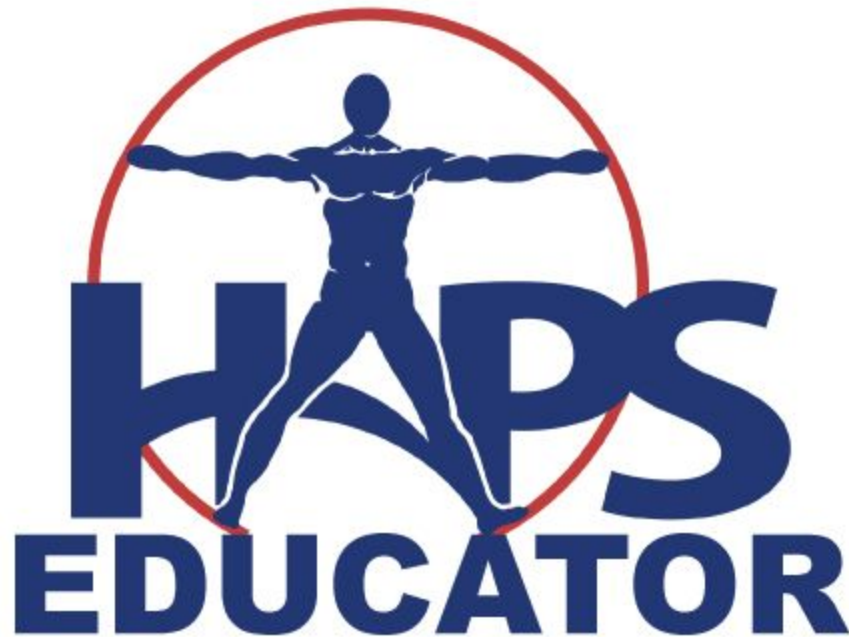**Finding CN XI: A Review of Defining the Spinal Accessory Nerve in Anatomical and Evolutionary Contexts**

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# Finding CN XI:  A Review of Defining the Spinal Accessory Nerve in Anatomical and Evolutionary Contexts

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## Abstract
The distinct pathway and controversial morphology of cranial nerve XI (spinal accessory nerve) make it unique among the cranial nerves.  In the past decade, several anatomical and embryological studies have further elucidated the structure and function of CN XI.  In this review, the evolutionary history of CN XI and its phylogenetic relationship to CN X, the vagus nerve, are considered in light of these recent investigations to provide a fuller anatomical picture of the CN XI.  Implications for anatomical education are also considered. doi: 10.21692/haps.2017.047

*The information contained in this article will enhance student comprehension of the nervous system and their appreciation for current research associated with the morphology of cranial nerve XI.  This information is applicable to the pedagogy of courses in Human Anatomy and Human Anatomy and Physiology.*

## Introduction

The morphology and function of the cranial nerves represent some of the most recognizable concepts in human anatomy.  The current criteria for a cranial nerve are that: 1) the nerve arises from the brain/brainstem and 2) the nerve exits through a foramen within the skull (Lachman *et al.* 2002).   Cranial nerve XI, the spinal accessory nerve seems to defy this definition.  While it exits the skull and may have nuclei within the brain/brainstem, it is the only cranial nerve to have fibers from nuclei in the spinal cord that enter the skull before the nerve exits via the jugular foramen.  This unique presentation is one of the defining features of an otherwise ordinary general somatic efferent nerve.  In the last decade, however, the function and structure of this cranial nerve have been further investigated.

The research conducted on cranial nerve XI conflicts with the textbook description of this well-known landmark.  In the review below, the historical and anatomical data are examined along with the phylogenetic data of the spinal accessory nerve.  Through tracing the proximate and ultimate development of this nerve, the story of the spinal accessory nerve can be expanded to include its rich history in the development of humans and other gnathostome descendants across the phylogenetic timeline.  By incorporating information from various scientific disciplines, the role of this nerve may be more accurately defined, which will assist human development researchers, clinicians, and anatomists in their scientific investigations.

