PERIPHERAL STIMULATION FOR TREATMENT OF TRIGEMINAL POSTHERPETIC NEURALGIA AND TRIGEMINAL POSTTRAUMATIC NEUROPATHIC PAIN: A PILOT STUDY

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OBJECTIVE: Trigeminal neuropathic pain (TNP) after facial trauma or herpes zoster infection is often refractory to treatment. Peripheral nerve stimulation has been used to treat occipital neuralgia; however, efficacy in controlling facial TNP or postherpetic neuralgia is unknown. A retrospective case series of patients who underwent subcutaneous placement of stimulating electrodes for treatment of V1 or V2 TNP secondary to herpetic infection or facial trauma is presented.

METHODS: Ten patients received implanted subcutaneous pulse generators and quadripolar electrodes for peripheral stimulation of the trigeminal nerve supraorbital or infraorbital branches. Long-term treatment results were determined by retrospective review of medical records (1998-2003) and by independent observers interviewing patients using a standard questionnaire. Surgical complication rate, preoperative symptom duration, degree of pain relief, preoperative and postoperative work status, postoperative changes in medication usage, and overall degree of therapy satisfaction were assessed. Mean follow-up was 26.6 ± 4.7 months.

RESULTS: Peripheral nerve stimulation provided at least 50% pain relief in 70% of patients with TNP or postherpetic neuralgia. Medication use declined in 70% of patients, and 80% indicated that they were mostly or completely satisfied with treatment overall. There were no treatment failures (<50% pain relief and a lack of decrease in medication use) in the posttraumatic group, and two failures (50%) occurred in the postherpetic group. The complication rate requiring reoperation was 30%.

CONCLUSION: Peripheral nerve stimulation of the supraorbital or infraorbital branches of the trigeminal nerve is an effective method for relief of TNP after facial trauma or herpetic infection. A prospective trial using this novel approach to treat these disorders is thus warranted.

KEY WORDS: Peripheral nerve stimulation, Postherpetic neuralgia, Posttraumatic neuropathic pain, Trigeminal

Unlike classic trigeminal neuralgia, facial pain occurring after traumatic injury or herpes zoster infection of the facial branches of the trigeminal nerve is a medical problem that is often very difficult to treat (5). Tricyclic antidepressants, topical anesthetics or capsaicin, intrathecally administered corticosteroids or local anesthetics, and gabapentin have all been shown to have limited efficacy in the treatment of postherpetic neuralgia (1, 2, 5, 10). Microvascular decompression is generally ineffective in this setting. Peripheral neurectomy and percutaneous gangliolysis have also been attempted in certain patients, but again with limited success (1, 2). Motor cortex stimulation and stereotactic trigeminal nucleotomy have been tried with reported success in 50 to 70% of patients (6, 9, 11-13, 15, 18). Patients are often quite disabled by their symptoms; consequently, a safer, more accessible, and more effective treatment is needed.

Peripheral nerve stimulation has been used to treat occipital neuralgia, although detailed series describing the efficacy and long-term outcome of this approach are lacking. Moreover, there are no reports in the medical literature describing the use or long-term efficacy of subcutaneous stimulation of branches of the trigeminal nerve for the treatment of facial pain occur-
ring after traumatic injury or herpes zoster infection. To determine whether peripheral trigeminal nerve stimulation might be an effective therapy for these disorders, either supraorbital or infraorbital stimulating electrodes were implanted in a cohort of patients who presented with refractory neuropathic facial pain (confined to the territory of the first or second branch of the trigeminal nerve) secondary to traumatic injury or herpetic infection. Medical records were reviewed retrospectively, and patient interviews were conducted to assess treatment outcome.

