

Treatment of Spinal Cord Injury Pain

Pain following spinal cord injury (SCI) is a significant problem for which no single treatment is effective over the long term. SCI pain is broadly classified into nociceptive (musculoskeletal and visceral) pain and neuropathic (above-level, at-level, and below-level) pain.¹ Different mechanisms subservise these various types of pain. It is possible that a careful analysis of underlying mechanisms may improve therapy options.² Pharmacological and nonpharmacological treatments have been applied, but only a few have been assessed in randomized controlled trials (RCTs).^{3,4} This issue of *Pain: Clinical Updates*, the third in a series of papers by the SCI Pain Task Force of IASP on this complex and challenging clinical condition,^{1,2} summarizes treatment of SCI pain.

Pharmacological Treatments

RCTs are now accepted as the "gold standard" in clinical analgesic trials. Of eight double-blind RCTs on drug treatment of pain after SCI (Table 1), four were negative. The small number of subjects per trial (7–21) raises the possibility of type II error (i.e., the trial is inadequate to detect a true positive effect). At present, therefore, the best available evidence includes case reports and uncontrolled trials.

Table 1. Randomized, double-blind, placebo-controlled trials of therapies for at-level or below-level pain in SCI patients.

Trial	Pain Condition	Sample Size	Drug (Final Daily Dose)	Design	Study Duration	Outcome	NNT (95% CI)
Davidoff et al. 1987 ⁷	At- or below-level neuropathic pain	18	Trazodone hydrochloride (150 mg)	Parallel	8 weeks	Tra = pla	9* (1.8–∞)
Loubser et al. 1991 ¹⁸	At- or below-level neuropathic pain	21	Lidocaine, s.a. (50–100 mg)	Cross-over	2 injections, 1 hour apart	Lid > pla	3.5 (1.8–37)
Herman et	Below-level	7	Baclofen, i.t. (50 μg)	Cross-	2 infusions on	Bac > pla	NA

al. 1992 ³⁶	neuropathic and spasm-related pain†			over	successive days		
Drewes et al. 1994 ¹³	At- or below-level neuropathic pain	20	Valproate (600–2400 mg)	Cross-over	2 x 3 weeks, 2 weeks washout	Val = pla	10 (2.7–∞)
Eide et al. 1995 ²⁴	At- or below-level neuropathic pain	9	Ketamine, i.v. (180 µg/kg) or alfentanil, i.v. (19 µg/kg)	Cross-over	3 infusions, 2 hours apart	Ket > pla Alf > pla Ket = alf	NA
Chiou-Tan et al. 1996 ¹⁹	At- or below-level neuropathic pain	11	Mexiletine (450 mg)	Cross-over	2 x 4 weeks; 1-week washout	Mex = pla	NA
Attal et al. 2000 ¹⁷	At- or below-level neuropathic pain	10	Lidocaine, i.v. (5 mg/kg)	Cross-over	2 x 30 min, 3 weeks apart	Lid > pla‡	5§ (1.6–∞)
Siddall et al. 2000 ²⁵	At- or below-level neuropathic pain	15	Morphine, i.t. (0.75 mg) and clonidine, i.t. (50 µg), singly + in combination	Cross-over	Minimum 4 injections, 1 day apart	Mor = pla Clon = pla Mor/clon > pla	7.5# (2.1–∞)

Abbreviations: i.t. = intrathecal; i.v. = intravenous; NNT = number needed to treat; NA = not accessible from article; pla = placebo; s.a. = subarachnoidal.

* Patient global assessment of efficacy as significant.

† Spinal cord lesions including multiple sclerosis, epidural abscess, and transverse myelitis.

‡ Conclusion based on all 16 patients in the study (SCI and stroke).

§ NNT based on SCI patients. Apparent insensitivity of NNT to differences in outcome reflects NNT estimation from dichotomized data.⁴

NNT for morphine in combination with clonidine. See comment on NNT in footnote above.