## Defining the Spinal Accessory Nerve
To compare the pathway of the human spinal accessory nerve with its counterparts along the evolutionary tree, it is vital to accurately define the morphology and function of the human cranial nerve XI.  The spinal accessory nerve was described in the 1600's and is traditionally defined as consisting of two parts: a cranial root and a spinal root (Liu *et al.* 2014, Marani and Lakke 2012).  It is the only cranial nerve to have nuclei outside the brain, the only cranial nerve to enter the skull before leaving it again, and the only cranial nerve to consist of two parts.  Its function is typically described as the motor supply for the trapezius and sternocleidomastoid (SCM) muscles.  The morphology and function of this cranial nerve have come under scrutiny in recent years.

The spinal root of the spinal accessory nerve consists of rootlets from nuclei in the upper cervical region that exit the spinal cord between the ventral and dorsal spinal rootlets.  These fibers enter the foramen magnum and often join with the cranial root as it leaves the caudal medulla.  The fibers from this spinal root have been described as continuing as the external branch of the spinal accessory nerve after its exit from the jugular foramen and providing motor innervation of the SCM and trapezius muscles (Moore *et al.* 2014).  Liu *et al.* (2013) in a gross tracing of fibers from both roots found that the most common composition of the external branch of the spinal accessory nerve was a mixture of spinal and cranial root fibers.  This composition occurred with an internal branch consisting of fibers from the cranial root and the vagus nerve.  The second most common presentation of the external branch consists of fibers from the cranial and spinal root along with fibers from the vagus nerve.  Figure 1 demonstrates the two most prevalent fiber compositions of the internal and external branches of the spinal accessory nerve.  The location of the cervical motor nuclei varies based on the source consulted with all cervical levels implicated in the literature (Bergman *et al.* 1988, Marani and Lakke 2012, Vanderwah and Gould 2016).
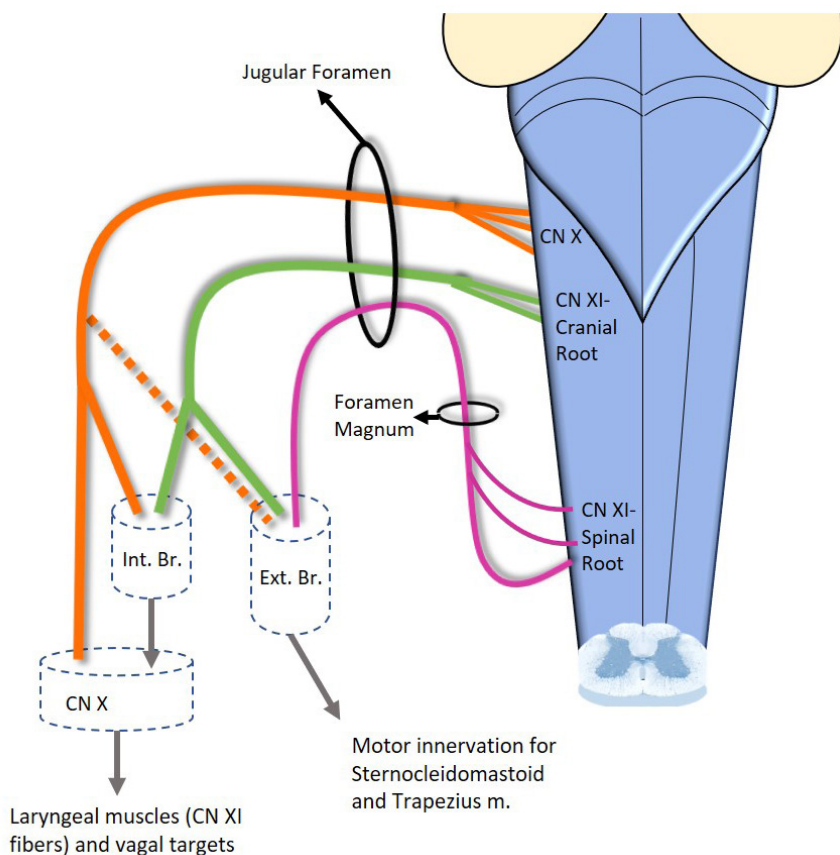
**Figure 1.** Diagrammatic representation of the two most prevalent presentation of the internal and external branch fibers of CN XI as discussed in Liu *et al.* (2013). The solid lines demonstrate the most prevalent presentation (IB = Cranial Root + CN X; EB = Cranial and Spinal Root) (n=18). The 2nd most prevalent presentation is identical to the first but adds vagal fibers to the external branch (represented by the dotted line) (n=8). Targets of this plexus are reported from Liu *et al.* (2013). Orange = CN X, Green = Cranial Root of CN XI, Purple = Spinal Root of CN XI. Adapted from Liu *et al.* 2013. Illustrated by Theodore C Smith.

