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THE PHYSIOLOGICAL ROLE OF THE JUGULAR NERVE IN THE INNERVATION OF INTRAORBITAL MUSCLES. EXOPHTHALMOS IN POSTERIOR FOSSA TUMORS

[Following is the translation of an article by L. A. Koreysha and I. M. Irger entitled K Fiziologicheskoy Roli N. Jugularis N. Sympathici v Innervatsii Vnutriorbital'nykh Myshts. Ekzoftal'miya pri Opukholey Zadney Cherepnoy Yamki, (English version above), in Voprosy Neyrokhirurgii (Problems of Neurosurgery), Vol. XXIV, No. 3, July 1960, Moscow, pages 31-37.]

The Diagnostic Value of Unilateral Exophthalmos in Cerebellar Tumors

Exophthalmos is not uncommonly encountered in posterior fossa tumors, particularly those of the fourth ventricle, where it is usually bilateral. In the analysis of 164 cases of cerebellar tumors in adults an insignificant degree of exophthalmos was found in 26 patients (16 percent); of these, it was unilateral in 17, and bilateral in nine. Unilateral exophthalmos usually is on the side of the cerebellar focus. We observed this in 14 patients. In three patients the exophthalmos was on the side opposite to the cerebellar focus.

In posterior fossa tumors exophthalmos usually is not accompanied by a simultaneous dilatation of the pupil. Nevertheless, regardless of whether it is or is not associated with the influence of the tumor process on the medulla, hypothalamus or on the cerebellum, it might have been expected that the sympathetic effect in posterior fossa tumors be manifested in the form of exophthalmos with simultaneous dilatation of the pupil.

In the case of tumors of the posterior fossa exophthalmos is usually associated with an irritation of sympathetic structures within the brain stem. It is well known that electrical stimulation of the hypothalamic areas produces a sympathetic effect in animals in the form of a maximum dilatation of the pupil, dilatation of the optic fissure and contraction of the third lid (Karpius and Kreidl, 1909, 1910, and others). In cases of foci in the medulla (for example, with obstruction of the posterior inferior cerebellar artery) or in the pons Horner's syndrome is manifested on the same side. This speaks for the fact that while sympathetic fibers which supply the intraorbital smooth musculature cross, this is accomplished above the medulla and above the pons.

Beginning in the posterior portion of the hypothalamus the efferent sympathetic fibers pass through the mid-brain and the medulla, the cervical portion of the spinal cord, being directed toward the centrum ciliospinale Budge. Part of the fibers crosses in the area of the reticular formation; part passes through this area without crossing (Beattie, Dull and Ballance, 1932; Gottschick, 1955). From the centrum ciliospinale the sympathetic fibers are pass within the cervical sympathetic trunk through the superior cervical ganglion to the orbit.

The discrepancy indicated cannot be explained either in the light of the experiments of L. A. Orbeli and A. M. Zimkina. N. M. Verzilov (1903) observed vegetative effects in animals on the part of the pupil and orbital muscles after electrical and mechanical stimulation of the cerebellum. A. M. Zimkina and L. A. Orbeli (1932) and A. M. Zimkina (1945) confirmed the observations of N. M. Verzilov and communicated the fact that under the influence of stimulation of even one-half of the cerebellum in dogs, cats and rabbits a sympathetic effect occurs in the form of protrusion of the eyeball, dilatation of the pupil, retraction of the third lid on both sides; after a unilateral transection of the cervical sympathetic nerve the effects of stimulation of the cerebellum on the side of the transection disappear or are expressed very slightly. In accordance with the data of A. M. Zimkina a bilateral transection of the cervical sympathetic trunk almost completely eliminates the effects of stimulation of the cerebellum.

The occurrence of exophthalmos in cerebellar tumors without simultaneous dilatation of the pupil becomes understandable to a certain degree when the physiological role of the jugular nerve is investigated.

Experimental Investigations

According to data in the literature, the route of sympathetic fibers to the eye and orbital muscles corresponds to the diagram (Fig.1). However, the investigations of L. A. Koreysha (1929), L. A. Koreysha and Ya. L. Rapoport (1929) and our own observations give us the basis for changing this diagram.

As is well known, the dorsal nucleus of the vagus nerve is functionally related to the cervical sympathetic ganglia, which served as the grounds for calling it the "vegetative nucleus of the medulla". Fibers from this nucleus, according to existing concepts, pass through the cervical portion of the spinal cord and only at the level of the inferior cervical and superior thoracic segments go off to the cervical sympathetic ganglia.

