NEUROPHYSIOLOGICAL STUDY OF CHRONIC SPINAL CORD STIMULATION

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ABSTRACT

Neurophysiological follow-up studies are in progress in 15 patients with implanted systems for epidural spinal cord stimulation. These studies are based on evoked spinal cord potentials, somatosensory evoked potentials, tendon jerks, vibratory reflexes and polyelectromyographic recordings of spinal reflexes and their dependence on brain influence. The procedures, done initially in all patients, were repeated at approximately 3, 6, and 12 month intervals post-implant. Evaluation of the evoked spinal cord and somatosensory potentials, and the interaction of tendon jerks and vibration revealed no significant changes in the neurophysiological characteristics of the four patients re-evaluated by the time of this writing. However, there was a noticeable decrease in the electromyographic features of spasticity and evidence of improved suprasegmental control in these patients.

INTRODUCTION

In a group of 15 patients with multiple sclerosis, spinal cord injuries and other disorders as described elsewhere in these proceedings, we have followed the effects of spinal cord stimulation (SCS) on motor disabilities and attempted to repeat the published observations that patients will benefit through decreased spasticity, improved locomotion and increased endurance (1). These effects are not equally pronounced in all patients. The degree of improvement generally depends on just how much motor control is preserved and how much this is disturbed by spasticity, i.e., to what degree spasticity covers up or blocks volitional activity. In this study, we sought to find if there are electrophysiological correlates of these effects, and to provide information from which conclusions might be drawn as to possible mechanisms.

Before the application of epidural stimulation, we conducted 4 studies in all patients, 2 devoted to the analysis of sensory system functions, and 2 devoted to the motor system. At this writing, we have completed follow-up studies in 4 of the 18 patients. These findings comprise the body of this text, together with a discussion of their implications.

METHODOLOGY

The patients in this study have been described elsewhere (1). All of the patients were evaluated prior to the application of epidural stimulation using four standardized protocols. The first two, involving evoked potentials from the spinal cord and brain, represent an attempt to measure the status of the patient's sensory system, while the other two map the segmental motor control by monitoring the interaction of phasic and tonic reflexes, and the suprasegmental influence on segmental reflexes through polyelectromyographic recordings during various maneuvers.

Evoked Spinal Cord Potentials: To monitor the activity associated with electrical stimulation of the peripheral nerves, Evoked Spinal Cord Potentials (ESCP) were recorded from the lumbo-sacral portion of the spinal cord and caudae equina. This non-invasive technique, described elsewhere (2), employed chlorided silver strip electrodes placed over the T12, L2, L4, and S1 vertebral processes, with an identical reference electrode at T3. For this study, the patients lay supine on a comfortable examination table. It was important to achieve good subject relaxation in order to reduce the artifacts from paraspinal muscle electrical activity. The responses to bilateral electrical stimulation of the tibial nerve at the popliteal fossae were differentially amplified with respect to the T3 reference (negative deflection upward), and averaged for 64 repetitions for a period of 40 ms following the stimulus. To avoid the large EKG artifact, the stimulus timing was controlled by the cardiac cycle through the use of a QRS-triggered delay.

The stimuli, delivered through 2.5 cm disc electrodes fixed over the nerve trunk, were 0.5 ms in duration, and were adjusted in amplitude to produce either a maximum amplitude Hoffman reflex response (H-wave) as monitored electromyographically from the soleus muscle, or a maximum direct motor response (M-wave).

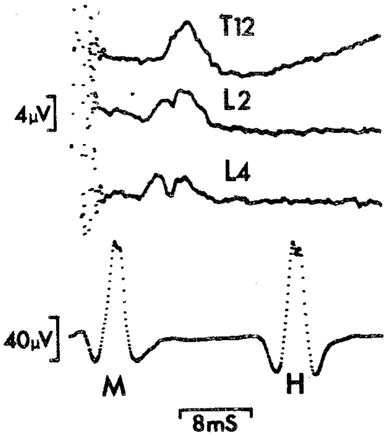

Figure 1. Typical ESCP responses from a normal subject. The monopolar potentials recorded with the reference at T6 (negative upward) and the simultaneously recorded EMG from the triceps surae muscle are the result of averaging 64 responses to bilateral tibial nerve stimulation with 0.5 mS pulses. The EMG trace was shifted to the left to eliminate the 8 mS M-wave delay, in effect moving the stimulus point from the popliteal fossae to the muscle itself.