The cranial root, while historically described as a part of cranial nerve XI, has recently been re-examined. The cranial portion of the spinal accessory nerve exits the medulla from the postolivary groove and unites with the spinal portion either before or within the jugular foramen (Ryan *et al.* 2007). Lachman *et al.* (2002) were among the first to describe the cranial root as a part of the vagus nerve, not the spinal accessory nerve. In their investigation of human cadavers (n = 15), they found that the medullary rootlets of the so-called cranial root could be bluntly dissected from the spinal root and that the medullary rootlets never made any connections with fibers in the spinal root. Instead, these cranial root fibers joined with vagal rootlets in the superior ganglion of the vagus nerve. This observation is disputed by several follow-up studies (Liu *et al.* 2014, Liu *et al.* 2013, Ryan *et al.* 2007, Tubbs *et al.* 2014).

Ryan *et al.* (2007) found a connection between the cranial root and the spinal root existed in one of the specimens dissected. Tubbs *et al.* (2014) found a cranial root (defined

as fibers joining the spinal portion proximal to the jugular foramen) present in 76% of their specimens (n=86 sides). The cranial root fibers are suggested to originate from the nucleus ambiguus and provide motor function for the laryngeal muscles (Liu *et al.* 2013).

Lachman *et al.* (2002) attribute the inclusion of a cranial root within the literature to a drawing made in 1838, which was then used as reference in the famous Gray's Anatomy (1858). While the drawing by Friedrich Arnold did not include a written description of the cranial root, the written description was included in Gray's Anatomy along with the illustration (Lachman *et al.* 2002). Before this time, the authors argue, descriptions of the spinal accessory nerve did not include a cranial portion. Whether the addition of a cranial root was a misrepresentation of the anatomy or the amount of anatomical variation in this area is much higher than previously thought, there is a need for further research into this "textbook" presentation.

Molecular studies like ones done by Pabst *et al.* (2003) may prove to be another valuable avenue for defining CN XI. Pabst *et al.* (2003) show there is disruption of the spinal root formation in Nkx2.9 (a homeodomain-containing transcription factor expressed in the ventral neural tube of mouse embryos) knockout mice but not the formation of the cranial root. The glossopharyngeal and vagus nerves were also found to be abnormal in about 50% of the Nkx2.9 knockout mice, demonstrating developmental connections between the spinal accessory, vagal and glossopharyngeal nerves. However, further investigations, from the gross, molecular, and developmental perspective are needed to provide a fuller description of the spinal accessory nerve.

