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Review Article

Unique Characteristics of the Dorsal Root Ganglion as a Target for Neuromodulation

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Abstract

Objective. The dorsal root ganglion (DRG) is a novel target for neuromodulation, and DRG stimulation is proving to be a viable option in the treatment of chronic intractable neuropathic pain. Although the overall principle of conventional spinal cord stimulation (SCS) and DRG stimulation—in which an electric field is applied to a neural target with the intent of affecting neural pathways to decrease pain perception—is similar, there are significant differences in the anatomy and physiology of the DRG that make it an ideal target for neuromodulation and may account for the superior outcomes observed in the treatment of certain chronic neuropathic pain states. This review highlights the anatomy of the DRG, its function in maintaining homeostasis and its role in neuropathic pain, and the unique value of DRG as a target in neuromodulation for pain. **Methods.** A narrative literature review was performed. **Results.** Overall, the DRG is a critical structure in sensory transduction and modulation, including pain transmission and the maintenance of persistent neuropathic pain states. Unique characteristics including selective somatic organization, specialized membrane characteristics, and accessible and consistent location make the DRG an ideal target for neuromodulation. Because DRG stimulation directly recruits the somata of primary sensory neurons and harnesses the filtering capacity of the pseudounipolar neural architecture, it is differentiated from SCS, peripheral nerve stimulation, and other neuromodulation options. **Conclusions.** There are several advantages to targeting the DRG, including lower energy usage, more focused and posture-independent stimulation, reduced paresthesia, and improved clinical outcomes.

Key Words: Neuromodulation; Neurostimulation; Dorsal Root Ganglion Stimulation; DRG Stimulation; Spinal Cord Stimulation; Chronic Pain; Neuropathic Pain; Pain Management

The role of the dorsal root ganglion (DRG) in chronic pain has long been recognized. With an early report in 1949 describing a technique for anesthetic infiltration of the DRG [1], this structure has been the focus of numerous other pain relief interventions, including dorsal rhizotomy or ganglionectomy, dorsal root entry zone (DREZ) lesioning (an adjacent related neural target), conventional radiofrequency denervation, pulsed radiofrequency, and steroid injection. In recent years, the DRG has been recognized as a viable option for neuromodulation therapy; electrical stimulation of primary sensory neuron somata may be an elegant solution for treating chronic pain and has generated compelling clinical findings [2–5]. This review describes the anatomic and physiologic evidence supporting clinical outcomes.

Anatomy of the DRG

The DRG is a critical structure in sensory transduction and modulation, including pain transmission [6]. The DRG,

located within the dural sheath with only a thin surrounding layer of cerebrospinal fluid (CSF) [7], is a bilateral structure found at every vertebral level and housed within fixed bony vertebral structures (neuroforamen) as it spans the transition from the spinal cord and vertebral column to the periphery. The DRG (about the size of a small peanut) is an enlargement of the dorsal root that houses somata (cell bodies) of primary sensory neurons (PSNs); up to 15,000 neurons are present in each DRG at limb-innervating segmental levels. Somata diameters range from 20 to 150 μm and can be categorized based on histologic staining of neurofilament density as "large-light" neurons (generally A-neurons, relaying non-noxious information) or "small-dark" neurons (generally C-neurons, relaying painful signals) [8]. The axons of these neurons are bundled into roots/nerves that contain a mix of fibers with varied excitability, including low-threshold mechanosensory fibers, higher-threshold Aβ nociceptors, and Aδ fibers. Aβ, Aδ, and C fibers all carry peripheral sensation information to their respective soma in the DRG. Myelinated Aδ fibers have a relatively high velocity to carry acute nociceptive information (temperature, mechanical, and chemical-induced) to the DRG, respectively. Unmyelinated C fibers have a smaller diameter and slower conduction velocity. They also carry nociceptive information to the DRG but contribute to the more diffuse and deeper secondary pain that occurs after an injury. In addition, DRGs have a large population of glial cells; there are approximately eightfold more glia than neurons in each DRG [9]. Satellite glial cells are a specialized form of glia in the DRG that envelop each PSN to create a functional unit that is physically separated from other PSN somata [9,10]. A rough somatotopy organizes PSN-receptive fields within each DRG [11].

