

Peripheral nerve stimulation in the treatment of intractable pain

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✓ Peripheral nerve stimulating devices were implanted for pain control in 33 patients with a variety of disabling chronic pain conditions, which had persisted despite usual medical and surgical therapy. The implants were placed on major nerves innervating the area of the patient's pain. Records were obtained of each patient's stated relief from pain produced by nerve stimulation, along with assessments of narcotic withdrawal, ability to return to work, sleep pattern, and relief from depression. Based on these five criteria 17 patients were judged to be treatment failures, while eight patients had excellent results, and seven had intermediate results. Twelve of the failures were in patients with either low back pain with sciatica, or pain from metastatic disease. The most dramatic successes occurred in patients with peripheral nerve trauma. The incidence of complications has been low, and two patients have used the stimulator for 5 years without adverse effects. Techniques of peripheral stimulator implantation, possible mechanisms of action, and conclusions regarding peripheral nerve stimulation in the treatment of chronic pain are discussed.

KEY WORDS • intractable pain • nerve stimulation

THE options for treatment of intractable pain are few. Until recent years they have been confined to psychotherapy, narcotics, or various neural ablative procedures. None of these methods has proved satisfactory for long-term patient management. The finding of Wall and Sweet²⁵ in 1967 that percutaneous sensory nerve electrical stimulation could produce hypesthesias distal to the point of stimulation, therefore, encouraged interest in the possibility that neural stimulation could be used to treat intractable pain. The two most common techniques described are transcutaneous electrical stimulation,⁷ and spinal cord stimulation via electrodes placed over the dorsal columns.^{13,17,18}

Transcutaneous stimulation has the disadvantage of being cumbersome; moreover adequate stimulation of the involved nerve

produces discomfort referred to the overlying skin. Spinal cord stimulation has the disadvantage of requiring a major operation. In addition, there are often difficulties with ideal placement of the electrodes, and a disturbingly high number of long-term technical failures occur, due in part to scar formation around the electrodes.^{9,15,16}

A third method of neural stimulation for pain control involves implantation of peripheral nerve stimulators (PNS). Bipolar electrodes are attached to major nerves of which the field of innervation contains the region in which pain arises, and are then connected to a radiofrequency receiver placed under the skin. The electrodes can then be activated by a transmitting device connected to an antenna taped in place over the receiver.

In the following report, we describe the results obtained in a series of 23 patients who

directed at the assessment of five variables:

1. Each patient's own impression of how much pain relief he was receiving from use of the stimulator device
2. Patterns of drug use
3. Sleeping habits
4. Activity level
5. Psychological well-being.

In addition, inquiries as to patterns of stimulator use and adverse effects were made.

Follow-up information was also obtained on nine of 10 patients with PNS implantation done at the University of Minnesota. Patient charts and information obtained from the patients' personal physician were used as sources of this information.

Summary of Patients

Johns Hopkins Hospital Series

A summary of the results for each patient is contained in Table 1 along with the patient's diagnosis, type of stimulator implanted, and length of follow-up period. An excellent result is defined by the following criteria:

1. The patient must continue to require the use of the stimulator for pain relief, thus all patients with a spontaneous remission are excluded. (Only one patient had a spontaneous remission, and this patient was considered a treatment failure by other criteria.)
2. Analgesic use must be confined to occasional use of Tylenol (acetaminophen) or aspirin.
3. All patients must have been able to resume their usual occupation, or at least be active at a level compatible with their neurological deficit.
4. All patients who previously had been depressed because of their pain must have had an improvement in mood.
5. Sleep disturbance previously associated with pain must have ceased.
6. Each patient must have felt that use of the peripheral nerve stimulator provided more than 50% relief of his pain.

Of the 23 patients, four were judged to have had excellent results. Another five patients met some of these criteria, and were judged to be partial successes. The remaining 14 patients were treatment failures. Eleven of the treatment failures occurred in patients with low back pain syndrome with sciatica, or pain

from metastatic disease. One of the treatment failures was in a patient (Case 4) who had had a traumatic amputation of his thumb with resulting dysesthesias. Trials of percutaneous stimulation preoperatively had failed to relieve his pain; however, because of his desperate situation, a brachial plexus stimulator was implanted although the chance for success was thought to be poor.