The discrepancy in the literature as to the constituents of the spinal accessory cranial nerve pathway and therefore its function makes further analysis difficult. In the broadest terms, the spinal accessory nerve originates from cervical and medullary nuclei and is responsible for motor innervation for the SCM and trapezius muscles as well as innervation of the laryngeal muscles, a function attributed more often to the vagus nerve, CN X (Liu *et al.* 2013, Tubbs *et al.* 2014). The relationship between CN XI and CN X is even more confounding. With the strong documentation of fiber exchange between these 2 nerves, the role of the cranial part of CN XI is unclear. In *Fundamental Neuroscience for Basic and Clinical Applications*, Haines compares the relationship between CN XI and X to that of the taste fibers of the facial nerve that also travel along the trigeminal nerve via the chorda tympani. Haines claims that the cranial root is a misnomer

and the spinal portion, the true component of CN XI, only temporarily joins the vagus and is not disseminated with vagal fibers. While research by Liu *et al.* (2013) disproves this lack of exchange, Haines provides an intriguing mental model for the relationship between the spinal accessory and vagus nerves. By examining the developmental and evolutionary origins of the spinal accessory nerve and its peripheral targets, the purpose for its circuitous route, its unique and controversial morphology and its strong relationship with the vagus nerve may be elucidated.

## Development and Evolution of the Spinal Accessory Nerve

In humans, motor innervation of the SCM and trapezius is attributed to the spinal accessory nerve with afferent proprioception innervation via cervical spinal nerves (Moore *et al.* 2014). However, these functions are not as clear-cut as reported in the Moore *et al.* study. Case studies have shown patients with spinal accessory injuries can retain motor function of the trapezius (Tubbs *et al.* 2011). Examination of rat cervical fibers and spinal accessory nerve fibers have shown that they often consist of a mixture of alpha and gamma motor neurons with cervical nerves containing a higher percentage of gamma motor neuron fibers (Tada and Kuratani 2015).

Other studies have found neural crest cells and myoblasts from occipital lateral plate mesoderm, which suggests a development similar to infrahyoid or trunk muscles, forming the cucullaris muscle (Ericsson *et al.* 2013, Tada and Kuratani 2015).

These conflicting results could be the product of several issues such as the differing stage of development of the specimens
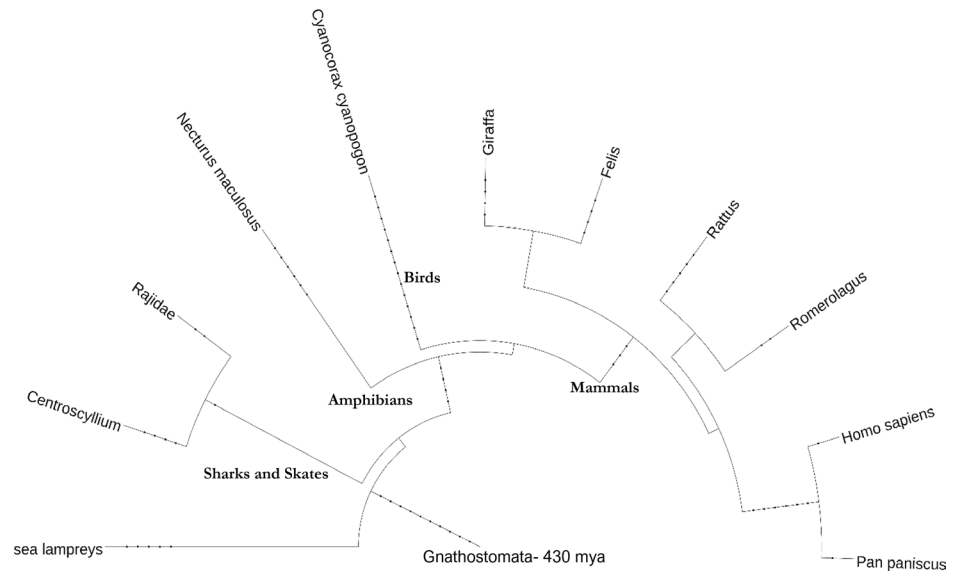


**Figure 2.** Phylogenetic tree of the Gnathostomata infraphylum showing select species. CN XI appears at the rise of the infraphylum, coinciding with the appearance of the pectoral girdle and jaw in the fossil record. Phylogenetic tree created with phyloT version 2017.7 (http://phylot.biobyte.de/index.html) and Interactive Tree of Life (iTOL) (Letunic and Bork 2016).