DRG neurons are pseudounipolar in nature; a single axon projects from the cell body and bifurcates at the unique T-junction. The peripheral portion of the axon extends to receptor endings in the periphery and is responsible for afferent signaling. The central portion of the axon extends into the central nervous system (CNS) and shows considerable axonal arborizations into the spinal cord [12], terminating in synapses at ipsilateral or contralateral wide dynamic range neurons, inhibitory interneuron networks, and other targets in the dorsal horn. In turn, other DRG fibers traverse the length of the dorsal columns to reach the dorsal column nuclei in the brainstem. It is these fibers—typically large-diameter central axons of Aβ primary sensory neurons—that comprise the dorsal columns and are most commonly recruited in spinal cord stimulation (SCS) [13]. Thus, a single PSN can span a dramatically large anatomy [8]. Additionally, DRGs are in intimate connection with the sympathetic chain via rami communicantes nerves [14,15]. The white rami communicantes nerve also serves as a conduit for discogenic afferents, which can convey intrinsic spinal pain signals, to the DRG [16]. The two preceding references present schematic diagrams that illustrate the relationships of DRGs with sympathetic ganglia.

At thoracic and lumbar levels, the DRG is consistently positioned under the vertebral pedicle; magnetic resonance imaging (MRI) in asymptomatic subjects identified the DRG in the foramen in 92% of L1, 98% of L2, 100% of L3 and L4, and 95% of L5 [17], with the remainder of DRGs located in intraspinal or extraforaminal (lateral) regions. Another MRI study in healthy volunteers corroborated that 97.8–100% of L1-L4 DRGs are located in the foramen, with a small percentage being located in extraforaminal sites. At L5, most DRGs (94.3%) were located in the foramen, with the remainder (5.7%) in the intraspinal region [18]. Confirmatory findings exist in the form of cadaveric studies [19]. Distinct from thoracic and lumbar DRGs, those located in the sacrum have been characterized as either being intracanalar (medial to the medial border of the sacral pedicle) or intraforaminal (lateral to the medial border of the sacral pedicle). Meticulous dissection of 20 cadavers revealed that 57.5% and 42.5% of the S1 DRGs were located in the intraforaminal and intracanalar regions, respectively. At S2 DRG, the intraforaminal proportion decreased to 32.5% (67.5% intracanalar), and 100% of S3 and S4 DRGs were located in the intracanalar region [20]. Figure 1 summarizes the extent of PSNs and DRG anatomy in the lumbar and sacral vertebral levels.

Homeostatic Function of the DRG

The role of the peripheral sensory neuron is to conduct action potentials from the peripheral sensory neurons to the central terminals for transmission to the central nervous system. Action potentials are characterized by ion currents across an excitable membrane: a sodium depolarization is followed by a potassium repolarization and elevation of intracellular calcium, which is a second messenger for development, excitability, neurotransmitter release, gene expression, and cell death [6]. Typically, action potentials are generated at the peripheral sensory endings in response to peripheral stimuli [21–23]. The neuron's axon transduces signals, whereas the somata provides metabolic support and acts as a gatekeeper—or de novo generator—for the transmission of signals from the periphery to the CNS. Action potentials that are generated by the peripheral sensory nerve may result in depolarization in DRG somata [24]. The DRG T-junction may normally impede the propagation of some action potentials arising in the periphery, thus acting as a filter [25–27].

DRG neurons have specialized membrane characteristics and are separated from one another within the ganglia. Each is wrapped in a layer of satellite glial cells, which have a supportive function. Nearly all DRG neurons undergo subthreshold excitation during the course of activation of other cell bodies. This may be referred to as DRG "cross-depolarization" (or "cross-excitation"). As many as 90% of DRG neurons undergo depolarization when stimulus is applied to the axon of a neighboring DRG neuron sharing the same ganglion [28,29].