L. A. Koreysha and Ya. L. Rapoport, while not excluding such a type of connection of the medulla with the cervical sympathetic ganglia, believe that these connections can be accomplished also through another route, namely, through the jugular nerve of the sympathetic system, which comes off the upper pole of the superior cervical ganglion and passes through the jugular foramen into the cavity of the skull along with the fibers of the vagus nerve. The subsequent course of the jugular nerve fibers is not known reliably as yet. L. A. Koreysha and Ya. L. Rapoport have shown that after the intracranial transection of the vagus nerve in dogs a degeneration of cells in the cervical sympathetic ganglia occurs. On this basis they believe that the fibers which travel within the jugular nerve of the sympathetic tract begin in the medulla, apparently in the dorsal nucleus of the vagus nerve, and end in the cervical sympathetic ganglia. This is confirmed also by the experiments of L. A. Koreysha with stimulation of the cephalic end of the cervical sympathetic nerve in dogs, which showed that this nerve participates in the regulation of blood pressure and cardiac activity and that impulses pass to the medulla along fibers which are not interrupted in the superior cervical sympathetic ganglion but rather remain within the jugular nerve.

For the purpose of elucidating the physiological role of the jugular nerve we have undertaken experimental research with the aim of studying the influence of the fibers of the jugular nerve on the intraorbital smooth muscles and pupils. After the isolated transection of the cervical sympathetic trunk in dogs (or the excision of it for several centimeters with the aim of preventing the possibility of union of the nerve fibers), a Horner's syndrome developed on the side of the transection in the form of enophthalmos, narrowing of the optic fissure, marked constriction of the pupil and relaxation of the nictitating membrane. This syndrome remained constant for the ten months of observation. One to two months after the operation the dogs were injected subcutaneously with apomorphine (one cubic centimeter of one percent solution), which, as is well known, causes an overstimulation of the medulla, and after five to 15 minutes a marked sympathetic effect occurred on the side of the Horner syndrome in the form of dilatation of the pupil, exophthalmus, contraction of the third lid and dilatation of the optic fissure. Signs of stimulation of the sympathetic fibers gradually disappeared after 25-30 minutes, and the Horner's syndrome recurred. Apomorphine was given to each dog several times, and in all seven experimental dogs this inevitably was associated with the same reactions.

The occurrence of the sympathetic reaction of the eye and orbital musculature after the injection of the apomorphine on the side of the transected cervical sympathetic trunk indicates the fact that part of the sympathetic fibers from the medulla reach the eye and the smooth musculature in the orbit, by-passing the cervical sympathetic trunk, to be sure, if we can exclude the humoral effect of apomorphine on the intraorbital structures or post-ganglionic sympathetic fibers. With the aim of excluding the humoral influence in two dogs a stimulation of the medulla was undertaken with a faradic current in the area where the nerve routes of the vagus come off on the side of a cervical sympathetic trunk which had been transected several months before this. Immediately after the current was turned on, a marked protrusion of the eyeball and dilatation of the pupil were noted on the side of the stimulation instead of the former Horner's syndrome; here, the protrusion was more distinctly pronounced than on the opposite side. After eight to ten minutes the Horner's syndrome could be observed again.

The investigations of V. Mayevskiy (1928) also speak against the humoral effect of apomorphine on the intraorbital structures or post-ganglionic sympathetic fibers. His experiments consisted of the fact that after the transection of the vagosympathetic trunk of dogs in the neck the central end of the vagus nerve was anastomosed with the peripheral end of the sympathetic nerve. The occurrence of a sympathetic reaction of the eyes and of the submaxillary gland after the injection of apomorphine was evidence of the functional relationship between the vagus and sympathetic nerves in the neck. The operative removal of the neuroma which formed in the neck eliminated the signs which had been observed before the operation.

B. I. Lavrent'yev and co-workers (1939) and other authors indicate that in all probability all the sympathetic fibers traveling along the internal carotid artery plexus to the orbit pass through the superior cervical ganglion. From the superior cervical ganglion large branches come off in the dog: one, to the internal carotid artery; the other, to join the jugular ganglion of the vagus nerve. From the lateral-posterior surface of the ganglion there are anastomoses with the ganglion nodosum of the vagus nerve. In man, according to the data of M. Clara (1953), the jugular nerve leaves the superior cervical ganglion and travels along the adventitia of the internal jugular vein to the area of the jugular foramen; here, the jugular nerve leaves the wall of the vein: one branch of it goes to the jugular ganglion of the vagus nerve; the other, to the extracranial ganglion of the glossopharyngeal nerve. These anatomic data in combination with the physiological data described above permit us to suppose that some sympathetic fibers for the smooth muscles of the eye pass from the cells of the dorsal nucleus of the vagus nerve to the jugular foramen, and penetrate into the superior cervical ganglion within the jugular nerve (Fig. 2).