The innervation of the SCM and trapezius is unique for muscles in the neck and pectoral girdle regions. The trapezius muscle is the only pectoral girdle muscle that is not innervated by branches of the brachial plexus while the SCM muscle does not share similar innervation with other neck muscles. Despite this difference in peripheral innervation of these muscles, the motor nuclei that innervate the pectoral girdle and neck muscles come from similar levels of the cervical spinal cord (Rosse and Gaddum-Rosse 1997). The different peripheral routes taken by these motor fibers may be evidence of a unique pattern of development in utero or indicate a unique phylogenetic history.

There is controversy surrounding the exact mode of development of the SCM and trapezius muscles. Phylogenetically, the SCM and trapezius muscles are homologous to the cucullaris muscle, which is present in all gnathostome vertebrates (See Figure 1 for a relevant phylogenetic tree) (Ericsson *et al.* 2013). Developmental studies, mainly with chick and quail embryos, have disagreed on the origin of the myoblasts that become the cucullaris muscle. Studies have found that neural crest cells (indicating a connective tissue formation similar to head muscles) and myoblasts from rostral somites (similar to other head and neck musculature development) join to form the cucullaris muscle.

used (Ericsson *et al.* 2013, Tada and Kuratani 2015). Haines (2013) claims that the SCM and trapezius muscles develop from paraxial mesoderm caudal to the 4th branchial arch. The unique nature of the cucullaris muscle as a neck muscle, which as a muscle in a transition area from trunk to head, may not follow definitive developmental pathways of the head and trunk may also be an issue (For more on the development and evolution of the neck, see Ericsson *et al.* 2013). This distinctive combination of head and trunk development does not, however, elucidate why motor innervation for the cucullaris muscle (SCM and trapezius muscles) takes such a circuitous path.

The route taken by the spinal accessory nerve in humans may seem less inefficient when examined in the context of evolution. Appearance of the cucullaris muscle coincides with the appearance of jaws and rudimentary pectoral girdles about 430 million years ago (Long 1999). One of the earliest species in which a spinal accessory nerve can be viewed is the skate, a primitive ancestor of the shark. However, the fibers that become the skate spinal accessory nerve travel within the intestinal ramus of the vagus nerve with its motor neuronal bodies in an area spanning the caudal aspect of the vagal nucleus to the lateral spinal gray matter near the 3rd and 4th ventral rootlets (Benninger and McNeil 2010).

Further down the evolutionary line, sharks provide a similar presentation of the spinal accessory nerve as a branch of the intestinal vagus nerve. Innervation of this muscle differs depending on the species of shark with either singular innervation by the accessory nerve or dual innervation by the accessory and cervical nerves. Retrograde tracking studies to locate the nuclei of this nerve are lacking due to the complex morphology of the nerve in sharks and fish (Benninger and McNeil 2010). Jumping further along the phylogenetic tree to mammals, the motor nuclei of cranial nerve XI have been mostly found in the caudal medulla and rostral spinal cord at varying levels. The variation of the location of the mammalian nuclei can be seen both between and within species (Benninger and McNeil 2010, Tada and Kuratani 2015). Figure 2 is a graphical representation of these nuclei in a variety of species.