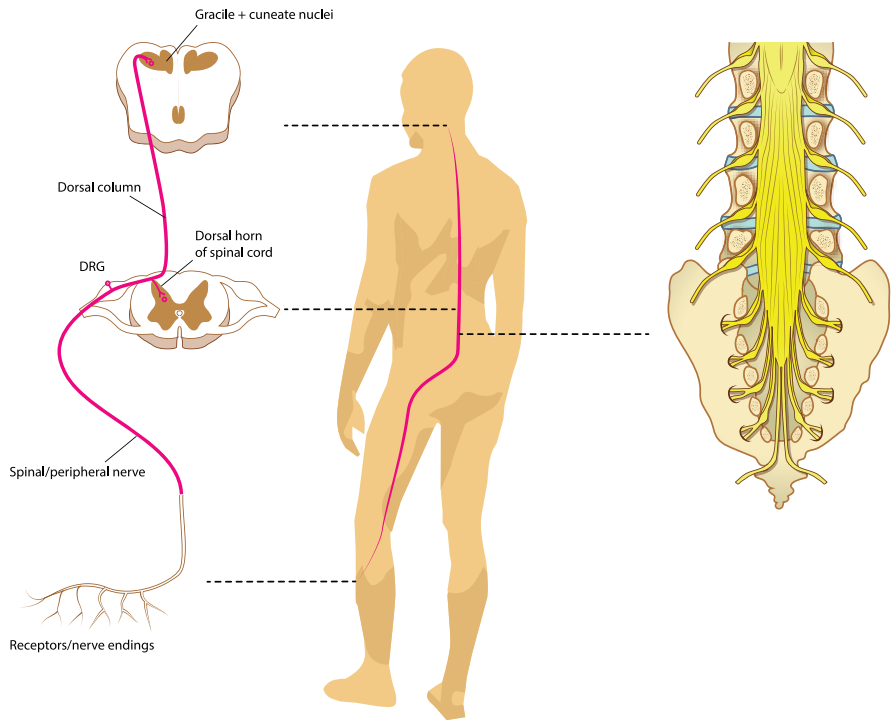

Figure 1. A schematic diagram showing the expanse of the primary sensory neuron (middle) and its terminations (left). The locations of dorsal root ganglia (DRGs) in the lumbar and sacral spine are illustrated (right); note the utility of vertebral pedicles as landmarks at lumbar levels and the greater variability of DRG location at sacral levels.

DRG neuron receptive fields and axonal arborizations are highly detailed. One-third of neurons in the substantia gelatinosa receive inputs from up to four different dorsal roots, and it has been hypothesized that C and Aδ fibers innervating a single cutaneous region will diverge at the level of the spinal nerve (before the DRG) and then re-converge at a single substantia gelatinosa neuron [30].

Function of DRG in Neuropathic Pain

The DRG is implicated in the development and maintenance of neuropathic pain [31]. After an injury, the DRG undergoes dramatic changes in phenotype and function, and these plastic changes establish the DRG as the originating site of pain signals that travel to the brain [32]. After a peripheral afferent nerve injury, an immune cascade is initiated that involves white cells, macrophages, T cells, glial cells, and Schwann cells in the DRG [31]. An increased number of T lymphocytes and major histocompatibility complex class II+ macrophages are found in DRGs of injured peripheral nerves several months after injury. The invasion of these inflammatory cells likely leads to prolonged release of excitatory cytokines, contributing to prolonged pain despite resolution of the original injury [33]. Glial cells also respond to injury of a peripheral nerve by multiplying and releasing inflammatory mediators [9]. Peripheral axotomy causes increased expression of neurotrophic factors in the satellite glial cells surrounding sensory neuron cell bodies in the DRG. These neurotrophins within the DRG trigger a persistent mechanical allodynia and can cause neuropathic pain after peripheral nerve injury [31,34].

There are also multiple changes in gene expression following axotomy of DRG neurons in rats, encompassing a large number of distinct family members including neuropeptides, receptors, ion channels, signal transduction molecules, synaptic vesicle proteins, and others. These cascades of gene expressions may be a prerequisite for neuropathic pain [35]. Chronic pain may be characterized by the upregulation of N- and T-type sodium channels after nerve injury and subsequent inflammatory responses [24,31].

The functional consequence of these changes, including alterations in gene regulation following injury, is sensitization and hyperexcitability of DRG neurons, which then leads to neuropathic pain [24,31,36]. After chronic constriction injury of a peripheral axon, low-threshold voltage gated calcium currents are significantly reduced, and this loss of inward calcium currents along with a decrease in extracellular shift of potassium can contribute to hyperexcitability after injury [31]. In addition, allodynia may be linked to increased noradrenaline levels [37].