PATIENTS AND METHODS

Surgical Technique

Informed consent for surgery was obtained before all surgical procedures. Patients were taken to the operating room and placed in a supine position. The face and neck were prepared and draped in a sterile manner. In most patients, a general anesthetic was used. In a minority of patients, however, the procedure was performed under a local anesthetic with the patient awake. With the head turned to expose the temporal and cervical region of the affected side, a preauricular vertical incision was made. Under fluoroscopic guidance, a four-contact Pisces-Quad stimulating electrode (Model 3487A; Medtronic, Inc., Minneapolis, MN) was advanced percutaneously into the region of either the supraorbital or infraorbital foramen with a Tuohy needle (Fig. 1). This electrode contained four linearly arranged 3-mm electrode contacts that were placed 6 mm apart. The proximal end of the electrode was then connected to an extension cable, which was subsequently tunneled subcutaneously to an exit point in the upper cervical region. A trial period of 2 to 7 days then ensued, during which the patient was given a temporary external pulse generator and was taught to self-adjust the stimulation parameters to maximize pain relief. Hospital staff assisted the patients in selecting parameters that provided effective coverage of their painful areas. Patients undergoing a 2-day trial were kept in hospital throughout the trial period. Those patients who underwent a longer trial period were discharged to home and brought back on an outpatient basis for implantation of the pulse generator.

Patients who experienced significant therapeutic benefit were taken back to the operating room for implantation of an IleEl3 Pulse Generator (Model 7425; Medtronic, Inc.). Patients were again placed in the supine position and anesthetized with general anesthesia. The temporary extension cable was removed, and a permanent extension cable was tunneled subcutaneously from an infracavicular site to a retroauricular incision. The proximal end of the stimulating electrode was also tunneled to this retroauricular site, where it was connected to the extension lead (Fig. 1). The pulse generator was then connected to the other end of the extension cable and placed into a surgically prepared infracavicular subcutaneous pocket above the pectoral fascia. Initial postoperative visits were scheduled within 14 days of the second surgical procedure.

FIGURE 1. Placement of peripheral trigeminal nerve-stimulating electrodes. Anteroposterior and lateral x-rays of the cranium demonstrating the placement of supraorbital (A and C) and infraorbital (B) quadrupolar stimulating electrodes for the treatment of postherpetic neuralgia and posttraumatic neuropathic pain. The lateral x-ray (C) also demonstrates the retroauricular location of the connector and extension cable, which was tunneled subcutaneously to an IleEl3 Pulse Generator located in the pectoral region.

Data Collection and Analysis

Medical records from 1998 to 2003 were reviewed to identify patients who had undergone placement of subcutaneous stimulating electrodes for the treatment of facial pain occurring after traumatic injury or herpetic infection. A brief questionnaire was then developed to assess preoperative symptom duration, patterns of stimulator use, postoperative changes in medication usage, degree of pain relief, preoperative and postoperative work status, and overall level of satisfaction with the therapy. Independent observers who were not members of the surgical team conducted telephone interviews to obtain follow-up data. Information on surgical complications was obtained from medical records and from patient interviews. Statistical analysis was performed with StatView (SAS Institute, Inc., Cary, NC), a commercially available software package. Data are presented as mean ± standard error of the mean. The procedures and data analysis for this study were performed in accordance with concurrent Oregon Health & Science University Institutional Review Board research guidelines.

RESULTS

Patient Demographics

A total of 11 patients who had undergone surgical implantation of a subcutaneous stimulating electrode in the facial region
were identified. With one exception, all patients presented with neuropathic facial pain in the context of a history of facial trauma or herpes zoster infection affecting the face. The exception was a patient with spontaneous atypical facial pain that was refractory to numerous forms of medical and surgical therapy. Typical symptoms included alodinia, hypesthesia or hyperesthesia, and chronic burning sensations in the distribution of the supraorbital or infraorbital nerves. No patient had complete anestesia in the involved dermatome. All of the patients had undergone unsuccessful trials of one or more other forms of therapy before surgery, including anticonvulstant and tricyclic antidepressant therapy, gabapentin administration, topical anesthetics, peripheral neuromectom, percutaneous trigeminal gangliolysis, or microvascular depression.

Eight of the patients were affected in the distribution of the supraorbital nerve, and three were affected in the distribution of the infraorbital nerve. Only patients with pain in the V1 or V2 distribution were considered for implantation of a nerve stimulator. The authors elected not to place stimulating electrodes in the V3 territory because of concerns about lead breakage caused by repeated movement of the mandible. One of the 11 patients who had sustained a traumatic infraorbital nerve injury failed to obtain significant relief after a 1-week trial period of peripheral nerve stimulation; consequently, no pulse generator was implanted.

