The contralateral effect of antidromic stimulation of the trigeminal nerve on the rabbit eye. Eugenio Maul and Marvin L. Sears.

The effect on contralateral eyes after injuries to one eye has been called the consensual reaction and has been postulated to be either the consequence of a neural reflex or one achieved by circulating substances. Trigeminal stimulation always causes ipsilateral miosis, ocular hypertension, intraocular hyperemia, and a disruption of the blood-aqueous barrier. Disruption of the blood-aqueous barrier in the contralateral eye after stimulation of the trigeminal nerve always occurs and depends on intact sensory innervation to that globe in rabbits. The disruption is not prevented by pretreatment of the animals with indomethacin.

The phenomenon of disruption of the barrier is sometimes accompanied by an elevation of intraocular pressure in the contralateral eye but not by the other irritative responses. Thus, unilateral stimulation of a sensory nerve, the trigeminal, in the rabbit, can produce ipsilateral contralateral disruption of the blood-aqueous barrier.

The action of the trigeminal nerve upon ocular structures was first reported by Magendie. He observed a constriction of the ipsilateral pupil upon intracranial section of the nerve. Bernard reported the same effect in the atropinized eye and in animals with a degenerated third nerve. Mauritius further studied this phenomenon and reproduced the effect on the pupil after mechanical stimulation of the trigeminal nerve in sympathetically denervated eyes. Perkins reported an increase in intraocular pressure after trigeminal stimulation, and in six of 36 experiments he observed a contralateral increase in the intraocular pressure. This contralateral effect was said to be mediated through crossed nerve fibers descending antidromically in the opposite trigeminal nerve. Humoral factors have been postulated as playing a role in consensual reactions, but among them prostaglandins probably cannot be listed because circulating prostaglandins would be inactivated by the lung and because blockade of prostaglandin synthesis does not prevent the reaction.

In this study the contralateral effect of trigeminal stimulation on the blood-aqueous barrier was singled out for study because changes in the barrier could affect intraocular pressure and in themselves be of interest in terms of regulatory mechanisms for the blood ocular barrier.

Materials and methods.

Animals. New Zealand, male, albino rabbits weighing 2 to 3 kilograms were anesthesitized with Urethane (1.3 Cm. per kilogram) administered intravenously over a period of 75 to 90 minutes. The animals retained their corneal reflexes, indicating the presence of an intact sensory neural pathway.

Stimulation of the trigeminal nerve. The nerve and trigeminal ganglion were exposed through a temporoparietal craniotomy after removal by aspiration of part of the temporal lobe of the brain. The nerve could be seen as a yellow track running longitudinally underneath the duramater in the base of the skull, 5 mm. from the sagittal plane. The trigeminal nerve was stimulated mechanically under observation through an operating microscope. The stimulation consisted of several (touch, strokes, punctures) of the nerve with a needle during a period of 60 to 80 seconds. All stimulations were done postganglionically.
Measurements. Aqueous humor was obtained by paracentesis 30 minutes after stimulation. The protein concentration was determined by refractometry. In the untreated group of animals the effect on the intraocular pressure was measured by a calibrated pneumotonometer and the pupil diameter was also recorded.

Experimental groups. Unilateral stimulation of the trigeminal nerve was carried out in seven untreated animals. Seven other animals were stimulated in which the contralateral orbits were infiltrated with 0.8 to 1 c.c. of 2 per cent lidocaine. Five animals were stimulated in which the contralateral trigeminal nerve was cut intracranially and allowed to degenerate over a period of 21 days. In two animals the maxillary branch of the trigeminal nerve was exposed under the skin of the face after its exiting from the orbit and stimulated. In three previously untreated rabbits, measurements were done after surgery and localization of the nerve in the base of the skull, but without stimulation. Indomethacin was divided into two parts and given intraperitoneally as a total base of 100 mg. per kilogram, 3 hours and 1 hour before stimulation. Statistical significance of the results was calculated with Student's t test for sample means.

Results.

Stimulation of untreated normal rabbits. The protein concentration in the aqueous humor of the ipsilateral eye was 1,553 ± 214 mg. per 100 ml. (7) and in the contralateral eye was 1,503 ± 171 mg. per 100 ml. (7) Surprisingly, the difference between eyes was not statistically significant, but obviously significantly greater than normal aqueous.

The pupil constricted immediately after stimulation from a baseline diameter of 6 ± 0.1 mm. (8) to 1.8 ± 0.1 mm., (8) showing a tendency to recover over a period of 60 minutes. The contralateral side remained unchanged. The intraocular pressure in the ipsilateral side increased from 15.6 ± 0.5 mm. Hg (6) to 34.5 ± 2 mm. Hg (6).

In the contralateral side the pressure pre-stimulation was 16 ± 1 mm. Hg (6) and 15.5 ± 0.7 mm. Hg (6) after stimulation. Only in one eye was an increase of 4 mm. Hg recorded.

Peripheral stimulation of the maxillary branch or exposure of the trigeminal nerve in the skull without stimulation did not change the preoperative values of intraocular pressure, pupil, ocular vessels, or aqueous protein concentration 30 minutes after stimulation.