Antidepressants

Numerous studies document the benefit of antidepressants (ADs) in peripheral neuropathic chronic pain conditions.^{5,6} In the only controlled study of an AD for SCI pain, Davidoff et al. found trazodone, a presynaptic serotonin reuptake blocker, to be no more effective than placebo in treating diffuse burning and tingling sensations.⁷ Side effects of trazodone included drowsiness, dry mouth, dizziness, increased spasticity, and urinary retention. An uncontrolled study by Heilporn found that 8 of 11 SCI patients with diffuse pain responded to a combination of melitracen (150 mg p.o.) and flupenthixol (3 mg p.o.) daily.⁸ Fennolosa and associates reported that 25 of 33 SCI patients with various types of pain obtained "satisfactory" pain relief with amitriptyline plus clonazepam in combination with either (1) an NSAID, (2) 5-OH-tryptophan and TENS, or (3) spinal cord stimulation.⁹ Two case reports document the benefit of a combination of an antidepressant and an anticonvulsant drug on neuropathic SCI pain.^{10,11}

Anticonvulsants

Anticonvulsant drugs have been used in pain management since the 1960s and are effective in trigeminal neuralgia, diabetic neuropathy, and migraine prophylaxis.¹² In the only controlled study to address SCI pain, Drewes et al. observed an insignificant analgesic beneficial effect of valproate, with a trend toward improvement in most of the

McGill Pain Questionnaire subscores.¹³ Gibson and White reported reduction of pain by carbamazepine in two patients with traumatic complete paraplegia.¹⁴ Zachariah et al. described the beneficial effect on both spasticity and pain in two of three patients with valproate.¹⁵ In a case of SCI pain, Ness et al. detected a good effect of gabapentin on episodic unilateral pain.¹⁶

Sodium Channel Blockers

Local anesthetics and antiepileptics are thought to reduce ectopic discharges from peripheral injured afferents by blocking voltage-gated sodium channels, but the exact mechanism by which lidocaine may reduce central pain is unknown. Lidocaine is not orally bioavailable, and its oral analogue mexiletine often is not tolerated because its unselective sodium channel-blocking action can produce side effects such as diarrhea. More selective blockers of sodium channels may be available in the future.

Three RCTs on lidocaine or mexiletine have been published. In a double-blind crossover trial, Attal et al. studied the effect of intravenous (i.v.) lidocaine on different components of neuropathic pain in 16 patients with chronic post-stroke pain ($n = 6$) or SCI pain ($n = 10$).¹⁷ Lidocaine decreased spontaneous ongoing pain, brush-induced allodynia, and mechanical hyperalgesia, but was no better than placebo against thermal allodynia and hyperalgesia. Six of 10 SCI patients receiving lidocaine showed a significant (50% or more) reduction in spontaneous pain compared to 4 of 10 with placebo, and brush-evoked allodynia (seen in 5 patients) was reduced in 3 after lidocaine compared to 1 after placebo. Loubser and Donovan gave subarachnoidal lidocaine (i.e., spinal anesthesia) or placebo to 21 patients with constant (most often burning) or paroxysmal stabbing pain at or below the level of traumatic SCI.¹⁸ Spinal anesthesia decreased pain significantly ($P < 0.01$) compared to placebo. Individual responses to diagnostic spinal anesthesia varied greatly. Chiou-Tan et al. reported that mexiletine had no significant beneficial effect on SCI pain as measured on visual analogue scales or the McGill Pain Questionnaire.¹⁹ Pollock et al. described the beneficial effect of intrathecal (i.t.) tetracaine hydrochloride delivered above the level of injury in four SCI patients with blocked spinal fluid flow and chronic distal pain.²⁰ Distal pain disappeared and returned at a time consistent with the patient's recovery from anesthesia. When i.t. tetracaine was given below the level of the lesion and spinal fluid block, the distal burning pain did not disappear. Backonja and Gombar observed partial pain relief after i.v. lidocaine in two patients with SCI.²¹

Opioids

Opioids are commonly believed to be ineffective in treating central pain, but some observations contradict this view (see reviews by Portenoy et al.²² and Hammond²³). Two placebo-controlled trials have evaluated opioids in the treatment of SCI pain. Eide and associates studied the effects of i.v. infusion of alfentanil, ketamine, or placebo on continuous, intermittent, and evoked pain in nine SCI patients.²⁴ Alfentanil (a μ -opioid receptor agonist) and ketamine (an NMDA-receptor antagonist) each had a significant analgesic effect on both continuous and evoked pain. Siddall et al. found that the combination of i.t. morphine and clonidine produced significantly greater relief of neuropathic SCI pain than saline placebo.²⁵ Neither morphine nor clonidine alone produced significant pain relief. The concentration of morphine in the cervical CSF was

