

## SHORT SCIENTIFIC COMMUNICATION

# The cranial nerve zero – mini review

Alexandra Diana Vrapciu, Maria Viorela Popescu

Division of Anatomy, Faculty of Dental Medicine, “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

### ABSTRACT

The terminal nerve (cranial nerve zero, cranial nerve XIII, the nerve “N”) was discovered in fish in 1894. In the early 90’s, it was found in human embryos and human adults. In the anterior fossa, it courses on the inner side of the olfactory tract and bulb; it then spreads fibers through the cribriform plate to distribute beneath the nasal septum mucosa. Being provided with intrinsic ganglion cells, its functions are weakly suggested by studies in different species. It may be connected with the visual system, it could act upon the intracranial vascular system, or it could ensure the pathway for pheromone-mediated behaviours. The cranial nerve zero deserves a better attention equally from anatomists and ENT specialists.

**KEYWORDS:** terminal nerve, cribriform plate, visual system, cranial nerves, nasal septum

### INTRODUCTION

The terminal nerve, also called the cranial nerve 0, the cranial nerve XIII or nerve “N” was discovered in certain fish species<sup>1</sup>. Samuel Thomas von Sömmerring (1755-1830) is the father of the modern organization and nomenclature of the cranial nerves, from I to XII, according to the location of skull passages, from anterior to posterior, the first cranial nerve traversing the skull base through the most anterior foramina, those of the cribriform plate of the ethmoid bone, and the 12<sup>th</sup> cranial nerve exiting through the hypoglossal canal<sup>2</sup>.

### THE BEGINNINGS...

Studying the anatomy of a fish, for comparative anatomy, Felix Pinkus discovered in 1894 a new cranial nerve, unreported, in close contact with the olfactory bulb, and decided to name it “*the new nerve*”<sup>1,3</sup>.

Thus, the terminal nerve was discovered after the other cranial nerves had been named. Many authors classified nerve XIII as the nerve 0 because it is rostral to the other cranial nerves, previously identified and named<sup>1,4</sup>. The term “*terminal*” was given by Loci in 1905 because in some species it expands in the region of the lamina terminalis<sup>5</sup>.

### ANATOMY OF THE TERMINAL NERVE IN HUMANS

The first description of this nerve in human embryos was given by Johnston in the early 1900’s<sup>6,7</sup>. At

the same time, Brookover reported this nerve in adults<sup>8</sup>. Both scientists provided information only regarding the intracranial paths of the nerve. According to them, the terminal nerve can be found on the surface of the gyrus rectus<sup>9</sup>.

McCotter studied the terminal nerve intracranially as well as in the nasal cavity, in human fetuses and adult individuals. The terminal nerve is visible on the brain surface in the olfactory trigone and passes rostrally between the crista galli, medially, and the olfactory tract and bulb, laterally. The terminal nerve consists of a compact bundle near the olfactory tract, which separates into a rich plexus of fibers dura mater-embedded, close to the olfactory fibers. The fibers pass through the holes of the cribriform plate. In the nasal cavity, the terminal nerve courses on the nasal septum and distributes to the septal mucosa<sup>9</sup>.

Although Johnston concluded in 1914 that the terminal nerve is vestigial in humans, being larger than in other species, 30 years later, studying its development in humans and observing that the central roots are small, Pearson notified that it is improbable for this nerve to be absolutely vestigial<sup>10</sup>.

The terminal nerve ganglion in fish species is placed near or within the olfactory nerve or bulb<sup>11</sup>. In the rabbit embryo, the terminal nerve has multiple ganglion cells, the biggest collection being considered the *ganglion terminale*<sup>10</sup>. In humans, this ganglion is still a subject of debate.

The development of the terminal nerve is uncertain: some authors indicate the origin of the nerve in the region of the olfactory cells, others suggest that it may result from the neural crest<sup>1,12</sup>.

## FUNCTIONS OF THE TERMINAL NERVE

For many years, the role of the terminal nerve has been uncertain.

The first convincing attempt to shed light in the field of the terminal nerve function was made by Silverman who demonstrated that the nerve and his ganglions contain neuroactive substances and are immunopositive for luteinizing hormone-releasing hormone (LHRH)<sup>13</sup>. The LHRH secreted by the terminal nerve acts in fact like a neuromodulator rather than a simple hormone<sup>14</sup>. Intriguingly, not all the terminal nerve neurons contain LHRH, this subset varying among species<sup>15</sup>.

The immunohistochemistry for LHRH revealed that fibers from the terminal nerve project into the adult retina of fish, frogs and voles<sup>16,17</sup>, but in other mammals, it happens only in the early stages of embryonic development<sup>18,19</sup>. Thus, it is speculated that the terminal nerve controls the visual function in some species<sup>12</sup>.

Another study, on goldfish, found that the terminal nerve is the principal chemosensory pathway pheromones-responder<sup>20</sup>. It is reported that in some species the terminal nerve coordinates environmental adaptive functions, sexual activity, reproductive and mating behaviours<sup>21-23</sup>. Other reports indicated the role of the terminal nerve in the development of the human hypothalamic-pituitary-gonadal axis<sup>15,24</sup>.