This new anatomical data provides a much fuller picture of the spinal accessory nerve than can be provided with just human anatomical and developmental data. The evidence points to a slight trend in the movement of the motor nuclei and location of the cucullaris muscle. Through progression along the phylogenetic line, the motor nuclei appear to descend along the brainstem as the neck develops in the species. This movement agrees with Kappers' theory of neurobiotaxis which states that a group of cell bodies for a group of axons will migrate in the direction they are receiving the most stimulus (Benninger and McNeil 2010, Tubbs *et al.* 2014). As organisms developed necks and the cucullaris muscle migrated further away, the motor nuclei migrated inferiorly within the brainstem and spinal cord. Thus, the spinal accessory nerve was stretched with the jugular foramen as an anchor point between the moving nuclei and its peripheral innervation. The retention of the nerve route seems inefficient with the motor

**Figure 3.** Comparison of locations of the vagus (x), spinal accessory (XI), and hypoglossal (XII) motor nuclei in the skate (A), salamander (B), toad (C), sand lizard (D), and human (E). They demonstrate a pattern of neurobiotaxis with the cell bodies of CN XI migrating towards their target. Images reprinted with permission from Tada & Kurantani (2015). Used with permission of Shigeru Kuratani, Chief Scientist Evolutionary Morphology Laboratory, RIKEN, 2-2-3 Minatojima-minami, Chuo-ku, Kobe, Hyogo 650-0047, JAPAN
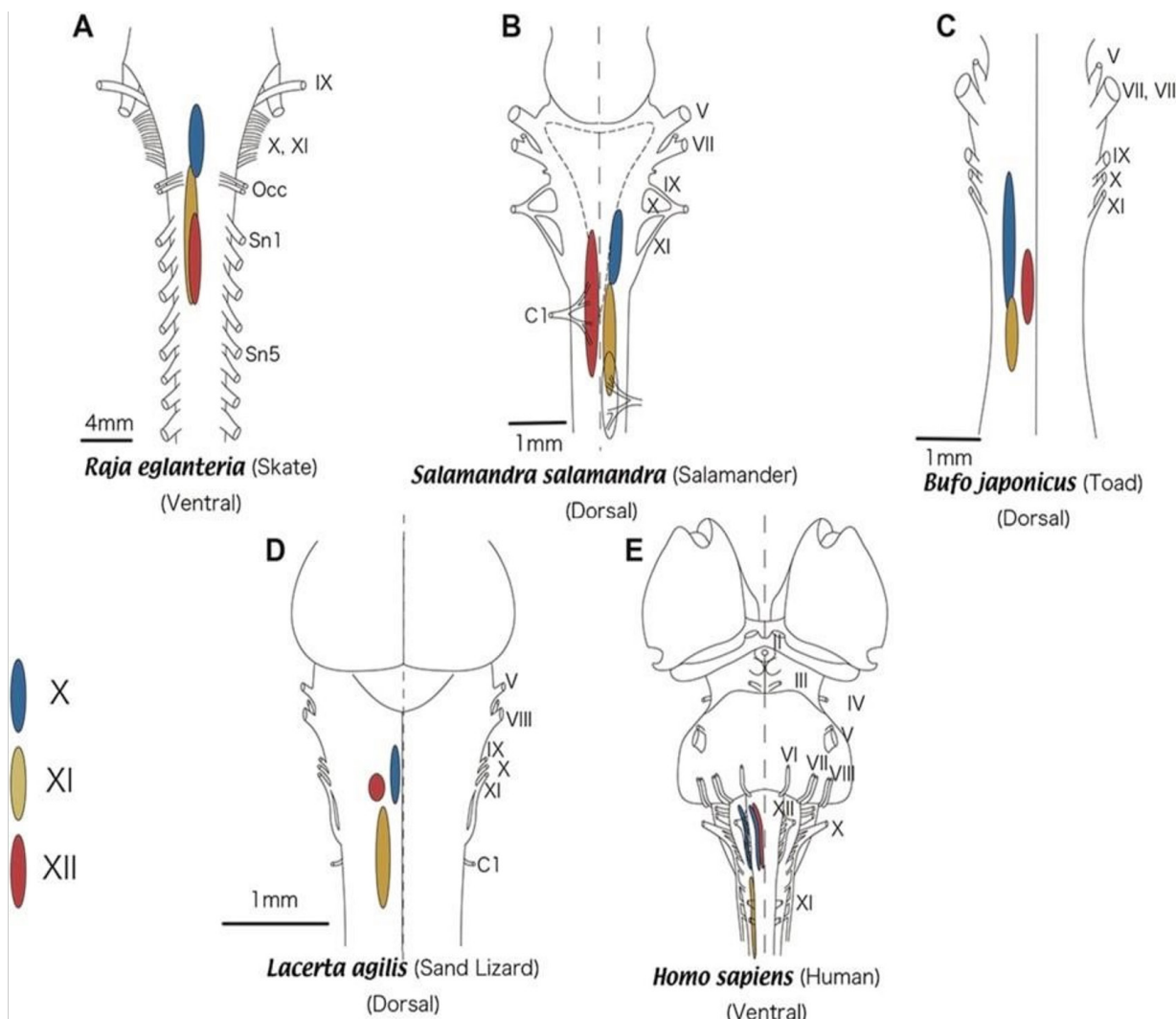
nuclei and peripheral innervation moving closer together. However, taking into account the ancestral relationship between the spinal accessory and the vagus nerve, this route may be logical. This pathway may have persisted due to a need for the exchange of fibers with the vagus, as an interaction of vagal and spinal accessory fibers can be found in the most ancestral and human forms of both structures. The cranial root of the spinal accessory nerve may be a remnant of this ancestral relationship. Or perhaps this pathway provides easier access for an innervation of the SCM muscle and trapezius together.

