Trigeminal pathway for afferent fibers from the oculomotor nerves

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Stimulation studies in the cat have shown that the afferent fibers for the oculorespiratory reflex travel with the motor nerves intraorbitally, but join the ophthalmic division of the fifth cranial nerve within the cavernous sinus. Degeneration studies confirm that these afferents join the fifth nerve in the cavernous sinus. From the size, number, and distribution of these nerves, it is concluded that this represents a major afferent pathway from the extraocular muscles to the brainstem.

Despite numerous anatomic and physiologic investigations in the past, there remains considerable controversy concerning the afferent fibers from the extrinsic muscles of the eye. This controversy involves the afferent fiber size, its distribution, and pathway to the brainstem. Consideration of previous histologic evidence reveals the following possibilities: (1) The afferents from the extraocular muscles immediately join the motor nerves in the orbit and remain with these nerves to the brainstem.[5, 7-12] (2) The afferents take the same course as mentioned in (1) with the exception that an insignificant number join the ophthalmic division of the fifth cranial nerve within the cavernous sinus.[13] (3) Afferent connections from the extraocular muscles follow the sympathetic pathway.[1]

Physiologic evidence has indicated one other pathway, namely that the afferents leave the extraocular muscles as separate and intact fiber bundles joining branches of the fifth nerve immediately within the orbit.[2-4, 14, 15]

In a previous publication[6] it was demonstrated physiologically that the oculorespiratory reflex in the cat could still be elicited when the motor nerves to the orbit had been transected at their brainstem exit. This would seem to eliminate the motor nerves as an afferent route to the brainstem, at least with respect to the oculorespiratory reflex. However, this left unconfirmed two possibilities: (1) that these afferents joined the fifth nerve peripherally, or (2) that they exited from the orbit with the sympathetics.

In the present paper, these pathways were investigated physiologically in the cat by fifth nerve section and sympathectomy. In addition, the peripheral pathways were demonstrated histologically by degeneration techniques.

Methods and materials

Physiologic studies. Two groups were used, with three cats in each group.

In one group of adult cats the ophthalmic

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division of the fifth cranial nerve was sectioned unilaterally by electrical cauterization immediately peripheral to the Gasserian ganglion. Using the technique described previously both orbits were then exposed and the third, fourth, sixth, and frontal branch of the fifth cranial nerves were stimulated ipsilaterally and contralaterally to the fifth nerve section.

In the second group of cats, one superior cervical ganglion was exposed and verified by electrical stimulation and observation of the pupil. The ganglion with its pre- and postsynaptic branches was then extirpated. These animals were then allowed to survive for one to two weeks to insure that the vagus nerve would be fully recovered from any possible injury. Following this period of recovery, the ipsilateral orbit was then exposed and stimulation was carried out as above.

Degeneration studies. Two groups were used, with 3 cats in each group.

In one group of adult cats the fifth and third cranial nerves were sectioned intracranially posterior to the cavernous sinus. In the second group, the third nerve was sectioned intracranially as before, and the ipsilateral superior cervical gan-

glion was removed. All cats were allowed to survive for a minimum of six weeks. They were killed by intra-aortic perfusion with 15 per cent formalin. The orbits and brain were exposed immediately after perfusion and placed in 10 per cent formalin solution where they remained a minimum of one week to ensure complete fixation. Using the dissecting microscope, the third nerve was then isolated and removed intact throughout its intracranial and intraorbital course. The various branches were then labeled and embedded separately. In the animals with third to fifth nerve transection, the frontal nerve was also studied to confirm adequacy of degeneration. In all animals, portions of the normal fourth and sixth nerves were also examined as a control of fixation, perfusion, and staining. All nerves were then stained with 1 per cent osmic acid and studied by serial section.

