PriMera Scientific Surgical
Research and Practice
Volume 5 Issue 6 June 2025
DOI: 10.56831/PSSRP-05-192
ISSN: 2836-0028

PriMera Scientific Publications

Collateral Sprouting in The Peripheral Nervous System (PNS) - The Silent Savior

Type: Short Communication
Received: May 20, 2025
Published: May 28, 2025

Citation:
Subramanya Adiga. "Collateral Sprouting in The Peripheral Nervous System (PNS) - The Silent Savior". PriMera Scientific Surgical Research and Practice 5.6 (2025): 40-42.

Subramanya Adiga[1,2]*

[1]*Rehab Medicine Specialist at Middlemore Hospital (Counties Manukau), Te Whatu Ora, Auckland, New Zealand*

[2]*Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand*

***Corresponding Author:** Subramanya Adiga, Middlemore Hospital, 100 Hospital Road Auckland, Auckland 2025, New Zealand.

In the PNS, regeneration takes place through either axonal regenerative sprouting (ARS) or collateral sprouting (CS). In ARS, the injured axon grows new processes to reconnect with its target; in CS, axons from adjacent uninjured nerves advance new branches into the denervated targets – such as skin, mucosa or muscle tissue.

The ARS process is well studied and publicised. It can only proceed well with certain grade of nerve injury (axonotmesis) unless surgically facilitated; it is a length-dependent slow process and the target organs may not be receptive due to the long delays; there may be the complication of cross-connection between sensory and motor fibres in higher grade injuries (neurotmesis), despite optimal surgical repair.

In contrast, the CS process is quite spontaneous and versatile, not requiring any surgical repair of peripheral nerves to facilitate it. It is not typically "length dependent" in that the intact adjacent nerves very distal to the site of the original nerves can extend collateral sprouts into the denervated area well before ARS mediated growth can reach there. For instance, following femoral nerve injury in groin or iliac fossa, it may take well over a year for the ARS mediated recovery to reach the skin over medial malleolus; in contrast, CS from the adjacent intact nerves re-innervate the whole saphenous nerve innervated skin over the shin within a matter of weeks to months, well before the ARS mediated recovery would creep even to the knee level. If at all anything, it may be appropriate to describe the CS mediated recovery as "width-dependent" or centripetal, as it is the width of the denervated skin area that determines the time taken for the CS from adjacent nerves to cover the gap. Despite such superiority of CS [1], with its spontaneous and versatile nature, it has received very little attention in the literature and clinical practice.

While CS is most evident in the situation of re-innervating the denervated skin, there are many other situations where it is likely to be active:

CS would work well in any tissue or organ that is laid down as a continuous sheet. In addition to the skin, other such areas include mucosae and serosae. Robinson et. al. [2] demonstrated regaining of sensation across the face by surgical denervation of trigeminal ganglion. Such CS mediated sensory recovery of the denervated mucosa inside the mouth would be very valuable in oral functions such as

chewing and swallowing.

CS also works for muscles when there is no fascial barrier between the donor and recipient muscles. This is particularly evident in the muscles with dual innervation as demonstrated by Lemaitre [3], who has elaborated on the molecular mechanisms and the transcriptome involved in this process. Edds [4] attributes the first recognition of this phenomenon to Exner's animal experiments in 1884-85. This is one of the likely mechanisms why the muscles at neurological level of injury (NLI) often progress from grade 3 power to grade 4 or 5, despite a complete spinal cord injury (SCI); here the intramuscular nerve fibres from the proximal intact nerve root extend collateral sprouts into the denervated part of the same muscle originally supplied by a distal root arising at or just below the SCI and in a lower motor neurone (LMN) injury state. The same is likely in case of certain muscles supplied by 2 different nerve plexuses. For instance, in cases of complete lumbar plexus palsy, hip abductor muscles may show some EMG evidence of partial denervation early on, due to the 4th lumbar nerve involvement and this gets eventually replaced by features of re-innervation (such as polyphasic potentials). Such re-innervation is taking place due to intramuscular collateral sprouts from the 5th lumbar root (sacral plexus) portion of the superior gluteal nerve extending to the denervated muscle fibres originally supplied by the 4th lumbar part of the same nerve.

CS is also likely to be operational is in the autonomic nervous system. Following heart transplantation, the transplanted organ remains largely unresponsive to vagal & sympathetic inputs. However, there is evidence supporting the idea of cardiac reinnervation, which has been shown to occur in 40% to 70% of recipients late after heart transplantation [5]. CS is the likely basis for this recovery, as the neural anastomosis is not routinely performed during heart transplantation.