Somatosensory Evoked Potentials: The cortical activity elicited by repetitive electrical stimulation of the median, peroneal and tibial nerves was assessed using standard techniques for recording the Somatosensory Evoked Potentials (SEP's). EEG electrodes were applied to the scalp using a collodian to fix them in position at the C3 and C4 positions, and 1 to 1.5 cm posterior to the Cz position, referred to the Fz position (international standard EEG convention). The signals were averaged for 128 repetitions, with an analysis time of 200 ms. The subjects were supine for this study also. The stimulus strength was adjusted for a threshold motor movement and delivered at a rate of 2 Hz for the upper extremity and 0.5 Hz for the lower extremity. Standard values for normal subject peroneal SEP's are shown in Figure 2.

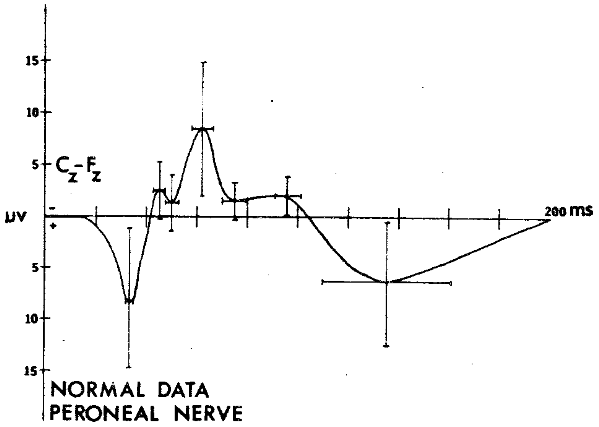

Figure 2. Normative values for Somatosensory Evoked Potentials. The values shown are derived from a series of normal subjects, with the waveform constructed from the mean values, with standard deviations indicated.

<u>Interaction of Phasic and Tonic Stretch Reflexes:</u> Pairs of silver - silver chloride electrodes were placed bilaterally over the quadriceps muscles of the patient, who was in a slightly reclining sitting position. Tendon tap responses were analyzed after differential amplification (gain 2000, bandwidth 10 Hz to 3 KHz) by full wave rectification, followed by integration of the signal over a response window at an appropriate latency. During the test protocol, 60 tendon taps were applied to the patellar tendon of one leg using an electrodynamic hammer which delivered a constant tap of 1 to 3 mm, with the strength adjusted to produce a tendon jerk response in the one-half to one millivolt peak-to-peak range. In order to assess the interaction of the Tendon Tap - Vibratory Reflex (TT-VR), the average integrated amplitude of 20 tap responses without vibration was compared to 20 responses with vibration. The vibration was applied ipsi- and contralaterally during successive trials, and the results were computed in terms of the percentage change. The average amplitudes of the responses to 20 taps immediately following vibration were compared to the control taps in the same way. (Figure 3).

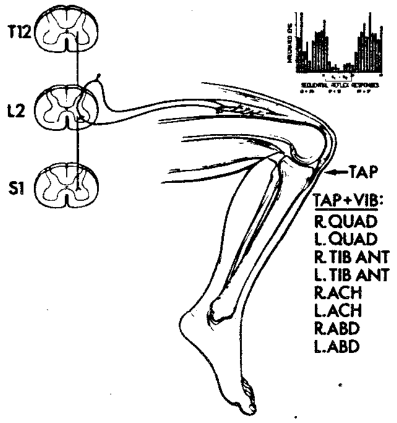

Figure 3. Interaction of Phasic and Tonic Stretch Reflexes. Vibration is applied to the muscles listed to modify the responses to patellar taps as illustrated in the bar graph.

Polyelectromyographic Analysis of Brain Influence on Segmental Reflexes: The analysis of brain influence on segmental reflexes was made by examining the activity of flexor and extensor muscles in the legs, along with the EMG activity of paraspinal and abdominal muscles, and hip adductors. Twelve pairs of Beckman recessed silver - silver chloride electrodes were placed over the muscle bellies approximately 5 cm apart, and connected to an ink-jet recorder (Elema Schonander), using a gain of 100 microvolts per division and a bandwidth of 6 to 800 Hz. The patients were then placed in a comfortable supine position on an examination table, and various maneuvers conducted such as volitional and passive movement of joints, elicitation of phasic and tonic stretch reflexes and withdrawal reflexes, and examination of clonus, Babinski signs, etc. When relevant, Jendrassik - like maneuvers or other volitional activation efforts were used to attempt to modify the segmental reflexes. Maneuvers were repeated three times to insure that the effects produced were repeatably related to the inducing maneuver.