Of the remaining 10 patients who received a permanent generator implant, 7 were men and 3 were women, yielding a male-to-female ratio of 2.3:1. The mean age at the time of implantation was 52.2 ± 6.0 years (range, 33-86 yr). As shown in Figure 2, 50% of the patients experienced posttraumatic neuropathic pain, 40% postherpetic neuralgia, and 10% atypical facial pain that was unresponsive to traditional treatment modalities for trigeminal neuralgia (including anticonvulstant therapy, percutaneous gangliolysis, and microvascular decompression). Eight (80%) of the 10 patients were contacted for completion of a standardized questionnaire. Data for the remaining 2 patients (1 with posttraumatic neuropathic pain and 1 with postherpetic neuralgia) were gleaned from medical records of postoperative clinic visits. The mean duration of symptoms before surgery was 47.5 ± 13.6 months (range, 7-144 mo). Data characterizing the patient population are summarized in Table 1 and Figure 2.

Therapeutic Efficacy

Several parameters were assessed to determine whether peripheral trigeminal nerve stimulation was effective in relieving posttraumatic or postherpetic neuropathic pain. These included degree of pain relief, preoperative and postoperative work status, changes in medication usage, and overall satisfaction rating.

Assessment of the degree of pain relief afforded by peripheral stimulation of the supraorbital or infraorbital branches of the trigeminal nerve revealed that 70% of patients experienced a 50% or greater degree of pain relief after undergoing this procedure. Overall, the mean degree of pain relief was 58 ± 10% (range, 0-100%), with a median of approximately 75%. The distribution of the results is shown in Figure 3. There was no correlation between the degree of postoperative pain relief and patient age, sex, or duration of preoperative symptoms.

Seven of the 10 patients reported a decrease in medication use after surgery, an effect that was statistically significant (P < 0.02, Student's t test). Two patients experienced no change in their medication use after surgery, and only one patient reported an increase in medication use (Fig. 3). This patient (Patient 4) had facial pain of uncertain pathogenesis, which may explain why she experienced less than 50% pain relief and an increase in medication use despite peripheral trigeminal stimulation. As expected, there was a close correlation between changes in medication use and the degree of pain relief experienced after surgery. Without exception, patients with 50% or greater pain relief experienced an overall decrease in medication use, whereas patients with less than 50% pain relief had either no change or an increase in their medication use.

Preoperative and postoperative work status was also determined in an effort to assay the efficacy of peripheral trigeminal nerve stimulation. Before surgery, 60% of the patients were employed, and 40% were unemployed. Half of those who were unemployed, however, were in the eighth decade of life and well beyond retirement age. Thus, six of the eight patients who were under retirement age were employed before surgery. After implantation of the trigeminal nerve-stimulating electrodes, seven of the eight patients returned to work. This small increase in the number of employed patients after surgery indicates that the surgical procedure had no deleterious effect on work status.

Degree of patient satisfaction was used as another measure of therapeutic efficacy. As shown in Figure 3, 70% of patients indicated that they were mostly or completely satisfied with
50% pain relief from the device during the initial trial period. Using a level of 50% pain relief or greater as a marker of therapeutic efficacy, the number of patients deriving therapeutic benefit from the device as a function of time after implantation of the pulse generator was determined and plotted. As shown in Figure 4, the number of patients reporting at least 50% pain relief gradually decreased with longer periods of follow-up. However, 80% of patients continued to experience at least 50% pain relief after 24 months of follow-up.

**Postherpetic versus Posttraumatic Neuropathic Pain**

An examination of whether there were differences in therapeutic efficacy between trigeminal nerve stimulation for postherpetic or posttraumatic neuropathic pain was conducted. All the patients who had pain secondary to traumatic injury experienced 50% or greater pain relief, compared with only half of those patients who had herpetic infection as the cause of their pain (Fig 5). There were similar differences between posttraumatic and postherpetic trigeminal pain patients in terms of the effects of surgery on medication use and on overall satisfaction rating. Of the patients with posttraumatic neuropathic facial pain (n = 5), 100% experienced a decrease in medication use after surgery, compared with 50% (n = 4) of those with postherpetic pain. Similarly, all of the patients with posttraumatic facial pain reported that they were mostly or completely satisfied with the procedure, compared with only 50% of those with postherpetic pain. Although these differences were not statistically significant (P < 0.1, Student's t test), the trend raises the possibility that a difference may exist between the ability of peripheral trigeminal nerve stimulation to treat posttraumatic and postherpetic neuropathic pain. However, the fact that half of the patients with postherpetic neuralgia experienced greater than 50% pain relief and a decrease in medication use after surgery indicates that this procedure can be an effective treatment in a subpopulation of patients with this difficult disorder.