One of the four partial success patients (Case 3) had had nerve trauma in the hand and had undergone a number of hand operations. He had two distinct types of pain, the worse being a sharp jabbing pain, and the other a burning dysesthesia. The stimulator relieved the former pain and allowed him to return to work. Subsequent to the stimulator implantation, he had a sympathectomy, and internal neurolysis of the median nerve, which has relieved his second type of pain. He is now able to resume a normal life without use of analgesics, but requires the use of the stimulator to control the sharp jabbing pain to which he is still subject.

Another partial success was a patient who had had excellent results for 9 months, but then developed an incomplete radial nerve palsy and a partial return of pain in the areas distal to the brachial plexus stimulation device. This patient is currently in the hospital undergoing diagnostic evaluation. The other partial successes were in patients with low back pain sciatica who claimed substantial pain relief with use of the stimulator, but who were unable to resume normal lives because of remaining pain.

Two of the excellent results occurred in patients with peripheral nerve trauma which had failed to improve despite multiple operations. Another was in a patient with brachial neuritis secondary to radiation therapy for breast carcinoma. The fourth case was in a patient who continued to have severe arm pain following removal of a cervical rib causing brachial plexus compression.

There was one infection, which occurred in the area where the receiver had been implanted on the anterior chest wall. The patient (Case 5) had had a radical mastectomy and radiation therapy to this area, and the infection probably resulted from poor healing. She has done well after relocation of the receiver. There was one noninfectious tissue reaction. This complication presumably reflects an idiosyncratic reaction to the PNS implant as

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TABLE 1

Results of peripheral nerve stimulator implants in 23 patients

Case No.	Age, Sex	Stimulator Location	Diagnosis	Complications	Result	Follow-Up (mos)
1	55 F	brachial	arm pain after cervical rib removal	none	excellent	12
2	32 F	brachial	crush injury to elbow	relief for 1 yr then wrist weakness and partial pain return	partial success	13
3	27 M	brachial	ringer injury to hand	none	partial success	12
4	51 M	brachial	traumatic amputation of thumb	none	failure	6
5	71 F	brachial	brachial plexitis from radiotherapy for breast carcinoma	infection, PNS removed then reimplanted	excellent	3
6	33 M	median	traumatic amputation of forefinger	noninfectious tissue reaction	technical failure	10
7	37 M	median	wrist crush with median nerve injury	none	excellent	8
8	17 M	ulnar	elbow crush with ulnar nerve injury	none	excellent	12
9	60 M	sciatic	metastasis to spine; colonic carcinoma	none	failure	12
10	57 F	bilateral sciatic	metastasis to spine, hip; hypernephroma	none	failure	17
11	54 F	sciatic	metastasis to hip; adrenal carcinoma	none	failure	13
12	33 F	sciatic	hyperesthesia, leg pain, ? cause	none	failure	11
13	56 F	sciatic	foot pain, ? cause	none	failure	15
14	43 F	sciatic	low back pain syndrome with sciatica	none	partial success	9
15	38 F	sciatic	low back pain syndrome with sciatica	none	partial success	14
16	42 F	sciatic	low back pain syndrome with sciatica	none	partial success	9
17	56 F	sciatic	low back pain syndrome with sciatica	none	failure	12
18	43 M	sciatic	low back pain syndrome with sciatica	soreness in area of receiver	failure	14
19	32 M	sciatic	low back pain syndrome with sciatica	none	failure	13
20	53 F	sciatic	low back pain syndrome sciatica	none	failure	16
21	78 F	sciatic	low back pain syndrome with sciatica	none	failure	13
22	38 F	sciatic	low back pain syndrome with sciatica	none	failure	12
23	51 F	sciatic	low back pain syndrome with sciatica	none	failure	16

no source of contamination could be found. Another patient had considerable tenderness in the area of the receiver leading to removal of the implant. There were no objective signs of inflammation.

