Commentary

Nerve resection for the treatment of chronic neuropathic pain

When empirical observations fly in the face of prior knowledge, it is likely that there are lessons to be learned. Peter Watson and coauthors [20] report in this issue of PAIN a case of a young woman with chronic debilitating complex regional pain syndrome (CRPS) 2 resulting from traumatic nerve injury in the ankle, exacerbated by a subsequent orthopedic procedure. Typical of CRPS, the pain spread beyond the ankle, resulting in severe burning pain and tactile allodynia on most of the lower leg. A variety of pharmacologic, physical, and psychological therapies failed to relieve the pain. After 13 years of suffering by the patient (and frustration by her physicians), the unusual step was taken to cut some of the nerves serving the injured ankle. According to the report, this surgery resulted in an immediate and dramatic improvement in the allodynia and associated neuropathic pain symptoms, which has so far lasted >2 years. There remains, however, a qualitatively different (and arguably nonneuropathic) residual ankle soreness which severely limits mobility.

The primary driver of the patient’s clearly neuropathic symptoms appears to have been in the ankle on the grounds that the initiating injury was there, ankle loading exacerbated the pain, and diagnostic nerve blocks transiently relieved it. On its face, cutting a nerve, like cutting a noisy telephone line, ought to stop pain generated distally. However, there are 2 theoretical caveats to this logic. First, resecting a neuroma, or cutting the nerve proximally, might simply trigger the formation of a new painful neuroma. The patient, after all, is apparently predisposed to developing neuropathic pain and may do so again. Second, many physicians believe that over time, generators of pain migrate from the periphery into the central nervous system (CNS), where they become refractory to treatment (centralization, transition to chronicity) [1,9,11]. After 13 years, it may be too late.

Theories aside, many surgeons have tried cutting nerves, dorsal roots, and spinal tracts in an attempt to stop pain. The prevailing conclusion after decades of experience has been that the pain relief provided by these operations is usually temporary, with pain typically recurring in weeks or months, often with a vengeance [4,14,18,21]. Since the 1980s, expert opinion in the pain community has been to avoid adding iatrogenic injury to already injured nerves. This was summarized succinctly in an influential article by Noordenbos and Wall [15], who wrote, “We propose that resection should not be done to damaged nerves associated with pain and abnormal sensitivity.” The number of neurosurgical interventions for pain indeed fell drastically since then. Watson et al. [20] specifically noted that the consensus among “experienced and highly respected pain neurosurgeons” today is against resection—and all the more so for CRPS, where the very diagnosis implies a disproportionate pain response to injury.

However, there are a few exceptions to this rule. Most notable is the situation where pain is primarily due to mechanical forces applied to a neuroma (eg, in an amputation stump). Here, mobilizing the neuroma to a padded location protected from external forces both makes sense and usually succeeds in practice [3]. It is against this background that the case report of Watson et al. is so striking. How can their success be understood? Is the general advice that nerves should not be recut misguided?

It is clear that a single case report is not enough to reverse decades of clinical experience. That said, might there be features of the case of Watson et al., and others like it, that mitigate against the sweeping statement, “This should not be done!” Several factors need to be considered.

1. The dorsal root ganglion (DRG) as a driver of neuropathic pain

The site of nerve injury is not the only source of ectopic impulse generation within the peripheral nervous system. Indeed, in head-to-head comparisons in animal models, the DRG emerges as the predominant source of spontaneous firing [2,12], although the neuroma is probably more important for mechanically evoked pain during weight bearing and movement. Tactile allodynia, which is thought to be maintained by peripheral input, could be due to either. In principle, it is straightforward to determine the balance between these sources in any given patient using diagnostic nerve blocks. Nerve block should not eliminate effects of DRG ectopia. Note, however, that, it is difficult to completely block large nerves (sciatic, brachial plexus), and comparison against the same anesthetic dose injected systemically is essential because DRG ectopia is sensitive to very low concentrations of circulating anesthetics [6].