**Durability of Peripheral Trigeminal Nerve Stimulation**

Studies in other systems indicate that the efficacy of peripheral nerve stimulation can decrease over time. Therefore, the durability of the therapeutic effect over time was determined. Patients were first questioned regarding their patterns of use of the generators. All of the patients used their stimulators at least 50% of the time, with 6 of the 10 patients keeping them turned on 100% of the time.

A necessary criterion for permanent implantation of the stimulating electrode and generator was that patients receive at least
Complications

There were three complications requiring surgical intervention, for an overall complication rate of 30%. All were associated with the retroauricular position of the connector and extension lead. In two patients, wound breakdown developed over the connector. Both required surgical revision. In one of these two patients, all hardware had to be explanted and subsequently reimplanted at a later date. The third patient complained of discomfort associated with tension on the extension lead when turning his head. He was taken back to the operating suite electively, where the extension lead was lengthened.

![Figure 4](image.png)

**FIGURE 4.** Graph illustrating the durability of peripheral trigeminal nerve stimulation, expressed as the number of patients reporting at least 50% pain relief as a function of time after surgery. The slope of the curve demonstrates a gradual decrease over time in the number of patients with good pain relief. By extrapolation, the point at which 50% of patients would experience 50% pain relief or greater would occur at approximately 70 months.

**DISCUSSION**

Facial neuropathic pain of peripheral origin characteristically has several important features, including a precipitating pathogenesis such as disease (e.g., herpes zoster infection) or trauma, a delay period of days to months before onset, and typical symptoms such as burning paroxysmal or constant pain and dysesthesias that often occur in an area of incomplete sensory deficit (5, 20). These features aid in distinguishing this entity from the more commonly encountered trigeminal neuralgia, which is usually spontaneous in origin, is characterized by sharp lancinating pains, and is often the result of intracranial vascular compression of the trigeminal root. Facial neuropathic pain of peripheral origin should also be distinguished.

![Figure 5](image.png)

**FIGURE 5.** Bar graph depicting the efficacy of peripheral trigeminal stimulation for relief of pain secondary to either posttraumatic neuropathic pain or postherpetic neuralgia. There was a trend toward greater efficacy for the treatment of posttraumatic neuropathic pain, although this difference was not statistically significant (P < 0.1).
from anesthesia dolorosa, which is a deafferentation type of pain that is characterized by marked sensory loss in the periphery and that is probably caused by activation of abnormal central pain mechanisms (3).

The pathophysiology of facial neuropathic pain of peripheral origin is poorly understood, although several studies suggest that multiple mechanisms may underlie its occurrence and that these may differ from patient to patient and may depend on the underlying cause of the pain (5, 7, 14). Increased tactile and temperature thresholds, as well as abnormal summation of pain, have been observed in patients with traumatic trigeminal nerve injury but not in patients with trigeminal pain of spontaneous origin (7). Postherpetic neuralgia most likely has a different underlying pathophysiology that involves abnormalities of both peripheral and central origin (14). Moreover, studies indicate that facial postherpetic neuralgia and truncal postherpetic neuralgia may be two separate pathophysiological entities (14).

As discussed previously, the treatment of facial neuropathic pain occurring after herpetic infection or traumatic injury is difficult. Evidence suggests that the early use of antiviral agents may aid in preventing the occurrence of postherpetic neuralgia (19). Once the disorder develops, however, it is often refractory to therapy. In this study, evidence for a novel approach to treatment of this disorder is presented. The data shown here indicate that the use of subcutaneous stimulating electrodes for peripheral stimulation of the supraorbital or infraorbital nerves yielded good to excellent pain control in 70% of patients, as measured by at least 50% pain relief, a decrease in medication usage, and high overall satisfaction ratings. The therapeutic benefits were durable, with 70% of patients reporting good to excellent results up to 4 years after the initiation of therapy.

