ISPRM Sydney 2024 congress workshop (PN 155, Monday June 3rd 5-6 PM) delegate pre-reading material

This Peripheral nerve (PN) workshop consists of 3 interactive lectures focusing on less appreciated and emphasised aspects of peripheral nerve pathophysiology including general principles of nerve injury and recovery, retroperitoneal nerve compression syndromes as well as a novel application of PN collateral sprouting properties to address neurological deficits in central nervous lesions. Accordingly, the reading material is organised in 3 sections below.

Section 1. General principles of nerve injury and healing (Talk 2, by Dr Robin Sekerak)

These topics will be touched upon, to the extent possible within the limited time. You may look up some of these topics before the workshop.
Nerve injury mechanisms & classifications (Seddon and Sunderland)
Clinical examination of peripheral nerve injuries (PNI) and LMN syndromes
Functional loss and recovery in neuropraxia – time course and clinical features
Wallarian degeneration – time course, clinical, Electrodiagnostic (EDX) (EMG and NCS) features
Axonal regeneration / motor march – time course, clinical, EDX features
Neuroma, cross-connection, CRPS, etc.
Compartment syndromes: muscle Vs. nerve pathology, recovery with and without decompression
Pitfalls of percutaneous interventions (Vs. open surgery)
Focal nerve compression syndromes
Neurotisation, end-to-side anastomosis
Motor end-plate and sensory end-organ organ death
Collateral sprouting as a mode of sensory recovery

Section 2. Retroperitoneal compression syndromes (Talk 1, by Dr Subramanya Adiga)

Retroperitoneal compartment / compression syndromes from psoas & Iliacus haematomas with resultant lower limb nerve palsies (lumbar plexus / femoral nerve) are not well-recognized. Literature is often confusing with misleading terminology such as and "lumbo-sacral" "radiculo-plexo-neuropathy" and "ilio-psoas" collection - meaning different things to different people; treatments and outcomes of different conditions under these umbrellas are often different. There are no prospective studies. The literature consists of case reports, case series and review articles, lacking guidance regarding timely recognition, appropriate acute and rehabilitation management or subsequent salvage options for established deficits. Acute retroperitoneal collections (haematomas and abscesses) in tight myofascial compartments of Psoas major and Iliacus muscles result in acute compartment syndromes, causing in nerve palsies that are amenable for acute decompression interventions. Due to a lack of awareness of this, opportunities for timely interventions decompressing lumbar plexus/femoral nerve are missed. This Results in poor outcomes with permanent deficits and significant disability in many cases.

In clinical practice, it is common to see missed or delayed diagnosis leading to lack of timely interventions and poor outcomes, with prolonged hospital stay and significant residual deficits. It is important to differentiate these acute and treatable conditions from other chronic plexopathies. Often these patients are quite unwell; it is easy and common to overlook major lower limb palsies. Clinicians are usually good at recognising deficit patterns of stroke and spinal paralysis; however, peripheral nerve injury diagnosis can often be missed by non-neurologists; delayed diagnosis and misdiagnosis are not uncommon, including confusing it with functional neurological deficits. Femoral and Obturator are the 2 main motor nerves arising from lumbar plexus. However, there may be subtle deficits in the muscles supplied by the sacral plexus (gluteus medius and tibialis anterior) on EMG, due to the 4th lumbar nerve branch extending from the lumbar to the sacral plexus. Clinicians and neurophysiologists may fall prey to this trap, misdiagnosing the condition as wide-spread lumbo-sacral plexus lesion. While early surgical decompression is arguably the best treatment for preventing / reversing nerve deficits, there is insufficient hard evidence and it is difficult to execute in time, even when the condition is correctly diagnosed in a timely manner. Clinicians, including radiologists, do not often appreciate that acute compartment syndrome cannot be adequately decompressed with percutaneous drains and that there is a high risk of converting a transient neurological deficit (Neuropraxia) into a permanent one (Neurotmesis) during insertion and/or removal of a percutaneous drain right next to (or through!) a bunch of nerves (lumbar plexus).

