ed more than half of the sixth instar (postapolysis) were fed small sucrose-impregnated glass fiber disks to which [^{14}C]gallic acid (up to 100,000 disintegrations per minute) in methanol had been added; 20 to 100 percent of the disk was consumed in 2 to 6 hours. The insects were then sealed in test chambers (30°C) for 24 hours without food. At the end of the period the insects were killed. Hemolymph samples were taken for counting, and the total hemolymph volume was estimated. The tissue samples, and the fecal pellets produced over the period, were dried in cellulose thimbles, oxidized, and counted in a liquid scintillation counter (Packard Tri-Carb 2660). The expired carbon dioxide was collected as carbamate in phenylethylamine through which air was drawn from the test chambers during the period of the experiment; this was also used for measuring labeled carbon dioxide.

8. A. C. Neville, *The Biology of the Arthropod Cuticle* (Springer-Verlag, Berlin, 1975).
9. S. O. Andersen, *Insect Biochem.* **1**, 157 (1971).
10. M. Kato, *Entomol. Exp. Appl.* **24**, 485 (1978).
11. E. A. Bernays, *Ecol. Entomol.* **6**, 353 (1981); R. J. Heron, *Can. J. Zool.* **43**, 247 (1955); T. H. Hsiao and G. Fraenkel, *Ann. Entomol. Soc. Am.* **61**, 485 (1968).
12. G. Popov and M. Ratcliffe, *Anti-Locust Mem.* **9** (1968), entire volume.
13. National Academy of Sciences, *Tropical Legumes: Resources for the Future* (1979).
14. Leaves of *Acacia senegal* and *Acacia albida* were collected by C. Strudwick near Maidugeri, Nigeria, and sun-dried before being sent to England. Analysis was as in (*4*).
15. W. J. Mattson, *Annu. Rev. Ecol. Syst.* **11**, 119 (1980).
16. R. D. Gibbs, *Chemotaxonomy of the Flowering Plants* (McGill-Queen's Univ. Press, Montreal, 1974).
17. G. A. Rosenthal, D. L. Dahlman, D. H. Janzen, *Science* **192**, 256 (1976); G. A. Rosenthal, D. H. Janzen, D. L. Dahlman, *ibid.* **196**, 658 (1977).
18. We thank N. Jago for *Anacridium melanorhodon* adults, the Royal Botanic Gardens, Kew, for the *Geranium endressi*, C. Strudwick for collection of *Acacia* leaves, D. J. Chamberlain for assistance, and R. F. Chapman for criticism and encouragement.

5 January 1982

Modulation of Spasticity: Prolonged Suppression of a Spinal Reflex by Electrical Stimulation

Abstract. *Electrical subcutaneous nerve stimulation of radial, median, and saphenous nerves has been shown to produce prolonged analgesia. In a double blind study, such stimulation also suppressed clonus for 3 hours after stimulation ceased in subjects with spasticity. Since the effect is contralateral, each subject was his own control. Because stimulation of the nerve in the wrist suppressed ankle clonus, the mechanism mediating the effect must be centrifugal inhibition. These results suggest that subcutaneous nerve stimulation may also be a tool in the management of spasticity.*

Evidence for a gating mechanism in the spinal cord that modulates nociception (*1*) provides the rationale for the clinical practice of epidural spinal cord stimulation for pain relief (*2*). Several workers have observed that this procedure also benefits subjects with spastic paraparesis in that it increases voluntary muscle control, reduces rigidity, and improves bladder function (*3*). Thus, the same procedure can be used to alleviate pain and depress spasticity. As an alternative to spinal cord stimulation, we have studied the effects of subcutaneous nerve stimulation (SCNS) for the treatment of pain (*4*). We now report that the same treatment produces depression of spinal reflex excitability as demonstrated by prolonged and complete suppression of clonus. Preliminary reports of these results have appeared elsewhere (*4*) and have been documented on film.