2. The CNS as a driver of neuropathic pain

Marked changes evolve in the CNS after peripheral nerve injury and the idea that the actual pain source migrates centrally is alluring [1,9,11]. However, assuming that some of these changes are indeed related to persistent pain, do they cause the pain, or are they effects of pain? Excepting cases of CNS injury (central pain), evidence of CNS drive (as opposed to amplification) is sparse. When
known peripheral sources are removed, eg, after total hip replacement or the passing of a kidney stone, pain reliably resolves. Likewise nerve, regional and spinal blocks consistently eliminate pain for the duration of the block. Note that there is no obvious reason to expect that pain relief should persist longer than this, although it occasionally does. Increasing knowledge of peripheral electrogenesis in neuropathy is rapidly undermining classic examples of CNS drive, such as fibromyalgia and phantom limb pain [6,10,13,16].

3. A painful neuroma will re-form

A structural neuroma always forms proximal to a nerve cut. However, it is not the neuroma that causes pain but rather the electrical discharge that arises in neurones in predisposed individuals [6]. It is likely that developing an electrically active neuroma at the initial nerve injury is a risk factor for developing pain at resection. However, this cannot be taken for granted. The subject awaits experimental study. The fact is that clinical case series, even the classical ones on which the stricture against resecting injured nerves is based, always include a fraction of successes. As noted by Watson et al. [20], the plastic and orthopedic surgical literature contains many claims of success for various different chronic pain conditions, including CRPS [5,7,8,17]. Unfortunately, this literature to the outcome?

The subject awaits experimental study. The fact is that clinical case series, even the classical ones on which the stricture against resecting injured nerves is based, always include a fraction of successes. As noted by Watson et al. [20], the plastic and orthopedic surgical literature contains many claims of success for various different chronic pain conditions, including CRPS [5,7,8,17]. Unfortunately, this literature tends to lack systematic documentation, lack controls for bias in reporting, and lacks long-term tracking of pain recurrence. An example is Morton’s neuroma (pain due to injury of a small digital nerve). Although it is a common condition that is frequently treated with nerve resection or neurolysis, and is one that has spawned many case studies, a recent Cochrane review found very few reports that meet minimum quality standards. In those that did, the interim conclusion about the efficacy of this treatment was equivocal [19].

It is entirely possible that systematic analysis of successes and failures, in a research setting, might yield new diagnostic criteria for patient screening in addition to the consideration of mechanical factors and the results of diagnostic nerve block (with systemic controls). Systematic analysis of the surgical techniques could also be informative [22]. In the case of Watson et al., for example, nerves were extensively exposed, subject to traction, distally cauterized, mobilized, and proximally crushed. Was all of this relevant to the outcome?

In conclusion, the dogma that recutting injured nerves in neuropathic pain patients necessarily has disastrous consequences has probably been overstated. We tend to agree with Watson et al. that the time has come to release the brakes a bit and move forward with clinical investigation. However, given clinical experience, this must be done with care. Studies must be conducted in a systematic, controlled manner and with careful, quantitative, and prolonged postsurgical follow-up. The sine qua non of therapeutic decision making with respect to neuropathic pain is locating the pain driver: from where are the impulses coming that cause the pain? This question is crucial to the initial treatment of neuropathic pain—no less so in the event of pain recurrence after surgical resection of a nerve.

Conflict of interest statement

The authors are aware of no conflicts of interest regarding this commentary.

References


Marshall Devor
Department of Cell and Developmental Biology, Institute of Life Science, Faculty of Natural Sciences, and the Center for Research on Pain, The Hebrew University of Jerusalem, Jerusalem 91904, Israel

Tel.: +972 2 658 5085; fax: +972 2 658 6027.
E-mail address: marshlu@mail.huji.ac.il

Michael Tal
Department of Medical Neurobiology, Faculties of Medicine and Dentistry, and the Center for Research on Pain, The Hebrew University of Jerusalem, Jerusalem 91120, Israel