Poor awareness of these nerve palsies often results in insufficient guidance to the therapy team. This results in recurrent falls and further injuries due to attempts to encourage the patients to stand on their paralysed limbs without any supporting orthotics. Skin burns and pressure injuries (including those from orthotic braces) due to unrecognised anaesthetic skin is not uncommon. Lack of understanding of nerve injury and recovery patterns result in further missed opportunities; clinicians fail to request appropriate investigations (EMG, NCS, MRI scan) and refer to reconstruction specialists in a timely manner. As motor end-plates tend to degenerate around 18 months post injury and as it takes a few months for new nerves to grow into their targets (post neurotisation surgery), delayed referral means permanent & severe neurological deficits.

With increasing use of anti-platelet and anticoagulant medications, often two or more of these together, retroperitoneal bleeds are probably on the increase. At times these occur as secondary complications in stroke patients; when nerve palsies of this kind occur in the limbs with UMN paralysis, these are difficult to diagnose and manage. The resulting new lower motor neurone palsy causes further disability, as the patients now lose their ability of automatic stance, which aided them in standing and pivot transfers.

Clinicians concerned (physicians, surgeons, radiologists and acute ward therapists) should be aware of the principles outlined above and help each other in achieving early diagnosis, appropriate investigations and management and avoidance of secondary complications and unnecessary disability (in addition to cost savings by reduced length of stay). It would be even better if everyone used precise terminology like "psoas haematoma causing acute lumbar plexus palsy" rather than vague one like "lumbo-sacral radiculo-plexopathy from ilio-psoas collection". In conclusion, there is need for more research, use of consistent terminology, consensus about diagnosis and management and education of clinicians in this area, making retroperitoneal compartment syndromes with lower limb neurological deficits a well-understood, leading to early recognition and timely interventions with better outcomes.

Ref: S. Adiga, Lumbar plexus/femoral nerve palsy resulting from retroperitoneal compartment syndromes (psoas and Iliacus)—double whammy in stroke patients—Diagnostic and management challenges, WCNR 2022 abstracts (P131)
Link: https://journals.sagepub.com/doi/epub/10.1177/15459683231159499

Section 3. Weeding applications on peripheral nerves to facilitate expansion of intact sensory-motor territories in central lesions (Talk 3, by Dr Subramanya Adiga)

In complete peripheral nerve injuries (PNI) cases, despite no motor recovery, shrinkage of insensate area takes place, by collateral sprouting from the adjacent intact nerves. This pattern is not observed in central lesions - stroke & spinal cord injury (SCI) as well as cauda equina syndrome (CES) andpre-ganglionic brachial plexus injuries (pBPI).

A different process is taking place in PNI, permitting take-over of the insensate territory by adjacent nerves. Nerve conduction studies (NCS) give us a clue: normal peripheral sensory conduction is seen in all higher sensory lesions mentioned above, in contrast to PNI. This is because of cell bodies of first-order sensory neurones (FSN) in dorsal root ganglions (DRG) retaining their connection to sensory end organs (SEO) in skin and mucosae through their peripheral processes; thus, FSN in DRGs maintain their territory, preventing take-over attempts. In contrast, in PNI, this peripheral continuity and control of FSN is lost; adjacent intact nerves take over these territories and shrink the insensate area.

With this understanding, the research hypothesis about possible interventions facilitating such recovery in proximal lesions is formulated: "Creating a new distal discontinuity (PNI) in cases of more proximal sensory discontinuity can help to expand the sensate area by facilitating take-over by the adjacent intact / sensate territories."

A literature review was conducted, searching Medline, Embase & Cochrane databases using 3 categories of terms - CNS conditions (stroke, SCI, CES, pBPI, related terms), nerve recovery (Nerve degeneration, regeneration, collateral sprouting, related terms) and peripheral interventions (lesioning, ablation, radiofrequency, alcohol, phenol, etc.) and combining these using 'AND' function. This yielded 852 results; however, on abstract screening, none of these were found to be related to this hypothesis. There were no high- or low-quality studies; nor editorials, letters to editor, nor publications of any other kind, exploring this idea. Therefore, this is very likely a new, hitherto unexplored concept.

