note that the vasodilator response is usually of greater magnitude than the vasoconstrictor response; in some instances this difference is particularly striking (compare Fig. 2 with Fig. 5 lower).

3. Trigeminal Rhizotomy

Acute transection of the trigeminal root did not depress the vasomotor response elicited by stimulation of the trigeminal divisions. When the trigeminal root (sensory and motor) was transected 6 days prior to testing, evoked cutaneous temperature rises were slightly smaller than the normal range, but the return to baseline or resting temperatures was significantly prolonged (Fig. 3).

The failure of chronic trigeminal rhizotomy significantly to depress these vasomotor responses suggested that the latter might be due to axon reflexes or to vasodilator fibers that joined the trigeminal divisions peripherally to the rhizotomy. We therefore investigated the probability that these fibers reached the divisions from the facial nerve via the greater superficial petrosal nerve.

4. Facial and Greater Superficial Petrosal Nerves

Stimulation of the facial nerve in the internal auditory canal resulted in temperature rises in the cutaneous distribution of all trigeminal divisions (Fig. 4). When the trigeminal division was transected the temperature rise was abolished in its corresponding area of distribution. Stimulation of the greater superficial petrosal nerve gave rise to similar vasodilator responses.

5. Trigeminal Divisions after Chronic Section of the Facial Nerve

When the facial nerve was chronically transected at its entrance into the internal auditory meatus (seven experiments), the vasomotor responses elicited by stimulation of the trigeminal divisions 1 week after the rhizotomy were negligible in the first and
moderately depressed in the second and third division by comparison with responses elicited on the intact side of the same animal. In Fig. 5 upper stimulation of the second division in one of these experiments illustrates the degree of depression by comparison with the control response on the opposite side; stimulation of the third division resulted in similar temperature changes. It should be noted also that the return of temperature to the baseline level was markedly delayed on the operated side and comparable in this respect to the experiments in which chronic trigeminal rhizotomy had been done. However, when combined section of the posterior root of the trigeminal nerve and the facial nerve (three experiments) was performed 1 week prior to testing, no vasomotor responses could be elicited by stimulation of the trigeminal divisions on the operated side, while responses on the control side were of normal amplitude.

6. Stimulation in the Brain Stem

The medulla was stimulated in a systematic grid pattern at 0.5-mm intervals from medial to lateral planes, and from the surface to a depth of 5 mm at coronal planes between 6 and 11 mm rostral to the obex. Two discrete loci were identified, stimulation of which caused vasomotor responses similar to those elicited from the peripheral system.

Figure 6 illustrates the cutaneous vasodilator responses evoked by stimulation at stereotaxic coordinates 6 and 7 mm rostral to the obex, 4 mm lateral to the midline, and between 3 and 4 mm deep to the floor of the fourth ventricle. The responses were highly specific to these loci, since when the electrode was displaced upward or downward 0.25 mm (that is, to 2.75 or 4.25 mm deep) stimulation no longer produced a vasodilator effect; stimulation along a track 0.5 mm medial or lateral to this site was similarly ineffective. It was also particularly interesting that within this discrete "active zone" vasodilator responses in the distribution of all three divisions could be obtained at one point, while if the electrode was advanced or withdrawn 0.25 mm, the response was limited to the first and second divisions. The rise in cutaneous temperature thus evoked ranged from 0.75°C in the area of the second division, to 2.75°C in the distribution of the third division, the latency to onset being 6 sec and the duration...
corresponded to the spinal nucleus of the trigeminal nerve at the level of subnucleus interpolaris. Here again the “active zone” was very discrete and confined to the spinal nucleus over a dorsoventral distance of 1 mm; the response was limited to the third division and slight displacements of the electrode within this vertical range resulted in disappearance of the vasodilator response. No evidence of vasomotor response was obtained from any other point in the grid area stimulated; this emphasizes the specificity of the reaction (Fig. 7).