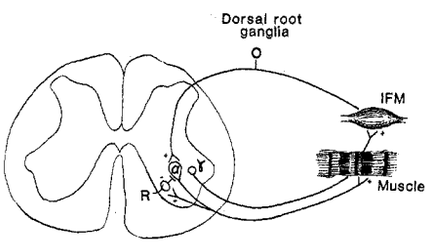


Fig. 1. Partial diagram of the basic stretch reflex. Stretching of intrafusal muscle (*IFM*) produces firing of stretch receptor which has its cell body in the dorsal ganglion. Activation of the stretch receptor results in firing of alpha motoneurons, which in turn produces muscle contraction and decreases activity of the stretch receptor of the IFM. The axon of the alpha motoneuron sends a collateral to a Renshaw cell (*R*) which inhibits the homonymous alpha motoneuron. The sensitivity of the stretch receptor is also regulated by gamma efferents, which are under bulbospinal control. Multiple inhibitory and excitatory factors regulate the output of the alpha motoneuron preventing the cyclic discharge that produces clonus.

Clonus is a 5- to 7-Hz pathological oscillation exhibited by spastic muscle after being passively stretched. After initial tendon jerk, the muscle relaxes and stretches the muscle spindles. Stretch produces a synchronous resumption of spindle afferent discharge. Figure 1 depicts the mechanism underlying the basic stretch reflex. Synchronous increased monosynaptic projection of spindles causes homonymous alpha motoneurons to discharge again, producing a second reflex contraction of the muscle. In neurologically intact spinal cord, input from muscle spindles is insufficient to initiate cyclical alpha motoneuron discharge. In spastic muscles, however, hyperexcitability of the alpha or gamma motoneurons is such that synchronous spindle firing produces cyclic alpha motoneuron firing and produces reflex contractions. Such a closed oscillating feedback loop indicates the importance of inhibitory control mechanisms that normally promote asynchrony of neural activity.

Subjects were pain-free patients in the multiple sclerosis clinic or on the neurosurgery ward at the UCLA Center for Health Sciences. Nine patients had multiple sclerosis, four had postlaminectomy irritability, and all had ankle clonus that persisted for 40 to 60 beats when triggered by patellar stretch.

The SCNS was delivered by subcutaneous placements of 30-gauge stainless steel needles in the median and radial nerves 5 cm proximal to the wrist flexure and in two points along the route of the saphenous nerve—at the metatarsal cuneiform junction and below the medial malleolus. The needles were attached to an electrical output (TA 4 stimulator), which delivered 20-Hz spike wave stimulation. The intensity of the current was increased gradually until it reached about 200 μA.

Correct placement of needles in the median and radial nerves was verified by reports of sensation of vibration along the distribution of each nerve. Stimulation of the saphenous nerve was frequently accompanied by a massive efferent outflow consisting of clonus, fanning of the toes, and occasional stepping movements. In normal subjects, stimulation of this nerve produced barely visible muscle twitches. Gross movements, which could be produced only in spastic patients, were presumably reflections of heightened neural irritability. In all cases, peripheral stimulation was accompanied by erythema (a reddening of surrounding tissue) and local elaboration of sympathetic signs, such as sweating, coldness, and piloerection.

Subjects were given SCNS or control SCNS (which consisted of stimulation of points distal from the three peripheral

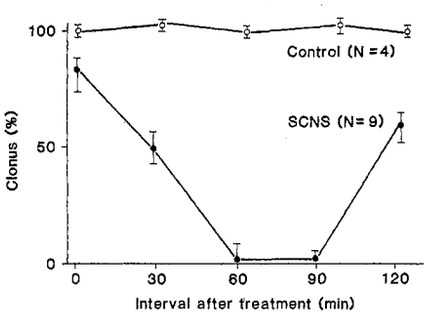


Fig. 2. Time course for inhibition of clonus by SCNS. Subjects were given SCNS or placebo, which consisted of electrical stimulation of distal points. Clonus was measured as a percentage of contractions before treatment.