CS is likely playing a silent, yet very significant role in reinnervating the denervated skin following surgical incisions. Many incisions are so placed that some damage to nerve branches is inevitable. Some examples include abdominal incisions such as subcostal & paramedian, transverse incisions across the limb joints (wrist, knee) and neck, etc. It is rare to see any significant sensory deficit following such incisions. This is very likely due to excellent reinnervation through CS from the adjacent intact nerves. Also, CS can work across clean surgical scars, as shown by swine alloflap experiments [6].

In a recently published hypothesis article [7], the author has proposed many neurectomy interventions affecting the areas of body disconnected from the central nervous system (CNS) through lesions such as stroke, SCI and cauda equina syndrome (CES), with a view to minimise sensory-motor deficits through CS from the adjacent unaffected nerves.

There is lack of clarity about the speed & extent of recovery through CS, though some estimations may be possible based on nerve harvest studies. In a meta-analysis of 12 studies of sural nerve biopsy and harvest, Ducic et al. [8] reported that all these studies found some extent of improvement in sensory deficit, including substantial CS-mediated recovery in one prospective study [9]. Further prospective studies of this type and the therapeutic applications suggested by the author [7] can help to establish the utility & limits of CS as well as the factors influencing it.

Brain's reorientation ability (cortical plasticity) after CS mediated reinnervation is not well studied. Baldassarre et al. [10] have conducted a detailed review of various aspects of cortical plasticity following nerve injury and surgery; this has included successful trans-hemispheric communication and control when the contralateral C7 nerve root was used to reconstruct brachial plexus injury. Such findings may also apply to the scenarios where CS is the mechanism to re-innervate the insensate skin and paralyzed muscles.

A good understanding about the science of CS will be useful to clinicians in many ways. Surgeons can explain to their patients with numbness around surgical scars about the probability of sensory recovery and the likely timeframe. Misinterpretation of certain clinical and electrophysiological findings can be avoided. For instance, one may identify that the concentric sensory recovery in the months following a complete lumbar plexus is due to CS and not true recovery of the plexus, thus avoiding giving false hopes to the patients. In situations of partial paralysis of muscles, as occurs in SCI, awareness about the likely intramuscular CS mediated recovery helps the clinician to plan the rehab strategies and timing of salvage surgeries accordingly. Also, peripheral nerve & muscle intervention strategies applying the phenomenon of CS will open the avenues of expanding the existing sensate and voluntary motor territories in those with more central lesions such as CES, SCI and stroke, thereby minimising the residual deficits & disability [7].

In conclusion, CS is a spontaneous & versatile, but underappreciated reinnervation mechanism that is at work in multiple areas & circumstances, helping us to compensate for the PNS denervation related deficits. With proper understanding and application of this mechanism, it may be possible to exploit this through novel pursuits such as minimising deficits resulting from more proximal neuraxial injuries. Such efforts will also help in further understanding the speed & extent of CS, factors affecting this process as well as the cortical plasticity aspects concerned in recognising & using reinnervated tissues.

References

1. Diamond J and Foerster A. "Recovery of sensory function in skin deprived of its innervation by lesion of the peripheral nerve". Exp Neurol 115.1 (1992): 100-103.
2. Robinson PP. "Recession of sensory loss from the midline following trigeminal sensory root section: collateral sprouting from the normal side?". Brain Res 259.1 (1983): 177-180.
3. Lemaitre D and Court FA. "New insights on the molecular mechanisms of collateral sprouting after peripheral nerve injury". Neural Regen Res 16.9 (2021): 1760-1761.
4. Edds MV Jr. "Collateral nerve regeneration". Q Rev Biol 28.3 (1953): 260-76.
5. Awad M., et al. "Early denervation and late reinnervation of the heart following cardiac transplantation: a review". J Am Heart Assoc 5.11 (2016): e004070.
6. Ibrahim Z., et al. "Cutaneous collateral axonal sprouting re-innervates the skin component and restores sensation of denervated Swine osteomyocutaneous alloflaps". PLoS One 8.10 (2013): e77646.
7. Adiga S. "Expansion of Intact Sensory-motor Territories in Proximal Neuraxial Lesions using Peripheral Nerve-muscle Weeding Interventions". Explor Res Hypothesis Med 9.2 (2024): 162-169.
8. Ducic I, Yoon J and Buncke G. "Chronic postoperative complications and donor site morbidity after sural nerve autograft harvest or biopsy". Microsurgery 40.6 (2020): 710-716.
9. Theriault M., et al. "A prospective quantitative study of sensory deficits after whole sural nerve biopsies in diabetic and nondiabetic patients. Surgical approach and the role of collateral sprouting". Neurology 50.2 (1998): 480-484.
10. Baldassarre BM., et al. "Principles of Cortical Plasticity in Peripheral Nerve Surgery". Surg Technol Int 36 (2020): 444-452.