Therefore, the diagram of the sympathetic innervation of the smooth musculature of the eye and the orbit presented in Fig. 1 should be changed, because the physiological and anatomic data permit us to consider, with a definite degree of probability, that the sympathetic fibers which innervate the smooth musculature inside the orbit and the muscles of the eye go by at least two routes: 1) from the hypothalamic area through the brain stem, spinal cord, cervical sympathetic trunk into the superior cervical ganglion and 2) from cells of the dorsal nucleus of the vagus nerve the fibers travel through the jugular foramen within the jugular nerve and penetrate into the superior cervical ganglion, from which the post-ganglionic fibers for the intraorbital and ocular smooth musculature take their origin.

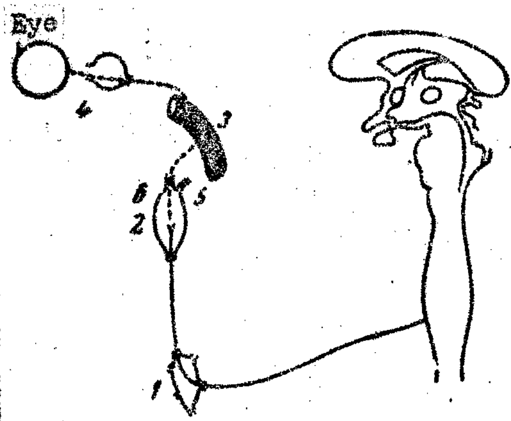

Fig. 1. Diagram of Sympathetic Innervation of the Eye.

1--stellate ganglion; 2--superior cervical ganglion; 3--internal carotid artery plexus; 4--ciliary ganglion; 5--n. jugularis n. sympathici; 6--internal carotid nerve

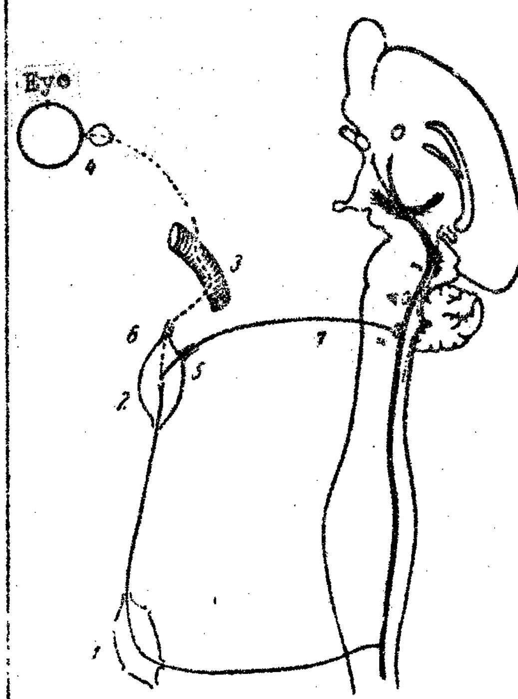

Fig. 2. Diagram of Sympathetic Innervation of the Eye, Made on the Basis of Research by L. A. Koreysha and I. M. Irger.

F--fibers connecting hypothalamic area with visceromotor nuclei of medulla; V--trigeminal nerve nucleus; X--vagal nucleus; 1--stellate ganglion; 2--superior cervical ganglion; 3--int. carot. artery plexus; 4--ciliary ganglion; 5--jugular nerve; 6- int. carot. nerve; 7--sympathetic fibers from cells of dorsal vagal nucleus travel within jugular nerve through jugular foramen to sup. cerv. ganglion.

If the schema of sympathetic innervation of the eye which we have proposed were not correct it might be expected that removal of the superior cervical ganglion should lead to an interruption of both sympathetic routes and to a complete elimination of the sympathetic innervation of the orbital and ocular muscles and that after the injection of apomorphine the sympathetic effect on the side of the lesion should be eliminated.

Experimental observations did not confirm this, but we were able to determine some interesting facts. If, one to two months after a unilateral removal of the superior cervical ganglion in dogs, an overstimulation of the medulla was produced by means of the injection of apomorphine, the sympathetic effect was shown differently on both sides. Five to six minutes after the injection on the healthy side a dilatation of the pupil, exophthalmos, dilatation of the optic fissure and retraction of the third lid occurred. On the side on which the cervical ganglion had been removed the exophthalmos, dilatation of the optic fissure and retraction of the third lid were even more marked than on the healthy side, and the pupil remained very much contracted. Sometimes, on the operated side the pupil was two to three times smaller than on the opposite side. Repeated injections with apomorphine in all three experimental dogs were accompanied by the same effect. Therefore, the schema which we have suggested is correct only for the sympathetic fibers of the pupil passing through the superior cervical ganglion, whereas another route aside from the two mentioned exists for the fibers which supply the intraorbital musculature stimulation of which causes exophthalmos. This is confirmed by the following experiment: when faradic stimulation of the medulla was performed in two dogs a month after the unilateral removal of the superior cervical ganglion, exophthalmos occurred on both sides.

