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Pupilodilator muscle fibers are sympathetically innervated and are arranged radially in the iris. First-order sympathetic nerve fibers arise in the posterolateral hypothalamus and descend uncrossed in the lateral tegmentum of the midbrain, pons, medulla, and cervical spinal cord to the intermediolateral cell column of the spinal cord from C8–2 (ciliospinal center of Budge-Waller). They synapse with lateral horn cells (neurotransmitter: ACh) and give off 2nd order neurons(preganglionics).

Second-order neurons exit the spinal cord at T1 and enter the sympathetic chain and ascend but do not synapse until they reach the superior cervical ganglion, where they give rise to 3rd order neurons.

Third-order neurons (postganglionics) course upward with the common carotid artery. Those that mediate sweat in the face split off with the ECA (exception: fibers to the medial forehead do not branch off). The rest travel with the ICA passing over the carotid sinus, entering the skull through the carotid canal, traversing the cavernous sinus where they follow the VI nerve for a short distance before they accompany V1 (ophthalmic division of trigeminal nerve), entering the orbit through the superior orbital fissure with the nasociliary nerve, passing through (without synapsing) the ciliary ganglion. Upon exiting the ciliary ganglion the sympathetic fibers divide, some reach the pupilodilator muscle of the eye as 2 long ciliary nerves (neurotransmitter: NE). Other fibers travel with the ophthalmic artery to innervate the lacrimal gland and Müller's muscle (the accessory levator muscle of the upper eyelid).

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