Normal DRG neurons generate sinusoidal oscillation patterns through voltage-sensitive mechanisms, and these oscillations increase in frequency after nerve injury. When these oscillations reach their threshold, an action potential is produced. An upregulation of transmembrane sodium ion channels and/or an increase in the transport of sodium ions is thought to play a large role in

the increased oscillations and, thus, the ectopic discharges associated with chronic neuropathic pain [38]. Injury to the DRG has also been shown to increase the number of Aβ fibers terminating into the dorsal horn of the spinal cord [39]. It has also been shown that following peripheral nerve injury, the majority of DRG neurons that develop spontaneous ectopic action potentials will respond to activation of the sympathetic postganglionic afferents innervating the DRG [40]. It is hypothesized that this sympathetic activity may increase spontaneous action potentials and reduce the threshold for stimulation at the DRG.

DRG cell types are important contributors in the mechanism of action underlying ectopic firing, which is associated with central sensitization in neuropathic pain. Early on in the algogenic cascade, ectopic firing begins in the Aβ fibers; it develops in the C fibers a few weeks later [41]. Although Aβ fibers typically transmit touch and vibratory sensations, during axonal injury, these neurons express receptors for and release glutamate, substance P, and calcitonin gene-related peptide (CGRP), among others, which allows them to transduce pain signals [42]. Spontaneous action potentials have been shown to originate in the DRG after peripheral nerve injury as well as injury to the DRG; however, it does not occur with injury proximal to the DRG [43]. These action potentials can arise from both the soma and the axon within the DRG [44]. Much of the ectopic discharge comes from Aβ fibers, which normally transmit sensations of touch and vibration [42]. After nerve injury, electrophysiologic changes occur that allow these fibers to transmit pain. This likely greatly contributes to central sensitization.

This was confirmed in a 2004 study utilizing a small animal model, which showed that peripheral axotomy causes massive spontaneous ectopic firing in DRG neurons, and also renders them capable of triggering and maintaining central sensitization due to a neurochemical switch in neuronal phenotype. This experimentally induced central sensitization could subsequently be interrupted by dorsal rhizotomy (transection proximal to the DRG) or via anesthetic agents delivered to the DRG [45]. This experiment emphasized the importance of the DRG in the development and continuation of chronic pain conditions.

The T-junction can impede, filter, or enhance the signal from the periphery toward the CNS. Injury to the peripheral axon is followed by loss of inward calcium current and a decrease in extracellular shift of potassium. This is associated with the T-junction of the DRG permitting higher-frequency bursts to pass more frequently, causing DRG hyperexcitability and ectopic activity [6].

Unique Value of DRG as a Target in Neuromodulation for Pain

The DRG stimulation lead implantation procedure has been described elsewhere [46], but briefly, it involves accessing the epidural space and guiding a lead into the neuroforamen and adjacent to the DRG. The procedure involves an interlaminar contralateral epidural access technique with a Tuohy needle using loss of resistance. After epidural access, a novel delivery system including a curved sheath is advanced en bloc through the needle toward the inferior aspect of contralateral pedicle, and the flexible lead is advanced through the foramen such that the electrodes are positioned adjacent to the DRG. Finally, an s-shaped strain relief loop is created in the epidural space, and the sheath and needle are removed. This novel approach to neuromodulation also allows for targeting of sacral and lumbar DRGs and pain arising from locations in those dermatomal regions. The Tuohy needle can easily access the sacral epidural space via a posterior transforaminal approach. The DRG is surrounded by the ligamentum flavum (posteriorly), midtransforaminal ligament (inferiorly), and the superior transverse ligament (superiorly) [47]. These ligaments create stabilization for neurostimulation leads. Figures 2 and 3 show an artist rendering of DRG leads in situ.