correlated with pain relief. In a single-blind case series by Glynn et al., epidural morphine had an analgesic effect in 5 of 14 patients with neuropathic pain after SCI.²⁶ In a single case report, oral Δ -9-tetrahydrocannabinol (THC, 5 mg) and codeine (50 mg) had a greater analgesic effect on painful dysesthesias in comparison with placebo.²⁷ In a case series, pain and spasticity improved in 8 of 12 SCI patients given continuous i.t. infusion of morphine (0.3–1.0 mg/day).⁹ Six of the eight patients were alive after 3 years of continuous i.t. morphine, with minimal tolerance.

Clonidine

There are few data on clonidine, an α_2 -adrenergic agonist, for the treatment of SCI pain. In the controlled study by Siddall et al. discussed above, i.t. clonidine in combination with i.t. morphine had an analgesic effect.²⁵ Glynn et al. reported that 10 of 15 patients receiving epidural clonidine (150 μ g) for neuropathic pain after SCI had a decrease in pain intensity.²⁶ Petros and Wright described a patient with paraplegia after SCI who obtained good relief of pain with epidural clonidine and moderate relief with oral clonidine.²⁸ Intrathecal infusion of morphine in combination with clonidine had a beneficial effect on continuous and shooting central pain in one patient after traumatic SCI.²⁹ The combination of i.t. baclofen (a GABA_B agonist) and clonidine relieved painful anal spasms in a patient with anterior spinal artery syndrome.³⁰

Potassium Channel Blockers

Several studies describe the positive effects of the potassium channel blocker 4-aminopyridine (4-AP) on neurological status in SCI patients, and some include pain as a secondary outcome. In a randomized, double-blind, dose-titration crossover trial of oral sustained release 4-AP in 26 SCI patients with incomplete lesions, the drug had no statistically significant benefits on pain (Present Pain Intensity, McGill Pain Questionnaire).³¹ A randomized, double-blind study evaluated the effect of i.v. 4-AP on neurological status in eight SCI patients.³² The authors noted improvement in neurological status and inferred an associated reduction in chronic pain and spasticity, but it was not quantified. In another investigation on six SCI patients, 4-AP reduced spasticity in two patients and reduced pain in one.³³

NMDA-Receptor Antagonists

Central *N*-methyl-d-aspartate (NMDA) receptors activated by the excitatory amino acid glutamate are involved in the central sensitization seen in neuropathic pain (see review by Sang³⁴). In a controlled trial by Eide and associates,²⁴ ketamine decreased both continuous and evoked pain in SCI patients.

GABA-Receptor Agonists

Animal studies suggest that a decreased inhibitory influence of GABAergic neurotransmission contributes to neuropathic pain (see review by Yeziarski³⁵). Baclofen, a GABA_B-receptor agonist, has been tested on SCI pain in one controlled and several uncontrolled trials. Herman et al. assessed the effect of i.t. baclofen (50 μ g) in seven patients with pain and spasticity from multiple sclerosis, spinal epidural abscess, and transverse myelitis in a double-blind randomized study.³⁶ Baclofen significantly decreased central neuropathic pain and spasm-related pain with temporal dissociation (the

effect of neuropathic pain occurred before the suppression of spasm-related pain), but did not influence pinch-induced or musculoskeletal (low back) pain. Opposite results were found in an uncontrolled study by Loubser and Akman.³⁷ Twelve SCI patients with spasticity and pain (six with neuropathic pain, three with musculoskeletal pain, and three with both pain components) were assessed prior to i.t. baclofen pump implantation and again 6 and 12 months postoperatively. At both 6- and 12-month intervals, two of nine patients with neuropathic pain and five of six patients with musculoskeletal pain experienced a significant decrease in pain intensity. In a pilot study by Taira et al., an i.t. bolus injection of baclofen reduced neuropathic pain in three of six patients with SCI.³⁸ The effect appeared 1–2 hours after the injection and persisted for 10–24 hours. Propofol, a GABA_A-receptor agonist, was studied in a placebo-controlled, double-blind crossover trial in 32 patients with nonmalignant pain, eight of whom had SCI pain.³⁹ Of these eight patients, all had better pain relief with propofol than with placebo, although *P* values were not reported. Allodynia (seen in five of the eight SCI patients) was abolished, while placebo had no effect. In seven patients assessed with SPECT scans, frontal, frontoparietal, thalamic, and cortical hypoperfusion were abolished or significantly reduced during propofol injection.