Finally, stimulation of the surface of the spinal tract of the fifth nerve at a point 3 mm caudal to the obex, where the tract lies superficially, and in the area corresponding to the fibers of the second division, regularly resulted in a temperature rise of 0.5°C limited to the peripheral distribution of the second division. No vasodilator responses could be evoked by stimulation in the area of the first and third divisions of the tract, although this was repeatedly attempted (Fig. 8).

**Discussion**

The experiments described in the preceding paragraphs indicate that vasomotor control of the facial area is considerably more complex than previously believed. The most probable source of the vasodilator fibers to the face initially was felt to be the facial nerve by way of its greater superficial petrosal nerve (GSP) branch. Since the trigeminal nerve's evoked vasomotor responses alone could not disprove this hypothesis, the characteristic distribution of the response in a divisional pattern by the trigeminal nerve made it necessary to rule out the possibilities that we might be dealing with trigeminal vasodilator efferent fibers, with a trigeminal axon reflex, or with a true reflex arc whose afferent limb was composed of trigeminal sensory fibers, the vasodilatation being a centrally mediated inhibition of the sympathetic outflow to the face. The latter possibility was immediately discarded from consideration when acute section of the trigeminal root failed to depress the vasodilator response elicited from the divisions.

Axon reflexes were considered next. The explanation proposed for this phenomenon is that cutaneous sensory fibers from dorsal root ganglia provide a collateral branch to

---

Fig. 6. **Upper:** Results of stimulation of the facial nucleus 6 mm rostral to obex; the response is limited to the first and second trigeminal divisions. **Center:** Results of stimulation of facial nucleus at 7 mm rostral to the obex; response is absent in the first division, the second division response is larger, and maximal response is present in the third division. Stimulation at progressively deeper sites (D1-4 from the floor of the fourth ventricle) shows that the response is limited to D-4. See Fig. 2 legend for key. **Lower:** Projection drawing of the placement of the electrode in the facial nucleus. Rest B = restiform body; Sp V = spinal tract of the trigeminal nerve; Pyr = pyramidal tract.

of the response approximately 9 to 11 min following stimulation for 1.5 to 2 min. Serial sections of the medulla from this experiment showed that the electrode tip had been located in the facial nucleus (Fig. 6 lower).

The other locus from which vasomotor responses were obtained on depth stimulation

---

G. Gonzalez, B. M. Onofrio and F. W. L. Kerr

J. Neurosurg. / Volume 42 / June, 1975
Vasodilator system for the face

cutaneous arterioles, and that antidromic activation of pure sensory nerves or dorsal roots would lead to a release of a histamine-like substance at the blood vessel level. The abolition of vasodilator responses in the experiments in which combined chronic section of the posterior root of the trigeminal and facial nerves was performed show conclusively that axon reflexes are not responsible for the cutaneous vasodilatation described in this study, since the anatomical substrate for axon reflexes was intact in those instances.

The present study indicates that the vasodilator responses were due to fibers that emerge mainly with the facial nerve but also directly with the trigeminal root; the former reach the trigeminal nerve via the GSP as shown in the experiments in which the facial root was stimulated or chronically severed or the GSP stimulated directly. It was demonstrated by Foley and Dubois that 15% of the axons of the facial nerve are autonomic efferents, and of these 70% leave by way of the GSP and 30% by way of the chorda tympani. Later, in a comparative study of the facial nerve, Van Buskirk confirmed this and found that autonomic efferents comprised 7% of the total in the dog, 2% in the cat, and as much as 24% in man; these studies emphasize the marked species differences and suggest that in man vasodilator phenomena should be much more pronounced. This is evidently so, since obvious facial vasodilatation is far more marked in man than in any other species.

The relationship of the GSP to vasomotor phenomena in pial vessels was demonstrated by Chorobski and Penfield, who described fibers that reached pial vessels from the facial nerve by way of the GSP, and proposed that some varieties of migraine headache might be explained on this basis. Cobb and Finesinger also showed that the GSP provides vasodilator fibers to the nasal mucosa in addition to those to the lacrimal glands. Gardner, et al., severed the GSP in 26 patients with unilateral migraine varieties of neuralgia and were successful in abolishing the syndrome in a third of their patients.