RESULTS

Evoked Spinal Cord Potentials:

In 4 of the 15 patients we have repeated the ESCP recording sessions after chronic use of epidural stimulation. Of these 4 subjects, 3 were M.S., and one, SCI. For two of the patients, the studies have been done a total of 3 times. The longest time interval after beginning SCS was 10 months and the shortest was 3 months.

Analysis of the S-wave (presumed to arise from spinal cord gray matter) did not reveal any changes in morphology. The amplitude of the S wave was larger after stimulation. The root potentials also showed increases in amplitude and better definition which corresponded to the increases seen in the S-wave. How much of the increase was due to a decrease in the background EMG activity from the paraspinals is not clear, since the presence of such activity contributes to the deterioration of the signal-to-noise ratio of the recordings.

Somatosensory Evoked Potentials:

Analysis of SEP responses to peroneal, tibial and median nerve stimulation in 4 patients (2 with M.S., 2 with SCI) did not reveal any profound changes in amplitude, morphology, or latency of the negative and positive components from 30 to 80 ms. However, in the case of R.T., follow-up studies showed a slight reduction of the waveform dispersion of moderate degree which is also the case in patient T.G.M., where waveforms are better defined in the follow-up studies, as shown in Figure 4.

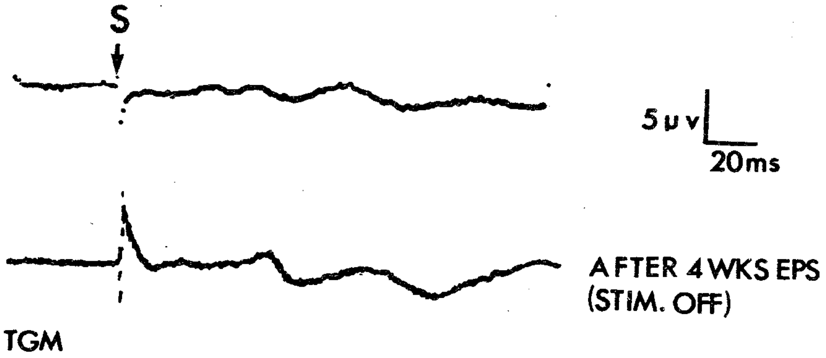

Figure 4. Spinal Cord Stimulation-Induced changes in Somatosensory Waveforms. Responses to peroneal nerve stimulation delivered at the motor threshold, averaged 128 times are shown, the top trace made prior to SCS, and the bottom, after 4 weeks of chronic SCS.

Interaction of Phasic and Tonic Stretch Reflexes:

In 4 patients we measured the suppression of knee jerk EMG responses during vibration of the ipsi- and contralateral responses before and after application of SCS. In all 4 instances, we were unable to demonstrate any consistent change in the percentage suppression of the tendon jerk responses during vibration or immediately after vibration. Figure 5 illustrates the degree of suppression of the patellar tendon tap before and after SCS in one M.S. patient (F.W.). Although there were some changes, they were not significant.

Polyelectromyographic Analysis of Segmental Reflexes:

Recordings were made of motor unit activity with surface electrodes during induced reflex activity (stretch reflex, vibration, cutaneous muscle reflexes, etc.). The modification of these reflexes through suprasegmental influence and volitional control revealed decreased spasticity and varying but marked