Nonpharmacological Treatments

Table 2. Literature review of relief of spinal cord injury pain with TNS, SCS, DBS, and motor cortex stimulation.

Trial	No.SCI Patients	Early Pain Relief (%)†	Late Pain Relief (%)†	Follow-up Period (months)‡
<i>Transcutaneous Electrical Nerve Stimulation</i>				
Banerjee 1974 ⁵⁵	5	100	-	-
Davis and Lentini 1975 ⁵⁶	31	35	-	-
Hachen 1978 ⁵⁷	39	49	28	3
Heilporn 1978 ⁸	3	0	-	-
Eriksson et al. 1979 ⁵⁸	11	-	64	3
Sindou and Keravel 1980 ⁵⁹	17	18	-	-
Bates and Nathan 1980 ⁶⁰	16	63	-	-
<i>Spinal Cord Stimulation</i>				
Nashold and Friedman 1972 ⁶¹	7	29	-	-

Lindblom and Meyerson 1975 ⁶²	2	50	-	-
Richardson et al. 1980 ⁶³	10	50	10	12
Meglio and Cioni 1982 ⁶⁴	3	0	-	-
Demirel et al. 1984 ⁶⁵	10	60	0	24
Wester 1987 ⁶⁶	4	-	25	4-60
Mittal et al. 1987 ⁶⁷	8	50	38	34-59
Meglio et al. 1989 ⁶⁸	16	44	19	1-40
Buchhaas et al. 1989 ⁶⁹	7	-	71	3-72
Spiegelmann and Friedman 1991 ⁷⁰	6	67	50	3-33
Simpson 1991 ⁷¹	8	-	63	1/2-108
Cole et al. 1991 ⁷²	4	0	-	-
Tasker et al. 1992 ⁷³	35	-	17	>12
Cioni et al. 1995 ⁷⁴	25	36	16	3-72
Kumar et al. 1998 ⁷⁵	15	60	13	6-179
Tseng 2000 ⁷⁶	1	-	100	19
<i>Deep Brain Stimulation</i>				
Hosobuchi 1980 ⁷⁷	11	55	45	6-114
Young et al. 1985 ⁴²	6	-	67	2-60
Siegfried 1987 ⁴³	4	-	50	6-72
Levy et al. 1987 ⁴⁴	11	36	0	24-168
Kumar et al. 1997 ⁴⁶	3	33	0	6-180
<i>Motor Cortex Stimulation</i>				
Canavero and Bonicalzi 1995 ⁷⁸	1	100	0	-
Sindou et al. 1999 ⁷⁹	3	-	100	21
Mertens et al. 1999 ⁸⁰	3	-	100	12-74

† Preferably $\geq 50\%$ pain relief, when this can be assessed from article.

‡ Range or mean follow-up periods, often given for all patients included in the trial, including non-SCI patients.

Transcutaneous Electrical Nerve Stimulation (TENS)

Reports on the use of TENS in SCI patients are limited (Table 2), and controlled trials are lacking. TENS appears to be effective in some patients with muscular pain or at-level neuropathic pain, but not in patients with below-level pain. Leyson and associates noted that the use of TENS was associated with postural detrusor-sphincter dyssynergia in acute and recent (<2 years post-injury) quadriplegics,⁴⁰ and recommended against the use of TENS in this group of patients. There is no evidence that TENS is useful for the treatment of central neuropathic pain secondary to SCI.

Spinal Cord Stimulation (SCS)

The gate control theory⁴¹ suggested that electrical stimulation of the dorsal columns of the spinal cord might alleviate SCI pain. Blinded trials are difficult to perform because of the need to evoke paresthesias. Published case series are presented in Table 2. Although these trials rarely report pain type, SCS appears to be effective in some patients with incomplete lesions, painful spasms, at-level pain, or postcordotomy pain. Poor results have been reported in patients with complete lesions and in patients with intermittent and burning pain. Most studies report a decline in efficacy of SCS over time.