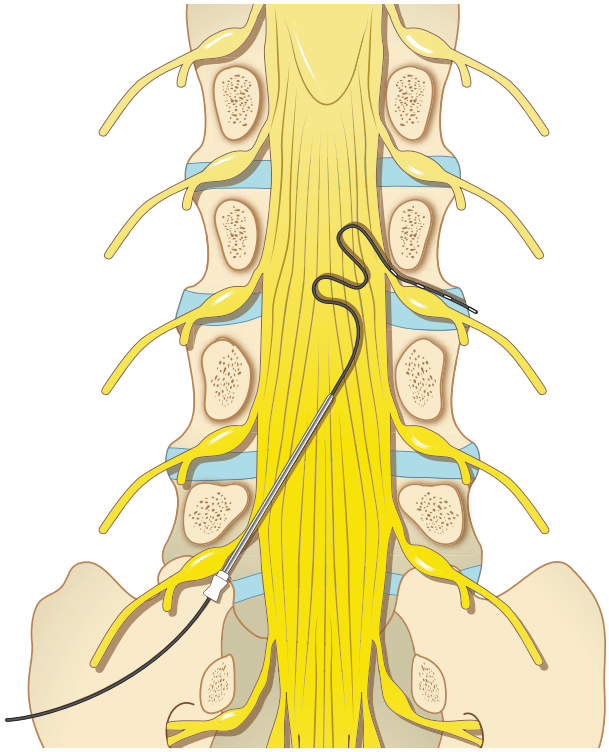

Figure 2. The narrow, flexible dorsal root ganglion (DRG) stimulation lead is maneuvered via an epidural needle into the vertebral foramen to appose the DRG. An S-shaped strain relief loop is placed in the epidural space, and tissue anchors (not pictured) are employed.

A risk of injury to the nerve or DRG injury exists during placement of a DRG lead. However, a recent report showed that safety in DRG stimulation is equivalent to that of SCS [48]. Evidence suggests that the DRG is a relatively resilient structure; cadaveric studies have shown that selective nerve root blocks often result in puncture

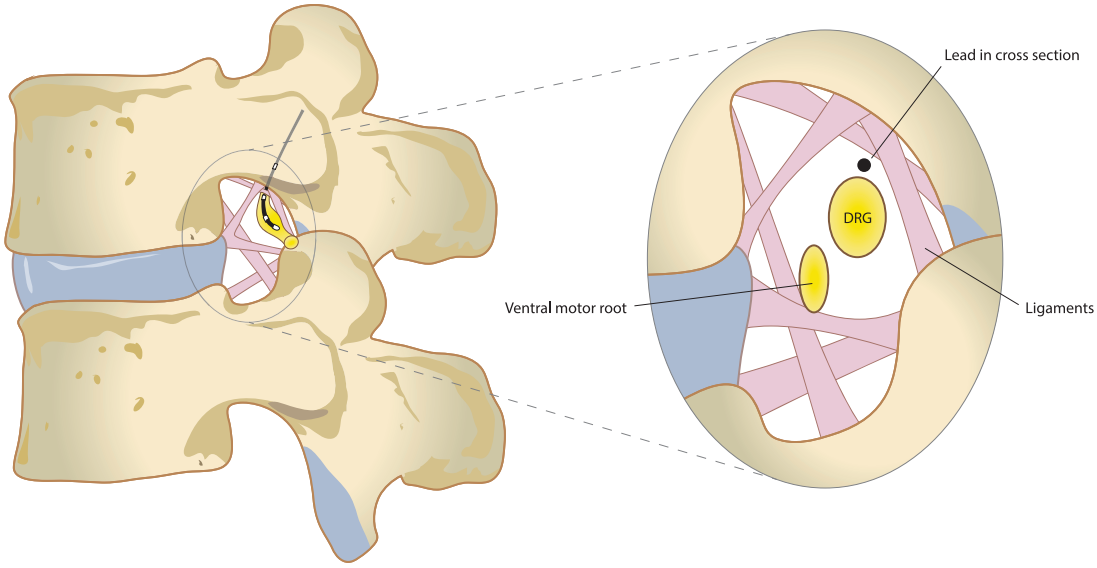

Figure 3. Sagittal schematics showing the location of the dorsal root ganglion (DRG) and proximal nerve roots in the spinal foramen (left) and a representation of the many intraforaminal ligaments (right). The DRG stimulation lead is inserted dorsally to lie closely along the DRG.

of the DRG and injection of medication within the epineurium without causing permanent injury [49]. The high density of capillaries surrounding the DRG may contribute to its robustness [50]. Methods to monitor for potential adverse events or damage/irritation of the targeted DRG during implantation include keeping the patient awake and conversant and using neuromonitoring with deep sedation or general anesthetic [51].

DRG stimulation is a clinically effective intervention. The earliest report, in 2013, demonstrated that DRG stimulation was an effective treatment for chronic intractable pain of the trunk and limbs, with an average of 70% pain relief and decreased medication usage among subjects over a four-week feasibility study [2]. In a multicenter prospective study, sustained pain relief was demonstrated at six and 12 months, along with excellent pain–paresthesia overlap with discrete coverage of hard-to-treat areas and no difference in paresthesia intensity due to postural changes [3,4]. These findings were subsequently recapitulated in a prospective multicenter study with patients with complex regional pain syndrome (CRPS) [52].

