Received: 31 May 2022 | Revised: 1 August 2022 | Accepted: 11 September 2022

DOI: 10.1002/ar.25079

REVIEW ARTICLE

The Anatomical Record WILEY

The tracts, cytoarchitecture, and neurochemistry of the spinal cord

Sheryl Tan | **Richard L. M. Faull** | **Maurice A. Curtis**

Centre for Brain Research and Department of Anatomy and Medical Imaging, University of Auckland, Auckland, New Zealand

Correspondence
Sheryl Tan, University of Auckland, PO Box 92019 Auckland 1142, New Zealand.
Email: sheryl.tan@auckland.ac.nz

Funding information
The CatWalk Spinal Cord Injury Trust

Abstract

The human spinal cord can be described using a range of nomenclatures with each providing insight into its structure and function. Here we have comprehensively reviewed the key literature detailing the general structure, configuration of tracts, the cytoarchitecture of Rexed's laminae, and the neurochemistry at the spinal segmental level. The purpose of this review is to detail current anatomical understanding of how the spinal cord is structured and to aid researchers in identifying gaps in the literature that need to be studied to improve our knowledge of the spinal cord which in turn will improve the potential of therapeutic intervention for disorders of the spinal cord.

KEYWORDS

cytoarchitecture, neuroanatomy, neurochemistry, Rexed laminae, spinal cord

1 | INTRODUCTION

Originating as a continuation of the brainstem and terminating in the *filum terminale*, the spinal cord is the primary information conduit connecting the brain and peripheral nervous system, controlling the trunk and limb musculature, as well as receiving sensory information from the same regions (Schwab, 2002; Watson & Kayalioglu, 2009). In contrast to other parts of the nervous system, the history of its characterization is relatively short and punctuated with large pauses, beginning with Blasius' distinction between gray matter and white matter in 1666, followed by the identification of several tracts and nuclei over the 18th and 19th Centuries (Naderi et al., 2004). Since the seminal subdivision of the spinal cord into laminae based on the localization and morphology of different cell types in the feline spinal cord by Bror Rexed (Rexed, 1952a), however, efforts to comprehensively articulate and describe the anatomy of the spinal cord has not kept up with advances in histochemical and imaging techniques, especially where the human is concerned. Consequently, there is a discontinuous series of studies spanning numerous species and animal models, spinal levels, and histochemical techniques. This review aims to comprehensively describe the spinal cord gray and white matter by consolidating available studies from the 19th Century to the present day. Unless otherwise stated, this review will refer to the human spinal cord, and considerable effort has been made to find data specific to humans. Experimental animal models will be referred to where there is no known human data available, or where comparisons across species are made. This is an essential foundation to fully understanding the structure and function of the key cell populations in the spinal cord and will serve as a reference when considering anomalies and disorders of the spinal cord (e.g., acute trauma, degeneration, or compression due to tumor growth).

2 | GENERAL DESCRIPTION OF HUMAN SPINAL CORD ANATOMY

Contiguous with the most caudal portion of the medulla oblongata, the spinal cord is ovoid in cross-section and extends within the vertebral column. In humans, it is approximately 45-cm long in males, and 43-cm long in females (Barson & Sands, 1977; McCotter, 1916). The cord is encased by the pia mater, the innermost layer of the spinal meninges. It is often considered as a single membrane with the intermediary arachnoid mater; collectively known as the leptomeninges (Figure 1b; Kayalioglu, 2009a). This continues to envelop the spinal roots as they leave the spinal cord, finally blending with the perineum of the spinal nerves. The pia mater also extends laterally between the attachments of the dorsal and ventral roots known as denticulate ligaments, which attach the spinal cord to the dura via the arachnoid mater (Figure 1b; Nicholas & Weller, 1988). These ligaments serve to anchor the spinal cord, providing stability when subject to movement in the lateral plane. Stress testing of denticulate ligaments in cadavers indicates greater tensile strength in the cervical spinal cord, gradually decreasing in the thoracic and lumbar regions (Tubbs et al., 2001). Like the cerebral meninges, the outermost layer of the spinal meninges is the dura mater; a tough and dense membrane composed of collagen, fibroblasts, and elastic fibers. It extends over the spinal ganglion and nerves, blending with the epineurium (Figure 1b).

The spinal cord is subdivided into five regions consisting of 31 paired segments from rostral to caudal, these are the cervical (8 segments), thoracic (12 segments), lumbar (5 segments), sacral (5 segments), and coccygeal (1 segment) (Figure 1a; Frostell et al., 2016). The cervical region is largely concerned with facilitating movement and sensation of the head, neck, shoulders, arms, and hands. In humans, this is a region where acute trauma to the spinal cord is commonly sustained and the most life-threatening (Kang et al., 2018). The thoracic region continues immediately from the cervical, which is responsible for controlling motor and sensory information about the abdomen, upper chest, and the upper back. Broadly speaking, this region is critical for providing stability to the body. The lumbar region continues from this, covering the movement and sensation of the lower abdomen and the legs. The sacral and coccygeal regions are found next, although in the human the spinal cord ceases to exist as a whole piece of tissue per se and instead frays out forming the *cauda equina* (Figure 1a); a series of nerve roots that facilitates motor and sensory function to the lower limbs and the pelvic organs (Orendáčová et al., 2001). While some nuclei have been identified in this region in non-human species, these will be omitted from this discussion for clarity. Specifically, the conus medullaris is considered the end of the spinal cord; typically occurring at the level of the L1 vertebra in the average adult (Figure 1c; Brouwers et al., 2017). It is surrounded by the pia mater and is connected to the filum terminale, a fibrous band of connective tissue extending from the conus medullaris to the dorsum of the coccyx (Figure 1c; Kwon et al., 2018). The filum terminale serves to anchor the spinal cord, stabilizing the distal aspect of the cord when subject to cephalic and caudal traction (Kwon et al., 2018). It is composed of type I collagen, elastic, and elaunin fibers (Fontes et al., 2006) and is made up of two parts: the filum terminale internum and the filum terminale externum (Saker et al., 2017). The former refers to the upper ¾ and is surrounded by the spinal dura and arachnoid meninges (Figure 1c; Saker et al., 2017). It is surrounded by ample sub-arachnoid space and is the region where a lumbar puncture is performed for the collection of cerebrospinal fluid (Saker et al., 2017). The latter is also known as the coccygeal ligament and refers to the remaining quarter and is adherent to the dura mater, connecting to the periosteum of the coccyx (Saker et al., 2017).

2.1 | Subdivisions of the spinal cord

The spinal cord is comprised of gray matter and white matter. The interior of the cord consists of gray matter and is immediately apparent by the distinctive, upside-down butterfly-like shape it resembles when viewed in the transverse plane (Figure 2). It consists of the cell bodies of neurons, interneurons, and both myelinated and unmyelinated axons. There are two key anatomical landmarks; the ventrolateral and dorsolateral sulci (Figure 2) from which the ventral and dorsal rootlets arise, respectively (Figure 1b). These rootlets cross the subarachnoid space and pierce the dura mater separately before converging to form the dorsal or ventral root and ultimately, the spinal nerve (Saito & Steinke, 2015). The functional subdivisions of the gray matter will be elaborated on further as the focus of the review. The white matter on the other hand encircles the gray matter (Figure 2). It is named so for the presence of heavily myelinated axons, facilitating saltatory conduction of signals along the length of the axon.

2.1.1 | White matter subdivisions

When viewed in the transverse plane, the white matter can be further subdivided into ventral (anterior), lateral, and dorsal (posterior) columns, or funiculi (Figure 2),

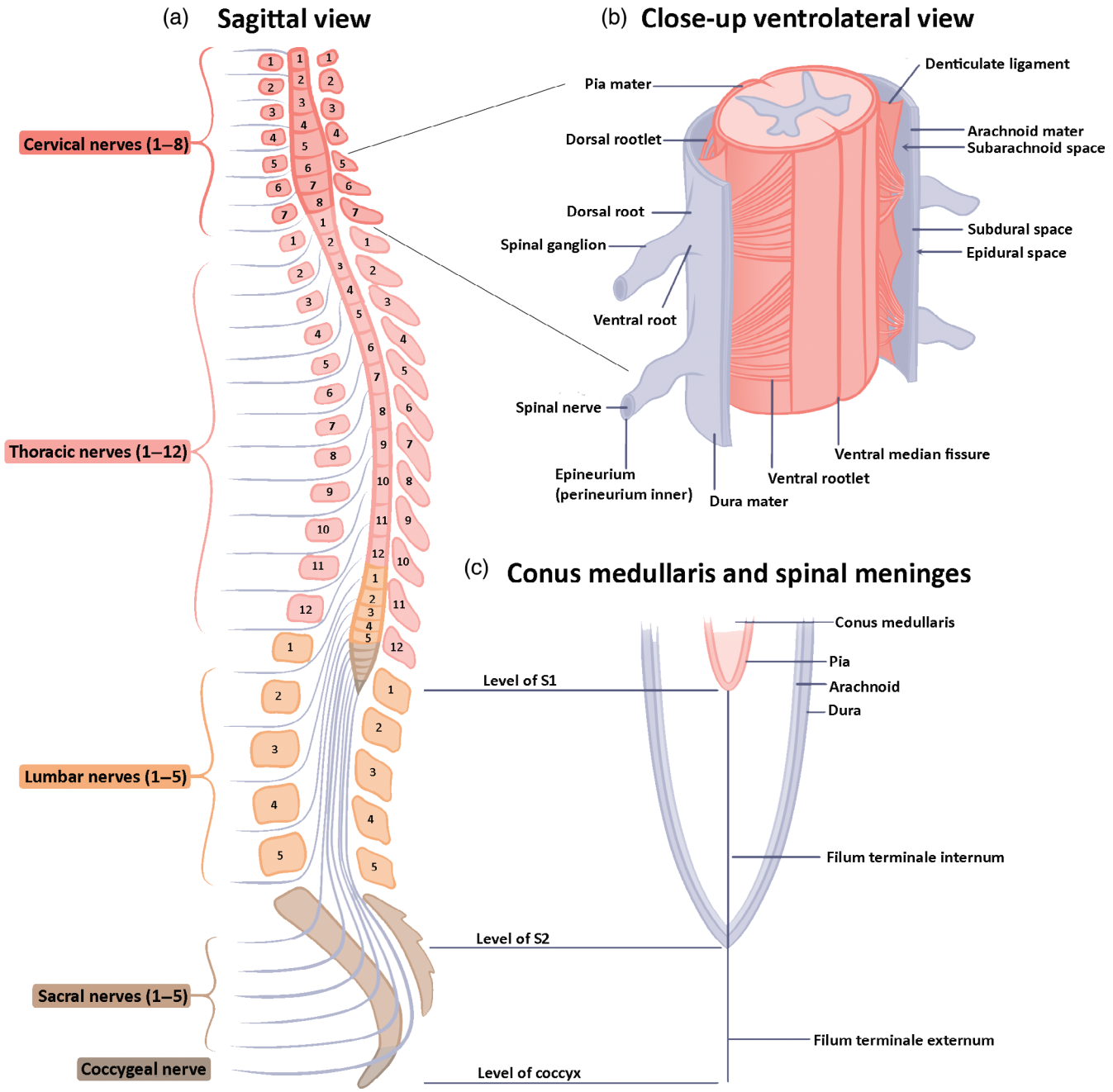

FIGURE 1 General anatomy of the human spinal cord. (a) Sagittal view of the spinal cord and vertebral column. The spinal column consists of 31 paired segments (8 cervical, 12 thoracic, 5 lumbar, and 1 coccygeal). The spinal cord is encased by the vertebral column (commonly known as the backbone or spine), which consists of 33 individual vertebrae [7 cervical, 12 thoracic, 5 lumbar, 5 sacral (fused), and 4 coccygeal (fused)]. (b) A close-up ventrolateral view over two spinal segments (C6–C7 is depicted as an example). The spinal cord itself is encased by the pia mater; together with the arachnoid mater it forms the leptomeninges. The leptomeninges envelops the spinal roots and blends with the perineum of the spinal nerves. The lateral extensions of the pia mater are known as the denticulate ligaments, which anchors the spinal cord to the dura via the arachnoid mater. The sub-arachnoid space is the gap in between the pia and arachnoid mater, and is filled with cerebrospinal fluid. Finally, the dura mater is the outermost layer; a tough, fibrous layer which serves to protect the spinal cord. The subdural space is a virtual space between the dura and arachnoid mater. Comprised of fat and small blood vessels, the epidural space is found in between the dura mater and vertebral column; it is a site of administration for some local anesthetics and analgesics. (c) Conus medullaris and spinal meninges. The conus medullaris is considered the end of the spinal cord. The filum terminale (internum, upper 3/4; externum, lower 1/4) is a fibrous band of connective tissue that serves to stabilize the distal end of the cord

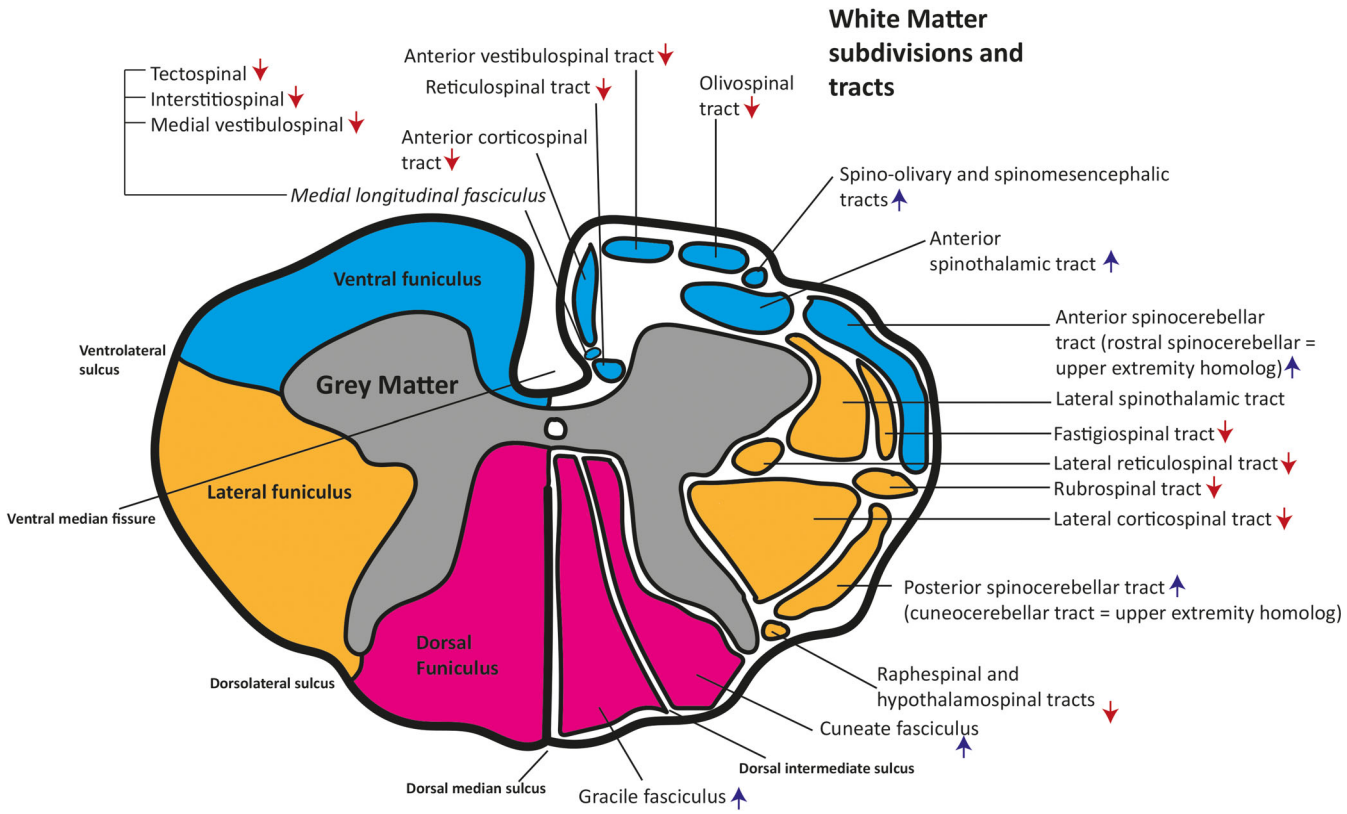

FIGURE 2 White matter subdivisions (left) and key tracts found within the white matter (right). Schematic transverse section of the human spinal cord (approximate spinal level = C7) with regional divisions (left-hand side) and key tracts (right-hand side; red arrow = descending, blue arrow = ascending). Tracts are colored the same as the regional division they are considered to be a part of

which are functionally distinct from one another (Schoenen & Faull, 2004; Sengul & Watson, 2012a); the anterior white commissure at the base of the latter connecting the halves (Çavdar et al., 2021; Raybaud, 2010). Ascending projections (Figure 3) travel from the spinal cord to supraspinal regions, communicating sensory information (pain, temperature, proprioception, and touch) not only from somatic structures (e.g., limbs) but also the viscera (Wang et al., 2022; Wercberger & Basbaum, 2019). These arise from neurons in the dorsal root ganglion or within the gray matter of the spinal cord, and project to the brainstem, cerebellum, midbrain, diencephalon, or the telencephalon (Wercberger & Basbaum, 2019). Descending projections (Figure 3) on the other hand are comprised of upper motor neurons whose role is to transmit motor information down the spinal cord where they synapse with lower motor neurons, ultimately facilitating movement (Lemon, 2008).

Ventral (anterior) funiculus

The ventral funiculus refers to the area of white matter between the anterior median fissure and the ventral root (Figure 2). *Ascending pathways* found in this column include the anterior (ventral) spinocerebellar tract, the spinovestibular tract, and the spinoolivary tract. *Descending pathways* found in this column include the ventral (anterior) corticospinal tract, medial longitudinal fasciculus (a sub-region consisting of the medial vestibulospinal tract, tectospinal tract, and interstitiospinal tract), the lateral vestibulospinal tract, pontine reticulospinal tract, and the olivospinal tract.

2.1.2 | Ascending pathways

In the heart of the lateral funiculus lies the anterior spinothalamic tract; dorsal to the lateral vestibulospinal tract and ventral to the ventral-most border of the ventral gray horn (Figure 2). The fibers of the anterior spinothalamic tract are widely distributed throughout the column (Honey et al., 2019; Kerr, 1975). These are axons of second-order neurons that originate in the contralateral gray matter [primarily lamina II (substantia gelatinosa)]; they receive input from first-order neurons that communicate with the periphery via the dorsal root ganglia. These axons travel up the ventral column and synapse with third-order neurons in the thalamus, facilitating neurotransmission to the somatosensory cortex, conveying

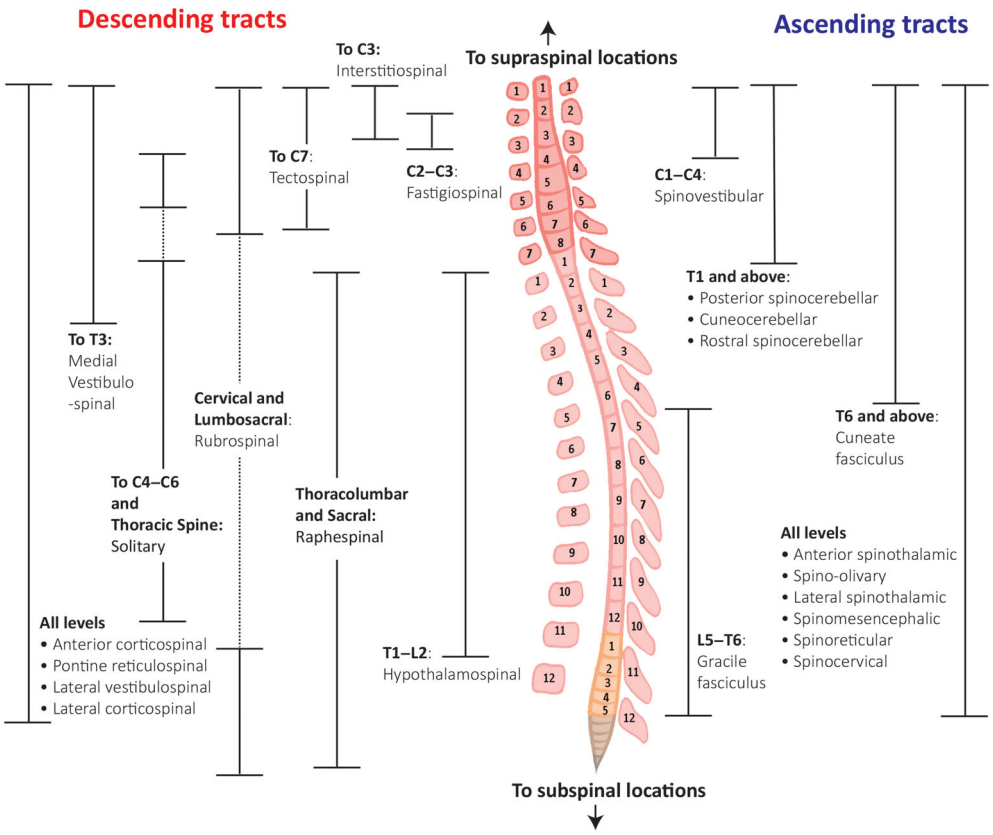

FIGURE 3 Tracts of the spinal cord white matter. Tracts are organized according to descending (left-hand side) and ascending (right-hand side). The approximate origin and termination points are described next to each tract; otherwise, "all levels" denotes tracts that are found throughout the entire length of the cord

primarily touch and light pressure information (Kerr, 1975). The anterior spinocerebellar tract (also known as Gower's column, after the British anatomist Sir William Gower), carries proprioceptive information from the lower limbs to the cerebellum and is key for the coordination of movement and postural maintenance (Sengul et al., 2015). In mice, optogenetic techniques to activate anterior spinocerebellar neurons and oppositely, silencing with clozapine N-oxide have demonstrated that this tract is involved in the initiation and maintenance of locomotion (Chalif et al., 2022). Retrograde tracing with wheatgerm-agglutinin conjugated to horseradish peroxidase indicates that in the lumbar and sacral regions, this tract is located within the ventral funiculus, and at more rostral levels its position becomes increasingly lateral (Xu & Grant, 2005). Its origins are dependent on the spinal level; in segments L4–L5 it begins in the lateral part of lamina VII and the neurons of the ventrolateral nucleus of lamina IX; the dorsolateral nucleus of lamina IX at levels L3–L6; and from the medial portion of lamina VII further down in the lumbrosacral regions (Xu & Grant, 2005). The axons comprising this tract decussate twice; firstly in the spinal cord to travel up to enter the contralateral cerebellum via the superior cerebellar peduncle, before recrossing and terminating in the ipsilateral cerebellum (Xu & Grant, 2005). The spinoolivary tract (Helweg's triangular tract; named so for its shape and after Hans Kristian Saxtorph Helweg, the Danish physician who first identified it) is the third ascending tract found in this region. Unlike the anterior spinocerebellar tract, this is found at all levels of the spinal cord and its origins lie in the medial aspect of the nucleus proprius (approximately lamina III) and the central cervical nucleus (Sengul & Watson, 2012b). In the cat and mouse, these axons decussate in the spinal cord and ascend contralaterally, terminating in the accessory olivary nucleus (Matsushita et al., 1992; Oscarsson & Sjölund, 1977; Pop et al., 2022). This tract plays a key role in transmitting proprioceptive information to the cerebellar sensorimotor zones via the accessory olivary nucleus (Schmahmann et al., 2019). The spinovestibular tract is also found in this white matter column and axons comprising this tract primarily belong to neurons of the central cervical nucleus [located in spinal levels C1–C4 (in the proximity of lamina X)], medial parts of the dorsal horn gray matter, and lamina VII of the ventral gray matter (Matsushita et al., 1995; Xiong & Matsushita, 2001). In the rat, these axons project to the lateral vestibular nuclei, spinal vestibular nuclei, and parts of the medial vestibular nuclei (Matsushita et al., 1995). This tract is comprised of bilateral inputs; axonal projections from the medial part of the dorsal gray horn remain ipsilateral and do not decussate; contralateral projections on the other hand originate from lamina VII and the central cervical nucleus (Xiong

& Matsushita, 2001). This tract is thought to play a role in the tonic neck reflex (Matsushita, 1991) as well as postural reflexes (Xiong & Matsushita, 2001).

2.1.3 | Descending pathways

The anterior corticospinal tract comprises ~12% of the corticospinal tract as a whole (Kwon et al., 2011) and is arguably the most important descending tract. Diffusion tensor imaging in humans indicates these fibers originate in the primary motor and somatosensory cortices, passing through the internal capsule and cerebral peduncle to form the longitudinal fibers of the pons and eventually the medullary pyramid upon leaving the basilar pons (Archer et al., 2017; Bürgel et al., 2006; Chenot et al., 2019; Kwon et al., 2011; Thiebaut de Schotten et al., 2011). Unlike fibers of the lateral corticospinal tract, this tract remains ipsilateral as it courses down the spinal cord (Kim et al., 2004), and is found in the most medial part of the ventral funiculus (Nathan et al., 1990). In the human, this tract lies along the entire median fissure at spinal levels C1–C4, spreading to reach the most ventral surface of the cord (Jang & Kwon, 2013; Kwon et al., 2011). Tracing experiments in the pig [an animal model whose spinal cord organization is remarkably similar to that of the human (Leonard et al., 2017)] demonstrated that projections from the primary and pre-motor cortex could be found up to spinal segment T6 (Del Cerro et al., 2021). In the humans, projections have been detected at around the upper thoracic levels; however, in isolated cases where the tract is particularly large, this has been seen as far down as the sacral segments (Nathan et al., 1990). Termination points are species-dependent. In primates and the pig, these are found in approximately laminae VII–VIII (Ralston & Ralston III, 1985); in rats and cats however these project slightly more dorsally, in laminae III–IV (Brösamle & Schwab, 1997; Nyberg-Hansen & Brodal, 1963). The anterior corticospinal tract is primarily responsible for innervating the musculature of the neck, trunk, and that of the proximal upper extremities such as the shoulder girdle (Kuypers & Brinkman, 1970; Kwon et al., 2011; Soteropoulos et al., 2011; Tazoe & Perez, 2014). Lesions in the motor cortex of the monkey thought to correspond to those muscle groups corresponded to elements of degeneration in their respective ipsilateral tracts (Kuypers & Brinkman, 1970). Functional studies corroborate this also. The failure to generate ipsilateral distal limb activity with a strong concomitant response in the contralateral limb following stimulation of neurons in the motor cortex demonstrates this (Soteropoulos et al., 2011). In addition, transcranial magnetic stimulation of neurons of the right motor cortex in individuals without neurological impairment did not yield discernible responses in distal muscles of the right upper limb (in particular, the deltoid and biceps brachii; responses were unable to be recorded from the flexor carpi radialis, extensor carpi radialis, and first dorsal interosseous muscle; Bawa et al., 2004). However, strong ipsilateral responses were recorded from the proximal muscles (trapezius and pectoral muscles; Bawa et al., 2004). Furthermore, a case study reported that an individual with a pre-existing hemiparesis on the right side (owing to an historical infarct in the left middle cerebral artery) had a worsening of the condition following a subsequent infarct in the right pontine basis; diffusion tensor tractography indicated discontinuation of the right anterior corticospinal tract below the site of the recent infarct (Jang & Kwon, 2013).

This tract is of particular interest as a putative mechanism for rewiring and functional recovery following damage to the complementary, contralateral corticospinal tract. Anterograde tracing in rats with a lesion to the sensorimotor cortex (induced by photothrombotic stroke) revealed sprouting of the anterior corticospinal tract fibers following treatment with an anti-*Nogo-A* antibody (an antibody blocking the inhibitory effects of the transcription factor *Nogo-A* on neurite growth (Freund et al., 2006; Lindau et al., 2014). Further, ipsilateral projections from the contra-lesional sensorimotor cortex were increased three-fold in treated animals, indicating an ability to reorganize the tracts when injury occurs (Lindau et al., 2014). Functionally, this resulted in forelimb recovery and successful grasp of food pellets compared with lesioned rats that received a control antibody (that does not block the function of *Nogo-A*), as well as those that received no treatment at all (Lindau et al., 2014). On the other hand, diffusion tensor imaging in stroke patients revealed that while fiber number increased in the anterior corticospinal tract in the contralesional (i.e., uninjured) side, this did not correspond to improvements in motor function (Jang & Kwon, 2015). Collectively, these results indicate a level of plasticity and capacity for somatotopic reorganization in the corticospinal system (Jang & Kwon, 2015; Netz et al., 1997) and highlight contributions of the anterior portion in facilitating recovery following damage sustained in stroke; however, interventions such as removing inhibitory factors like *Nogo-A* or targeted physical rehabilitation may be essential for functional and clinical improvement.

The *medial vestibulospinal tract* is in the ventral funiculus in a sub-region known as the medial longitudinal fasciculus (MLF), located near the medial surface of the ventral median fissure (Figure 2). In the cat, axons comprising this tract arise bilaterally from the medial and spinal vestibular nuclei, terminating in laminae VII and

VIII in the cervical and upper thoracic spine only (Sengul & Watson, 2015; Wilson et al., 1967). Diffusion tensor imaging in humans indicates an approximately similar pathway, originating from the medial vestibular nuclei, descending through the posteromedial medulla, and down through the ventral funiculus within the cervical region only (Jang et al., 2018). In addition, the organization and location are similar in the mouse (Liang et al., 2011). This tract is driven mainly by input from the semi-circular canals of the inner ear (Boyle, 1993), as well as receiving proprioceptive input from the neck (Gdowski & McCrea, 2000; Pettorossi & Schieppati, 2014) and the vestibulocochlear nerve (cranial nerve VIII; Boyle, 1993). Notably, the medial vestibulospinal tract is involved in mediating the vestibulocollic reflex, which is essential to stabilize cranial position (Wilson et al., 1995). It influences motor neuron activity controlling the movement of the neck (specifically, the sternocleidomastoid muscle (Kim et al., 2010)) as well as its position with respect to the rest of the body (Sengul & Watson, 2015). *The tectospinal tract* also makes up part of the medial longitudinal fasciculus (Figure 2). These axons are derived from neurons in the superior colliculus, and project to the cervical spinal cord (Figure 3; Nudo & Masterton, 1989; Nyberg-Hansen, 1964), and is conserved across a range of species including primates, marsupials, rodents, and cats (Nudo & Masterton, 1989). Its main function is to control head and neck movement, with the vast majority of axons crossing over in the dorsal tegmental decussation and traveling down to the cervical spine (Nyberg-Hansen, 1964). They terminate primarily in laminae V, VII, and VII of the gray matter (Yasui et al., 1998). A small percentage of these fibers, however, do not cross over and travel down ipsilaterally; and an observation was made in both rats (Redgrave et al., 1987) and cats (Olivier et al., 1994). As the superior colliculus itself receives and integrates visual, somatosensory, and auditory information, its influence on head and neck movement is thought to play a key role in orientation, avoidance, defense, and approach behaviors (in response to external stimuli; Dean et al., 1989). In the humans, damage to this tract is thought to contribute to truncal ataxia in a variant of Claude's syndrome (Amano et al., 2018). Finally, interstitiospinal fibers also form part of the MLF (Figure 2). These originate from the interstitial nucleus of Cajal, situated within the brainstem and descend bilaterally, terminating in laminae VII and VIII of the ventral gray matter, primarily in the upper cervical spine (Figure 3; Castiglioni et al., 1978; Satoda et al., 2002), directly innervating motoneurons of the neck (Fukushima et al., 1978). However, in an earlier study, projections were also found as far down as the sacral spine in the cat (Nyberg-Hansen, 1966). The interstitiospinal tract also projects to the vestibular nuclei (Dalezios et al., 1998; Fukushima et al., 1978); taken together, this tract is involved in oculomotor control, head posture, and vertical eye movement. Finally, a small number of reticulospinal fibers also comprise the MLF; however, for simplicity, they will be considered together with the pontine reticulospinal tract.