Stimulation after contralateral retrobulbar lidocaine. The protein concentration in the stimulated side increased to 1,121 ± 106 mg. per 100 ml. (7) and the contralateral increased only to 521 ± 50 mg. per 100 ml. (7). This value was significantly lower than that of the stimulated side in this group and lower than the contralateral aqueous protein concentration in untreated animals (P < 0.01).

Stimulation after contralateral degeneration of the trigeminal nerve. The protein concentration in the aqueous humor of the stimulated side increased to 1,080 ± 170 mg. per 100 ml. (5) and the value for the contralateral side was 77.5 ± 41 mg. per 100 ml. (5). This value was not significantly different from the normal value found for the rabbit eye with this method.

Discussion. The previously reported effects of the trigeminal nerve stimulation on the intraocular pressure of the rabbit eye are confirmed by this study. Ipsilateral increases regularly occurred. In this study only one of six animals developed an increase of the contralateral intraocular pressure. This effect is also an infrequent observation in other studies.

In seven of seven animals a disruption of the blood-aqueous barrier was found in the contralateral and ipsilateral eye. In several animals pretreatment with indomethacin did not block the effect. The contralateral effect was reduced to a 30 per cent level when the contralateral orbit was pretreated with lidocaine. This significant inhibition suggests the predominantly neural nature of the contralateral phenomenon. When the contralateral trigeminal nerve was allowed to degenerate, the disruption of the blood-aqueous barrier could be totally prevented. In all likelihood lidocaine produced only an incomplete block by comparison with total nerve section. This confirms the neural nature of the phenomenon and suggests that it is directly related to nerve fibers travelling in the trigeminal nerve. These fibers are undoubtedly crossed sensory fibers. The results suggest that in rabbits the effects of trauma on the blood ocular barrier can be mediated by the trigeminal nerve to affect the contralateral eye.

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Key words: trigeminal nerve, antidromic stimulation, intraocular pressure, blood-aqueous barrier, consensual effect, ocular trauma.

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Analysis of clonidine-induced mydriasis.

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In addition to its centrally mediated hypotensive action, clonidine causes a decrease in intraocular pressure associated with a long-lasting mydriasis. The present study was conducted to determine to what extent this drug-induced pupillary dilation is of central or peripheral origin. Pupil size was observed in cats anesthetized with pentobarbital. Clonidine (1 to 100 µg per kilogram, intravenously) resulted in a dose-dependent increase in pupillary diameter in intact as well as sympathectomized preparations. These same doses of clonidine produce no effect on the eserined, parasympathectomized iris. Epinephrine administration (0.1 to 30 µg, intra-arterially) produced an equivalent pupillary dilation in all preparations. In addition, clonidine caused a dramatic decrease in postganglionic ciliary nerve activity and both the decreased nerve activity and pupillary dilation were reversed by intravenous administration of yohimbine hydrochloride. These results suggest that the inhibition of parasympathetic tone by clonidine may involve a central adrenergic inhibitory mechanism.

The hypotensive drug clonidine lowers blood pressure by acting directly on the central nervous system. Recent investigations suggest that clonidine activates an alpha-adrenergic mechanism located in the medulla oblongata or hypothalamus. In conjunction with other long-lasting central nervous system (CNS) actions, such as sedation and inhibition of respiration, clonidine also exerts a transient sympathomimetic action on a variety of peripheral sympathetic systems.

In addition to its hypotensive action, clonidine has been shown to produce a therapeutically useful decrease in intraocular pressure associated with a long-lasting pupillary dilation. The aim of the present study was to quantitatively describe the mydriatic action of clonidine in the cat with regard to the site and mechanism of action involved.

Methods. Adult cats of either sex were anesthetized with pentobarbital (36 mg per kilogram, intraperitoneally). Following cannulation of the trachea, femoral artery, and vein, the animals were placed in a Kopf stereotaxic instrument. Blood pressure was recorded from the femoral artery by means of a Statham P23Dd pressure transducer and displayed on a Grass polygraph (Model 7B). Pupillary responses were measured directly with a millimeter ruler at the point of greatest horizontal diameter and photographed either directly or with the aid of a camera attached to an operation microscope (Olympus Model MTX). All observations were made under the same general ambient lighting conditions.

In some preparations the cervical sympathetic nerve trunk was sectioned preganglionically at the midcervical level and in others the medial and lateral short ciliary branches of the oculomotor nerve were cut following a lateral intraorbital approach. In these latter preparations, the subsequently dilated pupils were constricted by topical application of 1 to 2 drops of a 1 per cent solution of physostigmine salicylate. The direct effect of epinephrine was observed in both types of preparations following injection (0.2 ml) into the lingual artery.

In one series of experiments, bipolar platinum electrodes were placed beneath the lateral short ciliary nerve and the effect of clonidine on the activity in this postganglionic nerve was observed. The nerve was covered with warm mineral oil and the electrical activity amplified by a differential amplifier (Tektronix Model 26A2). These amplified potentials were displayed on a dual-beam storage oscilloscope (Tektronix Model D13) and were integrated (Grass Model 7P10B) for display on a polygraph (Grass Model 7D). A Hewlett Packard (Model 3600) F-M tape recorder was utilized for storage.

Drugs were dissolved in physiological saline and the doses are expressed in terms of their salts. Drugs employed were: clonidine hydrochloride (Boehringer Ingelheim, Ltd.), yohimbine...