Deep Brain Stimulation (DBS)

The number of studies on DBS for treatment of chronic pain has diminished in the last decade. In the studies listed in Table 2, DBS was used in patients who had not responded to conventional treatment modalities. Areas targeted for DBS included the periaqueductal gray (PAG) and periventricular gray (PVG), the thalamic nuclei (VPL and VPM), and the internal capsule. PVG/PAG stimulation generally has been used for nociceptive pain, and thalamic stimulation typically has been used for treatment of deafferentation pain. However, this pattern is not strictly followed as most studies in neuropathic pain patients have not limited DBS treatment to thalamic nuclei.

Many of the early studies on DBS did not present results according to the type or etiology of pain. Later studies stratified patient populations to determine which group had the best results with DBS, and increased the follow-up period. Young et al. published a study in 1985 in which four of six patients had at least 50% pain relief from DBS during follow-up of 2–60 months.⁴² In 1987, Siegfried conducted a study that included four patients with "paraplegic pain" who underwent DBS of thalamic nuclei (specifically VPL).⁴³ Two had excellent results and the other two showed an improvement in their pain profile. These early studies display optimism for DBS treatment of chronic intractable pain due to SCI, but none had an adequate follow-up period. In 1987, Levy et al. published a study on DBS for chronic intractable pain that included 11 patients with SCI.⁴⁴ The mean follow-up period for this study was substantial (mean 80 months, range 24–168 months). Patients received PAG/PVG or thalamic electrodes, and three patients had both thalamic and PAG/PVG electrodes. Although 4 of the 11 SCI patients had an initial response to DBS (6 weeks), none had long-term benefit. Two more studies by Kumar et al. were reported in the 1990s.^{45,46} In the first study, two patients with "trauma to cord/peripheral nerves" had long-term relief during a follow-up ranging from 6 months

to 10 years,^{45,46} but in the second study none of the three patients with "traumatic spinal cord injury" had long-term relief of pain (follow-up 6 months to 15 years).

In total, 14 of 26 patients (54%) in five case series had initial benefit from DBS, but only 2 of 16 had long-term benefit: If Kumar's first report is excluded due to lack of information regarding the type of pain and the length of follow-up, DBS provided no long-term benefit, and even its initial efficacy for SCI pain is unpredictable at best.

Cordotomy, Cordectomy, and Myelotomy

Uncontrolled case series on the effect of cordotomy, cordectomy, and myelotomy are presented in Table 3. Investigators have reported benefits of cordotomy and cordectomy for lancinating or shooting pain and possibly for evoked pain, as opposed to constant burning or aching pain and dysesthesias. Complications include intractable contralateral pain and dysesthesias, bladder dysfunction, impairment of sexual function, development of muscle spasms, and further impairment of residual nervous function below the lesion. Several authors have emphasized the need for cordotomies to be performed bilaterally, because unilateral cordotomy leads to a high incidence of intractable contralateral pain and dysesthesias. As with SCS and DBS, initially successful treatments are short-lived. In patients studied by White, attempts to reestablish analgesia after return of pain by a second or third tractotomy, although initially successful in half, nearly always ended in failure after a year or more.⁴⁷ Melzack and Loeser described five patients in whom an entire section of the spinal cord was removed.⁴⁸ One patient with shooting pain in the back and legs had complete pain relief after a spinal cordotomy, but pain recurred 11.5 years later with exactly the same characteristics and distribution as before. Reasons for the varied results after these surgical procedures include inconsistency in length of follow-up periods and pain types selected, surgical procedures, skill and experience of surgeons, and level of surgery. In a case report by Druckman and Lende, one SCI patient with pain after a traumatic L1 lesion first had a bilateral section of the 11th and 12th thoracic dorsal roots and then had a cord transection through the scarred 11th thoracic segment, both with only temporary relief of pain.⁴⁹ Finally he had a transection through apparently normal cord at the junction of the 10th and 11th thoracic segments, with lasting relief of pain during an 18-month follow-up.

There is no evidence that cordotomy or myelotomy are effective in managing the central neuropathic pains of SCI. Rostral lesions are not indicated in cervical SCI pain due to the likelihood of further impairment of the patient's functional status, including diaphragmatic innervation.