Complementary to the medial vestibulospinal tract is the *lateral vestibulospinal tract*. It is located separate to the MLF and is positioned laterally near the ventrolateral margin of the spinal cord (Figure 2). Axons comprising this tract arise from the lateral vestibular (Dieter's) nucleus (Frigon, 2020); unlike its medial counterpart, however, this tract remains ipsilateral (Hayes & Rustioni, 1981) and descends to reach the cervical, thoracic, and lumbar levels of the spinal cord (Figure 3; Petterson & Coulter, 1977), eventually terminating in laminae VII–IX (Holstege, 1988). As the lateral vestibular nucleus is driven by the activity of the otoliths of the inner ear (Watson & Harvey, 2009), this tract serves to modulate motoneuron activity related to head stabilization and positioning; specifically, the extensor musculature (Büttner-Ennever & Gerrits, 2004) and in postural reflexes (Xiong & Matsushita, 2001). This tract has also been implicated in locomotion, such as walking, trotting, and galloping (Clarac et al., 1998; Frigon, 2020).

Next, the pontine reticulospinal tract is comprised of axons whose neurons originate in the ipsilateral, rostral gigantocellular reticular nucleus and the pontine caudal reticular nucleus (Jang & Lee, 2019). They descend in the caudal brain stem, and travel down the medial and ventral parts of the ventral funiculus, terminating in laminae VI–IX of the ventral gray matter at all levels of the spinal cord (Figure 3; Nyberg-hansen, 1965). This tract is thought to be involved in the initiation of movement (Buford & Davidson, 2004; Deumens et al., 2005), maintenance of posture, and modulating somatosensory and autonomic activity (Watanabe et al., 2003). Indeed, lesion studies conducted in the rat have demonstrated that preservation of this tract led to higher BBB test performance scores compared with those whose ventral gray and white matter were completely damaged (Schucht et al., 2002). Given that the BBB locomotion test assesses functional recovery of hindlimbs following a spinal cord injury in rodents, with an emphasis on the initiation of stepping, it is thought that sparing this tract thus spares their ability to initiate movement, and in so doing allows for a greater degree of recovery compared with rats where this region is completely lesioned.

The final descending tract found in the ventral funiculus is the olivospinal tract. Little data is available, however, though it is directly reciprocal to the ascending spinoolivary tract in the rat (Ruigrok & Voogd, 2000).

Lateral funiculus

The lateral funiculus is the large area of white matter located in between the dorsolateral sulcus and the ventrolateral sulcus (Figure 2). This is a large area of white matter with numerous ascending and descending tracts. Ascending tracts include the anterior spinothalamic tract posterior spinocerebellar tract (the cuneocerebellar tract being the upper extremity homolog), the tracts of the anterolateral system found in this region (lateral spinothalamic tract, spinomesencephalic tract, spinoreticular tract, and the spinocervical tract). Descending tracts include the lateral corticospinal tract, rubrospinal tract, lateral reticulospinal tract, raphespinal tract, hypothalamospinal tract, solitary tract, fastigiospinal tract, and the lateral vestibulospinal tract (Haines et al., 2018).

2.1.4 | Ascending tracts

In the heart of the lateral funiculus lies the anterior spinothalamic tract; dorsal to the lateral vestibulospinal tract and ventral to the ventral-most border of the ventral gray horn (Figure 2). The fibers of the anterior spinothalamic tract are widely distributed throughout the column (Honey et al., 2019; Kerr, 1975). These are axons of second-order neurons that originate in the contralateral gray matter [primarily lamina II (substantia gelatinosa)]; they receive input from first-order neurons that communicate with the periphery via the dorsal root ganglia. These axons travel up the ventral column and synapse with third-order neurons in the thalamus, facilitating neurotransmission to the somatosensory cortex, conveying primarily touch and light pressure information (Kerr, 1975). The posterior spinocerebellar tract borders the lateral corticospinal tract, and is superficial to the lateral spinothalamic tract (Sengul & Watson, 2015). In the rat and cat, axons comprising this tract are derived from large neurons of the dorsal nucleus of Clarke, as well as those that lie in laminae V, VII, and VIII (Matsushita & Gao, 1997; Matsushita & Hosoya, 1979). It is found at approximately L3–L4, and extends up to the upper thoracic segments (Rivero-Melián & Grant, 1990). Unlike its anterior counterpart (a part of the ventral white matter column), it remains primarily ipsilateral and its axons enter the cerebellum via the inferior cerebellar peduncle (Matsushita & Gao, 1997). In conjunction with the anterior spinocerebellar tract, this tract carries proprioceptive and cutaneous information to the cerebellum, particularly from muscle spindles and Golgi tendon organs from the lower half of the body (Ross et al., 1979). Temporary lateropulsion (an involuntary tendency to tilt sideways) features in patients who have suffered a stroke in this region (Maeda et al., 2005). The rostral spinocerebellar tract is also found in this region and serves as the upper extremity homolog of the anterior spinocerebellar tract (Kayalioglu, 2009b). Neurons of axons comprising this tract originate within the medial part of lamina VI and the central part of lamina VII of the intermediate gray matter (Matsushita & Xiong, 1997). This tract too is primarily ipsilateral, but a few bilateral projections to the cerebellum have been reported (Matsushita & Xiong, 1997). Complementing the activity of the rostral spinocerebellar tract is the cuneocerebellar tract, which is also found within the lateral funiculus and conveys proprioceptive information from the upper extremities, neck, and upper trunk through to the cerebellum via the inferior cerebellar peduncle (Kayalioglu, 2009b), with its origins in lamina I, V, VI, and VII (Nyberg & Blomqvist, 1984). It is only found at spinal levels rostral to and including thoracic level 1 (Figure 3; Chandar & Freeman, 2014).

The anterolateral system is also found within this fasciculus; a major ascending pathway containing the lateral spinothalamic, spinomesencephalic, spinoreticular, spinobulbar, and spinocervical tracts (Haines et al., 2018). The lateral spinothalamic tract is complementary to the anterior spinothalamic tract previously described, transmitting pain and temperature information primarily to the thalamus (Jang & Seo, 2021), although projections to the medullary reticular formation (Kevetter & Willis, 1983), the parabrachial area (Hylden et al., 1989), periaqueductal gray (Harmann et al., 1988), and the nucleus accumbens (Kayalioglu et al., 1996) have also been reported. Third-order neurons then transmit this information to the somatosensory cortex, with the collateral projections of the spinothalamic tract contributing to the modulation of pain and temperature perception.

In the rat, cat, and monkey, axons of the spinomesencephalic tract are derived from neurons that lie in laminae I, IV, V, VI, X, lateral spinal, and lateral cervical nuclei (Yezierski, 1988). These fibers decussate in the spinal cord and ascend in the lateral funiculus with the exception of those derived from lamina I, which ascend bilaterally (Hylden et al., 1986). In addition, a number of axonal origins lie in the ventral gray matter (Kayalioglu et al., 1996). Studies in rats and monkeys indicate this tract projects to a variety of midbrain structures, namely the periaqueductal gray, intercollicular nucleus, superior nucleus, pretectal nuclei (the intercollicular nucleus, superior colliculus, and pretectal nuclei collectively form the spinotectal tract) the nucleus of Darkschewitsch (a small accessory oculomotor nucleus; Bianchi & Gioia, 1990), the Edinger–Westphal nucleus (another accessory oculomotor nucleus; McDougal & Gamlin, 2008), red nucleus, cuneiform nucleus, and the interstitial nucleus of Cajal, observing an approximately

TABLE 1 Summary of supraspinal targets of the spinomesencepahlic tract and their functions

Supraspinal target	Function	References
Periaqueductal gray	Motivational-affective responses to pain (e.g., the desire to terminate/reduce escape from painful stimuli	Sewards and Sewards (2002)
Spinotectal tract: Intercollicular nucleus, superior colliculus, and the pretectal nuclei	Transmitting tactile, thermal, and noxious stimuli for control of spinovisual reflexes	Antonetty and Webster (1975); Padula et al. (2017)
Red nucleus and cuneiform nucleus	Contributes to motor control in response to pain	Vinay and Padel (1990); Yezierski (1988)
Interstitial nucleus of Cajal and nucleus of Darkschweitsch	Oculomotor control	May et al. (2021)

somatotopic organization (Kayalioglu et al., 1999; Kerr, 1975; Mehler et al., 1960; Wiberg et al., 1987). As expected, the numerous projections of this tract mean that it plays a myriad of functions, summarized in Table 1:

The spinoreticular tract is the third component of the ALS situated within the lateral funiculus. It is located in the ventral most portion of the lateral funiculus (Figure 2) and for this reason, it is sometimes referred to as being located in the ventrolateral funiculus (Kayalioglu, 2009b; Sengul & Watson, 2015). Fluorescent neuron tracing in the rat revealed that neurons of axons forming this tract originate in the contralateral laminae VII, VIII, parts of lamina V and X throughout the length of the spinal cord (Figure 3; Garifoli et al., 2006), as well as the lateral spinal nucleus (Menétrey et al., 1983). This tract projects to a host of supraspinal nuclei in the reticular formation of the hindbrain, such as the reticular nuclei (lateral, dorsal, and gigantocellular), pontine reticular nuclei (oval and caudal), paragigantocellular nuclei (dorsal and lateral components), and the median raphe nuclei (Peschanski & Besson, 1984). Additionally, a bilateral projection has been reported in the cervical spine in the monkey and rat (Chaouch et al., 1983; Kevetter et al., 1982). The vast majority of spinoreticular tract neurons require noxious mechanical and radiant stimulation from first-order neurons in the periphery for activation and to a lesser extent, are responsive to light tactile stimuli (Fields et al., 1974; Haber et al., 1982).

The final component of the ALS is known as the spinocervical tract. Located in the dorsal part of the lateral funiculus (Figure 2) neurons of axons that form this tract originate primarily from lamina IV in a region known as the lateral cervical nucleus; an area identified only in the cat, dog, and monkey; its presence in human, however, was inconclusive owing to detection inconsistencies (Mizuno et al., 1967; Truex et al., 1970) and is regarded as vestigial (Nógrádi & Vrbová, 2006). Despite this, it has been implicated in cervicogenic headache in humans (Barmherzig & Kingston, 2019; Gondo et al., 2016; Shimohata et al., 2017); however, definitive histological confirmation remains to be seen. In addition, spinocervical projections have also been found in laminae I–III and V at all levels of the spinal cord in the rat, cat, and monkey (Baker & Giesler Jr., 1984; Brown, 1981; Bryan et al., 1974; Craig Jr, 1978). These axons decussate in the ventral white commissure, observing a somatotopic organization and ascends via the medial lemniscus to reach the contralateral thalamus (Boivie, 1970). Axons of these neurons receive input from the cutaneous receptors of first-order neurons in the periphery, and in particular respond to hair movement, noxious mechanical, and thermal stimulation (Brown et al., 1989; Cervero et al., 1977).

2.1.5 | Descending tracts

The *lateral corticospinal tract* occupies much of the lateral funiculus and is the larger of the two corticospinal tracts (the smaller anterior corticospinal tract has already been detailed as part of the ventral funiculus; Figure 2). Interestingly, there is considerable variation between species with regard to the position of the main corticospinal tract. In humans, non-human primates, and carnivores such as cats, this is located in the lateral funiculus (Petras, 1969). Perhaps unexpectedly, the lateral location also holds true for the pig (Leonard et al., 2017); porcine models may, therefore, serve as a useful translation tool over more conventional animal models like rats or mice (Miranpuri Gurwattan et al., 2018). However, in elephants, edentates (e.g., armadillos, sloths, and anteaters), and hedgehogs this is located in the ventral funiculus (Michaloudi et al., 1988; Verhaart, 1963); in rodents and marsupials, on the other hand, this is found in the dorsal funiculus (Brown, 1971; Watson, 1971). Irrespective of location, their function as the dominant corticospinal tract mediating voluntary motor function remains the same. Axons forming this tract belong to upper motor neurons that originate primarily from the primary motor,

somatosensory, and pre-motor cortex; specifically in cortical layer 5 (Nudo & Masterton, 1990a; Steward et al., 2020). This holds true across a number of mammalian species, including the rat, rabbit, hedgehodg, monkey, and cat (Nudo & Masterton, 1990a). Furthermore, in the rat, small numbers of corticospinal neurons have also been identified in the superior parietal lobule, occipital visual areas, anterior cingulate gyrus, and prefrontal areas (Miller, 1987). Projections from this area are thought to make contributions to the ability to execute fine/complex motor skills (Dum & Strick, 1991). Lateral corticospinal projections have also been identified in the macaque (Dum & Strick, 1991). These axons pass through the corona radiata and enter the posterior limb of the internal capsule. They descend further down the anterior cerebral peduncle (crus cerebri) in the midbrain, constitute the longitudinal fibers of the pons (alongside that of its anterior counterpart), and medullary pyramids before leaving the basilar pons (Nudo & Masterton, 1990a). Unlike the anterior corticospinal tract which remains ipsilateral, the vast majority of the lateral corticospinal tract decussates in the medulla, particularly, in primates, carnivores, lagomorphs (e.g., rabbits), and humans (Nudo & Masterton, 1990a; Yeo & Jang, 2011). In the macaque, the proportion of fibers that decussate is estimated to be around 85%–95% (Yoshino-Saito et al., 2010). Axons of the lateral corticospinal tract run throughout the length of the spinal cord in humans, with terminations found in the gray matter of the cervical, thoracic, lumbar, and sacral regions (Nathan et al., 1990). This holds true for most mammals (Masson Jr. et al., 1991; Nudo & Masterton, 1990b; Steward et al., 2020). These axons primarily serve the extremities and unsurprisingly, over half terminate in the gray matter of the cervical enlargement, and approximately one-quarter in the lumbosacral enlargement; the remainder terminating in the thoracic region (Nathan et al., 1990). Their specific terminations in the gray matter depend on their cortical origin. Anterograde wheatgerm–agglutinin–HRP tracing experiments in the monkey showed that projections from the motor cortex primarily terminated into contralateral lamina IX in the cervical enlargement (C7), entering the gray matter at the border of laminae III and IV (Ralston & Ralston III, 1985). Labeling was absent in the lumbar regions, which may be attributed to the relatively short survival time frame following injection (3–9 days). More recently, longer-term (32–33 days) tracing experiments with biotinylated dextran amine (BDA) injections originating in area 4 of the motor cortex of the monkey (corresponding to the hand/arm region) showed the vast majority of projections terminating in lamina VI, VIII, and IX primarily in the cervical (C5–C8) and upper thoracic region (Morecraft et al., 2013). Further, ipsilateral projections terminated heavily onto lamina VIII; a few were also found in lamina V and VI (Ralston & Ralston III, 1985). In the human and other anthropoid primates, its size and expansion over the course of evolution have been largely attributed to the acquisition of refined motor skills and increased dexterity of the digits (Bortoff & Strick, 1993; Heffner & Masterton, 1975). Another anterograde BDA tracing study demonstrated that lateral corticospinal projections to the lumbar region terminated in laminae V–VIII and critically, the laterodorsal motoneuronal pool of lamina IX (which is responsible for innervating the musculature of the distal extremities; Lacroix et al., 2004). Analogous to the approximate upper limb–cervical and lower limb–lumbar allocation in the monkey and humans, similar tracing experiments have also been conducted in the mouse. Tracing injections into the sensorimotor cortex (primarily controlling the forelimb musculature) showed that terminations were confined to the cervical regions and concentration in laminae IV–VIII, with the exception of the lateral aspect of lamina VII (Steward et al., 2020). Oppositely, injections into the caudal sensorimotor cortex (controlling the hindlimb musculature) showed that axons completely bypassed the cervical region and terminated in the thoracic and lumbosacral regions. In the thoracic regions, these were concentrated in contralateral laminae III–VI, with a few collaterals found in lamina VII; an approximately similar termination pattern was found in the lumbar region (laminae III–V; Steward et al., 2020).

Of particular interest is the ipsilateral lateral corticospinal tract when considering the mechanisms of recovery following a stroke (Otsuka et al., 2013). Photothrombotic destruction of the sensorimotor cortex in rats which abolished forelimb activity (and thus, the ability to grasp food) followed by physical rehabilitation and treatment with the aforementioned anti-*Nogo-A* antibody led to the recovery of function through the ipsilateral pathway (Wahl et al., 2014). In stroke patients, transcranial magnetic stimulation over the unaffected hand motor area (M1) led to the generation of ipsilateral motor-evoked potentials from the thenar (hand) muscles of the affected side; critically, the majority of patients showed near complete functional recovery, suggesting an activation or unmasking of the ipsilateral corticospinal pathway (Caramia et al., 2000). Further, functional imaging studies showed activation of the ipsilateral sensorimotor cortex; ipsilateral parietal region, and bilateral pre-frontal regions in stroke patients tasked with a finger–thumb opposition task (Marshall et al., 2000); again, this implicates the activation of the ipsilateral aspect, but also recruitment of additional cortical areas to regain function over time. Additional, similar studies in patients over the

course of their recovery report recruitment of the ipsilateral, lateral corticospinal tract and reogranisation of the motor cortex in the unlesioned hemisphere (Ahn et al., 2006; Hong et al., 2016; Jang et al., 2019; Peters et al., 2021; Yeo & Jang, 2012). However, others report that these ipsilateral contributions may be overstated and that they may even be maladaptive (Fregni & Pascual-Leone, 2006; Madhavan et al., 2010; Zaaimi et al., 2012). Similar to the proposed framework for treating traumatic spinal cord injury (Griffin & Bradke, 2020), the utility of the ipsilateral and anterior corticospinal tract in rewiring following damage to the main contralateral pathway will likely require both targeted physical rehabilitation and removal of inhibitory factors that may impede appropriate neurite outgrowth and rewiring.

The *rubrospinal tract* is a feature of vertebrates that have limbs or pectoral fins to enable movement (ten Donkelaar, 1988). Arising from the red nucleus in the rostral midbrain, it is found in the dorsal portion of the lateral funiculus, just ventral to the lateral corticospinal tract (Figure 2; Massion, 1967; Murray & Gurule, 1979; Wild et al., 1979). In mammals and birds, axons that comprise this tract cross over in the midbrain tegmentum and descend in a position ventral to the spinal trigeminal tract and lateral to the superior olive and facial nucleus (Watson & Harvey, 2009). In marsupials and rats, however, the tract remains ipsilateral (Küchler et al., 2002; Martin & Dom, 1970; Warner & Watson, 1972). The tract terminates in lamina V and VI of the dorsal gray matter in the cervical and lumbrosacral enlargements (Figure 3; Watson & Harvey, 2009). Axonal terminations have also been reported in lamina VII of the marsupial (Martin & Dom, 1970) and rodent (Brown, 1974). Furthermore, rubrospinal projections have been reported in cats and rats, directly innervating forepaw motoneurons of lamina IX in the ventral gray matter (Küchler et al., 2002; McCurdy et al., 1987). The rubrospinal tract is thought to work in conjunction with the lateral (or main corticospinal tract, in species where this tract is not located in the lateral funiculus) corticospinal tract to help facilitate general locomotion by excitation of flexor motoneurons and inhibition of extensor motoneurons (Haines et al., 2018; Muir & Whishaw, 1999). In addition, it helps to refine skilled motor tasks such as the grasping and handling of food in rats, for example, Whishaw et al. (1998).

The *lateral reticulospinal tract* is in the ventral part of the lateral funiculus, close to the ventral gray matter horn (Figure 2; Nyberg-hansen, 1965). In the cat, axons comprising this tract arise from the medial part of the gigantocellular reticular nucleus of the hindbrain, as do axons that eventually form the medial reticulospinal tract (previously discussed as part of the ventral funiculus; Peterson, 1979). Axons of this tract descend bilaterally next to the medial longitudinal fasciculus of the ventral funiculus before entering and descending down the spinal cord (Peterson et al., 1975). The majority of these fibers remain ipsilateral and only a small number cross over into the contralateral spinal cord (MacKinnon, 2018). This tract is found at all levels of the spinal cord, mainly terminating in, and synapsing with pre-motor interneurons in laminae V, VI, VII, and VIII of the dorsal and ventral gray matter (Figure 3; Nyberg-hansen, 1965; Peterson et al., 1975). In addition, a small number of these directly synapse with alpha and gamma motoneurons of laminae IX in the ventral gray horn (Nyberg-hansen, 1965). The reticulospinal tract is largely concerned with gross movement, which is in contrast to the anterior and lateral corticospinal tracts which are associated with refined and skilled motor control (Baker, 2011). In conjunction with its medial counterpart, the lateral reticulospinal tract is involved in the preparation of movement such as stepping (Schucht et al., 2002), postural control (Prentice & Drew, 2001; Schepens & Drew, 2004; Takakusaki et al., 2016), as well as modulating some somatosensory and autonomic function (Buford & Davidson, 2004; Deumens et al., 2005; Watanabe et al., 2003). Electromyographic studies in humans indicate this tract is involved in the coordination of finger movements in grasping tasks (Honeycutt et al., 2013; Riddle & Baker, 2010); given its activity as a complement to the corticospinal tract, it has been postulated as a site for therapeutic intervention following damage to the latter, such as in the case of stroke (Baker, 2011; Riddle et al., 2009). Further, following a hemisection lesion at the T10 level in rats, neurons of this tract formed new contacts with propriospinal interneurons, which translated into improvements in locomotor recovery (May et al., 2017).

The raphespinal tract is mainly comprised of serotonergic fibers and is found in the ventral portion of the lateral funiculus (Figure 2; Skagerberg & Björklund, 1985). This differs from the mouse, where the bulk of these fibers was located in the ventral funiculus, and a few were located in its lateral counterpart in the cervical spine (Liang et al., 2015). This tract originates from the raphe nuclei (magnus, obscurus, and pallidus) and is situated within the medulla oblongata (Skagerberg & Björklund, 1985). Axons of this tract are primarily serotonergic and descend bilaterally and terminate mainly in the dorsal gray horn (laminae I, II, and V in particular; Skagerberg & Björklund, 1985), although terminations in laminae X (intermediate gray horn), laminae VIII and IX (ventral gray horn) via anterograde biotinylated dextran amines have also been reported in the mouse and rat at the thoracolumbar and sacral segments (Liang et al., 2015; Skagerberg & Björklund, 1985). Tissue clearing and immunohistochemistry performed in the mouse

spinal cord indicates that the vast majority of this tract is serotonergic (Liang et al., 2016). Stimulation of the raphe nuclei releases serotonin into this tract (Hentall et al., 2006), and is thought to play a role in the modulation of spinal nociceptive transmission (Basbaum & Fields, 1979; Dickenson & Goldsmith, 1986; Zhuo & Gebhart, 1997).

The hypothalamospinal tract is a diffuse bundle of fibers that arise primarily from the paraventricular nucleus of the hypothalamus and to a lesser extent, lateral and posterior hypothalamic areas (Basbaum & Fields, 1979; Hancock, 1976; Holstege, 1987). These traverse the periaqueductal gray, dorsal tegmentum of the midbrain and pons before shifting to pass through the anterolateral medulla before descending to at least the upper lumbar region in the lateral fasciculus (Figure 4; Gofrit et al., 2019). Axonal projections terminate primarily in lamina I and X of the ventral gray matter, although terminations from this tract have also been identified in the preganglionic sympathetic and parasympathetic cell columns (Holstege, 1987). Further, in humans, injury to this tract leads to a loss of sympathetic outflow to the ipsilateral face, head, and body and results in a condition known as Horner's syndrome; a collection of symptoms that primarily affects the eye [excessive pupil constriction (miosis), drooping eyelid, and an inability to sweat from the face (facial anhidrosis)] (Kanagalingam & Miller, 2015). Similarly, lesions to this are a consequence of infarction or myelopathy also result in anhidrosis or hypohidrosis dependent on the spinal level where the damage was sustained (Saito, 2010).

The fastigiospinal tract refers to axons whose neurons originate in the fastigial nucleus of the cerebellum (Batton III et al., 1977; Fukushima et al., 1977; Wilson et al., 1978). In the cat, HRP tracing experiments have shown that it crosses over in the cerebellar midline before descending ventral to the spinal trigeminal nucleus in the pons, eventually terminating in the upper cervical spine (C2–C3; Figure 3) in the ventral gray horn (Fukushima et al., 1977; Matsushita & Hosoya, 1978). Projections from the fastigial nucleus are numerous and diverse, connecting with vestibular and reticular nuclei, the oculomotor system, hypothalamus, and limbic circuits (Batton III et al., 1977; Jones et al., 2013); however, little is known about the exact function of this particular tract and its connection with the upper cervical spine. Lesions of the fastigial nucleus are associated with the development of some spinocerebellar ataxias (Zhang et al., 2016); specifically, ataxia of gait and posture (Ilg et al., 2008; Konczak et al., 2005). While other fastigial tracts are undoubtedly affected by such lesions (e.g., such as the projections that connect the fastigial nucleus to the vestibular system), given its connections to the upper cervical spine it is feasible to suggest that input to the ventral gray matter in this region plays a role in the movement of the upper neck and maintenance of head posture.

Finally, the solitariospinal tract is yet another small, diffuse fiber bundle arising from the ipsilateral solitary nucleus of the medulla oblongata (Mtui et al., 1993). It is the shortest route in the entire CNS (Mtui et al., 1993). In the rat, these axons descend in the ventral part of the lateral funiculus (Figure 2) and terminate primarily to mid-cervical and thoracic spinal segments; specifically, the superficial laminae of the dorsal gray horn around the phrenic nucleus (C4–C6; Figure 3), laminae VII and X, and in the ventral gray horn in the thoracic region (Mtui et al., 1993). Ventral projections are contralateral, while dorsal and intermediate gray horn projections are primarily ipsilateral (Mtui et al., 1993). This tract is key to the control of respiratory function (by driving activity of inspiratory and some expiratory motoneurons; Rice et al., 2010), and has been implicated in the control of emesis (Sugino et al., 2021; Zoccal et al., 2014), presumably by modulating diaphragmatic and intercostal muscle activity via the phrenic nucleus during emesis.

The dorsal (posterior) funiculus

The dorsal funiculus is the white matter tract in between the left and right dorsal horns (Figure 2). Unlike the other funiculi that have ascending and descending tracts; the dorsal funiculus ascends in its entirety and is comprised of two parts. The gracile and cuneate fasciculi form the direct dorsal column pathway (Smith & Deacon, 1984), and the second pathway is known as the post-synaptic dorsal column pathway (Rustioni et al., 1979; Rustioni & Kaufman, 1977). Contrary to the conventional location of this tract, a recent MR-tractography of a single cadaveric human spine in its entirety suggests that the cuneate fasciculus has a wider fiber distribution into the lateral funiculus (Atik et al., 2019) and is supported by tracing experiments in the monkey (Liao et al., 2015).