Reports have suggested that DRG stimulation may be an ideal treatment for pain in areas such as the foot [4,53] and the groin [54–56]. These sites are more difficult to target with SCS because the relevant dorsal column fibers are relatively inaccessible to epidural stimulation and may require stimulation amplitudes that preferentially generate painful nerve root activation [57]. In DRG stimulation, recruitment at the somata avoids these issues. Furthermore, DRG stimulation has shown benefit in treating disease states that have been underserved by traditional SCS such as axial low back pain and discogenic pain [16], phantom limb pain [58,59], post-herpetic neuralgia [60], CRPS/causalgia [5], diabetic peripheral neuropathy [61], salvage for SCS in the treatment of CRPS [62], and perineal pain [63]. DRG stimulation can treat pain in a variety of locations across the body, as long as paresthesia coverage of the painful regions can be achieved [15].

In a landmark randomized controlled trial of DRG stimulation vs. conventional SCS (the ACCURATE study), outcomes with DRG stimulation were statistically superior to those with SCS after three months of treatment, and pain relief and superiority were sustained through 12 months. Additionally, this trial demonstrated that DRG stimulation, when compared with traditional tonic dorsal column SCS, provides greater specificity of stimulation for painful areas, less variation in stimulation intensity with postural variation, and the ability to deliver paresthesia-free analgesia in some subjects [5]. Recently, excellent pain relief outcomes with DRG stimulation, durable through three years, have been reported [64].

Outcomes with DRG stimulation are often compared with those with SCS, a treatment modality that has rightly earned a place in advanced treatment when conservative medical management has failed [65]. Its appeal has expanded as implantation techniques and neuromodulation technology have advanced. However, SCS may be effective against only a limited range of conditions and can provide incomplete relief. Furthermore, when SCS is successful in providing analgesia, therapeutic efficacy can fade with time, often due to loss of paresthesia distribution into the painful area [65–67] or compensatory spinal plasticity/habituation resulting in loss of therapeutic effect [68,69]. The failure rate of SCS due to loss of efficacy in patients initially responsive to SCS remains at approximately 10.1–13.7% [70,71]. Below, several of the limitations of SCS are reviewed, along with

descriptions of the unique characteristics of the DRG that allow these issues to be addressed in DRG stimulation.

A well-known limitation of traditional tonic SCS is its unstable stimulation relative to body position. Changes in posture alter the distance between the electrodes and the dorsal column because of its motion within the CSF [72]. With positions that decrease the distance between the dorsal columns and the electrode, there is an increase in the volume of neural tissue stimulated, higher-threshold fibers are recruited, and this is perceived as overstimulation, with side effects including uncomfortable paresthesias, extraneous paresthesias in unwanted locations, and muscle activation/cramping. Patients will usually decrease stimulation amplitude to avoid this painful stimulation, but this may also result in decreased therapeutic relief. Conversely, physical positions that increase the distance between the electrode and the dorsal columns will result in less dorsal column recruitment and insufficient stimulation, also leading to decreased pain relief. Even small movements can result in changes in neural recruitment and change SCS effectiveness [73]. In contrast, because DRGs and DRG stimulation leads are located inside the neuroforamen with little CSF space between lead and target and are stabilized by vertebral bone and ligaments, the leads are much less vulnerable to perturbations in their placement due to physical movements. DRG stimulation shows little in the way of postural changes [74]. This same physical feature may also be protective against lead migration; a recent report showed that of 62 patients (25 of whom were followed for three years after DRG stimulator implantation, the largest long-term cohort to date), only a single case of lead migration was observed (1.6%, 64). This contrasts favorably with the reported incidence rate of approximately 13% for migrations among percutaneous SCS leads in the published literature [75,76]. Recent work, however, suggests that the migration rate for both DRG stimulation and SCS may be approximately 3% [48]. For both devices, of course, lead migration that results in loss of therapeutic effect requires repositioning or replacement, with associated health care costs, risks, and patient dissatisfaction.