This is the limit of the conclusions based on experimental data. We can only express certain ideas about the direction of the third route, which do not exclude other possibilities.

Perhaps the sympathetic fibers pass to the intraorbital musculature within the so-called "vertebral nerve", which begins with several branches from the superior thoracic ganglion and follows the vertebral artery, entering the transverse foramen along with it, where at the level of the seventh cervical vertebra all the branches unite in the form of a vertebral nerve trunk. With the increase in the complexity of organization of the animal a tendency is noted toward a reduction in the size of the vertebral nerve. In man it is poorly developed, and some regard it as a vascular plexus of the vertebral artery, with which, taking into consideration the comparative-anatomic data, we can hardly agree. In the newborn the vertebral nerve is better developed and forms ganglia at the site of its connection with the cervical nerves (V. S. Baraboshkin, 1903).

On the basis of a comparative-anatomic analysis V. S. Baraboshkin concluded that in man, as in other mammals, it is not the superficial cervical sympathetic system which is the continuation of the sympathetic chain of the trunk but rather the deep sympathetic system which is represented by a number of ganglia on the grey rami in the canal of the vertebral artery. The vertebral artery plexus in man is formed from the ascending branches of the inferior cervical and the first thoracic sympathetic ganglia and passes in the vertebral canal. The views expressed by V. S. Baraboshkin have been supported by B. M. Sokolov (1943). The vascular plexus of the vertebral artery in man penetrates into the cranial cavity and along with the branches of the basilar artery enters into a connection with the nerves coming from the internal carotid artery plexus (A. Tsvetkov, 1938; V. L. Lesnitskaya, 1948).

These data do not exclude the possibility of the fact that part of the sympathetic fibers may travel to the smooth intraorbital musculature within the vertebral artery plexus.

Gellhorn and co-workers have observed a dissociation of the nictitating membrane and the pupil after stimulation of the sympathetic nervous system. In a waking cat the slightest stimulation, for example, noise in the room, produces a maximum contraction of the nictitating membrane. At the same time, the pupils may dilate, but this dilatation is the same for the normal and the sympathectomized eye and, therefore, is not the result of contraction of the muscle which dilates the pupil and which is innervated by the sympathetic nerve but rather the result of an inhibition of the oculomotor nerve. After transection of it even a very strong influence in the form of painful stimulation of the sciatic nerve does not produce any changes in the pupil. All this indicates the fact that after painful stimulation sympathetic discharges go to the nictitating membrane but do not go to the pupil (Üry and Gellhorn, 1939).

Similar results have been obtained in cats also after stimulation of the hypothalamus, when, along with a maximum contraction of the nictitating membrane, a dilatation of the normal and sympathectomized eyes /pupils?/ occurs (Carlson, Gellhorn and Darrow, 1941). Stimulation of the medulla also can produce an increase in blood pressure and contraction of the nictitating membrane, without being reflected on the degree of dilatation of the normal and sympathectomized eyes (Gellhorn, 1943, 1948).

After electrical stimulation of the first branch of the trigeminal nerve in rabbits, within which sympathetic fibers are found which go to the iris, A. V. Lebedinskiy and N. G. Savin (1947) observed the relationship of the pupillary reaction to the frequency and strength of the current. With stimulation with a current of low frequency or of low voltage symptoms of stimulation of the afferent fibers of the trigeminal nerve appeared in the form of a contraction of the pupil, and with an increase in frequency or voltage of the current to a degree sufficient for stimulation of sympathetic fibers also the pupil dilated.

The explanation of the dissociation of the reactions of the nictitating membrane and the pupil in stimulation of the sympathetic nervous system can be found in the work of Gellhorn (1943, 1948). He believes that excitation and inhibition in the sympathetic nervous system lead to a change in the number of fibers involved in the process of excitation, depending on the intensity of excitation, as well as to a change in the frequency of discharges in the individual fibers in accordance with the basic principles of Adrian.

In connection with the fact that the sympathetic pre-ganglionic fibers are in contact with several ganglia at different levels and that each nerve fiber transmits impulses to many cells located in the same ganglion, the excitation process in the sympathetic nervous system has a tendency toward a generalized distribution. However, under certain conditions not all of the branches of the sympathetic nervous system are subject to the same effect.

The method of the experiments performed for the purpose of studying the physiological role of the jugular nerve do not give us the basis for bringing in Gellhorn's conception for explaining the facts which we have established.

The aim of the present communication is to throw light on the mechanism of occurrence of exophthalmos in posterior fossa tumors, without dealing with the details of the clinical significance of this sign. Exophthalmos in patients with cerebellar tumors, as a rule, is very slight and is not uncommonly found only on attentive examination. In animals (dogs and cats) stimulation of the sympathetic fibers produces marked exophthalmos. This may be explained by the very slight development of Müller's muscle in man.

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