0036-8075/82/0409-0203$01.00/0

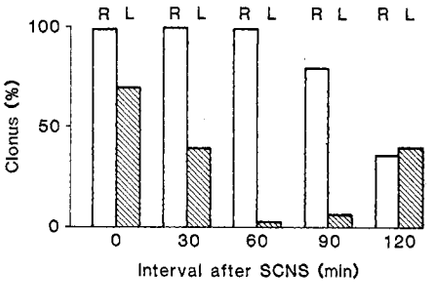
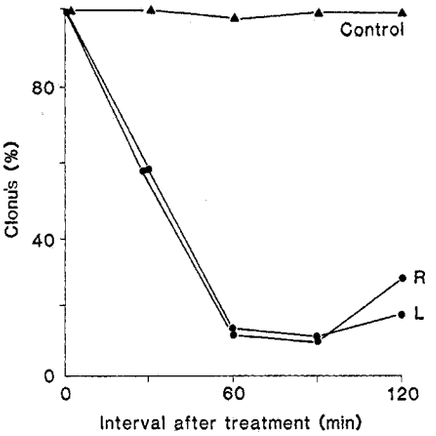


Fig. 3 (left). Laterality of SCNS-induced suppression of clonus. Fig. 4 (right). Stimulation of radial and median nerves suppressed ankle clonus, demonstrating that the mechanism mediating this response is suprasegmental.



nerves) for 1 hour twice daily for 1 week. Ankle clonus was elicited by patellar stretch by a physician who did not know the purpose of the study. The SCNS suppressed clonus for 2 hours on the first trial in all subjects, whereas none of the subjects given control stimulation responded (Fig. 2). With SCNS, slight inhibition was immediately observable, but maximum suppression did not occur until 1 hour after the treatment ended. This delay occurred in all instances and suggests the need for "processing time." Inhibition lasted for 3 hours and was observed in every subject.

The SCNS-induced clonus suppression did not depend on analgesia, as all subjects were pain-free at the time of the experiment. Clonus was inhibited but not abolished by the stimulation, as was demonstrated by the observation that it could be elicited, to a minor degree after multiple attempts, indicating that the threshold for eliciting the reflex was markedly raised. These results imply that SCNS decreases neural excitability and raises the threshold for clonus.

Administering SCNS to the right median, radial, and saphenous nerves produced clonus inhibition on the left side for as long as 90 minutes after treatment ended (Fig. 3), but inhibition occurred bilaterally for 2 hours after treatment. (Stimulation on the left side produced the opposite pattern of response.) Thus, SCNS did not produce its effect by global psychogenic factors such as sedation. The precise neuroanatomical pathways subserving altered excitability are not known, but these results imply that SCNS can be used as a tool to map functionally intact but latent human synaptic connections.

The SCNS suppresses clonus by dampening the oscillations in firing of alpha motoneurons either through segmental or suprasegmental inhibition. At the segmental level, a decrease in the excitability of muscle spindles or an increase in the potency of recurrent inhibition from Renshaw cells may decrease excitability of the basic stretch reflex. At the suprasegmental level, diverse brain regions regulate the threshold of alpha motoneurons by way of gamma efferents (*5*). In order to discern whether the suppression of clonus is the result of centrifugal inhibition, I stimulated the radial and median nerves bilaterally. Stimulation of the nerves in the wrists completely inhibited ankle clonus, indicating that stimulating neurons at the level of the sixth to eighth cervical segments suppresses neurons in the lumbosacral segments.

Spasticity is a global term covering phenomena as diverse as rigidity, clonus, hyperreflexia, overadduction of legs and ankles "scissoring," and the dorsiflexion of the toes. All of these signs are due to the release of spinal cord reflex mechanisms from inhibition by higher brain centers. The relative contribution of different brain areas in modulating postural reflexes is still unknown, but most authors agree that the analogy of spasticity to animal decerebrate rigidity is inadequate. The latter refers to an increase in extensor tone immediately after intercollicular transection; this increase in tone is transient in the case of animals, whereas human spasticity is permanent.