The gracile fasciculus (also known as the tract of Goll, after the Swiss neuroanatomist Friedrich Goll) is found throughout the entire length of the spinal cord and is made of axons of first-order neurons that coalesce and enter the spinal cord white matter via the dorsal root ganglia from the lower trunk and extremities below spinal cord T6 (Figure 3; Niu et al., 2013). Fibers entering the dorsal column white matter above spinal level T6 form the cuneate fasciculus (Burdach's column; named after the German anatomist Karl Friedrich Burdach; Niu et al., 2013). These two tracts are separated from one another by the dorsal intermediate sulcus and dorsal median fissure (Figure 2; Smith & Deacon, 1984). In macaques, this tract ascends ipsilaterally and synapse

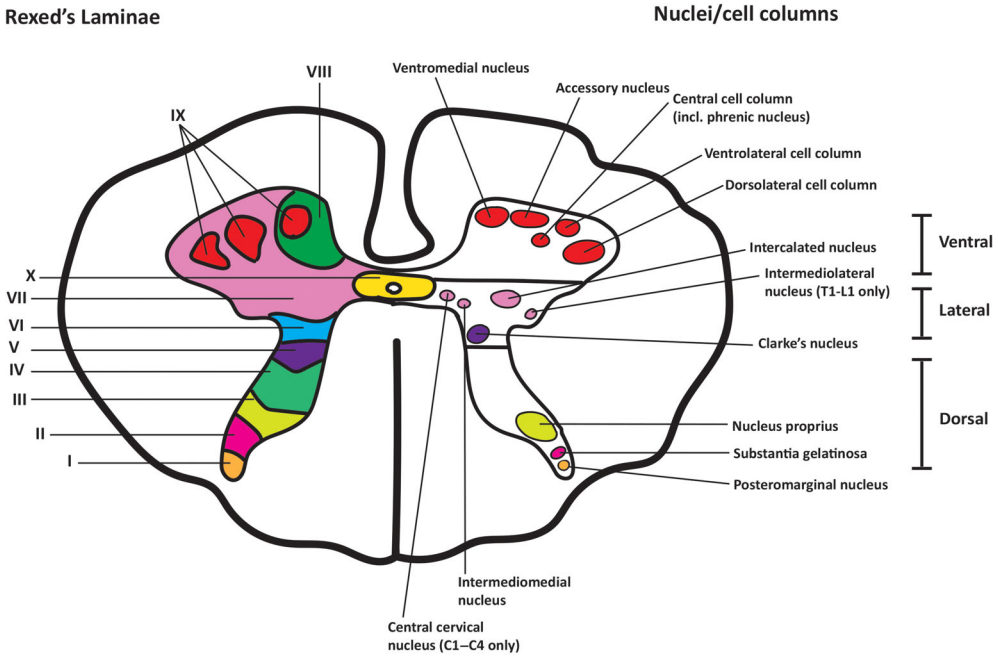

FIGURE 4 Schematic transverse section of the human spinal cord (approximate spinal level = C7) with Rexed's laminae outlined (left) and approximate locations of cell nuclei and cell columns within the gray matter (right). The left-hand side shows the 10 divisions identified by Rexed in 1952. These layers were identified on the basis of distinct cell morphologies revealed by cresyl violet (Nissl) staining. The right-hand side shows the approximate locations of key nuclei and cell columns. In most cases, these corresponded to a single Rexed's lamina, and are colored the same as the lamina they are most associated with. Regional deviations may be seen at the cervical, thoracic, and lumbar regions and are detailed in the description of the lamina they are mostly associated with. Ventral, lateral/intermediate, and dorsal horn regions are shown alongside for reference

with second-order neurons of the gracile and cuneate nuclei (collectively known as the dorsal column nuclei), which are situated in the midline of the dorsal medulla oblongata close to the junction with the spinal cord (Rustioni et al., 1979). These two nuclei give rise to internal arcuate fibers, which decussate and ascend in the contralateral medial lemniscus (Reil's band/ribbon), terminating in the ventro-posterolateral nucleus of the thalamus (Biedenbach, 1972; Hand & Van Winkle, 1977; Rodríguez-Mena et al., 2018). Collectively, this is known as the dorsal column-medial lemniscus pathway which is somatotopically organized and projects via the thalamic ventro-posterolateral nucleus to the primary somatosensory area of the cerebral cortex (Sengul & Watson, 2015). Collectively, axons of these two tracts are primarily myelinated, although a substantially smaller percentage is unmyelinated (~23%–29% in the cat and rat; Chung et al., 1987; Chung & Coggeshall, 1985). The unmyelinated population is thought to directly mediate transmission from nociceptors; injection of capsaicin in rats showed a decrease in the number of unmyelinated fibers in both gracile and cuneate fasciculi (Patterson et al., 1992). These fasciculi are responsible for transmitting information regarding discriminatory touch (Kitai & Weinberg, 1968), deep pressure (Loutit & Potas, 2020), proprioception (Granier et al., 2020), and vibration (Shintani et al., 2000). Indeed, lesions to the dorsal column have led to deficits in some or all of the above functions. For example, an incision to the dorsal column at the C1 region in rats produced deficits with object handling in rats, though they quickly learned to compensate with alternate limb or body movements (McKenna & Whishaw, 1999) and may be attributed to corticospinal and somatosensory sprouting (Fisher et al., 2018; McCann et al., 2020). In addition, myelopathy in these two fasciculi owing to a rare complication of intrathecal chemotherapy has been shown to produce lower limb numbness and a pronounced lack of proprioception in the same region (Joseph & Reyes, 2014).

Primary afferents from neurons entering the spinal cord from the periphery synapse with dorsal horn neurons [primarily III–VII and X (de Pommery et al., 1984; Rustioni et al., 1979; Wang et al., 1999)], and these axons form what is known as the post-synaptic dorsal column pathway (Rustioni et al., 1979). These fibers ascend ipsilaterally to the gracile and cuneate nuclei; in the rat, these constitute approximately a third of the input to

each (Giesler et al., 1984). Again, somatotopic organization of axonal fibers is observed in the indirect pathway and these also constitute the medial lemniscus, terminating in the contralateral, ventroposterolateral, and posterior thalamic nuclei (Giesler et al., 1984).

Further, these axons exhibit a pattern of termination dependent on the level of the spinal cord concerned. The post-synaptic dorsal column projections from the cervical enlargement terminate in the cuneate nucleus; those from the thoracic spine project to the medial cuneate and lateral gracile nuclei, those from the lumbar enlargement project to the gracile nucleus and finally, those from the sacral spine projects to the medial gracile nucleus (Cliffer & Giesler Jr., 1989). This pathway is primarily concerned with the transmission of innocuous mechanical (Giesler & Cliffer, 1985) as well as noxious peripheral stimuli (Bennett et al., 1984). A further role for this pathway has been implicated in determining the sensory-discriminate (the "intensity" or strength of the pain being felt) as well as the motivational-affective (avoidance or escaping) response to pain (Millan, 1999). It is also recognized as a major pathway for visceral nociception (Willis et al., 1999); minor surgical lesions of the gracile fasciculus are clinically utilized to relieve pain in the thoracic and pelvic regions (Nauta et al., 1997; Nauta et al., 2000).

3 | PROPRIOSPINAL PATHWAYS

In contrast to the ascending and descending pathways to and from supraspinal locations, propriospinal pathways refer to those that are intrinsic to the spinal cord; originating and largely terminating within the confines of the cord itself (Chung & Coggeshall, 1983); however, supraspinal targets also exist (Alstermark et al., 1984a). These pathways play an essential, integrative role in a host of functions, namely locomotion (Jordan & Schmidt, 2002), respiration (and its coordination with locomotion; Giraudin et al., 2012), limb coordination during movement (Juvin et al., 2005), and autonomic function (Darlot et al., 2012; Michael et al., 2019). Propriospinal neurons can be classed into two main groups. Short-axon propriospinal neurons project over short distances (up to six spinal segments), whose cell bodies lie in most laminae (with the exception of IX), terminating in lamina IX. The second group is long-axon propriospinal neurons, whose cell bodies originate mostly in lamina VII and VIII and axons extend over larger distances (>5–6 spinal segments), terminating in laminae V–VIII (Jacobi & Bareyre, 2015). These two groups are further subclassed according to function and the part of the body they exert influence over will be discussed as separate sub-sections.

3.1 | Short-axon propriospinal neurons

3.1.1 | Cervical propriospinal neurons

This group of neurons is often referred to as the C3–C4 pre-motoneuronal system and has been characterized in the cat (Alstermark et al., 2007; Illert et al., 1977). Receiving convergent input from the cortico-, rubro-, reticulo-, and tectospinal tract, the axons of these neurons originate in the C3–C4 level and primarily project to all motor neuron pools (lamina IX of the gray matter) across the C6–T1 spinal segments (which control forelimb muscles) and as such these motor neurons do not directly receive corticomotoneuronal input (Alstermark et al., 1987; Alstermark et al., 2007). Collectively, the descending tracts provide a combination of both excitatory and inhibitory input to these propriospinal neurons, thereby inhibiting or exciting motor neurons across the aforementioned spinal segments responsible for the control of forelimb musculature (Alstermark et al., 1984b). In the cat, this network has been implicated in visually guided forelimb movements (target reaching) such as reaching a piece of food (Alstermark et al., 1981). Noninvasive methods demonstrate a similar system in humans (Pauvert et al., 1998; Stinear & Byblow, 2004), and lesions to these neurons as a result of demyelination, compression, infarction, or syringomyelia are thought to be a contributing factor to the development of pseudoathetosis (a loss of proprioception) and dystonia of the hand (de Pasqua et al., 2016). Further, this particular propriospinal pathway is thought to act as an alternate pathway to facilitate forelimb activity when the corticospinal tract has been affected by stroke (Stinear & Byblow, 2004). In addition, viral-mediated blockade of this pathway in monkeys afflicted with a lesion to the corticospinal tract showed that the capacity to grip was impaired; restoration of grip and dexterity was restored when the block was removed (Tohyama et al., 2017).

3.1.2 | Lumbosacral propriospinal neurons

An equivalent of the C3–C4 premotoneuronal network also exists in the lumbosacral region of the spine. Originating in the L5–S1 segments, the cell bodies of these neurons are found in the intermediate gray matter; those that project to motor neurons innervating axial musculature is found primarily in the medial aspect of lamina VII

and VIII, and those that project to motor neurons of the lower limbs/distal hindlimbs originate in lamina V–VII (Rustioni et al., 1971). The reticulospinal and vestibulospinal tracts provide input to the propriospinal neurons that terminate in lamina VII and VIII; similarly, the rubrospinal and corticospinal tracts contribute to and modulate the activity of propriospinal neurons terminating in V–VII (Rustioni et al., 1971). This particular group of propriospinal neurons has been implicated in the function of the central pattern generator (CPG) for locomotion both in quadrupeds (rats; Zaporozhets et al., 2006) and bipeds (humans; Nadeau et al., 2010). Much of the evidence for a locomotor CPG in human is derived from those afflicted with a partial lesion to the spinal cord. Electrical stimulation over the L2 segment was sufficient to elicit step-like electromyogram activity in paraplegic individuals in the supine position (Dimitrijevic et al., 1998). In a similar vein, SCI patients with a complete motor injury and with stimulator devices implanted (for the control of pain and spasticity) receiving electrical stimulation in measured increments demonstrated rhythmic patterns of activity in the quadriceps, hamstrings, tibialis anterior, and triceps surae (the four muscles facilitating leg movement; Danner et al., 2015). Given the stimulators are typically placed around the T11–L1 level, this suggests the activity is derived from the lumbosacral propriospinal network since the main corticospinal pathway is completely lesioned (Danner et al., 2015).

3.1.3 | Short thoracic propriospinal neurons

The cell bodies of short thoracic propriospinal neurons are located in the mid-thoracic cord, extending for up to five spinal segments before synapsing with interneurons in laminae III–VIII and X (Giovanelli Barilari & Kuypers, 1969). Axons of these neurons have also been found caudally in the lumbosacral regions, terminating within lamina IX (Conta & Stelzner, 2004). Lesion studies in the cat indicate these neurons play a role in axial musculature control and maintenance of posture (Anderson, 1963; Vasilenko, 1975). Further, stimulation of this population also elicited stepping movements in rats with damage to the lumbar spinal cord (Cowley et al., 2015), which may indicate their involvement in CPG activity and reinforcing the notion that the propriospinal networks may serve as an alternate pathway following damage to the main tracts facilitating movement.

3.1.4 | Thoracic respiratory interneurons

The final class of short-axon propriospinal neurons is confined primarily to the thoracic spine, with axons innervating motor neuron pools of the abdominal and intercostal muscles (Merrill & Lipski, 1987). These neurons are thought to modulate descending respiratory drive from the medulla oblongata to these muscles (Merrill & Lipski, 1987). Further, studies in the rat have demonstrated that the activity of this population can be altered in response to a host of stimuli, such as esophageal distension, increased heart rate, and pressure, implicating a role of spinal interneurons in modulating viscero-respiratory reflexes (Qin et al., 2002). Further, and in line with the purported CPG activity of the propriospinal neurons, this particular population works in conjunction with the works in conjunction with the lumbosacral cohort to facilitate locomotor respiratory coupling; the coupling of locomotion with breathing (Sutor et al., 2022).

3.2 | Long-axon propriospinal neurons

3.2.1 | Long descending propriospinal neurons

Cell bodies of this population are found in laminae IV, V, VII, VIII, and the dorsal portion of lamina X in the cervical enlargement (spinal segments C4–C6). As aforementioned, these axons project caudally over long distances, and terminate in the lumbosacral equivalent of their origins (Conta & Stelzner, 2009). In doing so, the short-axon propriospinal networks of cervical and lumbosacral regions are connected (Jordan & Schmidt, 2002). Specifically, in mice, the ablation of these long-descending neurons with diphtheria toxin injections resulted in the impairment of exploratory locomotion, and when put on a treadmill, mice were unable to properly coordinate forelimb and hindlimb movement at higher speeds, suggesting this pathway is essential for the coordination of locomotion as well as the maintenance of posture and gait (Ruder et al., 2016). Interestingly, these neurons exhibit an element of plasticity and regenerative capacity. Following an incomplete spinal cord injury in rats, long propriospinal axons arborize on to lumbar motor neurons, indicating an endogenous mechanism for remodeling and relaying cortical input to its intended spinal targets (Bareyre et al., 2004).

3.2.2 | Long ascending propriospinal neurons

This population is reciprocal to the long descending population. Tracing experiments in rats demonstrated that cell bodies of this population originate in lumbar regions

of the cord, primarily in laminae VII and VIII and terminates in the C7–C8 region, within the ventrolateral aspect of lamina IX (Brockett et al., 2013). This pathway is thought to complement activity of the long descending propriospinal neurons, helping to synchronize the lumbar and cervical CPGs, and thus, coordination of fore- and hindlimb activity (Brockett et al., 2013). Indeed, viral transduction with tetanus to silence this population in the uninjured rat has resulted in the disruption of coordination of fore- and hindlimb as well as left–right movement, though the integrity of individual limb movement remained intact (Pocratsky et al., 2020; Shepard et al., 2021). However, following a lesion to the spinal cord, silencing the same population led to an improvement in left–right coordination and gait, though fore- and hindlimb coordination showed no such improvement (Shepard et al., 2021). Critically, the intrinsic pattern generator activity of the cervical and lumbosacral regions are independent of one another and neither can impose their activity upon the other; they rely on each other in a reciprocal fashion to facilitate limb coordination (Juvin et al., 2005).

3.2.3 | Upper cervical propriospinal neurons

The final population of propriospinal neurons in this class is known as upper cervical inspiratory neurons. In the rat, these are located in spinal segments C1–C2, modulating brain stem input to motor neuron pools corresponding to thoracic (T3–T4) and upper lumbar regions, where the abdominal and intercostal muscles are located (Douse et al., 1992; Lipski et al., 1993). These neurons are also thought to project to phrenic motor neurons and influence the activity of the diaphragm (C3–C5) as they course down to their canonical destination (Hoskin et al., 1988). This population plays a key role in modulating respiratory drive; however, rather than directly synapsing to motor neuron pools of abdominal and intercostal muscles, this population is thought to act on the thoracic respiratory propriospinal network (Conta & Stelzner, 2009). Slice culture spinal cord (C1–C2) preparations from mice generated respiratory burst activity which was synchronous with hypoglossal nerve activity (Kobayashi et al., 2010). Further, lesion studies indicate these neurons are sufficient to sustain breathing following a spinal cord injury. Collaterals from this population innervating the phrenic nerve facilitate phrenic motor neuron bursting and thus, restoration of diaphragm function following transection at the C1 level (Cregg et al., 2017). However, this also required the blockade of any inhibitory influence and required persistent glutamatergic excitation (Cregg et al., 2017). A subsequent study demonstrated that these neurons were not only essential for the maintenance of, but also necessary to promote recovery of breathing following a cervical-level injury (Satkunendrarajah et al., 2018). Further, in the absence of an injury, this population serves to enhance inspiratory amplitude (Satkunendrarajah et al., 2018). Collectively, this population of neurons represents an alternate mechanism to restore or recover respiratory activity following damage to the cord where phrenic innervation to the diaphragm is compromised.

4 | FUNCTIONAL DIVISIONS OF SPINAL CORD GRAY MATTER

Across all levels, the spinal cord gray matter can be divided into three functional zones (Figure 4) the dorsal (posterior), intermediate (lateral), and ventral (anterior) horns. Each of these horns differs from each other by function, and the laminae are categorized into each horn as follows:

- Dorsal horn: Laminae I–VI
- Intermediate: Laminae VII and X
- Ventral: Laminae VIII and IX

4.1 | Rexed's classification

Each of the functional zones can be further subdivided into laminae, based on the differences in cellular morphology and cytoarchitecture. This classification is based on the seminal work by Bror Rexed; arguably the most detailed and comprehensive description of the cell types present in the spinal cord to date. While Rexed's analysis was performed using post-mortem feline tissue, similar patterns of the organization have been observed in dog (Buxton & Goodman, 1967), monkey (Kuypers & Brinkman, 1970; Ralston & Ralston III, 1985), rat (Brichta et al., 2013), echidna (Ashwell & Zhang, 1997), and in the mouse (Watson, Paxinos, Sengul, & Heise, 2009). Bar a few differences related to species-specific function, it appears this organization is largely conserved across mammals. The methodology employed was relatively simple by modern standards; a modified toluidine blue protocol for use with thick sections (100 μm; Rexed, 1952a). A basic thiazine dye with an affinity for tissues rich in nucleic acid (Sridharan & Shankar, 2012), Rexed reported that staining was almost exclusive to neurons, with glia only visible as faint outlines (Rexed, 1952a). From this, Rexed deduced 10 different laminae: layers I–IV encompassing the dorsal horn, layers V and VI covering the intermediate zone/horn,

layers VIII–X covering the ventral horn, and layer VII being spread out over both the intermediate and ventral horns (Figure 4). More recently, single-cell RNA sequencing of sensory neurons in the dorsal horn indicates the presence of 15 inhibitory and excitatory neuronal subtypes that could be further categorized based on their sensitivity to thermal stimuli (Häring et al., 2018), suggesting a more complex organization based on functional domains rather than just morphology alone. Indeed, grouping according to functional domains may prove useful in instances where the morphology of adjacent laminae are virtually identical to one another (see Section 3.1.1.5: *Lamina V and VI)*; however, for simplicity, this review will adhere to the morphological classification into laminae as described by Rexed. Each layer will be described in detail from available anatomical studies, including cell types, neurochemical phenotypes, notable nuclei found in laminae, and their function.

4.1.1 | Dorsal horn

When viewed in the transverse plane, the dorsal (anterior) horn refers to the forewings or the "wing-tips" of the butterfly-shape that the gray matter adopts, and is responsible for receiving (from the periphery), modulating, and transmitting somatosensory information to higher order processing centers in the cerebral cortex (Harding et al., 2020), ultimately determining the body's response to painful stimuli and changes in touch, pressure, and temperature. Lesion studies in this region often result in the development of pain disorders (hyperalgesia, hypoalgesia, or allodynia) or deficits in touch, dexterity, and spatial awareness (Fisher et al., 2020; Harding et al., 2020; Lee et al., 2009), supporting its role in somatosensory perception and proprioception.

Lamina I

Lamina I is found in the dorsal horn and refers to the thin, dorsal-most layer (Figure 4); its lateral border tapering down the lateral aspect of the gray matter and ending rather suddenly down the medial aspect (Rexed, 1952a; Rexed, 1954). It is also referred to as the marginal zone, posteromarginal nucleus (Figure 4), or the *posterior marginalis* (Lima & Coimbra, 1986; Schoenen & Faull, 2004). It has a reticular appearance owing to the myriad of myelinated fibers amidst the few neurons present. In the cat, four distinct morphologies can be identified: *fusiform*, *multipolar*, *pyramidal*, and *flattened* neurons (Galhardo & Lima, 1999; Zhang et al., 1996). These morphologies have also been reported in lamina I of the rat (Lima & Coimbra, 1986), although this differs in human, where only fusiform and multipolar cells were present (Schoenen & Faull, 2004). Across these species, the dendritic organization of these neurons was described as tangential (Galhardo & Lima, 1999; Scheibel & Scheibel, 1968; Schoenen & Faull, 2004). A prominent and unique finding in fetal and adult human spinal cord is the presence of dendrites perpendicular to the edge of the dorsal horn (Schoenen & Faull, 2004). However, perpendicular dendrites were reported by Cajal in the developing cord of chicks and the medulla of newborn rabbits, suggesting that at least in non-human species, that these are immature structures that gradually disappear during development (Gobel, 1978). However, their continued persistence in the adult human spinal cord remains unknown. *Fusiform neurons* are distinguished by their ovoid, spindle-shaped soma and have a single primary dendrite extending from the apex and base of the soma (Galhardo & Lima, 1999; Lima & Coimbra, 1986). In lamina I, they are the most numerous of the four types present and located in the lateral-most third of the lamina (Galhardo & Lima, 1999; Lima & Coimbra, 1986). Their dendrites branch extensively within this lamina and are confined to the boundary of lamina I (Light et al., 1979); with the exception of the rat, where these reach out into the periphery of lamina II below (Lima & Coimbra, 1986; Todd et al., 2002). Fusiform neurons are further subdivided into two groups; the majority being Type A, whose dendrites are longitudinally oriented (Galhardo & Lima, 1999), and the remainder being Type B, whose caudal dendrite have been occasionally observed as far down into lamina III (Galhardo & Lima, 1999; Lima & Coimbra, 1986; Todd, 2017). This has also been observed in human and is thought to extend as far as lamina IV (Schoenen & Faull, 2004). Fusiform neurons exhibit immunoreactivity for GABA and dynorphin (Lima et al., 1993) and are thought to be inhibitory (Sardella et al., 2011). Recordings from these neurons in lamina I of the cat indicate they mediate nociception, displaying responses to pinch or heat only (Han et al., 1998). Furthermore, they exhibit a tonic pattern of firing that slowly and continuously fire, conveying information about the duration of the painful stimuli (Prescott & Koninck, 2002). *Multipolar neurons* are also found in the medial portion of this layer, which is characterized by their ovoid soma with several primary dendrites arising from it (Galhardo & Lima, 1999; Lima & Coimbra, 1986; Zhang et al., 1996). These neurons too can be subdivided into two classes; Type A multipolar neurons have dendritic spines extending primarily into the rostro-caudal plane and are densely arborized (Galhardo & Lima, 1999). Type B multipolar neurons in contrast are characterized by larger soma, dendritic arborizations that lack spines and are looser and fewer in comparison (Galhardo & Lima, 1999; Lima & Coimbra, 1986). These neurons are

GABA-ergic and in the mouse, exhibit a single spike firing pattern (Dougherty et al., 2005). Multipolar neurons are thought to be polymodal nociceptive, displaying sensitivity to heat, pinching, and cold in the cat (Han et al., 1998). The sensitivity of these neurons to each of these modalities differs, and variability in sensitivity exists between individual neurons as well (Craig et al., 2001; Han et al., 1998). *Pyramidal neurons* are also found in this layer, characterized by a distinct triangular shape (Galhardo & Lima, 1999; Lima & Coimbra, 1986). They are found primarily along the dorsal border of lamina I (Galhardo & Lima, 1999; Lima & Coimbra, 1986), and in the monkey (Dostrovsky & Craig, 1996) and cat (Han et al., 1998) are responsive to cold stimuli (Chisholm et al., 2021). For this reason, they are also known as COLD or COOL neurons (Craig et al., 2001; Dostrovsky & Craig, 1996; Han et al., 1998). Pyramidal neurons in this lamina are enkephalinergic (Lima et al., 1993); a small neuropeptide involved in nociception that is part of the opioid family and is involved in nociception (Takahashi, 2016). These neurons have a phasic pattern of firing, which fire at high frequency in response to a strong stimulus (Prescott & Koninck, 2002); in the monkey, the rate of firing increased with decreasing temperature, plateauing at about 12.5°C (Dostrovsky & Craig, 1996). *Flattened neurons* are the fourth morphological subclass of neurons found in lamina I. They are discoid and have small, sparsely ramified dendritic trees (Galhardo & Lima, 1999; Lima & Coimbra, 1986). They only comprise a small percentage of total neurons in this lamina [13% in the rat (Lima & Coimbra, 1986), and 16% in the cat (Galhardo & Lima, 1999)], and were not identified in the monkey (Zhang et al., 1996). Their firing pattern is thought to be the same as that of multipolar neurons, though the distinction between the two has not yet been made (Dougherty et al., 2005), presumably due to the scarcity of this morphological subtype compared with those aforementioned. Flattened neurons in the rat and cat are immunoreactive for substance P (Lima et al., 1993; Takahashi & Otsuka, 1975) but are completely absent in the non-human primate (Torres-da-Silva et al., 2016); a neuropeptide implicated in nociception (Simmons & Substance, 2010), the maintenance of hyperalgesia (Mantyh et al., 1997) and in particular, pain associated with inflammation (Doyle & Hunt, 1999; Simmons & Substance, 2010).

Lamina II

Immediately ventral to lamina I is lamina II, also known as the *substantia gelatinosa of Rolando* (Figure 4). It is one of the earliest regions identified in the spinal cord (Rexed, 1954). First identified by Luigi Rolando (Caputi et al., 1995), it was initially described as "jelly-like" (hence the term "gelatinous substance"), owing to its high neuronal and neuropil density, as well as a distinct paucity of myelinated fibers (Merighi, 2018; Rexed, 1954; Schoenen & Faull, 2004). In the transverse view, it largely follows the shape of the preceding lamina such that lamina I form its dorsal and lateral borders and medially, is bordered by the dorsal funiculus (white matter; Rexed, 1954). In addition, its thickness is not uniform throughout and differs amongst species; in the human, it is at its thickest in the lateral aspect (Schoenen & Faull, 2004), yet in rodents, the thickest enlargement occurs medially (Molander et al., 1984). This lamina can be further divided into two sub-laminae (Woodbury et al., 2000); a dorsal outer zone comprised of small, densely packed cells that occupy about 25% of the lamina, and a ventral inner zone comprising the remainder of the layer (Molander et al., 1984; Molander et al., 1989; Rexed, 1952b; Rexed, 1954). However, this subdivision has only been reported in the spinal cord of the cat (Rexed, 1952b; Rexed, 1954), rat (Pan & Pan, 2004), mouse (Woodbury et al., 2000), and monkey (Light & Perl, 1979); in the human, the neuronal population appears entirely homogenous (Schoenen & Faull, 2004).

In contrast to lamina I, the substantia gelatinosa is comprised of neurons whose morphologies follow a continuum as opposed to being categorized into specific subtypes (Todd & McKenzie, 1989) and many believe that a consensus to reach a unified classification may never be reached (Merighi, 2018). This is further compounded by substantial differences between species. Though Cajal attempted to classify lamina II neurons in 1909 as either central or limiting cells, these observations were made in new-born dogs and cats only; comparison between neonatal and adult mice, as well as adult rats and cats, indicate that the organization of the substantia gelatinosa is subject to further changes with advancing age (Woodbury et al., 2000). Stephen Gobel subsequently proposed a classification based on their dendritic and axonal branching, as well as the presence and distribution of dendritic spines (Merighi, 2018); this will form the basis of the morphological classification within this layer and will be discussed in this review. *Stalked* cells are the most numerous in the outer layer of this lamina (Schoenen, 1982a), characterized by a round or oval-shaped cell body with dendrites that project ventrally and obliquely such that the dendrites resemble a cone formation (Schoenen, 1982a). Furthermore, dendrites are particularly "spiny" and can pass deep into more ventral layers (Todd & Lewis, 1986; Todd & McKenzie, 1989). Stalked cells are glutamatergic (Todd et al., 1992) and immunopositive for somatostatin (Mather & Ho, 1992). In contrast, *islet* cells are entirely intralaminar and are named so owing to their presence occurring in discrete,

small islands. In human, this comprises about 30% of the total neuronal component (Schoenen, 1982a). This population is characterized by a rich network of branching axons. Islet cells are generally regarded as being mostly GABA-ergic (Heinke et al., 2004; Todd & McKenzie, 1989; Todd & Sullivan, 1990). Large islet cells assume GABA-ergic identity (Heinke et al., 2004; Todd & McKenzie, 1989) and colocalize with glycine and neuropeptide Y (Rowan et al., 1993; Todd et al., 1992). Oppositely, small islet cells tend to be glutamatergic and colocalize with neurotensin (Seybold & Elde, 1982) and somatostatin (Mather & Ho, 1992). The balance of glutamatergic and GABA-ergic activity in lamina II is of particular significance as it is a key player in the modulation of pain; specifically, the "gating" of noxious stimuli that are transmitted to higher order processing centers (Fields et al., 1995; Melzack & Wall, 1965). Specifically, the Gate Control Theory postulates that non-noxious stimuli/input carried by inhibitory GABA-ergic neurons within this lamina are necessary to "gate" noxious pain input, which is mediated by the glutamatergic population (Melzack & Wall, 1965). Damage to this area where GABA-ergic inhibition (presumably from the large islet cells) is insufficient to gate the glutamatergic activity of the stalked cells has been implicated in the development of neuropathic pain disorders such as allodynia (innocuous stimuli causing pain) or hyperalgesia (painful stimuli causing an extreme or heightened pain response (Price & Prescott, 2015). While stalked and islet cells have been documented in the rat (Todd & Lewis, 1986) and cat (Gobel, 1978), a different classification has been proposed in the human (Schoenen, 1982a). Sections stained using the Golgi impregnation method in humans have instead revealed three additional subtypes in addition to islet cells (Schoenen, 1982a). *Filamentous* cells comprise about 20% of the neurons in this layer, with soma found in both inner and outer portions of the lamina (Schoenen, 1982a). Their axons primarily project into either lamina I or Lissauer's tract in the white matter (Schoenen, 1982a). These cells have earnt the term "filamentous" owing to their dendrites being particularly spinous and extensive branching (Schoenen, 1982a). *Curly* cells make up ~10% of neurons in this layer and are found primarily in the outer portion of lamina II (Merighi, 2018; Schoenen, 1982a). They are characterized by a complex, tortuous dendritic tree rich in spines (Schoenen, 1982a), and are thought to resemble stalked cells in other species (Schoenen, 1982a). Finally, *stellate* cells make up the remainder (40%) and are multipolar neurons found in the inner zone of the lamina (Schoenen, 1982a). Their dendrites are straight with few spines, and encompass an area of about 500 μm, projecting in all directions and well into adjacent laminae I and III (Schoenen, 1982a).

Unlike in lamina I, and with the exception of stalked and islet cells where the morphological subtypes correspond to distinct neurochemical identities, further distinctions in lamina II are less clear. This is in part hampered by the substantial interspecies differences, and the methods employed to deduce these morphologies have since undergone substantial improvement over the decades; it is plausible that much of the contention and ambiguity between and within species may never be resolved. Therefore, much of what is known about the neurochemistry and chemoarchitecture of this lamina can be deduced by its role in nociception. Neuropeptides such as dynorphin, enkephalin, substance P, and neoendorphin have been localized to lamina II in the human (Przewłocki et al., 1983); further, the highest density of opiate receptors was localized to this region also (Faull & Villiger, 1987). Spinal administration of opiates has been demonstrated to induce profound analgesic effects (Yaksh, 1981); the effects of which are mediated via these receptors and reinforce the role of this lamina in nociception. In addition, autoradiographic studies in the human have revealed that benzodiazepine receptors are also at their highest density within this layer across the cervical, thoracic, lumbar, and sacral regions (Faull & Villiger, 1986), and GABA receptor expression matches this distribution also (Waldvogel et al., 1990). The presence of M_1 and M_2 muscarinic receptors in lamina II in the human has been reported (Villiger & Faull, 1985); in the mouse, knockdown with siRNA implicates the M_2 and M_4 subtype in the modulation of pain (specifically, reduced tolerance to a painful stimulus; Cai et al., 2009).