The use of the stimulator by patients in either the excellent or partial success category

changed little from the time immediately after implantation to the time of follow-up examination. Almost all of the patients used the device more than 12 hours a day. All used sufficient power output to produce a light-to-strong buzzing sensation, which radiated to the area of pain.

TABLE 2

Results of peripheral nerve stimulator implants in the University of Minnesota series

Case No.	Age, Sex	Stimulator Location	Diagnosis	Complications	Result	Follow-Up (mos)
1	47 M	ulnar	gunshot wound in elbow; ulnar palsy	none	excellent	68
2	42 M	ulnar	ulnar pain from olecranon fracture	none	excellent	68
3	42 M	ulnar	tardy ulnar palsy	none	excellent	46
4	41 F	ulnar	tardy ulnar palsy	none	excellent	54
5	19 M	sciatic	hip dislocation, sciatic injury	none	partial success	44
6	59 M	sciatic	spine injury, sciatic palsy	none	failure	44
7	31 M	brachial	traumatic amputation of arm, stump pain	infection, PNS removed then reimplanted	recent failure	44
8	57 M	brachial	traumatic amputation of arm, stump pain	wire disconnected (reimplanted)	initially excellent; lost to follow-up	48
9	64 M	sciatic	amputation above the knee; vascular disease, neuropathy, stump pain	muscle movement with stimulation	failure	48
10	63 M	sciatic and femoral	leg trauma, stump pain	none	failure	54

Patients were asked to characterize their pain in terms of various characteristics, such as steady, pulsating, hot, burning, heavy, pressing, aching. Patients in either the partial success or excellent category more often characterized their pain as sharp and stabbing (six patients) as compared to patients in the failure group (one patient). Two patients in the excellent result group had hyperesthesias as a major problem, and these disappeared with stimulation. Power output requirements from the transmitter did not increase with time, as has been noted with dorsal column stimulation,^{9,15,16} although the follow-up period is too short for this to be conclusive.

Muscle cramping from stimulation did not occur in any of the patients in either of the success groups. Furthermore, these patients did not find the stimulation distracting, but rather, that with the reduction in pain they had better ability to concentrate. Pain relief lasted for various lengths of time after a given stimulation period. In three patients the pain began again as soon as stimulation stopped; in two others pain returned within 30 to 60 minutes, and in four others pain returned in 1 to 8 hours.

Patients denied that the stimulation interfered with walking, coordination, sexual

functioning, driving, sensation, or muscular strength. These patients reported no tissue injury in the stimulated limb, or elsewhere, as a result of analgesia.

University of Minnesota Series

In 1973⁶ a series of 10 patients with chronic nerve injury treated with PNS implants was described. At that time six patients were judged to have excellent results, while two had good results, and two were treatment failures. Now, 3 years later, one of the patients in the excellent result series has been lost to follow-up, while another has become a failure. This latter patient, who had a traumatic arm amputation, continued to receive stimulation into the painful area, but no longer obtains pain relief. The longest follow-up period is in two of the patients with excellent results, who have now been using ulnar nerve stimulators for 5 years, and continue to obtain complete pain relief. These results are summarized in Table 2.

Discussion

The best predictor for success in using the PNS implant in the treatment of intractable pain was the patient's diagnosis. No patient treated with a sciatic implant for the low back

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pain syndrome had an excellent result. Patients with pain from metastatic disease also did poorly. Patients with chronic peripheral nerve injury had the best results, with six patients having excellent results, and four having partial success.

A high failure rate occurred in patients with low back pain syndrome, despite successful trials with percutaneous stimulation. The reason for this may be related to the observation noted by the present authors, and others,¹² that for stimulation to provide pain relief, it must be applied to an area proximal to the source of the pain. Thus bipolar stimulation of the sciatic nerve in patients with the low back pain syndrome would be expected to fail, since the source of the pain is proximal to the area stimulated. The temporary trials of sciatic stimulation may, on the other hand, succeed since this is done with unipolar stimulation, which allows for greater current spread. In support of this, preliminary work has shown that in such patients percutaneous bipolar epidural stimulation may be completely effective in relieving sciatic pain when the electrodes are placed over the ipsilateral L-4, L-5 or S-1 nerve roots under fluoroscopic control.