The studies indicating the close contact of the terminal nerve endings with blood vessels suggest also autonomic and sensory functions<sup>25</sup>, which could be performed in a similar manner as in the trigeminovascular system.

## CONCLUSIONS

Further studies are mandatory to establish the human anatomy, function and physiology of the terminal nerve. Neglected for so many years, the terminal nerve deserves to be introduced in anatomy and ENT atlases and manuals for students and young specialists.

**Conflicts of interests:** None

**Contribution of authors:** All authors have equally contributed to this work.

## REFERENCES

- Bordoni B., Zanier E. - Cranial nerves XIII and XIV: nerves in the shadows. *J Multidiscip Healthc.*, 2013;6:87-91.
- Sömmering S.T., Vandenhoeck A., Glassbach C.C. - *De basi encephali et originibus nervorum cranio egredientium libri quinque.* Prostant Apud Abr. Vandenhoeck viduam, 1778.
- Pinkus F. - Über einen noch nicht beschriebenen. Hirnnerven des *Protopterus annectens*, 1894.
- Demski L.S., Schwanzel-Fukuda M. - The terminal nerve (nervus terminalis): structure, function, and evolution. Introduction. *Ann N Y Acad Sci.*, 1987;519: ix-xi.
- Vilensky J.A. - The neglected cranial nerve: nervus terminalis (cranial nerve N). *Clin Anat.*, 2014;27(1):46-53.
- Johnston J. - Nervus terminalis in reptiles and mammals. *Journal of Comparative Neurology*, 1913;23(2):97-120. doi: 10.1002/cne.900230202
- Johnston J.B. - The nervus terminalis in man and mammals. *Anat Rec.*, 1914;8(4):185-198. doi: 10.1002/ar.1090080402
- Brookover C. - The nervus terminalis in adult man. *Journal of Comparative Neurology*, 1914;24(2):131-135. doi: 10.1002/cne.900240203
- McCotter R.E. - A note on the course and distribution of the nervus terminalis in man. *Anat Rec.*, 1915;9(3):243-246.
- Pearson A.A. - The development of the nervus terminalis in man. *Journal of Comparative Neurology*, 1941;75(1):39-66.
- Kawai T., Oka Y., Eisthen H. - The role of the terminal nerve and GnRH in olfactory system neuromodulation. *Zoolog Sci.*, 2009;26(10):669-680.
- Von Bartheld C.S. - The terminal nerve and its relation with extralbulbar "olfactory" projections: lessons from lampreys and lungfishes. *Microsc Res Tech.*, 2004;65(1-2):13-24.
- Schwanzel-Fukuda M., Silverman A.J. - The nervus terminalis of the guinea pig: a new luteinizing hormone-releasing hormone (LHRH) neuronal system. *J Comp Neurol.*, 1980;191(2):213-225.
- Oka Y., Matsushima T. - Gonadotropin-releasing hormone (GnRH)-immunoreactive terminal nerve cells have intrinsic rhythmicity and project widely in the brain. *J Neurosci.*, 1993;13(5):2161-2176.
- Wirsig-Wiechmann C.R., Wiechmann A.F., Eisthen H.L. - What defines the nervus terminalis? Neurochemical, developmental, and anatomical criteria. *Prog Brain Res.*, 2002;141:45-58.
- Uchiyama H., Reh T.A., Stell W.K. - Immunocytochemical and morphological evidence for a retinopetal projection in anuran amphibians. *J Comp Neurol.*, 1988;274(1):48-59.
- Wirsig-Wiechmann C.R., Wiechmann A.F. - Vole retina is a target for gonadotropin-releasing hormone. *Brain Res.*, 2002;950(1-2):210-217.
- Santacana M., de la Vega A.G., Heredia M., Valverde F. - Presence of LHRH (luteinizing hormone-releasing hormone) fibers in the optic nerve, optic chiasm and optic tract of the adult rat. *Brain Res Dev Brain Res.*, 1996;91(2):292-299.
- Witkin J.W. - Nervus terminalis, olfactory nerve, and optic nerve representation of luteinizing hormone-releasing hormone in primates. *Ann N Y Acad Sci.*, 1987;519:174-183.
- Demski L.S., Northcutt R.G. - The terminal nerve: a new chemosensory system in vertebrates? *Science*, 1983;220(4595):435-437.
- Doty R.L. - Olfaction. *Annu Rev Psychol.*, 2001;52:423-452.
- Mousley A., Polese G., Marks N.J., Eisthen H.L. - Terminal nerve-derived neuropeptide  $\gamma$  modulates physiological responses in the olfactory epithelium of hungry axolotls (*Ambystoma mexicanum*). *J Neurosci.*, 2006;26(29):7707-7717.
- Ramakrishnan S., Wayne N.L. - Social cues from conspecifics alter electrical activity of gonadotropin-releasing hormone neurons in the terminal nerve via visual signals. *Am J Physiol Regul Integr Comp Physiol.*, 2009;297(1):R135-R141.
- Fuller G.N., Burger P.C. - Nervus terminalis (cranial nerve zero) in the adult human. *Clin Neuropathol.*, 1990;9(6):279-283.
- Oelschläger H.A., Buhl E.H., Dann J.F. - Development of the nervus terminalis in mammals including toothed whales and humans. *Ann N Y Acad Sci.*, 1987;519:447-464.