In an excellent description of the gross anatomy of the autonomic innervation of the face, Pick demonstrated by dissection that the central arteries of the face received no nerve supply from the sympathetic nerves, but interestingly enough, they were innervated by fine branches arising from the trigeminal and facial nerves. As he noted, "the branches of the facial nerves may perhaps also subserve the function of vasodilation, thus being possibly responsible for blushing."

The amplitude of the response elicited by stimulation of the trigeminal is comparable in
the case of the second and third divisions, but is always much lower and often absent in the first division. However, in experiments in which a chronic cervical sympathectomy was done, or in which the facial vasomotor responses were elicited by stimulation of the facial nerve or the brain stem nuclei, the first division response was present and ranged between 0.5° and 1°C. This indicates that vasodilator fibers are present in this division although they are probably in smaller numbers than in the second and third divisions, since under optimal conditions the response elicited from this division is always of considerably smaller amplitude; this also indicates that activation of the closely adjacent sympathetic outflow at this level usually depresses the vasodilator response.

With regard to the central origin of the vasodilator fibers to the face, we still have only very limited data. The centers or fiber systems concerned with this phenomenon, however, are found in the two nuclei, facial and trigeminal, most directly concerned with the innervation of the face.

It is interesting that already at this central level evidence suggests that the vasodilator supply to the face is topically organized, since responses disappear in the distribution of one division and appear in another with slight advances or withdrawals of the stimulating electrode. Thus, while the divisional organization of the vasodilator fibers to the face may be due entirely to the pattern of distribution of the GSP to the trigeminal divisions peripherally, a central topical organization should not be excluded. However, if the latter does occur, there appears to be no reason for such an arrangement.

We interpret the occurrence of facial vasodilator responses to stimulation of both the spinal nucleus (pars interpolaris) and spinal tract of the fifth nerve below the obex level, as well as the presence of a significant degree of vasodilatation on stimulation of the second division of the trigeminal nerve in some experiments in which the facial nerve had been chronically transected at the internal auditory canal, as evidence for efferent vasodilator fibers in the trigeminal root. Some suggestion that they may arise from the subnucleus caudalis is provided by the experiments in which stimulation at that level resulted exclusively in vasodilatation in the second division area. The vasodilator responses obtained from more rostral levels of the trigeminal nucleus are tentatively ascribed to connections from the trigeminal nucleus to the facial vasomotor outflow.

It is interesting to note that Gardner7 has suggested that efferent parasympathetic fibers in the trigeminal divisions might be responsible for triggering the paroxysms of pain in trigeminal neuralgia by “cross talk” between damaged axons. However, he emphasized that this was purely speculation, since no evidence had ever been presented that such fibers existed with the exception of the experiments of Lewy, et al.8 They showed that following facial rhizotomy and cervical sympathectomy, stimulation of the trigeminal root produced slow separation of the whiskers on the upper lip of the cat; it was suggested that this might constitute a basis for pseudovasomotor phenomena in the tongue, lip, and eyelid. Whether the parasympathetic vasomotor outflow now demonstrated has any relationship to tic douloureux remains to be proven, but the observation does lend some weight to the argument put forth by Gardner.7

In summary, we have shown that in addition to the classically recognized sympathetic vasoconstrictor supply to the face, there exists another, equally significant vasodilator system; most of this emerges from the brain stem with the facial nerve, while some exits directly with the trigeminal nerve to be distributed by it in a divisional pattern. Concurrent studies aimed at identifying the neurotransmitter involved in this activity will be described in a separate report.

Acknowledgments

The authors express their appreciation for the assistance of Mr. Pat Bowron throughout and to Dr. Daniel Nijensohn for participating in some of the experiments.

References

Vasodilator system for the face


This work was supported in part by NINDS Grant 5995 from the U.S. Public Health Service.

Address reprint requests to: Guillermo Gonzalez, M.D., Section of Neurological Surgery, Mayo Clinic and Medical School, Rochester, Minnesota 55901.