Results

Physiologic studies. With the use of the oculorespiratory reflex as an indicator of afferent integrity, a typical respiratory
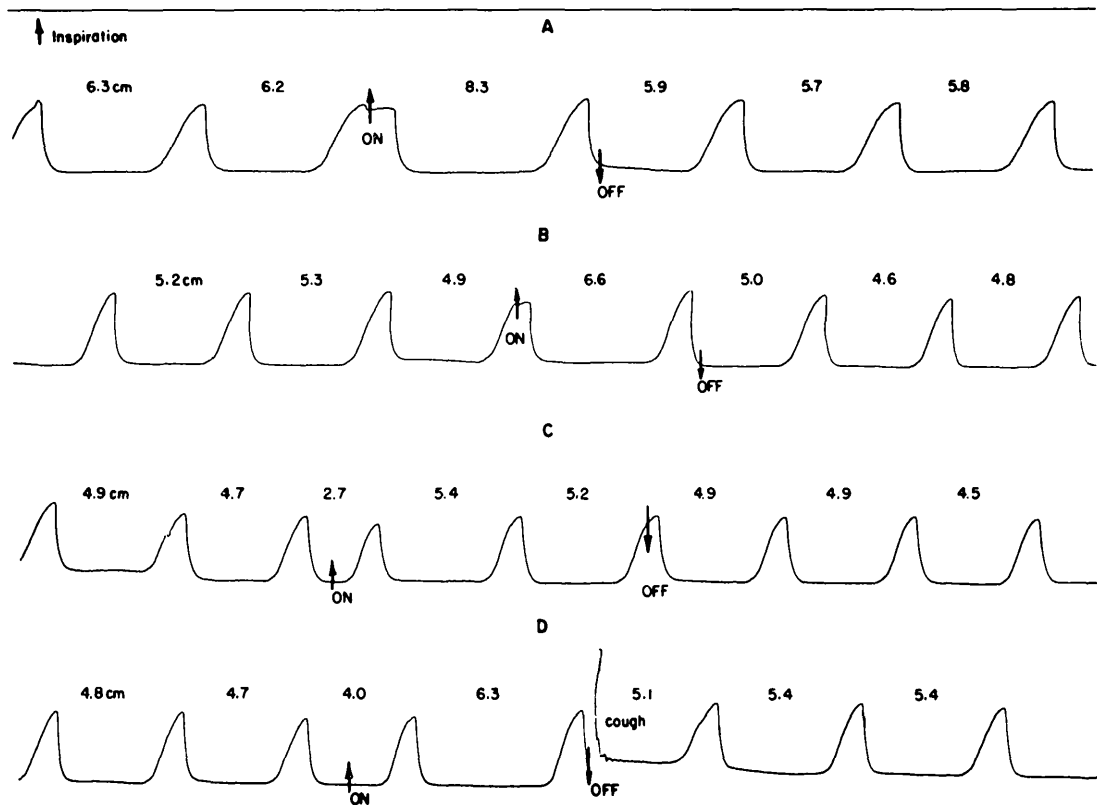