DRG stimulation may also differ from SCS in its lower rate of energy consumption. SCS carries high energy needs due to the significant energy loss to the relatively thick layer of CSF before stimulation reaches its dorsal column targets [77,78]. Because DRGs have a very thin layer of subdural CSF [17], there is less of a current sink, and lower amplitude may be required than for SCS. Indeed, DRG stimulation requires up to 92.5% less power than SCS [79]. This may benefit patients by increasing the interval between battery replacements (which decreases health care costs) and increasing the "invisibility" of treatments. This may be important because frequent interactions with one's neuromodulation system (e.g., frequent amplitude adjustments, battery recharging, or battery replacement procedures) may be perceived as burdensome and, for those prone to catastrophizing, can lead to rumination of one's pain and overall poorer outcomes [68,80,81].

The effectiveness of the DRG as a neuromodulation target and its differential outcomes relative to SCS are likely due to the unique anatomical and physiological properties that are afforded by stimulation at the somata of primary sensory neurons. In contrast, SCS shapes activity in some small proportion of fibers of passage. For example, conventional SCS results in neurotransmitter release, predominantly GABA, at second- and third-order neurons in the dorsal horn and supraspinal sites [82,83]. Similarly, pain relief from stimulation at the DREZ involves intersegmental processing and influencing of tract of Lissauer functions or the dorsal horn directly, including attenuation of wide dynamic range neuronal activity [84,85]. Some have postulated that stimulation of dorsal nerve roots is an adequate analog to DRG stimulation. However, published alternative methods to stimulate the DRG or nerve roots have shown no advantage over traditional SCS [86,87], and nerve root stimulation typically carries a high probability of painful segmental stimulation. Peripheral nerve stimulation is yet another form of axonal recruitment. In all cases, the DRG is a unique target because the somata themselves are modulated.

The DRG establishes somatotopy before the level of the spinal cord [11]. Thus, it is not necessary to recruit the spinal cord in order to deliver pain relief in classic dermatomal patterns. Because DRG stimulation may recruit only a subset of the primary sensory neurons housed in a DRG, subdermatomal specificity may be obtained. Furthermore, the neurons responsible for pain generation may also have lower fiber activation thresholds and can be selectively activated by appropriately titrated stimulation [21–23]. Together, these observations can explain the highly precise paresthesia localization that can be achieved with DRG stimulation, irrespective of the use of perceptible paresthesias during clinical treatment.

Clinical findings for the utility of DRG stimulation have been reinforced by preclinical work. DRG field stimulation relieves spontaneous and induced neuropathic pain in rats [88]. In addition to behavioral studies, a functional MRI study in rats showed that DRG stimulation attenuates the global blood oxygen level–dependent (BOLD) response to noxious stimulation in brain regions previously associated with sensory and pain-related response, identifying the specific brain region responses to neuromodulation at the DRG level and suggesting possible mechanisms for DRG-induced treatment of chronic pain [89].

Basic science work, computer modeling, in vitro studies, and animal models provide complementary results that may elucidate some of the mechanisms underlying the clinical effectiveness of DRG stimulation [90]. As discussed in an earlier section, although neuropathic pain