Dorsal Root Entry Zone (DREZ) Lesion

The first DREZ procedure was performed in 1976 on a patient with arm pain after brachial plexus avulsion.⁵⁰ Since then, many SCI patients have undergone this procedure for treatment of pain (Table 3). Patients with pain in dermatomes at or just below the level of injury, and those with unilateral pain have had good results after DREZ lesions, but results have been less satisfactory in patients with sacral pain and have been mixed in those with diffuse pain. Complications include CSF leaks; new weakness or sensory loss; new paresthesias or dysesthesias; exacerbation of bowel, bladder, and sexual dysfunction; and epidural or subcutaneous hematomas. The exact mode of action of the DREZ procedure remains unexplained, but may involve destruction of abnormal activity in pain

neurons in the dorsal horn rostral to the level of injury (epileptiform "pain-generating centers"), interruption of ascending pain pathways, or rebalancing of inhibitory and excitatory inputs within a damaged sensory network.^{51, 52} DREZ lesions are often performed from one or two dermatomal segments above the level of injury down to one segment below the level of the lesion. However, Edgar et al. suggested that standard DREZ microcoagulation may produce an insufficient degree of lesioning,⁵³ echoing the thoughts of Druckman and Lende.⁴⁹ Edgar et al. described computer-assisted DREZ microcoagulation in which recordings in the DREZ area at and above the injury level identified areas of abnormal focal hyperactivity that were then ablated. In 39% of cases, areas of focal hyperactivity were found higher than three levels above the injury site. This technique had a higher success rate (even though 93% of patients had diffuse and/or sacral pain, normally unresponsive to DREZ lesions), with fewer complications than standard DREZ operations. Falci et al. published an abstract describing a new technique to guide DREZ lesioning using spontaneous intramedullary recordings as well as intramedullary recordings during stimulation at C-fiber frequency.⁵⁴ With spontaneous intramedullary recordings alone, 9 of 11 patients achieved 50–100% pain relief. When both techniques were used, 21 of 25 patients achieved 50–100% pain relief.

Table 3. Literature review of relief of spinal cord injury pain with neuroablative procedures.

Trial	# SCI Patients	Pain Relief (%)†	Follow-up Period (months)‡
<i>Cordotomy/Corpectomy</i>			
Freeman and Heimburger 1946 ⁸¹	45	96	1 1/2
Davis and Martin 1947 ⁸²	18	28	-
Munro 1950 ⁸³	68	56	-
Botterell et al. 1953 ⁸⁴	8	63	24–96
White 1965 ⁴⁷	13	62	12–144
Porter et al. 1966 ⁸⁵	34	62	96–240
White and Sweet 1969 ⁸⁶	2	50	48
Melzack and Loeser 1978 ⁴⁸	5	20	138
Jefferson 1983 ⁸⁷	19	79	-
Tasker et al. 1992 ⁷³	88	31	>12
<i>Cordomyelotomy</i>			

Pagni and Canavero 1995 ⁸⁸	3	67	>120
<i>Dorsal Root Entry Zone Lesion</i>			
Nashold and Ost Dahl 1979 ⁸⁹	2	100	9
Nashold and Bullitt 1981 ⁵¹	13	85	5–38
Samii and Moringlane 1984 ⁹⁰	5	80	-
Richter and Seitz 1984 ⁹¹	2	0	-
Powers et al. 1984 ⁵²	9	67	2–19
Wiegand and Winkel Müller 1985 ⁹²	20	60	5–34
Friedman and Nashold 1986 ⁹³	56	50	6–72
Powers et al. 1988 ⁹⁴	11	45	24
Young 1990 ⁹⁵	26	62	Up to 60
Kumagai et al. 1990 ⁹⁶	4	50	11–30
Edgar et al. 1993 ⁵³	46	92	2–96
Sampson et al. 1995 ⁹⁷	39	74	36
Rath et al. 1997 ⁹⁸	14	50	52
Falci et al. 1999 ⁵⁴	36	83	3–60

† Preferably $\geq 50\%$ pain relief, when this can be assessed from article.

‡ Range or mean follow-up periods, often given for all included patients in the trial including non-SCI patients.

Conclusions

Pain is a major complaint in patients with SCI. Many patients experience several different types of pain and spasticity. Large-scale RCTs clearly are needed for both pharmacological and nonpharmacological treatments. Different types of pain must be characterized by careful clinical evaluation that may permit clinicians to make an even more effective choice for their patients among existing treatments. To complement this work, basic research must continue to identify central mechanisms and potential future therapeutic targets of SCI pain.

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