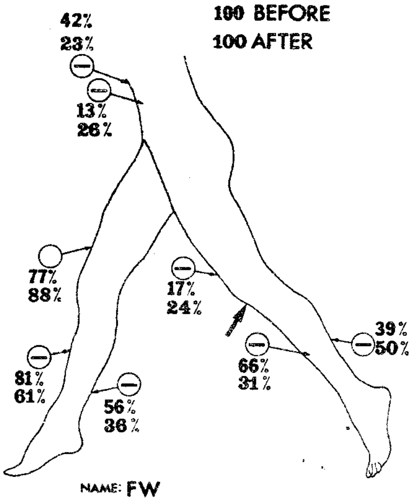

Figure 5. Changes in Vibratory-induced Suppression of Tendon Tap Responses. Comparing the results of 20 taps with vibration to 20 without, no significant changes in the percentage suppression of the tap responses are seen in this patient, regardless of the site of vibration. The responses were measured in response to taps to the left patella, both before and 4 weeks after beginning chronic SCS.

degrees of improved volitional control over motor unit activity. The most significant change found was the decreased reflex irradiation from one muscle group to another.

DISCUSSION AND CONCLUSIONS

Spinal cord stimulation is a method which has been found useful through application in patients with well-defined clinical diagnoses but poorly understood mechanisms of motor disorders. We have been able to satisfactorily modify the motor control of a relatively large group of patients, but with poor understanding of how this system works. This missing knowledge of the neural control mechanisms and how they are activated through SCS has contributed to the controversy over the effectiveness of the method in patients with upper motor neuron disorders.

We have attempted to evaluate the sensory functions of the posterior portion of the gray matter of the spinal cord, generated by activation of primary sensory neurons, since Sedgwick reported that there were changes in the amplitude of the cervical ESCP's in patients after long-term SCS (3). Preliminary analysis of the lumbo-sacral ESCP recordings we made revealed no changes which we wish to interpret as due to changes in the physiological functioning of the primary and secondary sensory neurones of the spinal cord. The increased amplitude observed in the spinal waves might suggest such changes in the neurons. However, our present interpretation is that the increase in amplitude seen is due to a reduction in spasticity, leading to improved recording conditions. This interpretation is strengthened by the observation that the root potentials, particularly the early phase or R-wave, are similarly changed, and it is not anticipated that spinal cord stimulation should have any effect on the synchronicity of firing, conduction velocity, excitability of the afferent fibers, or other parameters presumed to affect the R-wave amplitude. To what extent the underlying mechanisms generating the S-wave are changed is not yet clear. The results were obtained from only 4 patients, and it is therefore not appropriate to make any conclusive statements. However, within the limits of our ability to analyze the current data, we assume that spinal cord stimulation does not produce any permanent changes of the spinal "slow" waves.

Larson et al. (4) have shown that stimulation of the spinal cord simultaneously with the elicitation of somatosensory evoked potentials resulted in a decrease of the responses. When we repeated the procedure after long-term SCS, but while the stimulation was turned off, no significant changes in our first four patients were observed. The significance of the findings of slightly increased responses in two patients is not apparent, but might suggest that there are some changes in long-lasting descending functions from suprasegmental structures.

In normal man, vibration completely suppresses tendon tap responses due to induced presynaptic inhibition (5). However, in spastic patients, the tap responses are less suppressed, related to the absence of presynaptic inhibition (6). Therefore, we anticipated that any decrease in the patient's spasticity after SCS would be reflected in more suppression of the tap responses during vibration of the ipsilateral muscle. We did have a consistent report of suppression of spasticity from the patients, which agreed with our clinical observations of patient performance, and with our polyelectromyographic recordings. However, there were no consistent changes in suppression of tendon tap responses by vibration. It is not clear why these findings did not correlate with the clinical and PEMG findings. It may be that the suprasegmental mechanisms maintaining the abnormal segmental activity are modified during SCS, but that the simple oligosynaptic phasic reflexes do not reflect this modification. These findings are not yet conclusive, since we have not yet compared the data available on muscle tone obtained by passive stretch of the quadriceps muscle with data of vibratory suppression.

The results of PEMG recordings of reflex and voluntary activity showing improvement of voluntary control and reduction of spasticity in all 4 patients evaluated by this technique suggest the effects of SCS lie in modification of the interaction of brain and segmental reflexes. This seems to occur through improvement in the volitional and supraspinal control over segmental reflexes. The lack of substantial changes in the lumbo-sacral ESCP, the SEP, and vibratory-induced suppression of tendon jerks may be explained by assuming that the neurophysiological mechanisms evaluated in these measures are not directly affected by the SCS. These preliminary results are not conclusive, and leave many unanswered questions, which further follow-up studies in the entire group of patients may help to answer.

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