Lamina III

Immediately ventral to lamina II lies lamina III, which runs straight across the dorsal horn and parallel to lamina I (Figure 4). Its superior border bends along the apex of the dorsal horn in a similar fashion to lamina I and II, though not as sharply (Molander et al., 1984; Molander et al., 1989; Rexed, 1954). Historically, the distinction between lamina III from lamina II and IV has been difficult to make; indeed, initial studies in the cat classed lamina II and III as one (Scheibel & Scheibel, 1968; Szentágothai, 1964). In the cat and humans the neurons in lamina III are larger and less dense than in lamina II and equally, they are smaller and more dense compared with lamina IV (Schoenen & Faull, 2004). This does not hold true for the rat, where neuronal density and size are like lamina II, making demarcation less clear (Molander et al., 1984; Molander et al., 1989). However, these boundaries become more distinct when techniques used to distinguish neurochemical phenotypes and myeloarchitecture are employed. Tritiated diprenorphine which binds to, and detects opioid receptors via autoradiograms

revealed that while lamina II had overwhelmingly higher levels of bound ^{3}H-diprenorphine, lamina III had approximately 1/3 of the amount bound; and in lamina IV this dropped even further, to about a tenth of the amount found in lamina III (Faull & Villiger, 1987). The same can be said for the distribution of benzodiazepine receptors, probed for in the human spinal cord using tritiated flunitrazepam (Faull & Villiger, 1986). Further, sections stained for osmium tetroxide to highlight regions of myelination indicate that while lamina II is virtually devoid of myelin save for a few scant fibers, lamina III is densely myelinated and lamina IV is characterized by the presence of several prominent bundles (Faull & Villiger, 1987). In lamina III, neurons adopt a rounded, slightly elongated morphology (Rexed, 1954), and diameters range from 5-18 μm (Rexed, 1952a). Two neuronal populations can be distinguished based on their dendritic architecture. The first group is characterized by dendrites organized in the dorsoventral axis with the dorsal extension being the largest (Schoenen & Faull, 2004), and extended into lamina II (Maxwell et al., 1983; Schoenen, 1982a). The second group is those with dendrites that extend in the rostrocaudal axis and are largely confined within the lamina (Heise & Kayalioglu, 2009; Maxwell, 1985). These are GABA-ergic, making up nearly half of the neuronal population in this layer (Heise & Kayalioglu, 2009; Powell & Todd, 1992). In the rat and mouse, the GABA-ergic population can be further subdivided into those that colocalize with acetylcholine and glycine, respectively (Miranda et al., 2021; Todd, 1991). Lamina III receives input from the periphery via large unmyelinated Aβ-fibers, which primarily convey touch information (Field et al., 1999), and projects the sensory information to the spinocervical tract (involved in conveying tactile and pressure information (Brown, 1981; Whitehorn et al., 1969), or the post-synaptic dorsal column pathway (conveying cutaneous and visceral nociceptive information (Ekerot et al., 1991; Willis et al., 1999). Importantly, lamina III is partially home to the nucleus proprius (Figure 1b), which is also partly found in lamina IV and V (Lai et al., 2016). It is the first instance in this review where Rexed's classification based on morphology alone does not align neatly with nuclei previously found. The nucleus proprius (and by default and in part, lamina III) is implicated in the perception of light touch (Bennett et al., 1984; Bourane et al., 2015; Semba et al., 1984), proprioception (Heise & Kayalioglu, 2009; Logan et al., 2013), nociception (Gassner et al., 2013; Koch et al., 2018), and thermoception (through dendritic projections to lamina I and II; Sengul & Watson, 2012a). As such, lamina III can be viewed as an integration hub receiving a diverse range of inputs from the periphery and adjacent layers to modulate somatosensation. However, much of what is known about the function of lamina III neurons has been centered on nociception through various animal models of neuropathic pain where nerve injury alters the input to this lamina and thus, the excitability of GABA-ergic neurons within. Consequently, GABA-ergic activity is insufficient to "gate" the activity of glutamatergic interneurons (Gassner et al., 2013; Schoffnegger et al., 2008) like that described for lamina II, thus contributing to the pathogenesis of aberrant pain perception.

Lamina IV

The thickest of all the layers discussed so far, lamina IV does not curve laterally like the previous three (Rexed, 1952a, 1954; Figure 4). It can be distinguished from the other three layers by a low cell density and the presence of larger cells in comparison (Molander et al., 1984; Schoenen & Faull, 2004). It is described as a largely heterogenous cell layer of varying sizes interspersed among each other with the smallest cells ranging from 7 to 9 μm in diameter and at the other extreme, 35 to 45 μm (Rexed, 1952a). In this lamina, neurons are characterized by dendritic trees that are antenna-like (Schoenen, 1982a; Schoenen & Faull, 2004). These tend to be dorsally oriented and extend into lamina II and III (and can be found as far as lamina I; Heise & Kayalioglu, 2009). Furthermore, these dendritic trees are rich in spines (Schoenen, 1982a). This has been observed in human, cat (Schoenen & Faull, 2004), and the macaque monkey (Ralston III, 1982). The neurochemistry of this layer is diverse, and identities cannot be attributed to a specific morphology (unlike other laminae). GABA-ergic neurons predominately occupy the lateral third of the lamina, concentrated around the edge of the lamina (Barber et al., 1982; Häring et al., 2018) and are thought to participate in inhibitory modulation of signals from the periphery or other laminae projecting to laminae IV (Barber et al., 1982). In addition, transcriptomic analysis of the mouse spinal cord in the lumbar region indicates that this layer is enriched with glutamatergic neurons (Häring et al., 2018). Immunohistochemical, in situ hybridization, and transgenic studies revealed the presence of glycinergic nuclei scattered throughout this layer (Hossaini et al., 2007; Miranda et al., 2021), as have dopaminergic fibers (Holstege et al., 1996), dynorphin (Lima et al., 1993), enkephalin (de Lanerolle & LaMotte, 1982; Lima et al., 1993), somatostatin (Krukoff et al., 1986), and substance P (de Lanerolle & LaMotte, 1982), although it is unknown whether these identities colocalize or what their exact contributions to the function of this layer are.

Like the preceding layer, lamina IV plays a key role in the perception of pain and touch, with notable projections to the spinothalamic tract (Kayalioglu et al., 1996;

Schoenen & Faull, 2004), which is the main pathway conveying pain, touch, and temperature information to the thalamus. In particular, neurons in this lamina are responsive to light mechanical stimuli (e.g., brushing/stroking; Cervero et al., 1988). In addition, dendrites from this layer that project to and terminate in lamina II and III are likely to be modulated by nociceptive afferents in those layers, thus adding to the nociceptive output to the thalamus (Heise & Kayalioglu, 2009).

In addition to the nucleus proprius (previously discussed as part of lamina III), lamina IV is also home to the *internal basilar nucleus* and is confined to cervical segments C1–C6 in the rat (Torvik, 1956). It receives input from the sensorimotor cortex (Antal, 1984; Valtschanoff et al., 1993), primarily via the dorsal root ganglion (Rivero-Melián & Arvidsson, 1992), as well as the median and ulnar nerves (Lamotte et al., 1991) and projects to the thalamus (Kemplay & Webster, 1986) as well as the superior colliculus (Rhoades, 1981).

Lamina V and VI

Laminae V and VI are considered the final layers of the dorsal horn, occupying the base (Figure 4; Rexed, 1954; Schoenen & Faull, 2004). The cytoarchitecture, composition, and organization of laminae V and VI are very similar to each other (Rexed, 1952b, 1954) and virtually indistinguishable from one another in the human (Schoenen & Faull, 2004); therefore, for clarity the two will be considered as one in this review. These layers are organized into medial and lateral portions and exhibit different characteristics. In the rat, the demarcation between the two zones in lamina VI can only be seen in the lumbar segments 4–6 (Molander et al., 1984). The medial zone occupies approximately 2/3 of the laminae and is characterized by the presence of smaller neurons (8–10 μm) with a fusiform or triangular morphology (Rexed, 1954). Alternatively, neurons in lamina V can be functionally organized into three groups: nociceptive, mechanoreceptive, and multireceptive, wide dynamic range neurons (Ritz & Greenspan, 1985). These are also morphologically distinct from each other, though it is unknown if they can be neurochemically distinguished (as is the case with lamina I and II). *Nociceptive neurons* have small cell bodies and extensive dendrites that spread in all directions; their axons decussate and ascend to supraspinal targets in the ventral white matter (Ritz & Greenspan, 1985). As the name suggests, they are responsive to noxious/painful stimuli only. *Multireceptive, wide-dynamic-range* neurons have a similar morphology differing only by having a substantially larger cell body and respond to both innocuous and noxious/painful stimuli (Ritz & Greenspan, 1985). Finally, *mechanoreceptive* neurons were described as having smaller cell bodies and short, sparsely branched dendrites and are responsive to innocuous mechanical stimuli only (Ritz & Greenspan, 1985).

Projection neurons are predominately found in this in the medial zone (Molenaar & Kuypers, 1978) and project to a host of supraspinal regions such as the cerebellum (cat; as part of the cuneocerebellar tract; Edgley & Gallimore, 1988), the thalamus (rat; as part of the spinothalamic tract; Burstein et al., 1990; Kayalioglu et al., 1996), the periaqueductal gray (rat; as part of the spinomesencephalic tract; Liu, 1983), and the superior colliculus (rat; as part of the spinomesencephalic tract; Morrell & Pfaff, 1983). The lateral zone on the other hand occupies the remaining third of these layers and neurons in this sub-region are comparatively larger (30–45 μm; Rexed, 1952b) and adopt a multipolar morphology. Lamina VI differs slightly in that neurons are either propriospinal (connecting spinal segments to one another) or mainly project to motor neurons in the ventral layers; in addition, cerebellar and medullary projections have been observed (Rivero-Melián & Grant, 1990; Villanueva et al., 1991). The dendritic architecture of laminae V and VI are virtually identical, extending dorsoventrally and symmetrically (Schoenen & Faull, 2004). These dendrites extend dorsally as far up as laminae II and III; oppositely, dendrites extend down into lamina VII (Schoenen & Faull, 2004). Neurons in the lateral zone project more locally, particularly to preganglionic spinal neurons (Cabot et al., 1994). While lamina V neurons receive input from the periphery, mainly through large Aβ, small Aδ myelinated fibers, as well as C-fibers from distal dendrites that also extend into superficial laminae (Heise & Kayalioglu, 2009), Lamina VI differs slightly in that it also receives input from 1A muscle spindle afferents (Maxwell & Bannatyne, 1983) which is critical for proprioception, and both receive input from the red nucleus (Brown, 1974).

As seen in other laminae, GABA is a key neurotransmitter found in laminae V and VI; here, GABA is purported to be involved in switching signaling between cutaneous and visceral systems (Barber et al., 1982), highlighting its involvement in nociception both in the periphery as well as the viscera. Glycinergic immunoreactivity has also been observed (Hossaini et al., 2007), as has enkephalin (de Lanerolle & LaMotte, 1982), dopamine (Holstege et al., 1996), and somatostatin (Krukoff et al., 1986).

Immediately dorsolateral to lamina X lies the *dorsal nucleus of Clarke* (Clarke's Nucleus; Figure 1b) and is exclusive to the T1–L3 segments of the spinal cord in most species (Boehme, 1968; Heise & Kayalioglu, 2009; Snyder et al., 1978). Its exact location differs slightly amongst species; in cats (Merkul'eva et al., 2017;

Rexed, 1952b) and humans (Schoenen & Faull, 2004) it is found at the medial border of lamina V, VI, and VII; in the rat, at lamina IV and V (Snyder et al., 1978). Three classes of neurons have been identified based on dendritic architecture in the spinal cords of adult cats using silver impregnation and Nissl staining methods (Loewy, 1970). Class A nuclei are about 7–10 μm in diameter and are mostly ovoid with a varied dendritic branching patterns, and with a few class A dendrites extending into lamina V and X (Loewy, 1970). Class B neurons are slightly larger (termed "medium-sized") and are multipolar or fusiform with nuclei ranging from 7 to 15 μm in diameter (Loewy, 1970). Multipolar neurons have radially projecting dendrites, whereas the dendrites of fusiform neurons are oriented and project perpendicularly (Loewy, 1970). Finally, Class C neurons are the largest and arguably the most distinctive feature of this nucleus (Boehme, 1968; Loewy, 1970; Snyder et al., 1978) with nuclei ranging from about 20 to 25 μm (Loewy, 1970). Dendrites of these neurons extend in the rostrocaudal plane and can be traced as far as 200 μm into lamina VII (Loewy, 1970). Clarke's nucleus is primarily cholinergic (Schoenen & Faull, 2004) and somatotopically organized (Rivero-Melián, 1996), receiving input from the lower limb and neurons in this nucleus project to the cerebellum, with its axons forming the dorsal spinocerebellar tract (Heise & Kayalioglu, 2009; Snyder et al., 1978). Owing to its involvement in the movement of lower limbs, it is an attractive target for studying movement disorders, most notably amyotrophic lateral sclerosis (Averback & Crocker, 1982), and spinal cord injury (Attwell et al., 2018).

4.1.2 | Lateral horn

The lateral horn begins immediately above laminae VI but is only present in the thoracic and lumbar regions of the spinal cord, specifically T1–L2. The neurons encircling the central canal within the anterior commissure (corresponding to Rexed lamina X) also fall within this boundary. Nuclei related to autonomic function are found in this region, and is concerned with sympathetic innervation (Cho, 2015). Neurons in this region communicate with the brainstem, pelvic organs, viscera, and hypothalamus.

Lamina VII

Lamina VII marks the transition from the dorsal horn through to the intermediate zone/horn of the spinal cord (Figure 4). In the cat, it is bordered by lamina X in the medial aspect, and the white matter of the lateral funiculus laterally (Rexed, 1954). Dorsoventrally, it is distinct from lamina V and VI by having a lower neuronal density in comparison; ventrally, this is a lot more difficult to define and instead extends to the ventral borders of the gray matter with lamina VIII and IX found in between (Heise & Kayalioglu, 2009; Molander et al., 1984; Molander et al., 1989; Rexed, 1952b, 1954; Schoenen & Faull, 2004). In the lateral aspect of the lamina, neurons with a fusiform morphology predominate, multipolar neurons are found in the central and dorsal regions, and triangular/pyramidal-like neurons are found ventrally (Schoenen & Faull, 2004), particularly around lamina VIII and IX. Neurons generally have dendrites that extend horizontally or obliquely and can extend over the width of the gray matter (Schoenen & Faull, 2004); in addition, studies in the rat have identified smaller neurons with substantially shorter and sparsely branched dendrites (Ritz & Greenspan, 1985).

Lamina VII comprises mostly of GABA-ergic (Barber et al., 1982), premotor interneurons that project to the motor neurons of lamina IX (Heise & Kayalioglu, 2009). In addition, they also project to a host of supraspinal targets which highlights the contribution of this lamina to motor function, as well as the physical response to stress. This includes the amygdala and hypothalamus (Menétrey & de Pommery, 1991), which are thought to play a part in regulating the visceral (and pain from viscera) response to emotional and physical stress (Icenhour et al., 2020; Menétrey & de Pommery, 1991). Another target is the cerebellum (Krutki et al., 1998; Rivero-Melián & Grant, 1990). Axons of lamina VII are contributors to the formation of key spinocerebellar tracts, the functions of which are discussed in Section 2.1.2: *White matter subdivisions*. Specifically, the medial part of lamina VII and the spinal border cells [ventrolateral and dorsolateral parts of lamina VII (Snyder et al., 1978)] contribute to the anterior spinocerebellar tract (Sengul & Watson, 2015; Xu & Grant, 2005). Similarly, a major component of the posterior spinocerebellar tract is comprised of axons of the dorsal nucleus of Clarke (Sengul & Watson, 2015; Snyder et al., 1978); a nuclear column typically associated with lamina V, but located at the medial border of lamina VII in the cat and human (Heise & Kayalioglu, 2009; Rexed, 1952b). In addition, lamina VII contributes to the formation of the spinocuneocerebellar tract (Sengul & Watson, 2015). Other projection targets include the superior colliculus (Morrell & Pfaff, 1983) [indicating contributions to eye movement and coordinating the bodily response to visual stimuli (Dean et al., 1989)], the periaqueductal gray (Liu, 1983; suggesting involvement in autonomic body function; projections to the superior colliculus and periaqueductal gray ascend via the spinomesencephalic tract), and the pontomedullary reticular formation [Krutki et al., 1998; which is involved in the

regulation and maintenance of posture (Miller et al., 2017)].

The interneurons in this lamina act as a relay hub, receiving information of descending motor pathways and then transmitting this to motoneurons, which allows a single interneuron (or at most, a small number of interneurons) to initiate an entire movement that involves the engagement of multiple muscle groups (MacLean et al., 1995), including those that are not directly involved in the movement as such, but ones that are needed to maintain the balance or posture to execute the movement (Miller et al., 2017).

In addition, region-specific nuclei are found in lamina VII (Figure 4). In the cervical segments C1–C4 in the cat and dog, the *lateral cervical nucleus* can be found in the upper portion of the lamina, just next to lamina X; this nucleus was only observed in just 2 out of 16 human cadavers (Truex et al., 1970). This region can be characterized by large multipolar neurons whose dendrites extend dorsolaterally, laterally, and ventrally (Wiksten, 1979). Small triangular and spindle-shaped neurons with dendrites that extend and follow the round shape of the nuclear group were also found in small numbers (Wiksten, 1979). The central cervical nucleus plays a critical role in the movement and control of the neck by receiving input from the upper cervical muscles (Ammann et al., 1983) and vestibulospinal neurons of the vestibulospinal tract (Donevan et al., 1990); the latter being essential for the tonic neck reflex (Matsushita, 1991). Further, projections to the cerebellum (anterior and posterior spinocerebellar tracts, and the cuneocerebellar tract; Matsushita et al., 1995) and vestibular nuclei (spinovestibular tract; Bankoul & Neuhuber, 1992; Matsushita et al., 1995) indicate that this nucleus is key for the muscular coordination, balance, and the maintenance of posture. The *intermediolateral (IML) nucleus* can also be found in this lamina; in the human, this is found at the lateral-most edge of the lamina in thoracic segment T1 through to lumbar segment L1 in humans (Krassioukov et al., 1999) and extends as far down as lumbar segments L3 in the rat (Molander et al., 1984) and L4 in the cat (Rexed, 1954). It can be further subdivided into a principal portion (at the lateral-most edge) and a funicular portion (embedded in the lateral funiculus; Light & Metz, 1978). The IML contains preganglionic sympathetic neurons which are primarily cholinergic (Deuchars & Lall, 2015; Powis & Gillingwater, 2016) but also co-express a host of other modulators such as nitric oxide (Anderson, 1992), enkephalin, neurotensin, neurophysin, substance P, serotonin, somatostatin, and vasoactive intestinal polypeptide, as summarized by Heise & Kayalioglu (Heise & Kayalioglu, 2009). Sympathetic preganglionic neurons play a key role in a host of autonomic function, including cardiovascular control (Krassioukov et al., 1999), sudomotor (the control of sweat gland function), vasomotor control and the maintenance of blood pressure, and visceral control (Deuchars & Lall, 2015). The *intercalated nucleus* is also found in lamina VII and is seen as a "bridge" of sympathetic preganglionic dendrites that connect the IML to the central autonomic area, which is in lamina X, immediately dorsolateral to the central canal (Heise & Kayalioglu, 2009; Vera et al., 1986). Finally, lamina VII is also home to the *lumbar dorsal commissural nucleus* and is found in lumbar segments L1 and L2 only (Hancock & Peveto, 1979). Neurons in this nucleus can be round, ovoid, or spindle-shaped (Rexed, 1952a), and their cholinergic axons (Barber et al., 1984) innervate the hypogastric nerve and pelvic ganglia (Nadklhaft & McKenna, 1987; Yaïci et al., 2002), thus playing a role in regulating arterial blood supply to and control of the motility of the viscera and pelvic organs (Janig & McLachlan, 1987).

Lamina X

Lamina X is also found in the lateral horn, adjacent and medially to lamina VII, encircling the central canal (Rexed, 1954; Schoenen & Faull, 2004; Figure 4). Rexed initially identified and named this area as the *substantia grisea centralis* and is therefore also known as the central gray area (Rexed, 1952b, 1954). Rich in neuropil and low in cell body density (Rexed, 1952a, 1954), two morphological classes of neurons can be discerned in the human; in the cat, this population is more heterogenous with no obvious morphological differences (Honda & Perl, 1985). *Bipolar* neurons tend to occur in the mid and dorsal portions of the lamina with a fan-shaped, aspinous dendritic tree sprouting mainly from a single primary dendrite at both poles of the soma (Schoenen & Faull, 2004). These are thought to be the equivalent of the "*neurone fusiforme ou triangulaire*" (spindle-shaped and triangular neurons) initially identified in the cat by Cajal in 1909. Dendrites of these neurons project dorsally and reach into lamina VI; oppositely, these project ventrally into lamina VIII and in the adult human, these dendritic extensions measure no more than 600 μm dorsoventrally (Schoenen & Faull, 2004). The second morphological subtype is found in the ventral portion; while also classed as bipolar, their dendrites extend rostrocaudally (up to a distance of 1.5 mm) and are poorly ramified (Schoenen & Faull, 2004). These are thought to be equivalent to the "*cellule étoilée*" (star cells) that Cajal identified in the adult cat. Functionally, three classes of neurons have been identified in the cat; however, due to the morphological heterogeneity of neurons in this lamina versus the subtypes identified in the human, it is not possible to match morphology and function at present. *Low-*

threshold, mechanoreceptive neurons respond to moving, transient contact (e.g., light brushing of the skin) as well as evaporative cooling (Honda & Lee, 1985). *Multi-receptive neurons* were particularly receptive to noxious mechanical and heat stimuli (e.g., pinching, application of deep pressure, or heating of the skin; Honda & Lee, 1985). *Selectively nociceptive neurons* on the other hand were responsive to noxious cutaneous or subcutaneous stimulation (Honda & Lee, 1985).

When considering the response of these neurons to the above stimuli in the context of their afferent and efferent projections, this lamina is thought to be an integration hub for nociception, somatosensation, and visceroreceptive sensation (Matsushita, 1998; Schoenen & Faull, 2004). Lamina X receives input from the periphery via C- and Aδ-fibers and projects to a host of supraspinal structures such as the hypothalamus (Kayalioglu et al., 1996; Menétrey & de Pommery, 1991), periaqueductal gray (Liu, 1983), amygdala (Menétrey et al., 1989), as well as the contralateral lamina X (Nahin & Micevych, 1986). Input from ascending propriospinal axons has also been reported (Matsushita, 1998). Further, input from the raphe magnus nucleus (via the raphespinal tract; Holstege, 1987) which is involved in the inhibition of nociceptive transmission reinforces its involvement in the modulation of pain (Liang et al., 2015), as does the expression of various modulatory neuropeptides involved in the nociceptive response (Honda & Lee, 1985); for example, substance P, enkephalin, serotonin, cholecystokinin, vasointestinal peptide, and neurotensin (Gibson et al., 1981; LaMotte, 1988).

Lamina X is also partially home to the intermediomedial (IMM) nucleus and its location relative to other nuclei and laminae depends on the spinal level (Figure 4). In cervical segments C1–C4 it is dorsal to the central cervical nucleus; in C5–C8 it is found in lamina VI, and from spinal segments T1 and below it is partly embedded in lamina VII and X (Heise & Kayalioglu, 2009). Thus, for clarity, it will be discussed as part of this lamina. Unlike other nuclei previously discussed it is not a continuous cell column rostrocaudally; rather, it is more of a bead-like structure which means it may not be identified in every section (Molander et al., 1989; Schoenen & Faull, 2004). Neurons in the IMM receive input from the viscera and are cholinergic (Arvidsson et al., 1997; Borges & Iversen, 1986; Satoh et al., 1983; Schoenen & Faull, 2004), and are thought to provide inhibition to the adjacent IML, thus playing a role in modulating the autonomic response in the viscera.

4.1.3 | Ventral horn

Finally, the ventral (anterior) horn occupies the remainder of the gray matter, occupying the area that resembles the hindwings of a butterfly. This region contains the distinct, large motor neurons that terminate on striated muscle, facilitating the voluntary movement of the limbs and torso.

Lamina VIII

Lamina VIII signals the beginning of the ventral horn (Figure 4). Its size and shape differ depending on the level of the spinal cord. In the cervical and lumbar regions, it is confined to the medial base of the ventral horn (Heise & Kayalioglu, 2009; Molander et al., 1984, 1989; Rexed, 1954). In the thoracic region, however, it extends across the entire base of the ventral horn (Molander et al., 1984, 1989). An assortment of cell shapes and sizes are found here, with the smallest cells measuring ∼10 μm in diameter and the largest resembling motor neurons, measuring up to 50–60 μm in contrast (Rexed, 1952a). It is this heterogeneity that makes it distinct from lamina VII which extends to the edge of the ventral horn and surrounds lamina VIII and IX (Molander et al., 1984, 1989; Schoenen & Faull, 2004). The majority of neurons are triangular or multipolar in the human, (Schoenen & Faull, 2004), and in the cat those with a spindle-shaped morphology are frequently found along the medial border (Rexed, 1954). Large neurons that may be mistaken from motor neurons can be distinguished on the basis of Nissl staining; the former having finer granules (Schoenen & Faull, 2004). Small-medium sized neurons in this layer are immunopositive for GABA (Waldvogel et al., 1990) and are likely to comprise the interneuronal population. Furthermore, also in human, the glutamatergic, metabotropic mGluR1 receptor is strongly expressed in this layer (Aronica et al., 2001), suggesting responsiveness to glutamatergic inputs from projections to this area. In adult human, dendritic trees adopt a dorsoventral orientation (Schoenen & Faull, 2004). Dorsally they are directed toward the ventral gray commissure (but do not decussate) or project toward lamina VII. Ventrally, they branch out toward the ventromedial tip of the ventral horn, with a few crossing the border into the anterior funiculus (white matter; Schoenen & Faull, 2004). Their arborizations tend to be symmetrical and highly ramified (Abdel-Maguid & Bowsher, 1984), with very little spread in the mediolateral aspect (Schoenen & Faull, 2004).

Unlike the neurons in the previous laminae discussed, the majority of lamina VIII neurons do not project to supraspinal targets. However, there are a few exceptions. Lamina VIII projections to the contralateral cerebellum (Matsushita et al., 1979; cat), medulla (Villanueva et al., 1991; rat), and thalamus (Craig et al., 1989; rat). Further, a contralateral, reciprocal projection to the superior colliculus from lamina VIII has also been

identified in the rat (Morrell & Pfaff, 1983), suggesting a communication pathway where visual, auditory, and somatosensory information from the superior colliculus goes on to influence motor responses (and vice-versa; Ito & Feldheim, 2018). Spinal commissural neurons are found in lamina VIII and project more locally; to contralateral lamina VII, VIII, and IX (Harrison et al., 1986; Matsushita, 1970; Scheibel & Scheibel, 1968). Decussation of these neurons occurs during development and plays a critical role in ensuring the correct positioning of ventral interneurons, and genetic disruption of transcription factors that guide the axons along the correct routes results in abnormal positioning (and function, relative to the connections they need to make; Laumonnerie et al., 2015; Serafini et al., 1996). Following the development, spinal commissural neurons continue to play an important role in rhythmic and coordinated locomotion (Chédotal, 2014; Harrison et al., 1986; Kiehn, 2011; Scheibel & Scheibel, 1968; Stokke et al., 2002). Coordinated left–right movements include the reciprocal arm and leg swing (humans), or in quadrupeds like cats, the coordination of forelimbs and hindlimbs when walking. In addition, long propriospinal fibers that connect the lumbar and contralateral cervical segments originate in the medial portion of lamina VIII (and partially VII as well) and comprise the majority of neurons in this layer (Dutton et al., 2006; Sengul & Watson, 2012a). In the rat, the bulk of these axonal fibers is immunoreactive for vesicular glutamate transporter type 2 (VGLUT-2), suggesting a glutamatergic identity and therefore, excitatory output to their intended targets. Further, lamina VIII receives input from the superior colliculus (as aforementioned) the periaqueductal gray (Mouton & Holstege, 1994; cat), the interstitiospinal tract (Carpenter et al., 1970; monkey), vestibulospinal tract (Boyle & Johanson, 2003; squirrel monkey), reticulospinal tract (Matsuyama et al., 2004; cat), and cerebellospinal neurons (Sathyamurthy et al., 2020; mice; from both ipsilateral and contralateral aspects).

Lamina IX

The final layer discussed here is lamina IX, which is located at the base of the ventral horn (Figure 4). It is not a true lamina as such; rather, it is a series of longitudinally arranged motor neuron columns that are found embedded in lamina VII and VIII (Rexed, 1952a, 1954; Schoenen & Faull, 2004; Figure 4). Within each column, the group of motor neurons responsible for innervating a single muscle is termed a motoneuron pool. During development, positioning of motor neurons in the ventral horn is facilitated by the interactions of *Slit/Robo* (chemorepellants) and *Netrin1/DCC* (chemoattractants); mice with mutations for either of these led to aberrant migration, with motor neurons found in the hindbrain and spinal cord floor plate (*Slit/Robo* mutant) or shifted away from the floor plate (*Netrin1/DCC* mutant; Kim et al., 2015). These neurons are easily identified owing to their size; the smallest measuring ~20 μm, and larger ones measuring up to 50–70 μm (Rexed, 1952a). These neurons are multipolar and are characterized by their large nuclei, extensive dendrites, and large axons that form the ventral roots exiting the spinal cord (Sengul & Watson, 2012a). Golgi staining of longitudinal sections of the cat spinal cord revealed that the vast majority of these dendrites are oriented in a rostrocaudal direction (Scheibel & Scheibel, 1966; Sterling & Kuypers, 1967).