Fig. 1. Intraorbital stimulation following ipsilateral sympathectomy. Typical expiratory prolongation when the third (A), fourth (B), and sixth (C) nerves were stimulated with 1.5 volts. Similar expiratory changes when the frontal nerve (D) was stimulated with 3.0 volts.
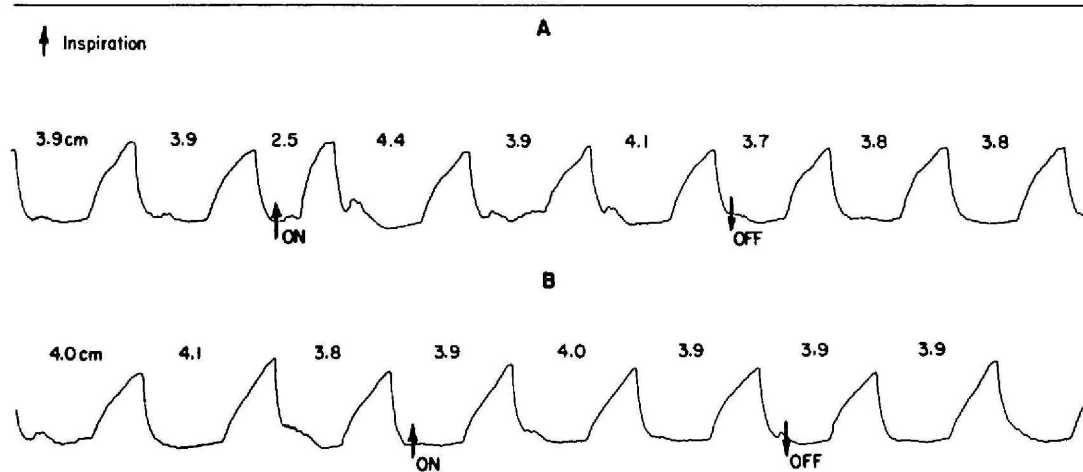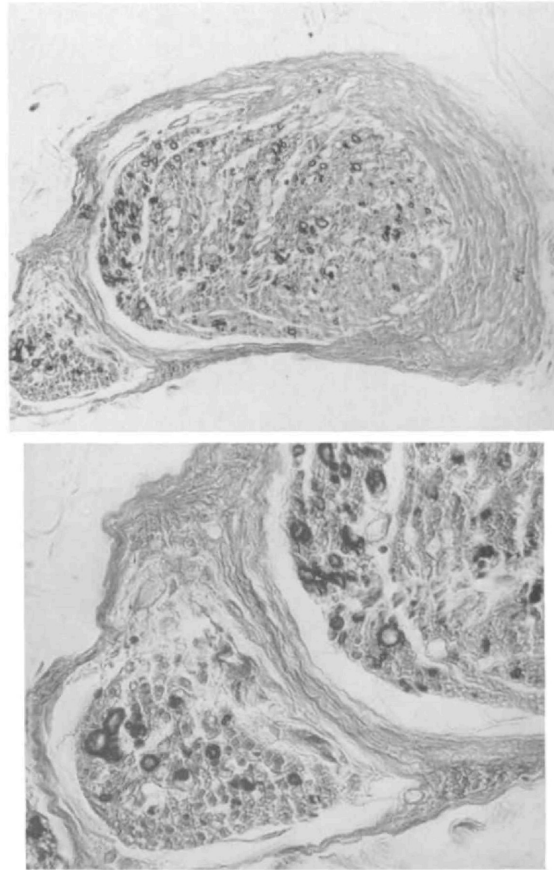
Fig. 2. Intraorbital stimulation of the third nerve to the inferior oblique of the right eye *(A)* with 3 volts, and of the left eye *(B)* with 15 volts, following intracranial transection of the ophthalmic division of the fifth nerve on the left. Note the typical expiratory prolongation in the top tracing from contralateral stimulation. Note also the absence of a respiratory response in the bottom tracing from ipsilateral stimulation despite a fivefold increase in the voltage.
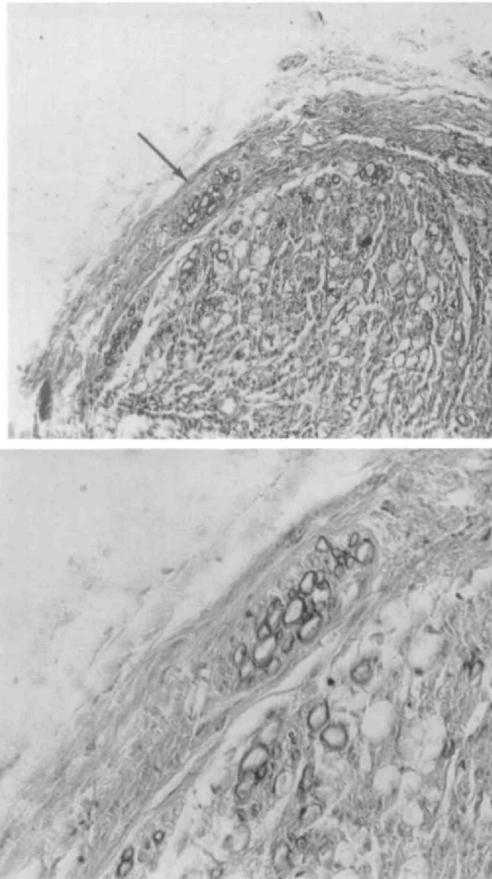
Figs. 3 (top) and 4 (bottom). Photomicrographs of the cavernous sinus portion of the degenerated third nerve following its intracranial transection and ipsilateral sympathectomy. Note numerous surviving myelinated fibers in cross section and their peripheral distribution (arrow). (Osmic acid. Fig. 3, ×175; Fig. 4, ×440.)