Despite some correlative trends, further research is needed to determine causation. More cadaveric studies examining the fibers from both roots of the spinal accessory nerve and their interaction with the vagus are needed. While there is an evolutionary precedent for a strong relationship between cranial nerves X and XI, the conflicting results concerning the morphology of the spinal accessory nerve need to be resolved. Further exploration into the development of the trapezius and SCM may provide further evidence into their place as trunk, head or intermediate muscles that may provide more information as to the function of cranial nerve XI. More nerve retrograde tracing studies in more species may also provide a more complete picture of the phylogenetic development of the spinal accessory nerve and its nuclei.

## Conclusion and Implications for Anatomical Education

Despite the more complete picture of CN XI resulting in the combination of developmental, evolutionary, and gross anatomical data, many questions remain concerning the function and morphology of this structure. Is the cranial root a part of CN XI or CN X? Should it be separated from both and given its own spot among the cranial nerves? Is the cranial root a remnant of the ancestral relationship shared by CN XI and CN X? These questions and more have the potential to allow us to rewrite the definitions of the cranial nerves and their functions. Regardless of the new questions, the spinal accessory nerve is a remarkable illustration of the nuances of neuroanatomy and gross anatomy. Not only does it demonstrate the range of human anatomical variation, it also shows that this variation extends across species.

For educators, CN XI provides a wealth of material for teaching anatomy at any level. Anatomy has always had a place at the core of medical science, making the connections from it to other topics such as developmental biology and evolutionary biology. Most importantly, CN XI's history has the ability to demonstrate the nuance of anatomy that anatomists rejoice in. As was demonstrated with the controversial definition of the cranial nerve itself, this structure is also a prime example of the inability of science to definitively generalize all structures to follow a singular definition. The goal of generalization is particularly difficult in anatomy due to the extent of

anatomical variation. Despite this, the investigation of the role of an anatomical structure is not any less important. Understanding the function of the spinal accessory nerve is vital for clinicians who are tasked with the up-keep of this vital structure. Future investigations into this area would greatly benefit from interdisciplinary work to gain a clearer picture of cranial nerve XI and its role in human biology.

## About the Author
Theodore Smith, MS is a second-year PhD student in the Anatomy and Cell Biology - Education Track program at Indiana University-Bloomington. He teaches undergraduate anatomy labs and is interested in classroom technology, spatial ability and student success, and curriculum re-design.

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