While the exact number of columns present differs among species and indeed, between regions of the spine, they can be broadly classed into medial and lateral columns. The medial column primarily innervates axial musculature (such as those involved in facilitating breathing and the maintenance of posture) and lateral columns innervate musculature of the limbs (Kanning et al., 2010; Molander et al., 1984, 1989; Routal & Pal, 1999a). A cadaveric examination of the human spinal cord in its entirety revealed the presence of 11 separate motor columns; the length and region in which they were found dependent on the musculature innervated (Routal & Pal, 1999a). Column 1 belonged to the medial subdivision and was found in all regions examined. Columns 2–11 on the other hand were considered part of the lateral subdivision and were found in specific spinal regions (e.g., Column 2, C1–C5 and C7–S3; columns 3–5 in the upper-mid cervical regions; columns 6–8 in the lower cervical/upper thoracic region; columns 9–11 mainly in the lumbosacral enlargement; Routal & Pal, 1999a). This organization is in general agreement with the observations made by Schoenen and Faull, who analyzed sections in the L5 region only. Here, they identified a ventromedial column (likely corresponding to Routal and Pal's columns 1–2), a central column (the equivalent of columns 2 and 9), a ventrolateral column (the equivalent of column 11), and a dorsolateral column (the equivalent of column 10; Schoenen & Faull, 2004). Therefore, in cervical and thoracic regions, it is feasible to suggest that the columns designated 1, 2, 3, and 4–8 by Routal and Pal (1999a) are further subdivisions of the ventromedial, central, ventrolateral, and dorsolateral columns of the ventral horn (Routal & Pal, 1999b). Based on their location, the authors deduced that the presence of columns 1 and 2 in the thoracic region likely innervated vertebral, intercostal, and abdominal musculature, columns 3–8 innervated upper limb musculature, and columns 9–11 innervated that of the lower limb (Routal & Pal, 1999a). Retrograde motor-end plate tracing in the rat also suggests that motor columns responsible for innervating a

specific group of muscles span several spinal segments, such as in the case of the hindlimb, which was traced to encompass spinal segments L2 through to the L6/S1 border (Mohan et al., 2015). An "upper-body" equivalent study from the same group investigating the origins of motor neurons of the forelimb musculature found these columns located in spinal levels C2 through to T1 (Tosolini & Morris, 2012). Further, these columns exhibited spatial organization, with cell columns innervating proximal muscles located ventrally, and those innervating distal muscles found laterally (Tosolini & Morris, 2012).

Furthermore, motor neuron dendrites are extensive and in the rat, these extend dorsally into lamina III and IV (Cook & Woolf, 1985). Dendritic bundling occurs only with dendrites from the same motor neuron column in the human [with the exception of the dorsolateral column, whose dendrites do not form bundles (Schoenen & Faull, 2004)] (Schoenen, 1982b); in the cat, however, this bundling can occur across multiple motor neuron columns and is thought to help synchronize the activity of a specific group of muscles (Scheibel & Scheibel, 1970a). In the cat and rat, these bundles can also decussate and mix with dendrites of motor neurons in the contralateral aspect (Light & Metz, 1978). It is thought that these bundles are involved in the development of programming appropriate reciprocal activity between agonist-antagonistic muscle groups (Scheibel & Scheibel, 1970b), so that movement such as crawling or walking can occur. In addition, the intermingling of longitudinal dendritic bundles with lamina VIII dendrites would also suggest communication between the two to facilitate coordination during locomotion.

Motor neurons are cholinergic (Barber et al., 1984; Satoh et al., 1983) and are further subdivided into three classes. The *α-motor neurons* are the larger, more prominent star-shaped neurons characteristic of this region that innervate striated (skeletal) muscle (Hunt & Kuffler, 1951). Physiologically, they are characterized by a high activation threshold and fire at a high frequency (Masakado, 1994). Their axons are heavily myelinated to facilitate rapid, saltatory conduction of electrical signals along the length of the axon and innervate fast-twitch (Type II) muscle fibers; the kind commonly associated with fatigue following physical exertion (Contessa et al., 2016). Single-cell transcriptomic analysis in the adult mouse suggests that these can be further subclassed into distinct pools corresponding to specific muscle groups (Blum et al., 2021). For example, *cpne4* (encoding copine-4) and *fign* (encoding fidgetin) were enriched in a pool of motor neurons associated with the innervation of intrinsic foot muscles, and *Sema3e* (encoding semaphorin 3a) was specific for motor neurons innervating the gluteus maximus and the shoulder muscles in the lumbar and cervical spinal cord, respectively (Blum et al., 2021). In both examples, these patterns of expression were present during development (Fukuhara et al., 2013; Mendelsohn et al., 2017; Pecho-Vrieseling et al., 2009). Another study identified *Erbb-4* [encoding the ERB-B2 receptor tyrosine kinase-4 and associated with amyotrophic lateral sclerosis (ALS; Blum & Gitler, 2022)] as unique to α-motor neurons innervating the diaphragm via the phrenic nerve (Alkaslasi et al., 2021). In addition to sub-classification according to specific muscle groups, this approach can be used to distinguish between pools of α-motor neurons innervating slow-firing, fast-fatigue-resistant, and fast-fatigable muscles (Blum et al., 2021), which has implications for diseases such as ALS where the three types of muscle fibers exhibit differential susceptibilities to degeneration (Nijssen et al., 2017). The *β-motor neurons* are the least abundant of all three subtypes, innervating both striated muscle and proprioceptors (skeletal muscle that plays a part in proprioception, receiving input from both dorsal and ventral horns; Bessou et al., 1965). Physiologically, they are further subdivided into static and dynamic subtypes; the former modulating the firing rate of sensory fibers for a given muscle length, and the latter increasing their stretch sensitivity (Barker et al., 1977). To date, β-motor neurons have not been conclusively defined transcriptomically, though a subset of γ-motor neurons (termed γ*) has been identified as a putatitve β population (Blum et al., 2021). Finally, lightly myelinated *γ-motor neurons* are the smallest of the three and innervate proprioceptors within the muscle spindle, exclusively controlling their sensitivity (Eccles et al., 1960). This population has a transcriptional profile characterized by the presence of *Htr1d* (encoding the 5-hydroxytryptamine receptor type 1D), *creb5* (encoding the cAMP-responsive element binding protein-5), and *Pard3b* (encoding the Par-3 family cell polarity regulator-beta protein; Blum et al., 2021). Perhaps counterintuitively, they do not possess any motor function and are physiologically characterized by a low activation threshold, and fire at a low frequency (Eccles et al., 1960; Taylor et al., 2000). Rather than participate in spinal reflexes, γ-motoneurons instead serve to modulate muscle contraction by adjusting the tension of intrafusal muscle fibers comprising the muscle spindle (Macefield & Knellwolf, 2018). Special mention must also be made of a notable interneuronal subtype; the Renshaw cells. Located medial to motor neuron pools that innervate striated muscle, these are primarily glycinergic and facilitate inhibition of α-motoneurons (Alvarez & Fyffe, 2007; Bhumbra et al., 2014; Özyurt et al., 2019). In doing so, these cells receive input from collaterals of motor neuron axons, and synapse with the cell bodies of motor neurons

TABLE 2 Comparison of spinal segments in the cervical, thoracic, lumbar, sacral, and coccygeal regions of the spinal cord compared with human

	Cervical	Thoracic	Lumbar	Sacral	Coccygeal
Human (Frostell et al., 2016)	8	12	5	5	1
Cat (Thomas et al., 1962)	8	13	7	3	At least 7
Mouse (Watson, Paxinos, Sengul, & Heise, 2009)	8	13	6	4	3
Rat (Watson, Paxinos, Kayalioglu, & Heise, 2009)	8	13	6	3	3

in a negative-feedback manner, thereby limiting their excitability (Eccles et al., 1954). The loss of this inhibition is thought to increase motor neuron vulnerability to excitotoxicity and alterations in the neuron-Renshaw cell circuit have been implicated in the pathogenesis of amyotrophic lateral sclerosis (Wootz et al., 2013).

5 | LIMITATIONS AND FUTURE DIRECTIONS

Much of our basic knowledge is derived mostly from a few animal models; as such, the mouse, rat, and cat feature heavily in this review. However, notwithstanding obvious size differences, there are key macrostructural differences immediately apparent. Table 2 summarizes the variation in spinal segments across humans, cats, rats, and mice.

Therefore, observations made at a given spinal segment in an animal model may not correlate well to the human equivalent, and could well have implications for the design of certain injury models (Jaumard et al., 2015). However, given the anatomical similarity of porcine models to humans as demonstrated by Leonard, et al., their utility as a pre-clinical translational model should be considered further (Leonard et al., 2017).

Further, a direct comparison to available human data is hampered by the analysis of a few spinal segments rather than the spinal cord in its entirety. In addition, regardless of the species studied, the spinal cord is a comparatively large area of the nervous system to study, with each level differing from the other. Consequently, studying just a single spinal cord entirely is a massive undertaking, let alone multiple cases or biological repeats. Nonetheless, further work to characterize the human spinal cord and accurately match spinal segments between species will play a role in designing better models of injury and disease.

The vast majority of studies cited in this review are from the mid-late 20th Century, using mostly manual staining and quantification techniques or offering a qualitative assessment only; often using just a single label or stain. Such approaches are prone to variability between experiments and qualitative observations are inherently subjective. However, detection and analytical techniques have evolved considerably since, particularly over the last 20 years. Simple improvements include the availability of staining kits for conventional histological stains (e.g., Golgi, silver, and Nissl) to improve efficiency and consistency. More complex advances include automated immunohistochemistry platforms to increase consistency and throughput (P, 2014), multiplexed immunohistochemical detection methods to detect multiple antigens in a single section (Maric et al., 2021), and automated imaging and analysis platforms to increase throughput and the amount of biological information gathered from a single section of tissue (Guirado et al., 2018). In addition, the use of spatial transcriptomics now allows one to quantify changes in gene expression in situ (Ståhl et al., 2016); a particularly powerful method to assess changes in gene expression as a consequence of injury or disease state. Equally and oppositely, this can also be employed to assess changes following a treatment or intervention. Making the most of these advances would certainly increase case/biological repeat throughput and build a more complete picture of the spinal cord at all levels in and between species. Such an approach would not only confirm or refute existing findings, but the ability to generate such a rich data set would substantially contribute to the overall goal of building a foundation for subsequent investigations of spinal disease.

AUTHOR CONTRIBUTIONS

Sheryl Tan: Conceptualization (lead); funding acquisition (lead); project administration (lead); writing – original draft (lead); writing – review and editing (equal). **Richard L. Faull:** Writing – review and editing (equal). **Maurice Curtis:** Conceptualization (supporting); supervision (lead); writing – review and editing (equal).

ACKNOWLEDGMENT

Open access publishing facilitated by The University of Auckland, as part of the Wiley - The University of

Auckland agreement via the Council of Australian University Librarians.

ORCID

Sheryl Tan https://orcid.org/0000-0003-1884-4378

REFERENCES

Abdel-Maguid, T. E., & Bowsher, D. (1984). Classification of neurons by dendritic branching pattern. A categorisation based on Golgi impregnation of spinal and cranial somatic and visceral afferent and efferent cells in the adult human. *Journal of Anatomy*, *138*(Pt 4), 689–702.

Ahn, Y. H., Ahn, S. H., Kim, H., Hong, J. H., & Jang, S. H. (2006). Can stroke patients walk after complete lateral corticospinal tract injury of the affected hemisphere? *Neuroreport*, *17*(10), 987–990.

Alkaslasi, M. R., Piccus, Z. E., Hareendran, S., Silberberg, H., Chen, L., Zhang, Y., Petros, T. J., & le Pichon, C. E. (2021). Single nucleus RNA-sequencing defines unexpected diversity of cholinergic neuron types in the adult mouse spinal cord. *Nature Communications*, *12*(1), 2471.

Alstermark, B., Isa, T., Pettersson, L.-G., & Sasaki, S. (2007). The C3–C4 propriospinal system in the cat and monkey: A spinal pre-motoneuronal Centre for voluntary motor control. *Acta Physiologica*, *189*(2), 123–140.

Alstermark, B., Kümmel, H., Pinter, M. J., & Tantisira, B. (1987). Branching and termination of C3-C4 propriospinal neurones in the cervical spinal cord of the cat. *Neuroscience Letters*, *74*(3), 291–296.

Alstermark, B., Lundberg, A., Norrsell, U., & Sybirska, E. (1981). Integration in descending motor pathways controlling the forelimb in the cat. *Experimental Brain Research*, *42*(3), 299–318.

Alstermark, B., Lundberg, A., & Sasaki, S. (1984a). Integration in descending motor pathways controlling the forelimb in the cat. 10. Inhibitory pathways to forelimb motoneurones via C3-C4 propriospinal neurones. *Experimental Brain Research*, *56*(2), 279–292.

Alstermark, B., Lundberg, A., & Sasaki, S. (1984b). Integration in descending motor pathways controlling the forelimb in the cat. *Experimental Brain Research*, *56*(2), 293–307.

Alvarez, F. J., & Fyffe, R. E. W. (2007). The continuing case for the Renshaw cell. *The Journal of Physiology*, *584*(1), 31–45.

Amano, E., Komatuzaki, T., Ishido, H., Ishihara, T., Otsu, S., Yamada, I., & Machida, A. (2018). Pitfalls in the diagnosis of pupil-sparing oculomotor nerve palsy without limb ataxia: A case report of a variant of Claude's syndrome and neuroanatomical analysis using diffusion-tensor imaging. *Journal of Clinical Neuroscience*, *47*, 120–123.

Ammann, B., Gottschall, J., & Zenker, W. (1983). Afferent projections from the rat longus capitis muscle studied by transganglionic transport of HRP. *Anatomy and Embryology*, *166*(2), 275–289.

Anderson, C. R. (1992). Nadph diaphorase-positive neurons in the rat spinal cord include a subpopulation of autonomic preganglionic neurons. *Neuroscience Letters*, *139*(2), 280–284.

Anderson, F. D. (1963). The structure of a chronically isolated segment of the cat spinal cord. *Journal of Comparative Neurology*, *120*(2), 297–315.

Antal, M. (1984). Termination areas of corticobulbar and corticospinal fibres in the rat. *Journal für Hirnforschung*, *25*(6), 647–659.

Antonetty, C. M., & Webster, K. E. (1975). The organisation of the spinotectal projection. An experimental study in the rat. *Journal of Comparative Neurology*, *163*(4), 449–465.

Archer, D. B., Vaillancourt, D. E., & Coombes, S. A. (2017). A template and probabilistic atlas of the human sensorimotor tracts using diffusion MRI. *Cerebral Cortex*, *28*(5), 1685–1699.

Aronica, E., Catania, M. V., Geurts, J., Yankaya, B., & Troost, D. (2001). Immunohistochemical localization of group I and II metabotropic glutamate receptors in control and amyotrophic lateral sclerosis human spinal cord: Upregulation in reactive astrocytes. *Neuroscience*, *105*(2), 509–520.

Arvidsson, U., Riedl, M., Elde, R., & Meister, B. (1997). Vesicular acetylcholine transporter (VAChT) protein: A novel and unique marker for cholinergic neurons in the central and peripheral nervous systems. *Journal of Comparative Neurology*, *378*(4), 454–467.

Ashwell, K. W., & Zhang, L. L. (1997). Cyto- and myeloarchitectonic organisation of the spinal cord of an echidna (Tachyglossus aculeatus). *Brain, Behavior and Evolution*, *49*(5), 276–294.

Atik, A. F., Calabrese, E., Gramer, R., Adil, S. M., Rahimpour, S., Pagadala, P., Johnson, G. A., & Lad, S. P. (2019). Structural mapping with fiber tractography of the human cuneate fasciculus at microscopic resolution in cervical region. *NeuroImage*, *196*, 200–206.

Attwell, C. L., van Zwieten, M., Verhaagen, J., & Mason, M. R. J. (2018). The dorsal column lesion model of spinal cord injury and its use in deciphering the neuron-intrinsic injury response. *Developmental Neurobiology*, *78*(10), 926–951.

Averback, P., & Crocker, P. (1982). Regular involvement of Clarke's nucleus in sporadic amyotrophic lateral sclerosis. *Archives of Neurology*, *39*(3), 155–156.

Baker, M. L., & Giesler, G. J., Jr. (1984). Anatomical studies of the spinocervical tract of the rat. *Somatosensory Research*, *2*(1), 1–18.

Baker, S. N. (2011). The primate reticulospinal tract, hand function and functional recovery. *The Journal of Physiology*, *589*(Pt 23), 5603–5612.

Bankoul, S., & Neuhuber, W. L. (1992). A direct projection from the medial vestibular nucleus to the cervical spinal dorsal horn of the rat, as demonstrated by anterograde and retrograde tracing. *Anatomy and Embryology*, *185*(1), 77–85.

Barber, R. P., Phelps, P. E., Houser, C. R., Crawford, G. D., Salvaterra, P. M., & Vaughn, J. E. (1984). The morphology and distribution of neurons containing choline acetyltransferase in the adult rat spinal cord: An immunocytochemical study. *Journal of Comparative Neurology*, *229*(3), 329–346.

Barber, R. P., Vaughn, J. E., & Roberts, E. (1982). The cytoarchitecture of gabaergic neurons in rat spinal cord. *Brain Research*, *238*(2), 305–328.

Bareyre, F. M., Kerschensteiner, M., Raineteau, O., Mettenleiter, T. C., Weinmann, O., & Schwab, M. E. (2004). The injured spinal cord spontaneously forms a new intraspinal circuit in adult rats. *Nature Neuroscience*, *7*(3), 269–277.

Barker, D., Emonet-Dénand, F., Harker, D. W., Jami, L., & Laporte, Y. (1977). Types of intra- and extrafusal muscle fibre innervated by dynamic skeleto-fusimotor axons in cat peroneus brevis and tenuissimus muscles, as determined by the

glycogen-depletion method. *The Journal of Physiology*, *266*(3), 713–726.

Barmherzig, R., & Kingston, W. (2019). Occipital neuralgia and cervicogenic headache: Diagnosis and management. *Current Neurology and Neuroscience Reports*, *19*(5), 20.

Barson, A. J., & Sands, J. (1977). Regional and segmental characteristics of the human adult spinal cord. *Journal of Anatomy*, *123* (Pt 3), 797–803.

Basbaum, A. I., & Fields, H. L. (1979). The origin of descending pathways in the dorsolateral funiculus of the spinal cord of the cat and rat: Further studies on the anatomy of pain modulation. *Journal of Comparative Neurology*, *187* (3), 513–531.

Batton, R. R., III, Jayaraman, A., Ruggiero, D., & Carpenter, M. B. (1977). Fastigial efferent projections in the monkey: An autoradiographic study. *Journal of Comparative Neurology*, *174*(2), 281–305.

Bawa, P., Hamm, J. D., Dhillon, P., & Gross, P. A. (2004). Bilateral responses of upper limb muscles to transcranial magnetic stimulation in human subjects. *Experimental Brain Research*, *158* (3), 385–390.

Bennett, G. J., Nishikawa, N., Lu, G.-W., Hoffert, M. J., & Dubner, R. (1984). The morphology of dorsal column postsynaptic spinomedullary neurons in the cat. *Journal of Comparative Neurology*, *224*(4), 568–578.

Bessou, P., Emonet-Dénand, F., & Laporte, Y. (1965). Motor fibres innervating extrafusal and intrafusal muscle fibres in the cat. *The Journal of Physiology*, *180*(3), 649–672.

Bhumbra, G. S., Bannatyne, B. A., Watanabe, M., Todd, A. J., Maxwell, D. J., & Beato, M. (2014). The recurrent case for the Renshaw cell. *The Journal of Neuroscience*, *34*(38), 12919–12932.

Bianchi, R., & Gioia, M. (1990). Accessory oculomotor nuclei of man. 1. The nucleus of Darkschewitsch: A Nissl and Golgi study. *Acta Anatomica*, *139*(4), 349–356.

Biedenbach, M. A. (1972). Cell density and regional distribution of cell types in the cuneate nucleus of the rhesus monkey. *Brain Research*, *45*(1), 1–14.

Blum, J. A., & Gitler, A. D. (2022). Singling out motor neurons in the age of single-cell transcriptomics. *Trends in Genetics*, *38*, 904–919.

Blum, J. A., Klemm, S., Shadrach, J. L., Guttenplan, K. A., Nakayama, L., Kathiria, A., Hoang, P. T., Gautier, O., Kaltschmidt, J. A., Greenleaf, W. J., & Gitler, A. D. (2021). Single-cell transcriptomic analysis of the adult mouse spinal cord reveals molecular diversity of autonomic and skeletal motor neurons. *Nature Neuroscience*, *24*(4), 572–583.

Boehme, C. C. (1968). The neural structure of Clarke's nucleus of the spinal cord. *Journal of Comparative Neurology*, *132*(3), 445–461.

Boivie, J. (1970). The termination of the cervicothalamic tract in the cat. An experimental study with silver impregnation methods. *Brain Research*, *19*(3), 333–360.

Borges, L. F., & Iversen, S. D. (1986). Topography of choline acetyltransferase Immunoreactive neurons and fibers in the rat spinal cord. *Brain Research*, *362*(1), 140–148.

Bortoff, G. A., & Strick, P. L. (1993). Corticospinal terminations in two new-world primates: Further evidence that corticomotoneuronal connections provide part of the neural substrate for manual dexterity. *The Journal of Neuroscience*, *13*(12), 5105–5118.

Bourane, S., Grossmann Katja, S., Britz, O., Dalet, A., Del Barrio, M. G., Stam, F. J., Garcia-Campmany, L., Koch, S., & Goulding, M. (2015). Identification of a spinal circuit for light touch and fine motor control. *Cell*, *160*(3), 503–515.

Boyle, R. (1993). Activity of medial vestibulospinal tract cells during rotation and ocular movement in the alert squirrel monkey. *Journal of Neurophysiology*, *70*(5), 2176–2180.

Boyle, R., & Johanson, C. (2003). Morphological properties of vestibulospinal neurons in primates. *Annals of the New York Academy of Sciences*, *1004*(1), 183–195.

Brichta, L., Greengard, P., & Flajolet, M. (2013). Advances in the pharmacological treatment of Parkinson's disease: Targeting neurotransmitter systems. *Trends in Neurosciences*, *36*(9), 543–554.

Brockett, E. G., Seenan, P. G., Bannatyne, B. A., & Maxwell, D. J. (2013). Ascending and descending propriospinal pathways between lumbar and cervical segments in the rat: Evidence for a substantial ascending excitatory pathway. *Neuroscience*, *240*, 83–97.

Brösamle, C., & Schwab, M. E. (1997). Cells of origin, course, and termination patterns of the ventral, uncrossed component of the mature rat corticospinal tract. *Journal of Comparative Neurology*, *386*(2), 293–303.

Brouwers, E., van de Meent, H., Curt, A., Starremans, B., Hosman, A., & Bartels, R. (2017). Definitions of traumatic conus medullaris and cauda equina syndrome: A systematic literature review. *Spinal Cord*, *55*(10), 886–890.

Brown, A. G. (1981). The spinocervical tract. *Progress in Neurobiology*, *17*(1), 59–96.

Brown, A. G., Maxwell, D. J., & Short, A. D. (1989). Receptive fields and in-field afferent inhibition of neurones in the cat's lateral cervical nucleus. *The Journal of Physiology*, *413*, 119–137.

Brown, L. T. (1971). Projections and termination of the corticospinal tract in rodents. *Experimental Brain Research*, *13*(4), 432–450.

Brown, L. T. (1974). Rubrospinal projections in the rat. *Journal of Comparative Neurology.*, *154*(2), 169–187.

Bryan, R. N., Coulter, J. D., & Willis, W. D. (1974). Cells of origin of the spinocervical tract in the monkey. *Experimental Neurology*, *42*(3), 574–586.

Buford, J. A., & Davidson, A. G. (2004). Movement-related and preparatory activity in the reticulospinal system of the monkey. *Experimental Brain Research*, *159*(3), 284–300.

Bürgel, U., Amunts, K., Hoemke, L., Mohlberg, H., Gilsbach, J. M., & Zilles, K. (2006). White matter fiber tracts of the human brain: Three-dimensional mapping at microscopic resolution, topography and intersubject variability. *NeuroImage*, *29*(4), 1092–1105.

Burstein, R., Dado, R. J., & Giesler, G. J. (1990). The cells of origin of the spinothalamic tract of the rat: A quantitative reexamination. *Brain Research*, *511*(2), 329–337.

Büttner-Ennever, J. A., & Gerrits, N. M. (2004). CHAPTER 33 - Vestibular system. In G. Paxinos & J. K. Mai (Eds.), *The human nervous system* (pp. 1212–1240). Academic Press.

Buxton, D. F., & Goodman, D. C. (1967). Motor function and the corticospinal tracts in the dog and raccoon. *Journal of Comparative Neurology*, *129*(4), 341–360.

Cabot, J. B., Alessi, V., Carroll, J., & Ligorio, M. (1994). Spinal cord lamina V and lamina VII interneuronal projections to sympathetic preganglionic neurons. *Journal of Comparative Neurology*, *347*(4), 515–530.

Cai, Y.-Q., Chen, S.-R., Han, H.-D., Sood, A. K., Lopez-Berestein, G., & Pan, H.-L. (2009). Role of M2, M3, and M4 muscarinic receptor subtypes in the spinal cholinergic control of nociception revealed using siRNA in rats. *Journal of Neurochemistry*, *111*(4), 1000–1010.

Caputi, F., Spaziante, R., de Divitiis, E., & Nashold, B. S. (1995). Luigi Rolando and his pioneering efforts to relate structure to function in the nervous system. *Journal of Neurosurgery*, *83*(5), 933–937.

Caramia, M. D., Palmieri, M. G., Giacomini, P., Iani, C., Dally, L., & Silvestrini, M. (2000). Ipsilateral activation of the unaffected motor cortex in patients with hemiparetic stroke. *Clinical Neurophysiology*, *111*(11), 1990–1996.

Carpenter, M. B., Harbison, J. W., & Peter, P. (1970). Accessory oculomotor nuclei in the monkey: Projections and effects of discrete lesions. *Journal of Comparative Neurology*, *140*(2), 131–153.

Castiglioi, A. J., Gallaway, M. C., & Coulter, J. D. (1978). Spinal projections from the midbrain in monkey. *Journal of Comparative Neurology*, *178*(2), 329–345.

Çavdar, S., Aydın, A. E., Algın, O., & Aydın, S. (2021). The complex structure of the anterior white commissure of the human brain: Fiber dissection and Tractography study. *World Neurosurgery*, *147*, e111–e117.

Cervero, F., Handwerker, H. O., & Laird, J. M. (1988). Prolonged noxious mechanical stimulation of the rat's tail: Responses and encoding properties of dorsal horn neurones. *The Journal of Physiology*, *404*(1), 419–436.

Cervero, F., Iggo, A., & Molony, V. (1977). Responses of spinocervical tract neurones to noxious stimulation of the skin. *The Journal of Physiology*, *267*(2), 537–558.

Chalif, J. I., Martínez-Silva, M. L., Pagiazitis, J. G., Murray, A. J., & Mentis, G. Z. (2022). Control of mammalian locomotion by ventral spinocerebellar tract neurons. *Cell*, *185*(2), 328–44.e26.

Chandar, K., & Freeman, B. K. (2014). Spinal cord anatomy. In M. J. Aminoff & R. B. Daroff (Eds.), *Encyclopedia of the neurological sciences* (2nd ed., pp. 254–263). Academic Press.

Chaouch, A., Menetrey, D., Binder, D., & Besson, J. M. (1983). Neurons at the origin of the medical component of the bulbopontine spinoreticular tract in the rat: An anatomical study using horseradish peroxidase retrograde transport. *Journal of Comparative Neurology*, *214*(3), 309–320.

Chédotal, A. (2014). Development and plasticity of commissural circuits: From locomotion to brain repair. *Trends in Neurosciences*, *37*(10), 551–562.

Chenot, Q., Tzourio-Mazoyer, N., Rheault, F., Descoteaux, M., Crivello, F., Zago, L., Mellet, E., Jobard, G., Joliot, M., Mazoyer, B., & Petit, L. (2019). A population-based atlas of the human pyramidal tract in 410 healthy participants. *Brain Structure and Function*, *224*(2), 599–612.

Chisholm, K. I., Lo Re, L., Polgár, E., Gutierrez-Mecinas, M., Todd, A. J., & McMahon, S. B. (2021). Encoding of cutaneous stimuli by lamina I projection neurons. *Pain*, *162*(9), 2405–2417.

Cho, T. A. (2015). Spinal cord functional anatomy. *Continuum*, *21* (1), 13–35.

Chung, K., & Coggeshall, R. E. (1983). Propriospinal fibers in the rat. *Journal of Comparative Neurology*, *217*(1), 47–53.

Chung, K., Langford, L. A., & Coggeshall, R. E. (1987). Primary afferent and propriospinal fibers in the rat dorsal and dorsolateral funiculi. *The Journal of Comparative Neurology*, *263*(1), 68–75.

Chung, K. S., & Coggeshall, R. E. (1985). Unmyelinated primary afferent fibers in dorsal funiculi of cat sacral spinal cord. *The Journal of Comparative Neurology*, *238*(3), 365–369.

Clarac, F., Vinay, L., Cazalets, J. R., Fady, J. C., & Jamon, M. (1998). Role of gravity in the development of posture and locomotion in the neonatal rat. *Brain Research Reviews*, *28*(1-2), 35–43.

Cliffer, K. D., & Giesler, G. J., Jr. (1989). Postsynaptic dorsal column pathway of the rat. III. Distribution of ascending afferent fibers. *The Journal of Neuroscience*, *9*(9), 3146–3168.

Conta, A. C., & Stelzner, D. J. (2004). Differential vulnerability of propriospinal tract neurons to spinal cord contusion injury. *Journal of Comparative Neurology*, *479*(4), 347–359.

Conta, A. C., & Stelzner, D. J. (2009). Chapter 12 - The propriospinal system. In C. Watson, G. Paxinos, & G. Kayalioglu (Eds.), *The spinal cord* (pp. 180–190). Academic Press.

Contessa, P., De Luca, C. J., & Kline, J. C. (2016). The compensatory interaction between motor unit firing behavior and muscle force during fatigue. *Journal of Neurophysiology*, *116*(4), 1579–1585.

Cook, A. J., & Woolf, C. J. (1985). Cutaneous receptive field and morphological properties of hamstring flexor alpha-motoneurones in the rat. *The Journal of Physiology*, *364*(1), 249–263.

Cowley, K. C., MacNeil, B. J., Chopek, J. W., Sutherland, S., & Schmidt, B. J. (2015). Neurochemical excitation of thoracic propriospinal neurons improves hindlimb stepping in adult rats with spinal cord lesions. *Experimental Neurology*, *264*, 174–187.