These are a few possible interventions based on this hypothesis:

Stroke (Thalamic / sensory): sectioning cutaneous nerves close to the midline – such as cervical plexus branches - to facilitate sensory territory take-over across the midline.
SCI (lower thoracic, AIS-A): Post-ganglionic lesioning of a few nerve roots below the neurological level of injury (NLI), facilitating sensory-motor (abdominal and back muscles) expansion from the last intact root above.
Complete CES: Creating alcohol, phenol, radiofrequency or surgical lesioning of the DRGs or nerves below the NLI – to facilitate sensory take-over by branches of L1-L4 nerve branches in the territories next to the insensate areas (Fig 1).
Preganglionic BPI: Similar to CES – creating post-ganglionic brachial plexus lesions, to facilitate sensory take-over of the proximal limb areas (C5, T1) from the neighbouring trunk nerves (C4, T2-3).
This type of collateral sprouting mediated take-over of the paralysed motor territories by the intact adjacent nerves is not seen as the muscles are separated by fascial & aponeurotic barriers that the nerves can't cross. We know from the TMR (Targeted Muscle Reinnervation) studies that such take-over of the new motor territories is possible, when surgically facilitated. Hence, there is a case for new surgical interventions – fasciectomy, opposing the paralysed and unaffected muscles. Based on our literature search, this is a novel idea too; application of this concept in some select situations will be deliberated in the workshop.

Relevant literature: Kirk, et al[1] demonstrated significantly larger sensory expansion after post-ganglionic (Vs preganglionic) division of the adjacent nerves in nerve-section experiments. There are reports of nerve collateral growth & sensate area expansion across midline & even surgical scars[2]. A meta-analysis on nerve harvest / biopsy studies showed a degree of collateral sprouting mediated sensory recovery in all included studies[3], with a prospective study showing more than 90% of the insensate area recovering. These are listed in references for further reading.

There are many research questions to be answered in coming years: Which nerves/injuries do better? How-far/how-long they grow? Factors that help/hinder? Intervention timing? Fatigue in future? Next step would be to test the hypothesis for effectiveness and safety. Focus groups consisting of patients, clinicians & other stakeholders maybe help to establish propriety. As stated by Sterling Bunnell: "To someone who has nothing, a little is a lot". Therefore, translation of this research hypothesis into clinical practice is likely to help many disabled individuals.