Figs. 5 (top) and 6 (bottom). Photomicrographs of the intraorbital portion of the third nerve to the superior rectus muscle following intracranial third nerve transection and ipsilateral sympathectomy. Note numerous osmium positive surviving myelinated fibers and their diffuse distribution. (Fig. 5, ×175; Fig. 6, ×440.)

dysrhythmia could be elicited following ipsilateral sympathectomy when either the third, fourth, sixth, or frontal branch of the fifth cranial nerves were stimulated intraorbitally (Fig. 1).

Secondly, when the third, fourth, sixth, and frontal branch of the fifth cranial nerves were stimulated ipsilaterally to transection of the ophthalmic division of the fifth intracranially, no respiratory response could be elicited. Nevertheless, in the same animal, stimulation of these nerves contralaterally produced a typical respiratory response (Fig. 2).

Degeneration studies. Serial sections of the entire third cranial nerve following its intracranial transection and ipsilateral sympathectomy revealed surviving myelinated fibers. In the cavernous sinus portion of the third nerve, these surviving fibers were noted to join the degenerated third nerve, peripherally, as separate and intact fiber bundles (Figs. 3 and 4). Sections of this same nerve intraorbitally showed numerous surviving myelinated fibers in a more diffuse distribution (Figs. 5 and 6).

When the ipsilateral third and ophthalmic fifth cranial nerves were transected, intracranially, no surviving fibers could be detected in serial sections of the entire third nerve (Fig. 7).

Discussion

As mentioned in the introduction, there are at least four possible pathways for the afferents from the extraocular muscles to
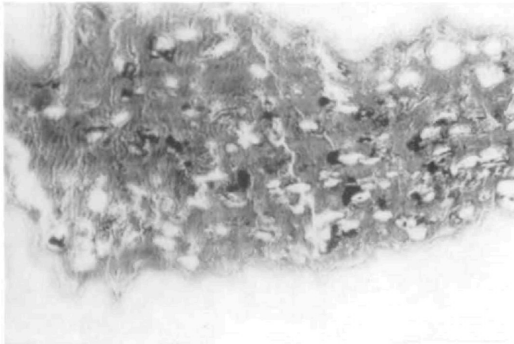
Fig. 7. Photomicrograph of the nerve to the inferior rectus muscle following intracranial transection of the ipsilateral third and ophthalmic fifth nerves. Note absence of surviving myelinated fibers. (Osmic acid. ×440.)

reach the brainstem. In a previous publication[6] it was demonstrated that the oculorespiratory reflex was not inhibited by intracranial transection of the third, fourth, and sixth cranial nerves. The present studies indicate further that ipsilateral sympathectomy does not influence this reflex. However, in a cat with the ophthalmic division of the fifth transected intracranially, no respiratory reflex could be elicited by ipsilateral stimulation. In this same animal, the integrity of the efferent pathway was demonstrated by the facility with which the reflex could be elicited by contralateral stimulation. From these data, it is concluded that the afferents mediating the oculorespiratory reflex in the cat are contained within the motor nerves intraorbitally but leave these same nerves to join the ophthalmic division of the fifth prior to its exit from the cavernous sinus.

The question could arise as to whether this represents an isolated pathway for this reflex only, or the course of the majority of the afferents from the extraocular muscles. This question cannot be answered categorically. However, the degeneration studies reveal that afferents do join the motor nerves within the cavernous sinus. At this point, they enter as peripherally situated intact bundles. From the size and number of these surviving fibers (Figs. 3 and 4) it would seem that this represents a major

afferent pathway. Further support of this can be drawn from the fact that these peripheral bundles mingle with the motor nerves and are distributed numerously and diffusely throughout their intraorbital branches (Figs. 5 and 6).

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Erratum

In the article, "Intertissue vascular relationships in the fundus of the eye," by Professor I. C. Michaelson, in the December, 1965, issue of the JOURNAL, page 1004, Figures 2 and 9 were original in the article. They were wrongly attributed to the *Archives of Ophthalmology* and the *British Medical Journal,* respectively.