Craig, A. D., Krout, K., & Andrew, D. (2001). Quantitative response characteristics of thermoreceptive and nociceptive lamina I spinothalamic neurons in the cat. *Journal of Neurophysiology*, *86* (3), 1459–1480.

Craig, A. D., Linington, A. J., & Kniffki, K. D. (1989). Significant differences in the retrograde labeling of spinothalamic tract cells by horseradish peroxidase and the fluorescent tracers fast blue and diamidino yellow. *Experimental Brain Research*, *74*(2), 431–436.

Craig, A. D., Jr. (1978). Spinal and medullary input to the lateral cervical nucleus. *Journal of Comparative Neurology*, *181*(4), 729–743.

Cregg, J. M., Chu, K. A., Hager, L. E., Maggard, R. S. J., Stoltz, D. R., Edmond, M., Alilain, W. J., Philippidou, P., Landmesser, L. T., & Silver, J. (2017). A latent propriospinal network can restore diaphragm function after high cervical spinal cord injury. *Cell Reports*, *21*(3), 654–665.

Dalezios, Y., Scudder, C. A., Highstein, S. M., & Moschovakis, A. K. (1998). Anatomy and physiology of the primate interstitial nucleus of Cajal. II. Discharge pattern of single efferent fibers. *Journal of Neurophysiology*, *80*(6), 3100–3111.

Danner, S. M., Hofstoetter, U. S., Freundl, B., Binder, H., Mayr, W., Rattay, F., & Minassian, K. (2015). Human spinal locomotor

control is based on flexibly organized burst generators. *Brain*, *138*(Pt 3), 577–588.

Darlot, F., Cayetanot, F., Gauthier, P., Matarazzo, V., & Kastner, A. (2012). Extensive respiratory plasticity after cervical spinal cord injury in rats: Axonal sprouting and rerouting of ventrolateral bulbospinal pathways. *Experimental Neurology*, *236*(1), 88–102.

de Lanerolle, N. C., & LaMotte, C. C. (1982). The human spinal cord: Substance P and methionine-enkephalin immunoreactivity. *The Journal of Neuroscience*, *2*(10), 1369–1386.

de Pasqua, S., Cevoli, S., Calbucci, F., & Liguori, R. (2016). Cervical demyelinating lesion presenting with choreoathetoid movements and dystonia. *Journal of the Neurological Sciences*, *368*, 203–205.

de Pommery, J., Roudier, F., & Menétrey, D. (1984). Postsynaptic fibers reaching the dorsal column nuclei in the rat. *Neuroscience Letters*, *50*(1-3), 319–323.

Dean, P., Redgrave, P., & Westby, G. W. (1989). Event or emergency? Two response systems in the mammalian superior colliculus. *Trends in Neurosciences*, *12*(4), 137–147.

Del Cerro, P., Rodríguez-De-Lope, Á., & Collazos-Castro, J. E. (2021). The cortical motor system in the domestic pig: Origin and termination of the corticospinal tract and cortico-brainstem projections. *Frontiers in Neuroanatomy*, *15*, 748050.

Deuchars, S. A., & Lall, V. K. (2015). Sympathetic preganglionic neurons: Properties and inputs. *Comprehensive Physiology*, *5*(2), 829–869.

Deumens, R., Koopmans, G. C., & Joosten, E. A. (2005). Regeneration of descending axon tracts after spinal cord injury. *Progress in Neurobiology*, *77*(1-2), 57–89.

Dickenson, A. H., & Goldsmith, G. (1986). Evidence for a role of 5-hydroxytryptamine in the responses of rat raphe magnus neurones to peripheral noxious stimuli. *Neuropharmacology*, *25*(8), 863–868.

Dimitrijevic, M. R., Gerasimenko, Y., & Pinter, M. M. (1998). Evidence for a spinal central pattern generator in humans. *Annals of the New York Academy of Sciences*, *860*, 360–376.

Donevan, A. H., Neuber-Hess, M., & Rose, P. K. (1990). Multiplicity of vestibulospinal projections to the upper cervical spinal cord of the cat: A study with the anterograde tracer Phaseolus vulgaris leucoagglutinin. *Journal of Comparative Neurology*, *302*(1), 1–14.

Dostrovsky, J. O., & Craig, A. D. (1996). Cooling-specific spinothalamic neurons in the monkey. *Journal of Neurophysiology*, *76*(6), 3656–3665.

Dougherty, K. J., Sawchuk, M. A., & Hochman, S. (2005). Properties of mouse spinal lamina I GABAergic interneurons. *Journal of Neurophysiology*, *94*(5), 3221–3227.

Douse, M. A., Duffin, J., Brooks, D., & Fedorko, L. (1992). Role of upper cervical inspiratory neurons studied by cross-correlation in the cat. *Experimental Brain Research*, *90*(1), 153–162.

Doyle, C. A., & Hunt, S. P. (1999). Substance P receptor (neurokinin-1)-expressing neurons in lamina I of the spinal cord encode for the intensity of noxious stimulation: A c-Fos study in rat. *Neuroscience*, *89*(1), 17–28.

Dum, R. P., & Strick, P. L. (1991). The origin of corticospinal projections from the premotor areas in the frontal lobe. *The Journal of Neuroscience*, *11*(3), 667–689.

Dutton, R. C., Carstens, M. I., Antognini, J. F., & Carstens, E. (2006). Long ascending propriospinal projections from lumbosacral to upper cervical spinal cord in the rat. *Brain Research*, *1119*, 76–85.

Eccles, J. C., Eccles, R. M., Iggo, A., & Lundberg, A. (1960). Electrophysiological studies on gamma motoneurones. *Acta Physiologica Scandinavica*, *50*(1), 32–40.

Eccles, J. C., Fatt, P., & Koketsu, K. (1954). Cholinergic and inhibitory synapses in a pathway from motor-axon collaterals to motoneurones. *The Journal of Physiology*, *126*(3), 524–562.

Edgley, S. A., & Gallimore, C. M. (1988). The morphology and projections of dorsal horn spinocerebellar tract neurones in the cat. *The Journal of Physiology*, *397*(1), 99–111.

Ekerot, C. F., Garwicz, M., & Schouenborg, J. (1991). The postsynaptic dorsal column pathway mediates cutaneous nociceptive information to cerebellar climbing fibres in the cat. *The Journal of Physiology*, *441*(1), 275–284.

Faull, R. L. M., & Villiger, J. W. (1986). Benzodiazepine receptors in the human spinal cord: A detailed anatomical and pharmacological study. *Neuroscience*, *17*(3), 791–802.

Faull, R. L. M., & Villiger, J. W. (1987). Opiate receptors in the human spinal cord: A detailed anatomical study comparing the autoradiographic localization of [3H]diprenorphine binding sites with the laminar pattern of substance P, myelin and nissl staining. *Neuroscience*, *20*(2), 395–407.

Field, M. J., Bramwell, S., Hughes, J., & Singh, L. (1999). Detection of static and dynamic components of mechanical allodynia in rat models of neuropathic pain: Are they signalled by distinct primary sensory neurones? *Pain*, *83*(2), 303–311.

Fields, H. L., Anderson, S. D., & Wagner, G. M. (1974). The spinoreticular tract: An alternate pathway mediating pain. *Transactions of the American Neurological Association*, *99*, 211–213.

Fields, H. L., Malick, A., & Burstein, R. (1995). Dorsal horn projection targets of ON and OFF cells in the rostral ventromedial medulla. *Journal of Neurophysiology*, *74*(4), 1742–1759.

Fisher, K. M., Garner, J. P., & Darian-Smith, C. (2020). Reorganization of the primate dorsal horn in response to a deafferentation lesion affecting hand function. *The Journal of Neuroscience*, *40*(8), 1625–1639.

Fisher, K. M., Lilak, A., Garner, J., & Darian-Smith, C. (2018). Extensive somatosensory and motor corticospinal sprouting occurs following a central dorsal column lesion in monkeys. *Journal of Comparative Neurology*, *526*(15), 2373–2387.

Fontes, R. B., Saad, F., Soares, M. S., de Oliveira, F., Pinto, F. C., & Liberti, E. A. (2006). Ultrastructural study of the filum terminale and its elastic fibers. *Neurosurgery*, *58*(5), 978–984.

Fregni, F., & Pascual-Leone, A. (2006). Hand motor recovery after stroke: Tuning the orchestra to improve hand motor function. *Cognitive and Behavioral Neurology*, *19*(1), 21–33.

Freund, P., Schmidlin, E., Wannier, T., Bloch, J., Mir, A., Schwab, M. E., & Rouiller, E. M. (2006). Nogo-A–specific antibody treatment enhances sprouting and functional recovery after cervical lesion in adult primates. *Nature Medicine*, *12*(7), 790–792.

Frigon, A. (2020). Chapter 13 - Fundamental contributions of the cat model to the neural control of locomotion. In P. J. Whelan & S. A. Sharples (Eds.), *The neural control of movement* (pp. 315–348). Academic Press.

Frostell, A., Hakim, R., Thelin, E. P., Mattsson, P., & Svensson, M. (2016). A review of the segmental diameter of the healthy human spinal cord. *Frontiers in Neurology*, *7*, 278.

Fukuhara, K., Imai, F., Ladle, D. R., Katayama, K., Leslie, J. R., Arber, S., Jessell, T. M., & Yoshida, Y. (2013). Specificity of monosynaptic sensory-motor connections imposed by repellent Sema3E-PlexinD1 signaling. *Cell Reports*, *5*(3), 748–758.

Fukushima, K., Peterson, B. W., Uchino, Y., Coulter, J. D., & Wilson, V. J. (1977). Direct fastigiospinal fibers in the cat. *Brain Research*, *126*(3), 538–542.

Fukushima, K., Pitts, N. G., & Peterson, B. W. (1978). Direct excitation of neck motoneurons by interstitiospinal fibers. *Experimental Brain Research*, *33*(3), 565–581.

Galhardo, V., & Lima, D. (1999). Structural characterization of marginal (lamina I) spinal cord neurons in the cat: A golgi study. *Journal of Comparative Neurology*, *414*(3), 315–333.

Garifoli, A., Maci, T., Perciavalle, V., & Perciavalle, V. (2006). Organization of bilateral spinal projections to the lateral reticular nucleus of the rat. *Archives Italiennes de Biologie*, *144*(3–4), 145–157.

Gassner, M., Leitner, J., Gruber-Schoffnegger, D., Forsthuber, L., & Sandkühler, J. (2013). Properties of spinal lamina III GABAergic neurons in naïve and in neuropathic mice. *European Journal of Pain*, *17*(8), 1168–1179.

Gdowski, G. T., & McCrea, R. A. (2000). Neck proprioceptive inputs to primate vestibular nucleus neurons. *Experimental Brain Research*, *135*(4), 511–526.

Gibson, S. J., Polak, J. M., Bloom, S. R., & Wall, P. D. (1981). The distribution of nine peptides in rat spinal cord with special emphasis on the substantia gelatinosa and on the area around the central canal (laminaX). *Journal of Comparative Neurology*, *201*(1), 65–79.

Giesler, G. J., & Cliffer, K. D. (1985). Postsynaptic dorsal column pathway of the rat. II. Evidence against an important role in nociception. *Brain Research*, *326*(2), 347–356.

Giesler, G. J., Nahin, R. L., & Madsen, A. M. (1984). Postsynaptic dorsal column pathway of the rat. I. Anatomical studies. *Journal of Neurophysiology*, *51*(2), 260–275.

Giovanelli Barilari, M., & Kuypers, H. G. J. M. (1969). Propriospinal fibers interconnecting the spinal enlargements in the cat. *Brain Research*, *14*(2), 321–330.

Giraudin, A., Le Bon-Jégo, M., Cabirol, M.-J., Simmers, J., & Morin, D. (2012). Spinal and pontine relay pathways mediating respiratory rhythm entrainment by limb proprioceptive inputs in the neonatal rat. *The Journal of Neuroscience*, *32*(34), 11841–11853.

Gobel, S. (1978). Golgi studies of the neurons in layer I of the dorsal horn of the medulla (trigeminal nucleus caudalis). *Journal of Comparative Neurology*, *180*(2), 375–393.

Gofrit, O. N., Yutkin, V., Pode, D., Duvdevani, M., Landau, E. H., Gielchinsky, I., & Hidas, G. (2019). A study of prostate volumes in patients with spinal cord injury. *Neurourology and Urodynamics*, *38*(2), 684–688.

Gondo, G., Watanabe, T., Kawada, J., Tanaka, M., Yamamoto, K., Tanaka, S., & Endo, S. (2016). A case of cervicogenic headache caused by C5 nerve root derived shwannoma: Case report. *Cephalalgia*, *37*(9), 902–905.

Granier, C., Schwarting, J., Fourli, E., Laage-Gaupp, F., Hennrich, A. A., Schmalz, A., Jacobi, A., Wesolowski, M., Conzelmann, K. K., & Bareyre, F. M. (2020). Formation of somatosensory detour circuits mediates functional recovery following dorsal column injury. *Scientific Reports*, *10*(1), 10953.

Griffin, J. M., & Bradke, F. (2020). Therapeutic repair for spinal cord injury: Combinatory approaches to address a multifaceted problem. *EMBO Molecular Medicine*, *12*(3), e11505.

Guirado, R., Carceller, H., Castillo-Gómez, E., Castrén, E., & Nacher, J. (2018). Automated analysis of images for molecular quantification in immunohistochemistry. *Heliyon*, *4*(6), e00669.

Haber, L. H., Moore, B. D., & Willis, W. D. (1982). Electrophysiological response properties of spinoreticular neurons in the monkey. *Journal of Comparative Neurology*, *207*(1), 75–84.

Haines, D. E., Mihailoff, G. A., & Yezierski, R. P. (2018). Chapter 9 - The spinal cord. In D. E. Haines & G. A. Mihailoff (Eds.), *Fundamental neuroscience for basic and clinical applications* (pp. 138–151). Elsevier.

Han, Z. S., Zhang, E. T., & Craig, A. D. (1998). Nociceptive and thermoreceptive lamina I neurons are anatomically distinct. *Nature Neuroscience*, *1*(3), 218–225.

Hancock, M. B. (1976). Cells of origin of hypothalamo-spinal projections in the rat. *Neuroscience Letters*, *3*(4), 179–184.

Hancock, M. B., & Peveto, C. A. (1979). A preganglionic autonomic nucleus in the dorsal gray commissure of the lumbar spinal cord of the rat. *Journal of Comparative Neurology*, *183*(1), 65–72.

Hand, P. J., & Van Winkle, T. (1977). The efferent connections of the feline nucleus cuneatus. *The Journal of Comparative Neurology*, *171*(1), 83–109.

Harding, E. K., Fung, S. W., & Bonin, R. P. (2020). Insights into spinal dorsal horn circuit function and dysfunction using optical approaches. *Frontiers in Neural Circuits*, *14*, 31.

Häring, M., Zeisel, A., Hochgerner, H., Rinwa, P., Jakobsson, J. E. T., Lönnerberg, P., la Manno, G., Sharma, N., Borgius, L., Kiehn, O., Lagerström, M. C., Linnarsson, S., & Ernfors, P. (2018). Neuronal atlas of the dorsal horn defines its architecture and links sensory input to transcriptional cell types. *Nature Neuroscience*, *21*(6), 869–880.

Harmann, P. A., Carlton, S. M., & Willis, W. D. (1988). Collaterals of spinothalamic tract cells to the periaqueductal gray: A fluorescent double-labeling study in the rat. *Brain Research*, *441*(1–2), 87–97.

Harrison, P. J., Jankowska, E., & Zytnicki, D. (1986). Lamina VIII interneurones interposed in crossed reflex pathways in the cat. *The Journal of Physiology*, *371*(1), 147–166.

Hayes, N. L., & Rustioni, A. (1981). Descending projections from brainstem and sensorimotor cortex to spinal enlargements in the cat. Single and double retrograde tracer studies. *Experimental Brain Research*, *41*(2), 89–107.

Heffner, R., & Masterton, B. (1975). Variation in form of the pyramidal tract and its relationship to digital dexterity. *Brain, Behavior and Evolution*, *12*(3), 161–200.

Heinke, B., Ruscheweyh, R., Forsthuber, L., Wunderbaldinger, G., & Sandkühler, J. (2004). Physiological, neurochemical and morphological properties of a subgroup of GABAergic spinal lamina II neurones identified by expression of green fluorescent protein in mice. *The Journal of Physiology*, *560*(1), 249–266.

Heise, C., & Kayalioglu, G. (2009). Chapter 6 - Cytoarchitecture of the spinal cord. In C. Watson, G. Paxinos, & G. Kayalioglu (Eds.), *The spinal cord* (pp. 64–93). Academic Press.

Hentall, I. D., Pinzon, A., & Noga, B. R. (2006). Spatial and temporal patterns of serotonin release in the rat's lumbar spinal cord

following electrical stimulation of the nucleus raphe magnus. *Neuroscience*, *142*(3), 893–903.

Holstege, G. (1987). Some anatomical observations on the projections from the hypothalamus to brainstem and spinal cord: An HRP and autoradiographic tracing study in the cat. *The Journal of Comparative Neurology*, *260*(1), 98–126.

Holstege, G. (1988). Brainstem-spinal cord projections in the cat, related to control of head and axial movements. *Reviews of Oculomotor Research*, *2*, 431–470.

Holstege, J. C., Dijken, H. V., Buijs, R. M., Goedknegt, H., Gosens, T., & Bongers, C. M. H. (1996). Distribution of dopamine immunoreactivity in the rat, cat, and monkey spinal cord. *Journal of Comparative Neurology*, *376*(4), 631–652.

Honda, C. N., & Lee, C. L. (1985). Immunohistochemistry of synaptic input and functional characterizations of neurons near the spinal central canal. *Brain Research.*, *343*(1), 120–128.

Honda, C. N., & Perl, E. R. (1985). Functional and morphological features of neurons in the midline region of the caudal spinal cord of the cat. *Brain Research*, *340*(2), 285–295.

Honey, C. M., Ivanishvili, Z., Honey, C. R., & Heran, M. K. S. (2019). Somatotopic organization of the human spinothalamic tract: In vivo computed tomography–guided mapping in awake patients undergoing cordotomy. *The Journal of Comparative Neurology*, *30*(5), 722–728.

Honeycutt, C. F., Kharouta, M., & Perreault, E. J. (2013). Evidence for reticulospinal contributions to coordinated finger movements in humans. *Journal of Neurophysiology*, *110*(7), 1476–1483.

Hong, J. S., Kim, J. M., & Kim, H. S. (2016). Correlation between ambulatory function and clinical factors in hemiplegic patients with intact single lateral corticospinal tract: A pilot study. *Medicine (Baltimore)*, *95*(31), e4360.

Hoskin, R. W., Fedorko, L. M., & Duffin, J. (1988). Projections from upper cervical inspiratory neurons to thoracic and lumbar expiratory motor nuclei in the cat. *Experimental Neurology*, *99*(3), 544–555.

Hossaini, M., French, P. J., & Holstege, J. C. (2007). Distribution of glycinergic neuronal somata in the rat spinal cord. *Brain Research.*, *1142*, 61–69.

Hunt, C. C., & Kuffler, S. W.. Further study of efferent small-nerve fibres to mammalian muscle spindles. Multiple spindle innervation and activity during contraction. *The Journal of Physiology.* 1951;*113*:283–97.

Hylden, J. L. K., Hayashi, H., & Bennett, G. J. (1986). Lamina I spinomesencephalic neurons in the cat ascend via the dorsolateral funiculi. *Somatosensory Research*, *4*(1), 31–41.

Hylden, J. L. K., Nahin, R. L., Traub, R. J., & Dubner, R. (1989). Expansion of receptive fields of spinal lamina I projection neurons in rats with unilateral adjuvant-induced inflammation: The contribution of dorsal horn mechanisms. *Pain*, *37*(2), 229–243.

Icenhour, A., Labrenz, F., Roderigo, T., Benson, S., & Elsenbruch, S. (2020). The role of chronic stress in normal visceroception: Insights from an experimental visceral pain study in healthy volunteers. *Frontiers in Psychiatry*, *11*, 107.

Ilg, W., Giese, M. A., Gizewski, E. R., Schoch, B., & Timmann, D. (2008). The influence of focal cerebellar lesions on the control and adaptation of gait. *Brain*, *131*(11), 2913–2927.

Illert, M., Lundberg, A., & Tanaka, R. (1977). Integration in descending motor pathways controlling the forelimb in the cat. 3. Convergence on propriospinal neurones transmitting disynaptic excitation from the corticospinal tract and other descending tracts. *Experimental Brain Research*, *29*(3–4), 323–346.

Ito, S., & Feldheim, D. A. (2018). The mouse superior colliculus: An emerging model for studying circuit formation and function. *Frontiers in Neural Circuits*, *12*, 10.

Jacobi, A., & Bareyre, F. M. (2015). Regulation of axonal remodeling following spinal cord injury. *Neural Regeneration Research*, *10*(10), 1555–1557.

Jang, S. H., Chang, C. H., Jung, Y. J., & Seo, Y. S. (2019). Recovery of an injured corticospinal tract via an unusual pathway in a stroke patient: Case report. *Medicine (Baltimore)*, *98*(7), e14307.

Jang, S. H., & Kwon, H. G. (2013). Deterioration of pre-existing hemiparesis due to injury of the ipsilateral anterior corticospinal tract. *BMC Neurology*, *13*(1), 53.

Jang, S. H., & Kwon, H. G. (2015). Change of the anterior corticospinal tract on the normal side of the brain in chronic stroke patients: Diffusion tensor imaging study. *Somatosensory & Motor Research*, *32*(1), 25–30.

Jang, S. H., Kwon, J. W., & Yeo, S. S. (2018). Three dimensional identification of medial and lateral vestibulospinal tract in the human brain: A diffusion tensor imaging study. *Frontiers in Human Neuroscience*, *12*, 229.

Jang, S. H., & Lee, S. J. (2019). Corticoreticular tract in the human brain: A mini review. *Frontiers in Neurology*, *10*, 11.

Jang, S. H., & Seo, J. P. (2021). Anatomical location of the spinothalamic tract in the subcortical white matter in the human brain: A diffusion tensor imaging study. *Clinical Anatomy*, *34*(5), 736–741.

Janig, W., & McLachlan, E. M. (1987). Organization of lumbar spinal outflow to distal colon and pelvic organs. *Physiological Reviews*, *67*(4), 1332–1404.

Jaumard, N. V., Leung, J., Gokhale, A. J., Guarino, B. B., Welch, W. C., & Winkelstein, B. A. (2015). Relevant anatomic and morphological measurements of the rat spine. *Spine*, *40*(20), E1084–E1092.

Jones, H. R., Burns, T., Aminoff, M. J., & Pomeroy, S. (2013). Part 1-Brain. In F. H. Netter (Ed.), *The Netter collection of medical illustrations: Nervous system*. Elsevier Health Sciences.

Jordan, L. M., & Schmidt, B. J. (2002). Chapter 10 - Propriospinal neurons involved in the control of locomotion: Potential targets for repair strategies? In L. McKerracher, G. Doucet, & S. Rossignol (Eds.), *Progress in Brain Research* (Vol. 137, pp. 125–139). Elsevier.

Joseph, P. J., & Reyes, M. R. (2014). Dorsal column myelopathy following intrathecal chemotherapy for acute lymphoblastic leukemia. *The Journal of Spinal Cord Medicine*, *37*(1), 107–113.

Juvin, L., Simmers, J., & Morin, D. (2005). Propriospinal circuitry underlying interlimb coordination in mammalian quadrupedal locomotion. *The Journal of Neuroscience*, *25*(25), 6025–6035.

Kanagalingam, S., & Miller, N. R. (2015). Horner syndrome: Clinical perspectives. *Eye and Brain*, *7*, 35–46.

Kang, Y., Ding, H., Zhou, H., Wei, Z., Liu, L., Pan, D., & Feng, S. Q. (2018). Epidemiology of worldwide spinal cord injury: A literature review. *Journal of Neurorestoratology*, *6*(1), 3.

Kanning, K. C., Kaplan, A., & Henderson, C. E. (2010). Motor neuron diversity in development and disease. *Annual Review of Neuroscience*, *33*(1), 409–440.

Kayalioglu, G. (2009a). Chapter 3 - The vertebral column and spinal meninges. In C. Watson, G. Paxinos, & G. Kayalioglu (Eds.), *The spinal cord* (pp. 17–36). Academic Press.

Kayalioglu, G. (2009b). Chapter 10 - Projections from the spinal cord to the brain. In C. Watson, G. Paxinos, & G. Kayalioglu (Eds.), *The spinal cord* (pp. 148–167). Academic Press.

Kayalioglu, G., Hariri, N., Govsa, F., Erdem, B., Peker, G., & Maiskii, V. (1996). Laminar distribution of the cells of origin of the spinocerebral pathways involved in nociceptive transmission and pain modulation in the rat. *Journal of Neurophysiology*, *28*(2-3), 111–118.

Kayalioglu, G., Robertson, B., Kristensson, K., & Grant, G. (1999). Nitric oxide synthase and interferon-gamma receptor immunoreactivities in relation to ascending spinal pathways to thalamus, hypothalamus, and the periaqueductal grey in the rat. *Somatosensory & Motor Research*, *16*(4), 280–290.

Kemplay, S. K., & Webster, K. E. (1986). A qualitative and quantitative analysis of the distributions of cells in the spinal cord and spinomedullary junction projecting to the thalamus of the rat. *Neuroscience*, *17*(3), 769–789.

Kerr, F. W. L. (1975). The ventral spinothalamic tract and other ascending systems of the ventral funiculus of the spinal cord. *The Journal of Comparative Neurology*, *159*(3), 335–355.

Kevetter, G. A., Haber, L. H., Yezierski, R. P., Chung, J. M., Martin, R. F., & Willis, W. D. (1982). Cells of origin of the spinoreticular tract in the monkey. *Journal of Comparative Neurology*, *207*(1), 61–74.

Kevetter, G. A., & Willis, W. D. (1983). Collaterals of spinothalamic cells in the rat. *The Journal of Comparative Neurology*, *215*(4), 453–464.

Kiehn, O. (2011). Development and functional organization of spinal locomotor circuits. *Current Opinion in Neurobiology*, *21*(1), 100–109.

Kim, M., Fontelonga, T., Roesener, A. P., Lee, H., Gurung, S., Mendonca, P. R. F., & Mastick, G. S. (2015). Motor neuron cell bodies are actively positioned by Slit/Robo repulsion and Netrin/DCC attraction. *Developmental Biology*, *399*(1), 68–79.

Kim, S., Lee, H.-S., & Kim, J. S. (2010). Medial vestibulospinal tract lesions impair sacculo-collic reflexes. *Journal of Neurology*, *257* (5), 825–832.

Kim, Y. H., Sung, H. J., Bong, S. H., Kwon, Y. H., You, S. H., Byun, W. M., Park, J. W., & Yoo, W. K. (2004). Ipsilateral motor pathway confirmed by diffusion tensor tractography in a patient with schizencephaly. *Neuroreport*, *15*(12), 1899–1902.

Kitai, S. T., & Weinberg, J. (1968). Tactile discrimination study of the dorsal column-medial lemniscal system and spino-cervicothalamic tract in cat. *Experimental Brain Research*, *6*(3), 234–246.

Kobayashi, S., Fujito, Y., Matsuyama, K., & Aoki, M. (2010). Spontaneous respiratory rhythm generation in in vitro upper cervical slice preparations of neonatal mice. *The Journal of Physiological Sciences*, *60*(4), 303–307.

Koch, S. C., Acton, D., & Goulding, M. (2018). Spinal circuits for touch, pain, and itch. *Annual Review of Physiology*, *80*(1), 189–217.

Konczak, J., Schoch, B., Dimitrova, A., Gizewski, E., & Timmann, D. (2005). Functional recovery of children and adolescents after cerebellar tumour resection. *Brain*, *128*(Pt 6), 1428–1441.

Krassioukov, A. V., Bunge, R. P., Pucket, W. R., & Bygrave, M. A. (1999). The changes in human spinal sympathetic preganglionic neurons after spinal cord injury. *Spinal Cord*, *37*(1), 6–13.

Krukoff, T. L., Ciriello, J., & Calaresu, F. R. (1986). Somatostatin-like immunoreactivity in neurons, nerve terminals, and fibers of the cat spinal cord. *Journal of Comparative Neurology*, *243* (1), 13–22.

Krutki, P., Grottel, K., & Mrówczyński, W. (1998). Cervical and cerebellar projections of lamina VII and VIII neurones of the S2 segment in the cat's spinal cord. *Archives Italiennes de Biologie*, *136*(3), 181–189.

Küchler, M., Fouad, K., Weinmann, O., Schwab, M. E., & Raineteau, O. (2002). Red nucleus projections to distinct motor neuron pools in the rat spinal cord. *Journal of Comparative Neurology*, *448*(4), 349–359.

Kuypers, H. G. J. M., & Brinkman, J. (1970). Precentral projections to different parts of the spinal intermediate zone in the rhesus monkey. *Brain Research*, *24*(1), 29–48.

Kwon, H. G., Lee, D. G., Son, S. M., Byun, W. M., Hong, C. P., Lee, D. H., Kim, S., & Jang, S. H. (2011). Identification of the anterior corticospinal tract in the human brain using diffusion tensor imaging. *Neuroscience Letters*, *505*(3), 238–241.

Kwon, M., Je, B.-K., Hong, D., & Choi, B. M. (2018). Ultrasonographic features of the normal filum terminale. *Ultrasonography*, *37*(2), 129–133.

Lacroix, S., Havton, L. A., McKay, H., Yang, H., Brant, A., Roberts, J., & Tuszynski, M. H. (2004). Bilateral corticospinal projections arise from each motor cortex in the macaque monkey: A quantitative study. *Journal of Comparative Neurology*, *473*(2), 147–161.

Lai, H. C., Seal, R. P., & Johnson, J. E. (2016). Making sense out of spinal cord somatosensory development. *Development (Cambridge, England)*, *143*(19), 3434–3448.

LaMotte, C. C. (1988). Lamina X of primate spinal cord: Distribution of five neuropeptides and serotonin. *Neuroscience*, *25*(2), 639–658.