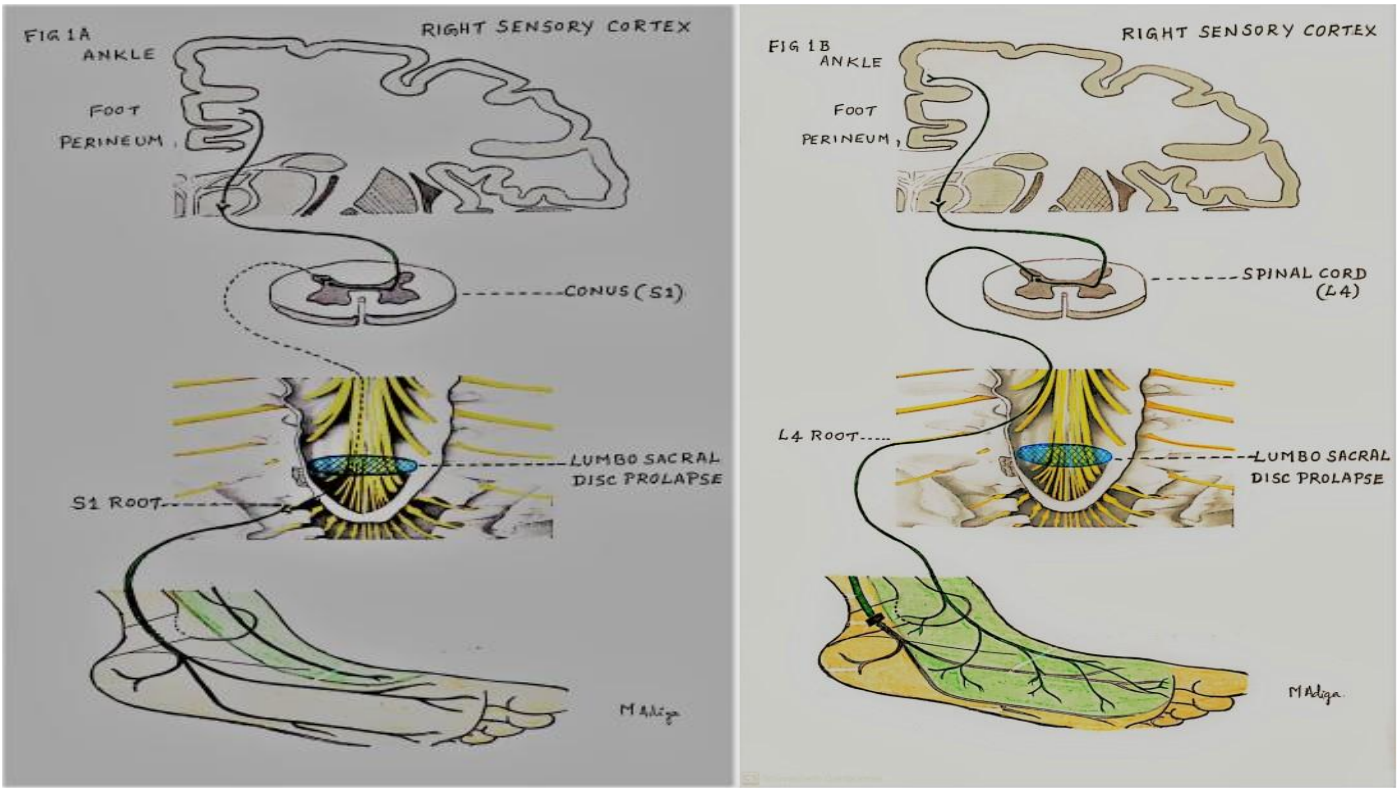

Figure 1. Depiction of rerouting of sensory conduction to the brain in a complete cauda equina syndrome (L5-S1 level central disc prolapse) case. Figure 1A. Tibial nerve (territory shown in beige color) is continuous peripherally from the dorsal root ganglion at the first sacral foramen to the skin at the sole of the foot. Therefore, though it is disconnected from the spinal cord by the disc herniation, it opposes any attempts of territory take-over through collateral sprouting by the adjacent intact saphenous nerve (green-shaded territory). While the second- and third-order sensory neurones are still intact, reaching the foot area of sensory homunculus, the sensation does not reach the brain due to the degeneration of the proximal process of the first-order neurone from the level of disc prolapse up to conus medullaris. Figure 1B. The same case after the neurectomy (shown as a black solid rectangle over the tarsal tunnel area) of cutaneous branches of the tibial nerve in the tarsal tunnel. Now, the sensate saphenous nerve (connecting to the central nervous system at L4, above the disc prolapse) extends collateral sprouts into this newly denervated territory on the sole of the foot, thus expanding its sensate territory. The newly acquired sensory territory on the sole of the left foot is now connected to the right sensory cortex through the L4 sensory root. As the rediscovered sensation from the sole of the foot now reaches the ankle area on the same sensory homunculus, very close to the original foot area, re-orientation through cortical plasticity may be easier (compared to the stroke scenario discussed in the workshop).

Link to my recently published hypothesis article:

https://www.xiahepublishing.com/2472-0712/ERHM-2023-00020/pdf

Other References cited above:

1. Functional variation in dermatomes in macaque monkey following dorsal root lesions, EJ Kirk, et. al, J Comp Neurol. 1970 Jul: 139(3): 307-20

2. Collateral axonal sprouting re-innervates the skin & restores sensation of denervated swine alloflaps, Zuhaib Ibrahim, et. Al, PLoS One, 2013; 8(10): e77646, published online Oct 18, 2013

3. Chronic post-op complications & donor site morbidity after sural nerve harvest or biopsy, Ivica Ducic, et. Al, Microsurgery, 2020 Sep; 40(6): 710-16