The first reported use of permanent peripheral nerve implants for pain control was made by Sweet and Wepsic in 1968;¹³ however, these results have not been published, and detailed follow-up data are not available. Picaza, *et al.*,¹⁴ reported that 20 out of 23 patients had excellent results after a follow-up period ranging from 6 to 20 months. Nine patients in their series had low back pain syndrome. The stimulation was applied to an area remote from the location of pain in nine patients. The reason for the discrepancy in results between their series and our own is not clear.

The mechanism by which peripheral nerve stimulation relieves pain is still uncertain. Campbell and Taub⁴ confirmed that normal human subjects had sensory loss during transcutaneous nerve stimulation in the distribution of the stimulated nerve. This change began with decreased touch sensation at low levels of stimulation, and progressed to analgesia with higher levels of stimulation. The development of analgesia was associated with loss of the A-delta elevation in the compound action potential recording, which suggests that a peripheral axonal blockade

was responsible for the observed analgesia.

This hypothesis was supported by work of Torebjörk and Hallin,²¹ who showed that repeated electrical stimulation of human peripheral nerves resulted in excitation failure in C fibers, followed to a lesser extent by excitation failure in A fibers. That electrical stimulation may relieve clinical pain by this mechanism was shown by Wall and Gutnick.²⁴ Experimentally induced neuromas in rats were shown to have an abundance of hyperirritable small myelinated fibers (recording techniques did not allow for recording from C fibers), that showed prolonged silent periods after a brief antidromic tetanus. A mechanism by which electrical stimulation may selectively block small fiber activity was described by Accornero, *et al.*,¹ who showed that cathodal current can stimulate both large and small fibers, while the anodal current selectively inactivates the smaller fibers. The axonal blockade hypothesis is in keeping with the observation that electrical stimulation must be applied to an area proximal to the source of pain, and to a nerve of which the peripheral field of innervation includes the site of origin of the pain.

Alternatively, peripheral nerve stimulation may inhibit pain perception by way of central nervous system effects. There are numerous examples of inhibitory and facilitatory interactions of sensory stimuli. It is postulated that electrical stimulation of a peripheral nerve may block more distal nociceptive input by inhibitory action at the dorsal horn, brain stem, thalamus, or even the parietal cortex.

The "gate theory" proposed by Melzack and Wall in 1965¹⁰ represents a specific hypothesis involving this general mechanism. This proposal along with increasing Western awareness of the application of acupuncture in China, led to the popularization of electrical stimulation techniques for the treatment of pain. In the "gate theory" it is proposed that electrical stimulation activates large fiber activity in peripheral nerves, which induces a suppression of transmission of large and small fiber activity to high CNS structures, and thereby blocks pain perception. The specific assumptions of this hypothesis have not been supported by subsequent investigations,^{2,3,5,9,11,20,22} and Wall himself has stated, "The least, and perhaps the best, that can be said for the 1965 paper was that it provoked discussion and experiment."²³ The

role of central effects as a means by which electrical stimulation relieves pain, therefore, remains unsettled.

Conclusions as to the role of peripheral nerve stimulation in the treatment of chronic pain can only be made tentatively. In a select group of patients in this series this mode of treatment has provided a relatively safe, effective means of controlling pain. This success is evidenced by pain relief, improvements in life style, cessation of narcotic intake, normalization of sleep-wake cycles, and improvement in psychological well-being with no disturbance of other neurological functions. The most promising group of patients for this mode of treatment appears to be those with peripheral nerve injuries in which the stimulation can be attached to the affected nerve at a point proximal to the site of injury. The incidence of complications appears to be relatively low. The use of sciatic nerve stimulators in the treatment of the low back pain syndrome and pain from metastatic disease is not advocated, for in our series these patients have done poorly. Future research will be directed toward determining the safety of this technique and its mechanism of action, and toward a better definition of the patient population that will respond favorably to its use.

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