Lamotte, C. C., Kapadia, S. E., & Shapiro, C. M. (1991). Central projections of the sciatic, saphenous, median, and ulnar nerves of the rat demonstrated by transganglionic transport of cholera-genoid-HRP (B-HRP) and wheat germ agglutinin-HRP (WGA-HRP). *Journal of Comparative Neurology*, *311*(4), 546–562.

Laumonnerie, C., Tong, Y. G., Alstermark, H., & Wilson, S. I. (2015). Commissural axonal corridors instruct neuronal migration in the mouse spinal cord. *Nature Communications*, *6*(1), 7028.

Lee, J. W., Siegel, S. M., & Oaklander, A. L. (2009). Effects of distal nerve injuries on dorsal-horn neurons and glia: Relationships between lesion size and mechanical hyperalgesia. *Neuroscience*, *158*(2), 904–914.

Lemon, R. N. (2008). Descending pathways in motor control. *Annual Review of Neuroscience (Palo Alto, CA)*, *31*(1), 195–218.

Leonard, A. V., Menendez, J. Y., Pat, B. M., Hadley, M. N., & Floyd, C. L. (2017). Localization of the corticospinal tract within the porcine spinal cord: Implications for experimental

modeling of traumatic spinal cord injury. *Neuroscience Letters*, *648*, 1–7.

Liang, H., Paxinos, G., & Watson, C. (2011). Projections from the brain to the spinal cord in the mouse. *Brain Structure and Function*, *215*(3), 159–186.

Liang, H., Schofield, E., & Paxinos, G. (2016). Imaging serotonergic fibers in the mouse spinal cord using the CLARITY/CUBIC technique. *JoVE*, *108*, e53673.

Liang, H., Wang, S., Francis, R., Whan, R., Watson, C., & Paxinos, G. (2015). Distribution of raphespinal fibers in the mouse spinal cord. *Molecular Pain*, *11*, 42.

Liao, C.-C., DiCarlo, G. E., Gharbawie, O. A., Qi, H.-X., & Kaas, J. H. (2015). Spinal cord neuron inputs to the cuneate nucleus that partially survive dorsal column lesions: A pathway that could contribute to recovery after spinal cord injury. *Journal of Comparative Neurology*, *523*(14), 2138–2160.

Light, A. R., & Metz, C. B. (1978). The morphology of the spinal cord efferent and afferent neurons contributing to the ventral roots of the cat. *Journal of Comparative Neurology*, *179*(3), 501–515.

Light, A. R., & Perl, E. R. (1979). Reexamination of the dorsal root projection to the spinal dorsal horn including observations on the differential termination of coarse and fine fibers. *Journal of Comparative Neurology*, *186*(2), 117–131.

Light, A. R., Trevino, D. L., & Perl, E. R. (1979). Morphological features of functionally defined neurons in the marginal zone and substantia gelatinosa of the spinal dorsal horn. *Journal of Comparative Neurology*, *186*(2), 151–171.

Lima, D., Avelino, A., & Coimbra, A. (1993). Morphological characterization of marginal (lamina I) neurons immunoreactive for substance P, enkephalin, dynorphin and gamma-aminobutyric acid in the rat spinal cord. *Journal of Chemical Neuroanatomy*, *6*(1), 43–52.

Lima, D., & Coimbra, A. (1986). A Golgi study of the neuronal population of the marginal zone (lamina I) of the rat spinal cord. *The Journal of Comparative Neurology*, *244*(1), 53–71.

Lindau, N. T., Bänninger, B. J., Gullo, M., Good, N. A., Bachmann, L. C., Starkey, M. L., & Schwab, M. E. (2014). Rewiring of the corticospinal tract in the adult rat after unilateral stroke and anti-Nogo-A therapy. *Brain*, *137*(3), 739–756.

Lipski, J., Duffin, J., Kruszewska, B., & Zhang, X. (1993). Upper cervical inspiratory neurons in the rat: An electrophysiological and morphological study. *Experimental Brain Research*, *95*(3), 477–487.

Liu, R. P. C. (1983). Laminar origins of spinal projection neurons to the periaqueductal gray of the rat. *Brain Research*, *264*(1), 118–122.

Loewy, A. D. (1970). A study of neuronal types in clarke's column in the adult cat. *Journal of Comparative Neurology*, *139*(1), 53–79.

Logan, S. M., Romero, M. I., Nguyen, D. H., & Benson, M. D. (2013). Ephrin-B2 expression in the proprioceptive sensory system. *Neuroscience Letters*, *545*, 69–74.

Loutit, A. J., & Potas, J. R. (2020). Restoring Somatosensation: Advantages and current limitations of targeting the brainstem dorsal column nuclei complex. *Frontiers in Neuroscience*, *14*, 156.

Macefield, V. G., & Knellwolf, T. P. (2018). Functional properties of human muscle spindles. *Journal of Neurophysiology*, *120*(2), 452–467.

MacKinnon, C. D. (2018). Chapter 1 - Sensorimotor anatomy of gait, balance, and falls. In B. L. Day & S. R. Lord (Eds.), *Handbook of clinical neurology* (Vol. 159, pp. 3–26). Elsevier.

MacLean, J. N., Hochman, S., & Magnuson, D. S. (1995). Lamina VII neurons are rhythmically active during locomotor-like activity in the neonatal rat spinal cord. *Neuroscience Letters*, *197*(1), 9–12.

Madhavan, S., Rogers, L. M., & Stinear, J. W. (2010). A paradox: After stroke, the non-lesioned lower limb motor cortex may be maladaptive. *European Journal of Neuroscience*, *32*(6), 1032–1039.

Maeda, K., Saikyo, M., Mukose, A., Tomimatsu, H., & Yasuda, H. (2005). Lateropulsion due to a lesion of the dorsal spinocerebellar tract. *Internal Medicine*, *44*(12), 1295–1297.

Mantyh, P. W., Rogers, S. D., Honore, P., Allen, B. J., Ghilardi, J. R., Li, J., Daughters, R. S., Lappi, D. A., Wiley, R. G., & Simone, D. A. (1997). Inhibition of hyperalgesia by ablation of lamina I spinal neurons expressing the substance P receptor. *Science*, *278*(5336), 275–279.

Maric, D., Jahanipour, J., Li, X. R., Singh, A., Mobiny, A., Van Nguyen, H., Sedlock, A., Grama, K., & Roysam, B. (2021). Whole-brain tissue mapping toolkit using large-scale highly multiplexed immunofluorescence imaging and deep neural networks. *Nature Communications*, *12*(1), 1550.

Marshall, R. S., Perera, G. M., Lazar, R. M., Krakauer, J. W., Constantine, R. C., & DeLaPaz, R. L. (2000). Evolution of cortical activation during recovery from corticospinal tract infarction. *Stroke*, *31*(3), 656–661.

Martin, G. F., & Dom, R. (1970). The rubro-spinal tract of the opossum (*Didelphis virginiana*). *Journal of Comparative Neurology*, *138*(1), 19–29.

Masakado, Y. (1994). Motor unit firing behavior in man. *The Keio Journal of Medicine*, *43*(3), 137–142.

Massion, J. (1967). The mammalian red nucleus. *Physiological Reviews*, *47*(3), 383–436.

Masson, R. L., Jr., Sparkes, M. L., & Ritz, L. A. (1991). Descending projections to the rat sacrocaudal spinal cord. *Journal of Comparative Neurology*, *307*(1), 120–130.

Mather, C. S., & Ho, R. H. (1992). Golgi impregnated somatostatin immunoreactive neurons in lamina II of the rat spinal cord. *Brain Research Bulletin*, *28*(2), 305–309.

Matsushita, M. (1970). The axonal pathways of spinal neurons in the cat. *Journal of Comparative Neurology*, *138*(4), 391–417.

Matsushita, M. (1991). Cerebellar projections of the central cervical nucleus in the rat: An anterograde tracing study. *Neuroscience Research*, *12*(1), 201–216.

Matsushita, M. (1998). Ascending propriospinal afferents to area X (substantia grisea centralis) of the spinal cord in the rat. *Experimental Brain Research*, *119*(3), 356–366.

Matsushita, M., & Gao, X. (1997). Projections from the thoracic cord to the cerebellar nuclei in the rat, studied by anterograde axonal tracing. *The Journal of Comparative Neurology*, *386*(3), 409–421.

Matsushita, M., Gao, X., & Yaginuma, H. (1995). Spinovestibular projections in the rat, with particular reference to projections from the central cervical nucleus to the lateral vestibular nucleus. *Journal of Comparative Neurology*, *361*(2), 334–344.

Matsushita, M., & Hosoya, Y. (1978). The location of spinal projection neurons in the cerebellar nuclei (cerebellospinal tract

neurons) of the cat. A study with the horseradish peroxidase technique. *Brain Research*, *142*(2), 237–248.

Matsushita, M., & Hosoya, Y. (1979). Cells of origin of the spinocerebellar tract in the rat, studied with the method of retrograde transport of horseradish peroxidase. *Brain Research*, *173*(2), 185–200.

Matsushita, M., Hosoya, Y., & Ikeda, M. (1979). Anatomical organization of the spinocerebellar system in the cat, as studied by retrograde transport of horseradish peroxidase. *Journal of Comparative Neurology*, *184*(1), 81–105.

Matsushita, M., & Xiong, G. (1997). Projections from the cervical enlargement to the cerebellar nuclei in the rat, studied by anterograde axonal tracing. *The Journal of Comparative Neurology*, *377*(2), 251–261.

Matsushita, M., Yaginuma, H., & Tanami, T. (1992). Somatotopic termination of the spino-olivary fibers in the cat, studied with the wheat germ agglutinin-horseradish peroxidase technique. *Experimental Brain Research*, *89*(2), 397–407.

Matsuyama, K., Nakajima, K., Mori, F., Aoki, M., & Mori, S. (2004). Lumbar commissural interneurons with reticulospinal inputs in the cat: Morphology and discharge patterns during fictive locomotion. *Journal of Comparative Neurology*, *474*(4), 546–561.

Maxwell, D. J. (1985). Combined light and electron microscopy of Golgi-labelled neurons in lamina III of the feline spinal cord. *Journal of Anatomy*, *141*, 155–169.

Maxwell, D. J., & Bannatyne, B. A. (1983). Ultrastructure of muscle spindle afferent terminations in lamina VI of the cat spinal cord. *Brain Research*, *288*(1), 297–301.

Maxwell, D. J., Fyffe, R. E. W., & Rethelyi, M. (1983). Morphological properties of physiologically characterized lamina III neurones in the cat spinal cord. *Neuroscience*, *10*(1), 1–22.

May, P. J., Bohlen, M. O., Perkins, E., Wang, N., & Warren, S. (2021). Superior colliculus projections to target populations in the supraoculomotor area of the macaque monkey. *Visual Neuroscience*, *38*, E017.

May, Z., Fenrich, K. K., Dahlby, J., Batty, N. J., Torres-Espín, A., & Fouad, K. (2017). Following spinal cord injury transected reticulospinal tract axons develop new collateral inputs to Spinal interneurons in parallel with locomotor recovery. *Neural Plasticity*, *2017*, 1932875.

McCann, M. M., Fisher, K. M., Ahloy-Dallaire, J., & Darian-Smith, C. (2020). Somatosensory corticospinal tract axons sprout within the cervical cord following a dorsal root/dorsal column spinal injury in the rat. *Journal of Comparative Neurology*, *528*(8), 1293–1306.

McCotter, R. E. (1916). Regarding the length and extent of the human medulla spinalis. *The Anatomical Record*, *10*(9), 559–564.

McCurdy, M. L., Hansma, D. I., Houk, J. C., & Gibson, A. R. (1987). Selective projections from the cat red nucleus to digit motor neurons. *Journal of Comparative Neurology*, *265*(3), 367–379.

McDougal, D. H., & Gamlin, P. D. R. (2008). Chapter 1.26 - Pupillary control pathways. In: R. H. Masland, T. D. Albright, P. Dallos, D. Oertel, S. Firestein, G. K. Beauchamp, M. Catherine Bushnell, A. I. Basbaum, J. H. Kaas, & E. P. Gardner (Eds.), *The senses: A comprehensive reference* (521–36). Academic Press.

McKenna, J. E., & Whishaw, I. Q. (1999). Complete compensation in skilled reaching success with associated impairments in limb synergies, after dorsal column lesion in the rat. *The Journal of Neuroscience*, *19*(5), 1885–1894.

Mehler, W. R., Feferman, M. E., & Nauta, W.-J. H. (1960). Ascending axon degeneraton following anterolateral cordotomy. An experimental study in the monkey. *Brain*, *83*(4), 718–750.

Melzack, R., & Wall, P. D. (1965). Pain mechanisms: A new theory. *Science*, *150*(3699), 971–979.

Mendelsohn, A. I., Dasen, J. S., & Jessell, T. M. (2017). Divergent Hox coding and evasion of retinoid signaling specifies motor neurons innervating digit muscles. *Neuron*, *93*(4), 792–805 e4.

Menétrey, D., & de Pommery, J. (1991). Origins of spinal ascending pathways that reach central areas involved in visceroception and visceronociception in the rat. *European Journal of Neuroscience*, *3*(3), 249–259.

Menétrey, D., Gannon, A., Levine, J. D., & Basbaum, A. I. (1989). Expression of c-fos protein in interneurons and projection neurons of the rat spinal cord in response to noxious somatic, articular, and visceral stimulation. *Journal of Comparative Neurology*, *285*(2), 177–195.

Menétrey, D., Roudier, F., & Besson, J. M. (1983). Spinal neurons reaching the lateral reticular nucleus as studied in the rat by retrograde transport of horseradish peroxidase. *Journal of Comparative Neurology*, *220*(4), 439–452.

Merighi, A. (2018). The histology, physiology, neurochemistry and circuitry of the substantia gelatinosa Rolandi (lamina II) in mammalian spinal cord. *Progress in Neurobiology*, *169*, 91–134.

Merkul'eva, N. S., Veshchitskii, A. A., Shkorbatova, P. Y., Shenkman, B. S., Musienko, P. E., & Makarov, F. N. (2017). Morphometric characteristics of the dorsal nuclei of Clarke in the rostral segments of the lumbar part of the Spinal cord on cats. *Neuroscience and Behavioral Physiology*, *47*(7), 851–856.

Merrill, E. G., & Lipski, J. (1987). Inputs to intercostal motoneurons from ventrolateral medullary respiratory neurons in the cat. *Journal of Neurophysiology*, *57*(6), 1837–1853.

Michael, F. M., Patel, S. P., & Rabchevsky, A. G. (2019). Intraspinal plasticity associated with the development of autonomic dysreflexia after complete spinal cord injury. *Frontiers in Cellular Neuroscience*, *13*, 505.

Michaloudi, H., Dinopoulos, A., Karamanlidis, A. N., Papadopoulos, G. C., & Antonopoulos, J. (1988). Cortical and brain stem projections to the spinal cord of the hedgehog (*Erinaceus europaeus*). A horseradish peroxidase study. *Anatomy and Embryology*, *178*(3), 259–270.

Millan, M. J. (1999). The induction of pain: An integrative review. *Progress in Neurobiology*, *57*(1), 1–164.

Miller, D. M., DeMayo, W. M., Bourdages, G. H., Wittman, S. R., Yates, B. J., & McCall, A. A. (2017). Neurons in the pontomedullary reticular formation receive converging inputs from the hindlimb and labyrinth. *Experimental Brain Research*, *235*(4), 1195–1207.

Miller, M. W. (1987). The origin of corticospinal projection neurons in rat. *Experimental Brain Research*, *67*(2), 339–351.

Miranda, C. O., Hegedüs, K., Wildner, H., Zeilhofer, H. U., & Antal, M. (2021). Morphological and neurochemical characterization of glycinergic neurons in laminae I–IV of the mouse spinal dorsal horn. *Journal of Comparative Neurology*, *530*(3), 607–626.

Miranpuri Gurwattan, S., Schomberg Dominic, T., Stan, P., Chopra, A., Buttar, S., Wood, A., Radzin, A., Meudt, J. J.,

Resnick, D. K., & Shanmuganayagam, D. (2018). Comparative morphometry of the Wisconsin miniature SwineTM thoracic spine for modeling human spine in translational Spinal cord injury research. *Annals of Neurosciences*, *25*(4), 210–218.

Mizuno, N., Nakano, K., Imaizumi, M., & Okamoto, M. (1967). The lateral cervical nucleus of the Japanese monkey (*Macaca fuscata*). *Journal of Comparative Neurology*, *129*(4), 375–383.

Mohan, R., Tosolini, A. P., & Morris, R. (2015). Segmental distribution of the motor neuron columns that supply the rat hindlimb: A muscle/motor neuron tract-tracing analysis targeting the motor end plates. *Neuroscience*, *307*, 98–108.

Molander, C., Xu, Q., & Grant, G. (1984). The cytoarchitectonic organization of the spinal cord in the rat. I. The lower thoracic and lumbosacral cord. *Journal of Comparative Neurology*, *230*(1), 133–141.

Molander, C., Xu, Q., Rivero-Melian, C., & Grant, G. (1989). Cytoarchitectonic organization of the spinal cord in the rat: II. The cervical and upper thoracic cord. *Journal of Comparative Neurology*, *289*(3), 375–385.

Molenaar, I., & Kuypers, H. G. J. M. (1978). Cells of origin of propriospinal fibers and of fibers ascending to supraspinal levels. A HRP study in cat and rhesus monkey. *Brain Research*, *152*(3), 429–450.

Morecraft, R. J., Ge, J., Stilwell-Morecraft, K. S., McNeal, D. W., Pizzimenti, M. A., & Darling, W. G. (2013). Terminal distribution of the corticospinal projection from the hand/arm region of the primary motor cortex to the cervical enlargement in rhesus monkey. *The Journal of Comparative Neurology*, *521*(18), 4205–4235.

Morrell, J. I., & Pfaff, D. W. (1983). Retrograde hrp identification of neurons in the rhombencephalon and spinal cord of the rat that project to the dorsal mesencephalon. *American Journal of Anatomy*, *167*(2), 229–240.

Mouton, L. J., & Holstege, G. (1994). The periaqueductal gray in the cat projects to lamina VIII and the medial part of lamina VII throughout the length of the spinal cord. *Experimental Brain Research*, *101*(2), 253–264.

Mtui, E. P., Anwar, M., Gomez, R., Reis, D. J., & Ruggiero, D. A. (1993). Projections from the nucleus tractus solitarii to the spinal cord. *The Journal of Comparative Neurology*, *337*(2), 231–252.

Muir, G. D., & Whishaw, I. Q. (1999). Complete locomotor recovery following corticospinal tract lesions: Measurement of ground reaction forces during overground locomotion in rats. *Behavioural Brain Research*, *103*(1), 45–53.

Murray, H. M., & Gurule, M. E. (1979). Origin of the rubrospinal tract of the rat. *Neuroscience Letters*, *14*(1), 19–23.

Nadeau, S., Jacquemin, G., Fournier, C., Lamarre, Y., & Rossignol, S. (2010). Spontaneous motor rhythms of the back and legs in a patient with a complete spinal cord transection. *Neurorehabilitation and Neural Repair*, *24*(4), 377–383.

Naderi, S., Türe, U., & Pait, T. G. (2004). History of the spinal cord localization. *Neurosurgical Focus*, *16*(1), E15.

Nadklhaft, I., & McKenna, K. E. (1987). Sexual dimorphism in sympathetic preganglionic neurons of the rat hypogastric nerve. *Journal of Comparative Neurology*, *256*(2), 308–315.

Nahin, R. L., & Micevych, P. E. (1986). A long ascending pathway of enkephalin-like immunoreactive spinoreticular neurons in the rat. *Neuroscience Letters*, *65*(3), 271–276.

Nathan, P. W., Smith, M. C., & Deacon, P. (1990). The corticospinal tracts in man. Course and location of fibres at different segmental levels. *Brain*, *113*(Pt 2), 303–324.

Nauta, H. J. W., Hewitt, E., Westlund, K. N., & Willis, W. D. (1997). Surgical interruption of a midline dorsal column visceral pain pathway: Case report and review of the literature. *Journal of Neurosurgery*, *86*(3), 538–542.

Nauta, H. J. W., Soukup, V. M., Fabian, R. H., Lin, J. T., Grady, J. J., Williams, C. G. A., Campbell, G. A., Westlund, K. N., & Willis, W. D. (2000). Punctate midline myelotomy for the relief of visceral cancer pain. *The Journal of Comparative Neurology*, *92*(2), 125–130.

Netz, J., Lammers, T., & Hömberg, V. (1997). Reorganization of motor output in the non-affected hemisphere after stroke. *Brain*, *120*(9), 1579–1586.

Nicholas, D. S., & Weller, R. O. (1988). The fine anatomy of the human spinal meninges: A light and scanning electron microscopy study. *Journal of Neurosurgery*, *69*(2), 276–282.

Nijssen, J., Comley, L. H., & Hedlund, E. (2017). Motor neuron vulnerability and resistance in amyotrophic lateral sclerosis. *Acta Neuropathologica*, *133*(6), 863–885.

Niu, J., Ding, L., Li, J. J., Kim, H., Liu, J., Li, H., Moberly, A., Badea, T. C., Duncan, I. D., Son, Y. J., Scherer, S. S., & Luo, W. (2013). Modality-based organization of ascending somatosensory axons in the direct dorsal column pathway. *The Journal of Neuroscience*, *33*(45), 17691–17709.

Nógrádi, A., & Vrbová, G. (2006). Anatomy and physiology of the spinal cord. In A. Nógrádi (Ed.), *Transplantation of neural tissue into the spinal cord* (pp. 1–23). Springer US.

Nudo, R. J., & Masterton, R. B. (1989). Descending pathways to the spinal cord: II. Quantitative study of the tectospinal tract in 23 mammals. *The Journal of Comparative Neurology*, *286*(1), 96–119.

Nudo, R. J., & Masterton, R. B. (1990a). Descending pathways to the spinal cord, III: Sites of origin of the corticospinal tract. *Journal of Comparative Neurology*, *296*(4), 559–583.

Nudo, R. J., & Masterton, R. B. (1990b). Descending pathways to the spinal cord, IV: Some factors related to the amount of cortex devoted to the corticospinal tract. *Journal of Comparative Neurology*, *296*(4), 584–597.

Nyberg, G., & Blomqvist, A. (1984). The central projection of muscle afferent fibres to the lower medulla and upper spinal cord: An anatomical study in the cat with the transganglionic transport method. *The Journal of Comparative Neurology*, *230*(1), 99–109.

Nyberg-Hansen, R. (1964). The location and termination of tectospinal fibers in the cat. *Experimental Neurology*, *9*(3), 212–227.

Nyberg-hansen, R. (1965). Sites and mode of termination of reticulo-spinal fibers in the cat. An experimental study with silver impregnation methods. *Journal of Comparative Neurology*, *124*(1), 71–99.

Nyberg-Hansen, R. (1966). Functional organization of descending supraspinal fibre systems to the spinalcord. Anatomical observations and physiological correlations. *Ergebnisse der Anatomie und Entwicklungsgeschichte*, *39*(2), 3–48.

Nyberg-Hansen, R., & Brodal, A. (1963). Sites of termination of corticospinal fibers in the cat. An experimental study with silver impregnation methods. *Journal of Comparative Neurology*, *120*(3), 369–391.

Olivier, E., Kitama, T., & Grantyn, A. (1994). Anatomical evidence for ipsilateral collicular projections to the spinal cord in the cat. *Experimental Brain Research*, *100*(1), 160–164.

Orendáčová, J., Čížková, D., Kafka, J., Lukáčová, N., Maršala, M., Šulla, I., Maršala, J., & Katsube, N. (2001). Cauda equina syndrome. *Progress in Neurobiology*, *64*(6), 613–637.

Oscarsson, O., & Sjölund, B. (1977). The ventral spino-olivocerebellar system in the cat. III. Functional characteristics of the five paths. *Experimental Brain Research*, *28*(5), 505–520.

Otsuka, N., Miyashita, K., Krieger, D. W., & Naritomi, H. (2013). Compensatory contribution of the contralateral pyramidal tract after stroke. *Frontiers of Neurology and Neuroscience*, *32*, 45–53.

Özyurt, M. G., Piotrkiewicz, M., Topkara, B., Weisskircher, H. W., & Türker, K. S. (2019). Motor units as tools to evaluate profile of human Renshaw inhibition. *The Journal of Physiology*, *597*(8), 2185–2199.

Padula, W. V., Capo-Aponte, J. E., Padula, W. V., Singman, E. L., & Jenness, J. (2017). The consequence of spatial visual processing dysfunction caused by traumatic brain injury (TBI). *Brain Injury*, *31*(5), 589–600.

Pan, Y.-Z., & Pan, H.-L. (2004). Primary afferent stimulation differentially potentiates excitatory and inhibitory inputs to spinal lamina II outer and inner neurons. *Journal of Neurophysiology*, *91*(6), 2413–2421.

Patterson, J. T., Chung, K., & Coggeshall, R. E. (1992). Further evidence for the existence of long ascending unmyelinated primary afferent fibers within the dorsal funiculus: Effects of capsaicin. *Pain*, *49*(1), 117–120.

Pauvert, V., Pierrot-Deseilligny, E., & Rothwell, J. C. (1998). Role of spinal premotoneurones in mediating corticospinal input to forearm motoneurones in man. *The Journal of Physiology*, *508*(1), 301–312.

Pecho-Vrieseling, E., Sigrist, M., Yoshida, Y., Jessell, T. M., & Arber, S. (2009). Specificity of sensory–motor connections encoded by Sema3e–Plxnd1 recognition. *Nature*, *459*(7248), 842–846.

Peschanski, M., & Besson, J. M. (1984). A spino-reticulo-thalamic pathway in the rat: An anatomical study with reference to pain transmission. *Neuroscience*, *12*(1), 165–178.

Peters, D. M., Fridriksson, J., Richardson, J. D., Stewart, J. C., Rorden, C., Bonilha, L., Middleton, A., & Fritz, S. L. (2021). Upper and lower limb motor function correlates with Ipsilesional corticospinal tract and red nucleus structural integrity in chronic stroke: A cross-sectional, ROI-based MRI study. *Behavioural Neurology*, *2021*, 3010555.

Peterson, B. W. (1979). Reticulospinal projections to spinal motor nuclei. *Annual Review of Physiology*, *41*, 127–140.

Peterson, B. W., Maunz, R. A., Pitts, N. G., & Mackel, R. G. (1975). Patterns of projection and branching of reticulospinal neurons. *Experimental Brain Research*, *23*(4), 333–351.

Petras, J. M. (1969). Some efferent connections of the motor and somatosensory cortex of simian primates and felid, canid, and procyonid carnivores. *Annals of the New York Academy of Sciences*, *167*(1), 469–505.

Petterson, B. W., & Coulter, J. D. (1977). A new long spinal projection from the vestibular nuclei in the cat. *Brain Research*, *122*(2), 351–356.

Pettorossi, V. E., & Schieppati, M. (2014). Neck proprioception shapes body orientation and perception of motion. *Frontiers in Human Neuroscience*, *8*, 895.

Pocratsky, A. M., Shepard, C. T., Morehouse, J. R., Burke, D. A., Riegler, A. S., Hardin, J. T., Beare, J. E., Hainline, C., States, G. J. R., Brown, B. L., Whittemore, S. R., & Magnuson, D. S. K. (2020). Long ascending propriospinal neurons provide flexible, context-specific control of interlimb coordination. *eLife*, *9*, e53565.

Pop, I. V., Espinosa, F., Blevins, C. J., Okafor, P. C., Ogujiofor, O. W., Goyal, M., Mona, B., Landy, M. A., Dean, K. M., Gurumurthy, C. B., & Lai, H. C. (2022). Structure of long-range direct and indirect spinocerebellar pathways as well as local spinal circuits mediating proprioception. *The Journal of Neuroscience*, *42*(4), 581–600.

Powell, J. J., & Todd, A. J. (1992). Light and electron microscope study of GABA-immunoreactive neurones in lamina III of rat spinal cord. *Journal of Comparative Neurology*, *315*(2), 125–136.

Powis, R. A., & Gillingwater, T. H. (2016). Selective loss of alpha motor neurons with sparing of gamma motor neurons and spinal cord cholinergic neurons in a mouse model of spinal muscular atrophy. *Journal of Anatomy*, *228*(3), 443–451.

Prentice, S. D., & Drew, T. (2001). Contributions of the reticulospinal system to the postural adjustments occurring during voluntary gait modifications. *Journal of Neurophysiology*, *85*(2), 679–698.

Prescott, S. A., & Koninck, Y. D. (2002). Four cell types with distinctive membrane properties and morphologies in lamina I of the spinal dorsal horn of the adult rat. *The Journal of Physiology*, *539*(3), 817–836.

Price, T. J., & Prescott, S. A. (2015). Inhibitory regulation of the pain gate and how its failure causes pathological pain. *Pain*, *156*(5), 789–792.

Prichard, J. W. (2014). Overview of automated immunohistochemistry. *Archives of Pathology & Laboratory Medicine*, *138*(12), 1578–1582.

Przewłocki, R., Gramsch, C., Pasi, A., & Herz, A. (1983). Characterization and localization of immunoreactive dynorphin, α-neoendorphin, met-enkephalin and substance P in human spinal cord. *Brain Research*, *280*(1), 95–103.

Qin, C., Chandler, M. J., Foreman, R. D., & Farber, J. P. (2002). Upper thoracic respiratory interneurons integrate noxious somatic and visceral information in rats. *Journal of Neurophysiology*, *88*(5), 2215–2223.

Ralston, D. D., & Ralston, H. J., III. (1985). The terminations of corticospinal tract axons in the macaque monkey. *Journal of Comparative Neurology*, *242*(3), 325–337.

Ralston, H. J., III. (1982). The fine structure of laminae IV, V, and VI of the macaque spinal cord. *Journal of Comparative Neurology*, *212*(4), 425–434.

Raybaud, C. (2010). The corpus callosum, the other great forebrain commissures, and the septum pellucidum: Anatomy, development, and malformation. *Neuroradiology*, *52*(6), 447–477.

Redgrave, P., Mitchell, I. J., & Dean, P. (1987). Descending projections from the superior colliculus in rat: A study using orthograde transport of wheatgerm-agglutinin conjugated horseradish peroxidase. *Experimental Brain Research*, *68*(1), 147–167.

Rexed, B. (1952a). The cytoarchitectonic organization of the spinal cord in the cat. *The Journal of Comparative Neurology*, *96*(3), 414–495.

Rexed, B. (1952b). The cytoarchitectonic organization of the spinal cord in the cat. *Journal of Comparative Neurology*, *96*(3), 415–495.

