# Introduction to the Anatomy and Function of the Nervus Terminalis

From early studies of nasal chemosensory systems came a description of a ganglionated nerve which at first was assumed to belong to the olfactory or vomeronasal systems. Fritsch (1878) first described an "überzähliger Nerv" (supernumerary nerve) in *Galeus canis*, the smooth dogfish. Kingsbury (1895) observed a small bundle of fibers in the region caudal to the olfactory bulbs of the mudpuppy. He called this the "diencephalic olfactory tract." Likewise, Bochenek (1899) found a similar nerve in the salamander and gave it the nomenclature of "tractus olfacto-commissuralis and tractus olfacto-diencephalicus," believing it to be an extension of the olfactory system proper. However, Pinkus (1894) realized that this ganglionated nerve was a separate "neuen Nerv" (new nerve). He based this on his studies of *Propterus annectens*, the African lungfish, in which this nerve entered the brain in the region of the lamina terminalis and not in the region of the olfactory bulbs. Soon after Pinkus proclaimed the significance of this new nerve, Locy (1899) confirmed its presence in *Squalus acanthias*, the spiny dogfish, and referred to it as the "median nerve," "the new nerve," and the "accessory olfactory nerve." He reported that the fibers of this median nerve and the olfactory nerve never anastomosed. In 1905, Locy conducted a study of the median nerve using 27 species of selachians. Because the nerve consistently entered the brain at the lamina terminalis, he called this new nerve the *nervus terminalis*. From 1905 until 1980 there was only speculation about this unique nerve's function.

Now more commonly referred to as the *terminal nerve*, this neural plexus is only slightly less of an enigma than it was over 100 years ago. We now know that it contains several neuroactive substances including gonadotropin hormone-releasing hormone (Schwanzel-Fukuda and Silverman, 1980), that it projects to the chemosensory mucosa and into the brain (and sometimes to the retina), that it is present in all vertebrates except perhaps jawless fish (Eisthen and Northcutt, 1996; however, its cells are perhaps hidden among the hypothalamic GnRH neurons in these animals, Nozaki et al., 2000), and that it acts as a neuromodulatory system in the peripheral olfactory system and retina (Eisthen et al., 2000; Stell et al., 1987). The terminal nerve group of GnRH neurons is also one of three distinct brain GnRH systems. These systems include GnRH neurons found within the nasal cavity and forebrain (terminal nerve GnRH III system), preoptic/hypothalamic area (hypothalamo-hypophyseal GnRH I system), and midbrain (mesencephalic GnRH II system). Because this new information sets the terminal nerve GnRH system apart from the hypothalamic system, it has become apparent that the terminal nerve is more than merely a group of GnRH neurons that failed to migrate into the brain. This system has the potential to coordinate peripheral and central sensory and motor system functions that relate to reproduction.

The following three articles introduce the terminal nerve as a separate cranial nerve, and cover aspects of its unique development, neuroanatomical characteristics, and functional projections. In the first article by Kathleen Whitlock (pages 2–12), the most current information on the developmental origins of the terminal nerve is presented. During the neural plate stage of nervous system development cells destined to become part of the GnRH component of the terminal nerve are derived from the rostral-most edge of the neural crest. In the article by Christopher von Bartheld (pages 13–24), the criteria for defining what neural components can be included as constituents of the terminal nerve are discussed in light of the multitude of potential markers for both the olfactory system and the terminal nerve. The neural system that bypasses the olfactory bulb may be a component of the terminal nerve. In the last article, by Uwe Behrens and Hans-Joachim Wagner (pages 25–32), the projections of the terminal nerve to the retina and the functional considerations are presented. The projection of terminal nerve to the retina has a direct influence on dopaminergic interplexiform cells in fish, and thus the terminal nerve can influence light adaptation. These reviews are intended to bring us up to date on some of the most current information relating to the function of the terminal nerve. They also are meant to set the stage for a second series of reviews that will delve into additional unique aspects of terminal nerve anatomy and physiology in a host of model systems.

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