In this report, I document a decrease in clonus subsequent to SCNS. Rigidity also decreases, but I have been unable to find any change in the extent of scissoring, hyperreflexia, or the Babinski sign. Similar dissociation of the behavioral components of spasticity has been reported after administration of Baclofen (*6*). SCNS may provide an analytical tool for dissecting the various behavioral components of spasticity. In conjunction with metabolic mapping techniques such as positron emission, it may provide a clue to the identity of brain regions mediating the individual behavioral components.

Suppression of clonus is reminiscent of "consolidation," defined here as the time-dependent transfer of information across diverse regions of the central nervous system. One example of this phenomenon is the fixation of postural asymmetry (*7*): transection of the spinal cord of 45 minutes after a unilateral cerebellar lesion abolishes asymmetry, whereas later transection does not. To my knowledge, this is the first demonstration that any procedure can abolish a grossly observable spinal reflex in an awake, intact animal.

JUDITH B. WALKER
Walker Pain Institute,
1100 Glendon Avenue,
Los Angeles, California 90024

References and Notes

1. R. Melzack and P. D. Wall, *Science* **150**, 971 (1965).
2. C. N. Shealy, J. T. Mortimer, J. B. Resnick, *Anesth. Analg. (Cleveland)* **46**, 489 (1965); W. H. Sweet and J. G. Wespic, *Adv. Neurol.* **4**, 737 (1974); D. M. Long and N. Hagfors, *Pain* **1**, 109 (1975); R. R. Richardson, P. R. Meyer, L. J. Cenillo, *ibid.* **8**, 75 (1980); B. J. Urban and B. S. Nashold, *J. Neurosurg.* **48**, 323 (1978).
3. A. W. Cook and S. Weinstein, *N.Y. State J. Med.* **73**, 2826 (1973); L. Illis, E. M. Sedgwick, A. E. Oygar, M. A. Sabbaki Awadalla, *Lancet* **1967-I**, 1383 (1976); R. R. Richardson and D. G. McLone, *Surg. Neurol.* **9**, 153 (1978); L. S. Illis, E. M. Sedgwick, R. C. Tallis, *J. Neurol. Neurosurg. Psychiatry* **43**, 1 (1980).
4. J. B. Walker and R. L. Katz, *Lancet* **1979-II**, 1307 (1979); *Soc. Neurosci, Abstr.* **7**, 340 (1981); *Proc. Am. Pain Soc.* **2**, 54 (1980); *Pain*, in press; *Pain* **1** (Suppl.), 141 (1981).
5. M. R. Dimitrijevic, P. Nathan, A. M. Sherwood, *Prog. Clin. Neurol.* **5**, 171 (1978); R. Granit, B. Holmgren, P. A. Merton, *J. Physiol. (London)* **130**, 213 (1955).
6. G. W. Duncan, B. T. Shahani, R. R. Young. *Neurology* **26**, 441 (1976).
7. T. J. Chamberlain, P. Halick, R. W. Gerard, *J. Neurophysiol.* **26**, 662 (1963); G. C. Palmer, J. W. Ward, G. R. Davenport, *Anat. Rec.* **160**, 405 (1968); G. C. Palmer and G. R. Davenport *Brain Res.* **13**, 394 (1969); _____, J. W. Ward, *Psychopharmacologia* **17**, 59 (1970).
8. I thank E. Eldred and J. Beatty for critical review of this manuscript.

17 June 1981; revised 27 January 1982

Receptive Fields and the Optimal Stimulus

Albrecht *et al.* (*1*) have suggested that the "spatial frequency channel" hypothesis provides more insight into the functional nature of visual cortical neurons than does the bar-width, or "size" view. They also pointed out that their results—that such cortical cells in both the cat and the monkey are more sharply tuned to gratings than to bars—are consistent with an opponent center-surround receptive field (RF) with subsidiary disinhibitory flanks.

0036-8075/82/0409-0204$01.00/0