One advantage of the procedure described here is that it uses hardware that is currently available for clinical use. The Pisciie Quad stimulating electrode and Itrel3 Pulse Generator system are commonly used for epidural spinal cord stimulation. The device has been adapted for use in the facial region with good results. In fact, the results reported here closely parallel those for use of the Pisciie Quad stimulating electrode in spinal cord stimulation, which produced 50% pain relief in 55% of patients after 1 year of therapy (4). Unlike spinal cord stimulation, which had no effect on medication usage, peripheral trigeminal nerve stimulation resulted in a decrease in medication usage in 70% of patients. The results of this study may also be compared with those reported for direct stimulation of the gasserian ganglion (17) for treatment of posttraumatic or postherpetic facial pain (19% good or excellent outcome) and peripheral nerve stimulation (12) for the treatment of peripheral pain (75% with good or excellent outcome).

The complication rate of 30% observed in the present study is somewhat higher than the 17% reported for use of stimulating electrodes for spinal cord stimulation (4) but is comparable to that of 30 to 40% reported for stimulation of the gasserian ganglion (17). All of the observed complications in the present study were related primarily to wound break-down or discomfort associated with the retroauricular position of the extension cable. The dermal and subcutaneous layers in this area are generally thin, and this undoubtedly contributed to the observed complication rate. The recent availability of smaller connectors with a lower profile makes it likely that this complication rate will decrease in the near future.

**CONCLUSIONS**

These findings indicate that peripheral stimulation of the supraorbital or infraorbital branches of the trigeminal nerve may be an effective method for relief of neuropathic facial pain occurring after trauma or herpes zoster infection in a majority of patients. A prospective trial of this novel approach to the treatment of these disorders is thus warranted.

**REFERENCES**

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Peripheral Stimulation for Treatment of Trigeminal Pain

It is well known that painful trigeminal neuropathy is extremely difficult to manage, and most of the treatment modalities available rarely are of much assistance. These conditions are not uncommon and may occur as a result of frequently performed surgical procedures, for example, the maxillary sinus (Caldwell-Luc procedure). Until motor cortex stimulation was demonstrated to be a potentially effective therapy for this condition, direct stimulation of the gasserian ganglion and intracisternal trigeminal rootlets often was attempted. In some patients, such stimulation could provide effective pain relief for many years, but it failed in the majority of patients. Furthermore, the placement of the stimulation electrode via a subtemporal approach required major surgery, and maintenance of the position of a percutaneously implanted electrode in the gasserian cistern often was problematic. Therefore, the novel stimulation approach presented in this article is of much interest. Although the number of patients is small, the follow-up period is relatively long and the outcome impressively favorable. A possible drawback is that this method, at least at this stage, seems to be limited to first- and second-branch neuralgia.

It is somewhat surprising that the concept of peripheral nerve stimulation has not been applied previously to the trigeminal nerve. In the early literature regarding transcutaneous electrical nerve stimulation, there are reports that transcutaneous stimulation was applied for various forms of facial pain. In the late 1970s, when we developed the technique for direct trigeminal stimulation, the patients were screened with transcutaneous electrical nerve stimulation. In addition to the discomfort of having a large rubber-plate taped to their face, however, several of the patients experienced aggravated cutaneous abnormalities in the form of allodynia, hyperalgesia, and so forth as a result of the stimulation.

In the present study, pain relief is assessed as a percentage in a global evaluation. Trigeminal neuropathy typically is associated with profound changes of cutaneous sensibility, which gives rise to evoked pain in addition to ongoing, spontaneous pain components. Both gasserian stimulation and motor cortex stimulation effectively suppressed the cutaneous signs of neuropathy, and it would have been interesting if the same effects were observed with peripheral trigeminal stimulation; that seems to be the case. A detailed assessment with quantitative sensory testing would have permitted analysis of and insight to possible mechanisms of action of the stimulation.

It is not surprising that the outcome tended to be less positive in patients presenting with postherpetic neuralgia than in those with a history of trigeminal trauma, considering the complexity of the latter condition. There is evidence that the form and extent of sensibility changes in postherpetic neuralgia relate to different pain-generating mechanisms and, hence, presumably also to the likeliness of response to the stimulation. It might therefore be that a thorough analysis of these changes could help to predict the responsiveness. The probability of alleviating pain associated with trigeminal neuropathy by use of peripheral stimulation, and the simplicity of the implantation procedure as compared with motor cortex stimulation, make it an attractive treatment option.