Rexed, B. (1954). A cytoarchitectonic atlas of the spinal cord in the cat. *Journal of Comparative Neurology*, *100*(2), 297–379.

Rhoades, R. W. (1981). Cortical and spinal somatosensory input to the superior colliculus in the golden hamster: An anatomical and electrophysiological study. *Journal of Comparative Neurology*, *195*(3), 415–432.

Rice, C. D., Weber, S. A., Waggoner, A. L., Jessell, M. E., & Yates, B. J. (2010). Mapping of neural pathways that influence diaphragm activity and project to the lumbar spinal cord in cats. *Experimental Brain Research*, *203*(1), 205–211.

Riddle, C. N., & Baker, S. N. (2010). Convergence of pyramidal and medial brain stem descending pathways onto macaque cervical spinal interneurons. *Journal of Neurophysiology*, *103*(5), 2821–2832.

Riddle, C. N., Edgley, S. A., & Baker, S. N. (2009). Direct and indirect connections with upper limb motoneurons from the primate reticulospinal tract. *The Journal of Neuroscience*, *29*(15), 4993–4999.

Ritz, L. A., & Greenspan, J. D. (1985). Morphological features of lamina V neurons receiving nociceptive input in cat sacrocaudal spinal cord. *The Journal of Comparative Neurology*, *238*(4), 440–452.

Rivero-Melián, C. (1996). Organization of hindlimb nerve projections to the rat spinal cord: A choleragenoid horseradish peroxidase study. *The Journal of Comparative Neurology*, *364*(4), 651–663.

Rivero-Melián, C., & Arvidsson, J. (1992). Brain stem projections of rat lumbar dorsal root ganglia studied with choleragenoid conjugated horseradish peroxidase. *Experimental Brain Research*, *91*(1), 12–20.

Rivero-Melián, C., & Grant, G. (1990). Distribution of lumbar dorsal root fibers in the lower thoracic and lumbosacral spinal cord of the rat studied with choleragenoid horseradish peroxidase conjugate. *The Journal of Comparative Neurology*, *299*(4), 470–481.

Rodríguez-Mena, R., Piquer-Belloch, J., Llácer-Ortega, J. L., Riesgo-Suárez, P., & Rovira-Lillo, V. (2018). 3D microsurgical anatomy of the cortico-spinal tract and lemniscal pathway based on fibre microdissection and demonstration with tractography. *Neurocirugía (English Edition)*, *29*(6), 275–295.

Ross, E. D., Kirkpatrick, J. B., & Lastimosa, A. C. B. (1979). Position and vibration sensations: Functions of the dorsal spinocerebellar tracts? *Annals of Neurology*, *5*(2), 171–176.

Routal, R. V., & Pal, G. P. (1999a). A study of motoneuron groups and motor columns of the human spinal cord. *Journal of Anatomy*, *195*(Pt 2), 211–224.

Routal, R. V., & Pal, G. P. (1999b). Location of the phrenic nucleus in the human spinal cord. *Journal of Anatomy*, *195*(Pt 4), 617–621.

Rowan, S., Todd, A. J., & Spike, R. C. (1993). Evidence that neuropeptide Y is present in gabaergic neurons in the superficial dorsal horn of the rat spinal cord. *Neuroscience*, *53*(2), 537–545.

Ruder, L., Takeoka, A., & Arber, S. (2016). Long-distance descending spinal neurons ensure quadrupedal locomotor stability. *Neuron*, *92*(5), 1063–1078.

Ruigrok, T. J., & Voogd, J. (2000). Organization of projections from the inferior olive to the cerebellar nuclei in the rat. *The Journal of Comparative Neurology*, *426*(2), 209–228.

Rustioni, A., Hayes, N. L., & O'Neill, S. (1979). Dorsal column nuclei and ascending spinal afferents in macaques. *Brain*, *102*(1), 95–125.

Rustioni, A., & Kaufman, A. B. (1977). Identification of cells of origin of non-primary afferents to the dorsal column nuclei of the cat. *Experimental Brain Research*, *27*(1), 1–14.

Rustioni, A., Kuypers, H. G. J. M., & Holstege, G. (1971). Propriospinal projections from the ventral and lateral funiculi to the motoneurons in the lumbosacral cord of the cat. *Brain Research*, *34*(2), 255–275.

Saito, H. (2010). Hypothalamo-spinal tract somatotopic organization determined from thermal sudomotor function in patients with localized cervical spinal cord lesions. *Autonomic Neuroscience*, *158*(1), 135.

Saito, T., & Steinke, H. (2015). Chapter 32 - The dorsal rootlets, ventral rootlets, spinal nerve, and rami. In R. S. Tubbs, E. Rizk, M. M. Shoja, M. Loukas, N. Barbaro, & R. J. Spinner (Eds.), *Nerves and nerve injuries* (pp. 451–469). Academic Press.

Saker, E., Henry, B. M., Tomaszewski, K. A., Loukas, M., Iwanaga, J., Oskouian, R. J., & Tubbs, R. S. (2017). The filum terminale internum and externum: A comprehensive review. *Journal of Clinical Neuroscience*, *40*, 6–13.

Sardella, T. C. P., Polgár, E., Garzo, F., Furuta, T., Kaneko, T., Watanabe, M., & Todd, A. J. (2011). Dynorphin is expressed primarily by GABAergic neurons that contain galanin in the rat dorsal horn. *Molecular Pain*, *7*, 76.

Sathyamurthy, A., Barik, A., Dobrott, C. I., Matson, K. J. E., Stoica, S., Pursley, R., Chesler, A. T., & Levine, A. J. (2020). Cerebellospinal neurons regulate motor performance and motor learning. *Cell Reports*, *31*(6), 107595.

Satkunendrarajah, K., Karadimas, S. K., Laliberte, A. M., Montandon, G., & Fehlings, M. G. (2018). Cervical excitatory neurons sustain breathing after spinal cord injury. *Nature*, *562*(7727), 419–422.

Satoda, T., Matsumoto, H., Zhou, L., Rose, P. K., & Richmond, F. J. R. (2002). Mesencephalic projections to the first cervical segment in the cat. *Experimental Brain Research*, *144*(3), 397–413.

Satoh, K., Armstrong, D. M., & Fibiger, H. C. (1983). A comparison of the distribution of central cholinergic neurons as demonstrated by acetylcholinesterase pharmacohistochemistry and choline acetyltransferase immunohistochemistry. *Brain Research Bulletin*, *11*(6), 693–720.

Scheibel, M. E., & Scheibel, A. B. (1966). Terminal axonal patterns in cat spinal cord I. The lateral corticospinal tract. *Brain Research*, *2*(4), 333–350.

Scheibel, M. E., & Scheibel, A. B. (1968). Terminal axonal patterns in cat spinal cord II. The dorsal horn. *Brain Research*, *9*(1), 32–58.

Scheibel, M. E., & Scheibel, A. B. (1970a). Organization of spinal motoneuron dendrites in bundles. *Experimental Neurology*, *28*(1), 106–112.

Scheibel, M. E., & Scheibel, A. B. (1970b). Developmental relationship between spinal motoneuron dendrite bundles and patterned activity in the hind limb of cats. *Experimental Neurology*, *29*(2), 328–335.

Schepens, B., & Drew, T. (2004). Independent and convergent signals from the pontomedullary reticular formation contribute to the control of posture and movement during reaching in the cat. *Journal of Neurophysiology*, *92*(4), 2217–2238.

Schmahmann, J. D., Guell, X., Stoodley, C. J., & Halko, M. A. (2019). The theory and neuroscience of cerebellar cognition. *Annual Review of Neuroscience*, *42*(1), 337–364.

Schoenen, J. (1982a). The dendritic organization of the human spinal cord: The dorsal horn. *Neuroscience*, *7*(9), 2057–2087.

Schoenen, J. (1982b). Dendritic organization of the human spinal cord: The motoneurons. *The Journal of Comparative Neurology*, *211*(3), 226–247.

Schoenen, J., & Faull, R. L. M. (2004). CHAPTER 7 - Spinal cord: Cyto- and chemoarchitecture. In G. Paxinos & J. K. Mai (Eds.), *The human nervous system* (2nd ed., pp. 190–232). Academic Press.

Schoffnegger, D., Ruscheweyh, R., & Sandkühler, J. (2008). Spread of excitation across modality borders in spinal dorsal horn of neuropathic rats. *Pain*, *135*(3), 300–310.

Schucht, P., Raineteau, O., Schwab, M. E., & Fouad, K. (2002). Anatomical correlates of locomotor recovery following dorsal and ventral lesions of the rat spinal cord. *Experimental Neurology*, *176*(1), 143–153.

Schwab, M. E. (2002). Repairing the injured. *Spinal Cord*, *295* (5557), 1029–1031.

Semba, K., Masarachia, P., Malamed, S., Jacquin, M., Harris, S., & Egger, M. D. (1984). Ultrastructure of Pacinian corpuscle primary afferent terminals in the cat spinal cord. *Brain Research*, *302*(1), 135–150.

Sengul, G., Fu, Y., Yu, Y., & Paxinos, G. (2015). Spinal cord projections to the cerebellum in the mouse. *Brain Structure and Function*, *220*(5), 2997–3009.

Sengul, G., & Watson, C. (2012a). Chapter 6 - Spinal cord: Regional anatomy, cytoarchitecture and chemoarchitecture. In J. K. Mai & G. Paxinos (Eds.), *The human nervous system* (3rd ed., pp. 186–232). Academic Press.

Sengul, G., & Watson, C. (2012b). Chapter 13 - Spinal cord. In C. Watson, G. Paxinos, & L. Puelles (Eds.), *The mouse nervous system* (pp. 424–458). Academic Press.

Sengul, G., & Watson, C. (2015). Chapter 8 - Ascending and descending pathways in the spinal cord. In G. Paxinos (Ed.), *The rat nervous system* (4th ed., pp. 115–130). Academic Press.

Serafini, T., Colamarino, S. A., Leonardo, E. D., Wang, H., Beddington, R., Skarnes, W. C., & Tessier-Lavigne, M. (1996). Netrin-1 is required for commissural axon guidance in the developing vertebrate nervous system. *Cell*, *87*(6), 1001–1014.

Sewards, T. V., & Sewards, M. A. (2002). The medial pain system: Neural representations of the motivational aspect of pain. *Brain Research Bulletin*, *59*(3), 163–180.

Seybold, V. S., & Elde, R. P. (1982). Neurotensin immunoreactivity in the superficial laminae of the dorsal horn of the rat: I. Light microscopic studies of cell bodies and proximal dendrites. *Journal of Comparative Neurology*, *205*(1), 89–100.

Shepard, C. T., Pocratsky, A. M., Brown, B. L., Van Rijswijck, M. A., Zalla, R. M., Burke, D. A., Morehouse, J. R., Riegler, A. S., Whittemore, S. R., & Magnuson, D. S. (2021). Silencing long ascending propriospinal neurons after spinal cord injury improves hindlimb stepping in the adult rat. *eLife*, *10*, e70058.

Shimohata, K., Hasegawa, K., Onodera, O., Nishizawa, M., & Shimohata, T. (2017). The clinical features, risk factors, and surgical treatment of cervicogenic headache in patients with cervical spine disorders requiring surgery. *Headache: The Journal of Head and Face Pain*, *57*(7), 1109–1117.

Shintani, S., Tsuruoka, S., & Shiigai, T. (2000). Pure sensory stroke caused by a cerebral hemorrhage: Clinical-radiologic correlations in seven patients. *American Journal of Neuroradiology*, *21* (3), 515–520.

Simmons, M. A., & Substance, P. (2010). In S. J. Enna & D. B. Bylund (Eds.), *xPharm: The comprehensive pharmacology reference* (pp. 1–4). Elsevier.

Skagerberg, G., & Björklund, A. (1985). Topographic principles in the spinal projections of serotonergic and non-serotonergic brainstem neurons in the rat. *Neuroscience*, *15*(2), 445–480.

Smith, M., & Deacon, P. (1984). Topographical anatomy of the posterior columns of the spinal cord in man: The long ascending fibres. *Brain*, *107*(3), 671–698.

Snyder, R. L., Faull, R. L. M., & Mehler, W. R. (1978). A comparative study of the neurons of origin of the spinocerebellar afferents in the rat, cat and squirrel monkey based on the retrograde transport of horseradish peroxidase. *Journal of Comparative Neurology*, *181*(4), 833–852.

Soteropoulos, D. S., Edgley, S. A., & Baker, S. N. (2011). Lack of evidence for direct corticospinal contributions to control of the ipsilateral forelimb in monkey. *The Journal of Neuroscience*, *31* (31), 11208–11219.

Sridharan, G., & Shankar, A. A. (2012). Toluidine blue: A review of its chemistry and clinical utility. *The Journal of Oral and Maxillofacial Pathology*, *16*(2), 251–255.

Ståhl, P. L., Salmén, F., Vickovic, S., Lundmark, A., Navarro, J. F., Magnusson, J., Giacomello, S., Asp, M., Westholm, J. O., Huss, M., Mollbrink, A., Linnarsson, S., Codeluppi, S., Borg, Å., Pontén, F., Costea, P. I., Sahlén, P., Mulder, J., Bergmann, O., … Frisén, J. (2016). Visualization and analysis of gene expression in tissue sections by spatial transcriptomics. *Science*, *353* (6294), 78–82.

Sterling, P., & Kuypers, H. G. J. M. (1967). Anatomical organization of the brachial spinal cord of the cat. II. The motoneuron plexus. *Brain Research*, *4*(1), 16–32.

Steward, O., Yee, K. M., Metcalfe, M., Willenberg, R., Luo, J., Azevedo, R., Martin-Thompson, J. H., & Gandhi, S. P. (2020). Rostro-caudal specificity of corticospinal tract projections in mice. *Cerebral Cortex*, *31*(5), 2322–2344.

Stinear, J. W., & Byblow, W. D. (2004). The contribution of cervical propriospinal premotoneurons in recovering hemiparetic stroke patients. *Journal of Clinical Neurophysiology*, *21*(6), 426–434.

Stokke, M. F., Nissen, U. V., Glover, J. C., & Kiehn, O. (2002). Projection patterns of commissural interneurons in the lumbar spinal cord of the neonatal rat. *The Journal of Comparative Neurology*, *446*(4), 349–359.

Sugino, S., Konno, D., Abe, J., Imamura-Kawasawa, Y., Kido, K., Suzuki, J., Endo, Y., & Yamauchi, M. (2021). Crucial involvement of catecholamine neurotransmission in postoperative nausea and vomiting: Whole-transcriptome profiling in the rat

nucleus of the solitary tract. *Genes, Brain and Behavior*, *20*(6), e12759.

Sutor, T. W., Fuller, D. D., & Fox, E. J. (2022). Locomotor-respiratory coupling in ambulatory adults with incomplete spinal cord injury. *Spinal Cord Series and Cases*, *8*(1), 49.

Szentágothai, J. (1964). Propriospinal pathways and their synapses. In J. C. Eccles & J. P. Schadé (Eds.), *Progress in Brain Research* (Vol. 11, pp. 155–177). Elsevier.

Takahashi, A. (2016). Subchapter 7A - Enkephalin. In Y. Takei, H. Ando, & K. Tsutsui (Eds.), *Handbook of hormones* (pp. 55–7A). Academic Press.

Takahashi, T., & Otsuka, M. (1975). Regional distribution of substance P in the spinal cord and nerve roots of the cat and the effect of dorsal root section. *Brain Research*, *87*(1), 1–11.

Takakusaki, K., Chiba, R., Nozu, T., & Okumura, T. (2016). Brainstem control of locomotion and muscle tone with special reference to the role of the mesopontine tegmentum and medullary reticulospinal systems. *Journal of Neural Transmission*, *123*(7), 695–729.

Taylor, A., Durbaba, R., Ellaway, P. H., & Rawlinson, S. (2000). Patterns of fusimotor activity during locomotion in the decerebrate cat deduced from recordings from hindlimb muscle spindles. *The Journal of Physiology*, *522*(3), 515–532.

Tazoe, T., & Perez, M. A. (2014). Selective activation of ipsilateral motor pathways in intact humans. *The Journal of Neuroscience*, *34*(42), 13924–13934.

ten Donkelaar, H. J. (1988). Evolution of the red nucleus and rubrospinal tract. *Behavioural Brain Research*, *28*(1-2), 9–20.

Thiebaut de Schotten, M., ffytche, D. H., Bizzi, A., Dell'Acqua, F., Allin, M., Walshe, M., Murray, R., Williams, S. C., Murphy, D. G., & Catani, M. (2011). Atlasing location, asymmetry and inter-subject variability of white matter tracts in the human brain with MR diffusion tractography. *NeuroImage*, *54*(1), 49–59.

Thomas, C. E., & Combs, C. M. (1962). Spinal cord segments. A gross structure in the adult cat. *American Journal of Anatomy*, *110*(1), 37–47.

Todd, A. J. (1991). Immunohistochemical evidence that acetylcholine and glycine exist in different populations of GABAergic neurons in lamina III of rat spinal dorsal horn. *Neuroscience*, *44*(3), 741–746.

Todd, A. J. (2017). Identifying functional populations among the interneurons in laminae I-III of the spinal dorsal horn. *Molecular Pain*, *13*, 17448069917693003.

Todd, A. J., & Lewis, S. G. (1986). The morphology of Golgi-stained neurons in lamina II of the rat spinal cord. *Journal of Anatomy*, *149*, 113–119.

Todd, A. J., & McKenzie, J. (1989). GABA-immunoreactive neurons in the dorsal horn of the rat spinal cord. *Neuroscience*, *31*(3), 799–806.

Todd, A. J., Puskar, Z., Spike, R. C., Hughes, C., Watt, C., & Forrest, L. (2002). Projection neurons in lamina I of rat spinal cord with the neurokinin 1 receptor are selectively innervated by substance p-containing afferents and respond to noxious stimulation. *The Journal of Neuroscience*, *22*(10), 4103–4113.

Todd, A. J., Russell, G., & Spike, R. C. (1992). Immunocytochemical evidence that GABA and neurotensin exist in different neurons in laminae II and III of rat spinal dorsal horn. *Neuroscience*, *47*(3), 685–691.

Todd, A. J., & Sullivan, A. C. (1990). Light microscope study of the coexistence of GABA-like and glycine-like immunoreactivities in the spinal cord of the rat. *Journal of Comparative Neurology*, *296*(3), 496–505.

Tohyama, T., Kinoshita, M., Kobayashi, K., Isa, K., Watanabe, D., Kobayashi, K., Liu, M., & Isa, T. (2017). Contribution of propriospinal neurons to recovery of hand dexterity after corticospinal tract lesions in monkeys. *Proceedings of the National Academy of Sciences*, *114*(3), 604–609.

Torres-da-Silva, K. R., Da Silva, A. V., Barioni, N. O., Tessarin, G. W., De Oliveira, J. A., Ervolino, E., Horta-Junior, J. A., & Casatti, C. A. (2016). Neurochemistry study of spinal cord in non-human primate (*Sapajus* spp.). *European Journal of Histochemistry*, *60*(3), 2623.

Torvik, A. (1956). Afferent connections to the sensory trigeminal nuclei, the nucleus of the solitary tract and adjacent structures. An experimental study in the rat. *Journal of Comparative Neurology*, *106*(1), 51–141.

Tosolini, A. P., & Morris, R. (2012). Spatial characterization of the motor neuron columns supplying the rat forelimb. *Neuroscience*, *200*, 19–30.

Truex, R. C., Taylor, M. J., Smythe, M. Q., & Gildenberg, P. L. (1970). The lateral cervical nucleus of cat, dog and man. *Journal of Comparative Neurology*, *139*(1), 93–103.

Tubbs, R. S., Salter, G., Grabb, P. A., & Oakes, W. J. (2001). The denticulate ligament: Anatomy and functional significance. *The Journal of Comparative Neurology*, *94*(2), 271–275.

Valtschanoff, J. G., Weinberg, R. J., & Rustioni, A. (1993). Amino acid immunoreactivity in corticospinal terminals. *Experimental Brain Research*, *93*(1), 95–103.

Vasilenko, D. A. (1975). Propriospinal pathways in the ventral funicles of the cat spinal cord: Their effects on lumbosacral motoneurones. *Brain Research*, *93*(3), 502–506.

Vera, P. L., Ellenberger, H. H., Haselton, J. R., Haselton, C. L., & Schneiderman, N. (1986). The intermediolateral nucleus: An 'open' or 'closed' nucleus? *Brain Research*, *386*(1), 84–92.

Verhaart, W. J. C. (1963). Pyramidal tract in the cord of the elephant. *Journal of Comparative Neurology*, *121*(1), 45–49.

Villanueva, L., de Pommery, J., Menétrey, D., & Le Bars, D. (1991). Spinal afferent projections to subnucleus reticularis dorsalis in the rat. *Neuroscience Letters*, *134*(1), 98–102.

Villiger, J. W., & Faull, R. L. M. (1985). Muscarinic cholinergic receptors in the human spinal cord: Differential localization of [3H]pirenzepine and [3H]quinuclidinylbenzilate binding sites. *Brain Research*, *345*(1), 196–199.

Vinay, L., & Padel, Y. (1990). Spatio-temporal organization of the somaesthetic projections in the red nucleus transmitted through the spino-rubral pathway in the cat. *Experimental Brain Research*, *79*(2), 412–426.

Wahl, A. S., Omlor, W., Rubio, J. C., Chen, J. L., Zheng, H., Schröter, A., Gullo, M., Weinmann, O., Kobayashi, K., Helmchen, F., Ommer, B., & Schwab, M. E. (2014). Asynchronous therapy restores motor control by rewiring of the rat corticospinal tract after stroke. *Science*, *344*(6189), 1250–1255.

Waldvogel, H. J., Faull, R. L. M., Jansen, K. L. R., Dragunow, M., Richards, J. G., Mohler, H., & Streit, P. (1990). GABA, GABA receptors and benzodiazepine receptors in the human spinal cord: An autoradiographic and immunohistochemical study at

the light and electron microscopic levels. *Neuroscience*, *39*(2), 361–385.

Wang, C. C., Willis, W. D., & Westlund, K. N. (1999). Ascending projections from the area around the spinal cord central canal: A *Phaseolus vulgaris* leucoagglutinin study in rats. *The Journal of Comparative Neurology*, *415*(3), 341–367.

Wang, L.-H., Ding, W.-Q., & Sun, Y.-G. (2022). Spinal ascending pathways for somatosensory information processing. *Trends in Neurosciences*, *45*, 594–607.

Warner, G., & Watson, C. R. (1972). The rubrospinal tract in a diprotodont marsupial (*Trichosurus vulpecula*). *Brain Research*, *41*(1), 180–183.

Watanabe, S., Kitamura, T., Watanabe, L., Sato, H., & Yamada, J. (2003). Projections from the nucleus reticularis magnocellularis to the rat cervical cord using electrical stimulation and iontophoretic injection methods. *Anatomical Science International*, *78*(1), 42–52.

Watson, C., & Harvey, A. R. (2009). Chapter 11 - Projections from the brain to the spinal cord. In C. Watson, G. Paxinos, & G. Kayalioglu (Eds.), *The spinal cord* (pp. 168–179). Academic Press.

Watson, C., & Kayalioglu, G. (2009). Chapter 1 - The organization of the spinal cord. In C. Watson, G. Paxinos, & G. Kayalioglu (Eds.), *The Spinal cord* (pp. 1–7). Academic Press.

Watson, C., Paxinos, G., Kayalioglu, G., & Heise, C. (2009). Chapter 15 - Atlas of the rat spinal cord. In C. Watson, G. Paxinos, & G. Kayalioglu (Eds.), *The spinal cord* (pp. 238–306). Academic Press.

Watson, C., Paxinos, G., Sengul, G., & Heise, C. (2009). *Atlas of the mouse spinal cord* (pp. 308–379). Elsevier.

Watson, C. R. (1971). The corticospinal tract of the quokka wallaby (Setonix brachyurus). *Journal of Anatomy*, *109*(Pt 1), 127–133.

Wercberger, R., & Basbaum, A. I. (2019). Spinal cord projection neurons: A superficial, and also deep analysis. *Current Opinion in Physiology*, *11*, 109–115.

Whishaw, I. Q., Gorny, B., & Sarna, J. (1998). Paw and limb use in skilled and spontaneous reaching after pyramidal tract, red nucleus and combined lesions in the rat: Behavioral and anatomical dissociations. *Behavioural Brain Research*, *93*(1-2), 167–183.

Whitehorn, D., Morse, R. W., & Towe, A. L. (1969). Role of the spinocervical tract in production of the primary cortical response evoked by forepaw stimulation. *Experimental Neurology*, *25*(3), 349–364.

Wiberg, M., Westman, J., & Blomqvist, A. (1987). Somatosensory projection to the mesencephalon: An anatomical study in the monkey. *Journal of Comparative Neurology*, *264*(1), 92–117.

Wiksten, B. (1979). The central cervical nucleus in the cat. I. A Golgi study. *Experimental Brain Research*, *36*(1), 143–154.

Wild, J. M., Cabot, J. B., Cohen, D. H., & Karten, H. J. (1979). Origin, course and terminations of the rubrospinal tract in the pigeon (*Columba livia*). *Journal of Comparative Neurology*, *187*(4), 639–654.

Willis, W. D., Al-Chaer, E. D., Quast, M. J., & Westlund, K. N. (1999). A visceral pain pathway in the dorsal column of the spinal cord. *Proceedings of the National Academy of Sciences*, *96*(14), 7675–7679.

Wilson, V. J., Boyle, R., Fukushima, K., Rose, P. K., Shinoda, Y., Sugiuchi, Y., & Uchino, Y. (1995). The vestibulocollic reflex. *Journal of Vestibular Research*, *5*, 147–170.

Wilson, V. J., Uchino, Y., Maunz, R. A., Susswein, A., & Fukushima, K. (1978). Properties and connections of cat fastigiospinal neurons. *Experimental Brain Research*, *32*(1), 1–17.

Wilson, V. J., Wylie, R. M., & Marco, L. A. (1967). Projection to the Spinal cord from the medial and descending vestibular nuclei of the cat. *Nature*, *215*(5099), 429–430.

Woodbury, C. J., Ritter, A. M., & Koerber, H. R. (2000). On the problem of lamination in the superficial dorsal horn of mammals: A reappraisal of the substantia gelatinosa in postnatal life. *The Journal of Comparative Neurology*, *417*(1), 88–102.

Wootz, H., Fitzsimons-Kantamneni, E., Larhammar, M., Rotterman, T. M., Enjin, A., Patra, K., André, E., Van Zundert, B., Kullander, K., & Alvarez, F. J. (2013). Alterations in the motor neuron-renshaw cell circuit in the Sod1(G93A) mouse model. *The Journal of Comparative Neurology*, *521*(7), 1449–1469.

Xiong, G., & Matsushita, M. (2001). Ipsilateral and contralateral projections from upper cervical segments to the vestibular nuclei in the rat. *Experimental Brain Research*, *141*(2), 204–217.

Xu, Q., & Grant, G. (2005). Course of spinocerebellar axons in the ventral and lateral funiculi of the spinal cord with projections to the posterior cerebellar termination area: An experimental anatomical study in the cat, using a retrograde tracing technique. *Experimental Brain Research*, *162*(2), 250–256.

Yaïci, E. D., Rampin, O., Tang, Y., Calas, A., Jestin, A., Leclerc, P., Benoit, G., & Giuliano, F. (2002). Catecholaminergic projections onto spinal neurons destined to the pelvis including the penis in rat. *International Journal of Impotence Research*, *14*(3), 151–166.

Yaksh, T. L. (1981). Spinal opiate analgesia: Characteristics and principles of action. *PAIN*, *11*(3), 293–346.

Yasui, Y., Ono, K., Tsumori, T., Yokota, S., & Kishi, T. (1998). Tectal projections to the parvicellular reticular formation and the upper cervical spinal cord in the rat, with special reference to axon collateral innervation. *Brain Research*, *804*(1), 149–154.

Yeo, S. S., & Jang, S. H. (2011). Medullary decussation of the lateral corticospinal tract. *European Neurology*, *66*(5), 296–297.

Yeo, S. S., & Jang, S. H. (2012). A change in injured corticospinal tract originating from the premotor cortex to the primary motor cortex in a patient with intracerebral hemorrhage. *Neural Regeneration Research*, *7*(12), 939–942.

Yezierski, R. P. (1988). Spinomesencephalic tract: Projections from the lumbosacral spinal cord of the rat, cat, and monkey. *The Journal of Comparative Neurology*, *267*(1), 131–146.

Yoshino-Saito, K., Nishimura, Y., Oishi, T., & Isa, T. (2010). Quantitative inter-segmental and inter-laminar comparison of corticospinal projections from the forelimb area of the primary motor cortex of macaque monkeys. *Neuroscience*, *171*(4), 1164–1179.

Zaaimi, B., Edgley, S. A., Soteropoulos, D. S., & Baker, S. N. (2012). Changes in descending motor pathway connectivity after corticospinal tract lesion in Macaque monkey. *Brain*, *135*(7), 2277–2289.

Zaporozhets, E., Cowley, K. C., & Schmidt, B. J. (2006). Propriospinal neurons contribute to bulbospinal transmission of the locomotor command signal in the neonatal rat spinal cord. *The Journal of Physiology*, *572*(Pt 2), 443–458.

Zhang, E.-T., Han, Z.-S., & Craig, A. D. (1996). Morphological classes of spinothalamic lamina I neurons in the cat. *Journal of Comparative Neurology*, *367*(4), 537–549.

Zhang, X.-Y., Wang, J.-J., & Zhu, J.-N. (2016). Cerebellar fastigial nucleus: From anatomic construction to physiological functions. *Cerebellum & Ataxias*, *3*(1), 9.

Zhuo, M., & Gebhart, G. F. (1997). Biphasic modulation of spinal nociceptive transmission from the medullary raphe nuclei in the rat. *Journal of Neurophysiology*, *78*(2), 746–758.

Zoccal, D. B., Furuya, W. I., Bassi, M., Colombari, D. S. A., & Colombari, E. (2014). The nucleus of the solitary tract and the coordination of respiratory and sympathetic activities. *Frontiers in Physiology*, *5*, 238.

How to cite this article: Tan, S., Faull, R. L. M., & Curtis, M. A. (2023). The tracts, cytoarchitecture, and neurochemistry of the spinal cord. *The Anatomical Record*, *306*(4), 777–819. https://doi.org/10.1002/ar.25079