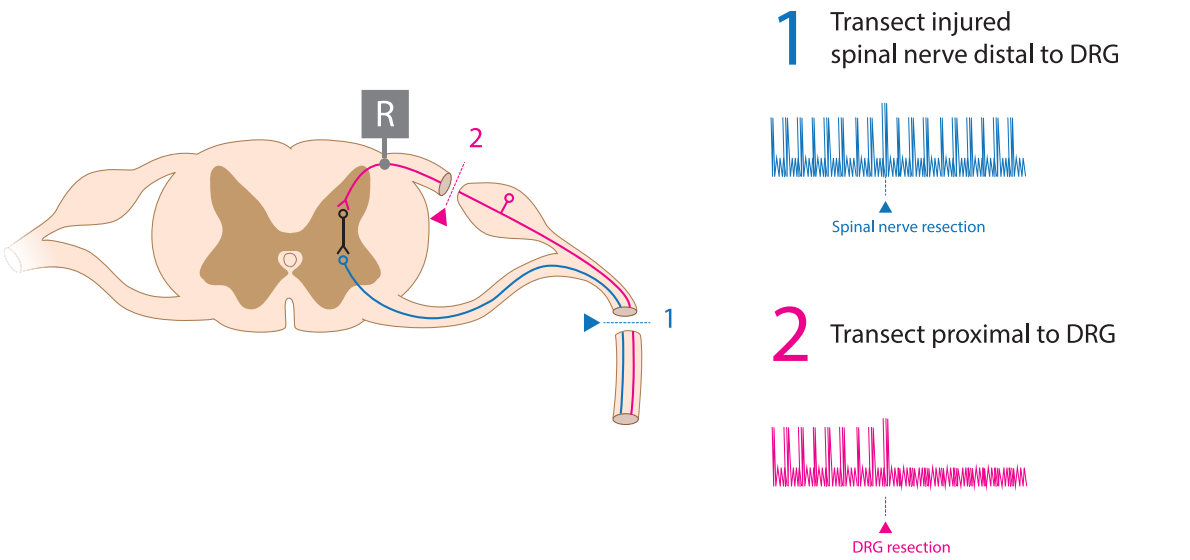

Figure 4. In an animal model of neuropathic pain induced via experimental spinal nerve axotomy injury, ectopic activity was recorded at dorsal root fibers before entry into the spinal cord (represented by the "R" symbol and two activity traces). 1) Transection of the spinal nerve distal to the dorsal root ganglion (DRG), analogous to the clinical removal of a neuroma, did not prevent the ectopic neural activity from entering the spinal cord. 2) Transection proximal to the DRG did, however, stop all ectopic activity from reaching the recording electrode.

may be initiated by peripheral damage, it is the DRG somata themselves that appear to maintain neuropathic pain because they are the source of ectopic discharges. This was confirmed in an animal model of experimental neuropathic pain in distal nerve transection did not prevent ectopic activity from reaching the spinal cord. Instead, the researchers found that surgical removal of the DRG immediately silenced the hyperactive action potentials (Figure 4) [32]. These findings suggesting that peripheral interventions on the presumed peripheral source of pain—such as excision of neuromas—would not be effective, which is all too often the case in clinical practice [91]. Instead, this animal study posits that the DRG is the source of the chronic pain and is the more relevant target for treating the root cause. Within in vitro preparations of isolated DRG neurons, electrical field stimulation reverses or normalizes the aberrant hyperactivity that characterizes these cells' discharge patterns [92]. This suggests that irreversible dorsal rhizotomy or another neuroablation method is unnecessary due to deafferentation pain syndromes, denervation pain, and central sensitization [93,94], as DRG stimulation is a reversible and minimally invasive intervention that similarly effectively stops ectopic discharges to relieve chronic pain.

The unique electrical properties of pseudo-unipolar DRG neurons may be another mechanism for the effectiveness of DRG stimulation. The T-junction, the meeting point of the peripheral axon, central axon, and the DRG stem axon, is the site of potential endogenous neuromodulation because, in addition to afferent spikes invading the cell body [8,31], the soma's contribution can also affect the signal that is being sent to the CNS via the T-junction [31]. The T-junction allows electrical impulses from the periphery to bypass, be blocked by, or be filtered by the soma. In vivo intracellular recordings describe a low-pass filter located at the T-junction, which is functionally altered to be more permissive under conditions of chronic pain [25]. The effect of DRG stimulation on the function of the T-junction appears to be the enhancement of its bandpass filtering properties. Stimulation of the DRG blocks the passage of impulse trains through the sensory neuron T-junction where the peripheral process and central process join the stem process. Recent computer modeling showed that action potentials generated in the peripheral axon of a modeled DRG neuron, which would ordinarily pass unimpeded into the central axon, were blocked from passing the T-junction when electrical field stimulation was applied to the DRG soma. In addition, ectopic action potentials arising from the DRG soma, which would ordinarily pass unimpeded into the central axon, were similarly blocked at the T-junction by DRG stimulation [27]. In vivo animal research has shown that the relief of neuropathic pain via DRG stimulation is due to conduction block of sensory impulses through the DRG via a neural blockade to prevent transmission of action potentials along primary sensory neuron fibers [95], appearing to confirm the existence of a T-junction filter.

Conclusions

This review has covered the anatomic and physiologic characteristics that make the DRG an important target for neuromodulation. Because DRG stimulation directly recruits the somata of primary sensory neurons and

harnesses the filtering function of the T-junction, it is differentiated from spinal cord stimulation (including dorsal nerve root or "gutter" stimulation) and peripheral nerve stimulation (in which ortho- and antidromic action potentials are induced in fibers). Current evidence suggests that DRG stimulation has an important role in the pain management physician's arsenal. More research is required to fully characterize the value of this intervention.

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