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The authors provide their outcome data for 11 patients with facial neuropathic pain, including trigeminal postherpetic neuralgia, trigeminal posttraumatic neuropathic pain, and failed trigeminal neuralgia, who underwent trigeminal peripheral stimulation. Satisfactory pain relief was obtained in 70% of patients. Although peripheral stimulation has been used previously in the treatment of occipital neuralgia, the reported efficacy of trigeminal peripheral stimulation in patients with facial pain and the technical aspects of the procedure are original. The study demonstrates promising results of this new treatment modality in patients with intractable facial pain, whose management presents great difficulty. Stimulation of the trigeminal nerve is not a new concept, however, and gasserian and retrogasserian neurostimulation have been performed by several authors since 1980 (1, 3). Although the technique described is a more peripheral application, these procedures may be considered as a group.

The efficacy of such procedures is not well understood. Neuropathic pain is known to be a result of pathological changes in the central nervous system. Surgical procedures usually are performed on targets within the central nervous system such as the dorsal root entry zone, substantia gelatinosa, trigeminal tract, nucleus, and motor cortex. Peripheral interventions principally are avoided, as they may increase central neural degeneration. The beneficial effect of very peripheral stimulation of the trigeminal nerve is obvious but surprising. The selection criteria for stimulation of the compartment of the trigeminal nerve are unclear, and a rationale is needed for choosing peripheral rather than gasserian or retrogasserian stimulation. Finally, technical difficulty in stimulating the third branch of the trigeminal nerve seems to be a disadvantage of trigeminal peripheral stimulation.

Percutaneous trigeminal tractotomy-nucleotomy also should be considered in patients with facial neuropathic pain of various causes, including postherpetic neuralgia (2). We performed this procedure in 53 cases, and complete or satisfactory pain control was obtained in 77.3% of cases. Four of patients had postherpetic neuralgia, and complete pain was obtained in two patients. In a third patient, pain relief was unsatisfactory; a trigeminal dorsal root entry zone operation was performed and complete pain relief was obtained. Trigeminal tractotomy-nucleotomy was not effective in the fourth patient. This procedure is efficient and minimally invasive. Although it has been classified as a neuronally destructive procedure, it is associated with a low rate of complications. Conversely, neurostimulation is a technologically
Sophisticated treatment method, it may increase the patient's dependence on the physician and hospital, and it is expensive.

Trigeminal peripheral stimulation is a new surgical treatment option in patients with facial neuropathic pain. The authors present an interesting, original, and efficient treatment modality. However, the mechanism of its efficacy needs to be explained with physiological studies, and selection criteria of the trigeminal nerve compartment for stimulation should be more clearly established with further studies. Larger series with longer follow-up periods are needed to facilitate the decision to conduct trigeminal nerve stimulation in patients with intractable facial pain.

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Treatment of facial pain caused by trigeminal neuralgia has an extremely good neurosurgical track record. The results of surgery for trigeminal posttraumatic neuropathy and post-therapeutic pain, however, are abysmal. That treatment for neuropathic pain in the territory of the trigeminal nerve should have such disparate results depending on the origin of the neuropathic process is vexing for any neurosurgeon who treats such patients. The lack of neurosurgical options for patients with trigeminal neuropathy and posttherapeutic pain seems to be changing with the publication of reports such as the present study. The authors describe a novel application of peripheral nerve stimulation to isolated V₁ or V₂ region trigeminal pain caused by postherpetic neuralgia or nerve injury. The surgical procedures described in this manuscript are straightforward and are associated with low morbidity. The quality of the data collection in this retrospective study seems high, given the usual caveats of retrospective studies. There was an 80% direct data completion rate, with the remaining 20% of data gleaned from charts. This excellent data collection rate for this type of study further strengthens the quality of the data. The follow-up period is relatively long, although the number of patients studied is fairly small. A larger retrospective series would allow clinicians to obtain more information specific to each of these disparate processes, as well as a better idea of the precise symptoms best alleviated by use of these devices. Prospective study of this surgical intervention should prove fairly straightforward given the intractable nature of these disease processes and clear clinical criteria to define them.

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Future Meetings—Congress of Neurological Surgeons

The following are the planned sites and dates for future annual meetings of the Congress of Neurological Surgeons:

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Future Meetings—American Association of Neurological Surgeons

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