History of PNS

Therapeutic electrical stimulation was proposed by Wall and Melzack in 1965 with the introduction of the gate control theory of pain perception.[1] This led to the development of neuromodulation, the dosing of electric current by implanted electrode leads to treat pain and neurologic dysfunction. One of the earliest reports on neuromodulation was published in 1967 and involved PNS, which is defined as applying electrical stimulation directly to a named nerve. In this study, Wall and Sweet applied this theory, experimentally developed in cats and tested on their own infraorbital nerves. They reported an eight-patient case series involving neuropathic pain from a variety of etiologies. They found that two-minute electrical stimulation produced pleasant paresthesia and decreased pain, but yielded only temporary benefit.[2] Despite this early application, however, the growth of PNS was limited for several decades due to impracticalities of early PNS because of the requirement for surgical dissection to the affected nerve and associated complications, including direct nerve trauma, fibrosis of surrounding tissues, lead migration, and frequent need for hardware revisions.[3,4]

In 1967, Shealy and Mortimer described their analgesic results with dorsal column spinal cord stimulation (SCS) using a modified electrical stimulator initially designed to stimulate the carotid sinus to treat hypertension and angina.[5] Due to its success, the device was made commercially available the following year, and dorsal column stimulation became the most popular modality of electrical neuromodulation for several decades. Developing reports of improvement in symptoms of torticollis,[6] spasticity in multiple sclerosis,[7] increased blood flow[8] and thereby decreasing painful peripheral vascular disease[9] and angina[10] further pushed research focus away from PNS in favor of SCS. Over that time, significant advances were made in SCS system technology, but PNS remained static with little innovation.

In 1999, however, Weiner and Reed brought attention back to PNS with a case series of 13 patients suffering from occipital neuralgia. Each patient underwent a diagnostic peripheral nerve block, a five to seven-day temporary lead trial, followed by percutaneous lead and subcutaneous implantable pulse generator (IPG) implantation. At follow-ups between one and six years, 66% of patients described >75% pain relief, and 33% described 50% relief.[11] In more recent years, there has been an explosion of interest in stimulating the C- and A-delta fibers in the periphery, especially as imaging modalities (eg, ultrasound) have improved targeting of nerves and the technology has supported less invasive means of treatment to improve PNS treatment efficacy, durability, and safety.

History of Trial, 60-Day Temporary, and Permanent Implant

With renewed interest in PNS, new techniques developed with advancing technology to address previous shortcomings. Ultrasound-guided PNS was described by Huntoon et al,[12–14] a technique that allows for a percutaneous and minimally invasive approach to lead placement to obviate the need for a surgical cut-down. Lead advancement has also improved significantly in recent years. Historically, PNS was offered through cylindrical leads that were designed for SCS. In the PNS application, they were large and had a high migration rate (9–25%), prohibiting implantation across joints and with increased risk of infection (3.6–17.9%).[15] Patients often went to a temporary trial with percutaneous lead placement and connection to an external generator as is customary for SCS. More recently, a new proprietary lead design [SPRINT® PNS System, SPR® Therapeutics, Cleveland, Ohio, USA] was developed using a helically coiled monopolar lead (versus solid and cylindrical). This coiled design encourages fibrotic ingrowth around the lead, significantly decreasing migration and infection rates (up to 25-fold reduction).[16–18] United States Food and Drug Administration (FDA)-cleared for up to 60 days of use, this system allows for extended periods of stimulation, which can act as a definitive course of treatment and possibly decrease the need for permanent systems.

The exact mechanism by which electrical stimulation of peripheral nerves provides analgesia has not fully been elucidated. Still, there has been considerable progress in our understanding since the initial gate control theory. Chronic inflammation of peripheral nerves leads to hyperexcitability and an increased rate of depolarization, a phenomenon known as peripheral sensitization. These nerves repeatedly fire an abnormal afferent signal to the wide dynamic range neurons in the dorsal column of the spinal cord. The overstimulation of wide dynamic range neurons leads to multiple changes in the spinal cord and brain, leading to central sensitization of pain. At the spinal cord, activation of glial cells increases inflammation and hyperexcitability of nociceptive pathways. In addition, glycinergic and gamma-aminobutyric acid (GABA)-ergic inhibitory neuronal activity decreases, thereby increasing abnormal afferent nociceptive signaling to the brain. A similar process then affects the supraspinal nociceptive circuits, ultimately resulting in neuroplastic changes