ELECTROPHYSIOLOGICAL RESPONSES ASSOCIATED WITH SPINAL CORD STIMULATION

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Summary

Cervical somatosensory evoked potentials and brainstem click evoked potentials were recorded from 10 patients with multiple sclerosis before and after a trial of spinal cord stimulation. An improvement in amplitude of the cervical somatosensory evoked potential was seen in 7 out of 8 patients while 3 out of 10 showed a decrease in latency of the brainstem evoked potential.

Introduction

Abnormalities of the cervical somatosensory evoked potentials (CSEP) after median nerve stimulation have been reported in up to 69% of definite M.S. cases (1). The abnormalities were a reduction in amplitude or absence of the different components but sometimes a slight prolongation of latency was seen. Abnormalities were seen even in patients with no clinical symptoms referable to the arm or even to the spinal cord.

Brain stem evoked potentials (BSEP) following click stimuli have also been shown to be abnormal in latency and/or amplitude in patients with M.S. and are used as an aid to diagnosis (2,3).

Both the CSEP and BSEP are stable in normal subjects from day to day and year to year. Studies on the stability of potentials in M.S. are incomplete but there are indications that patients in remission show stable potentials, even though they may be abnormal, whereas clinical relapses are accompanied by a change of potentials.

CSEP and BSEP were recorded in 10 cases of patients selected for a trial of spinal cord stimulation to see if there were any changes accompanying alteration of the patients' clinical condition.

Methods

All patients had definite M.S. and had been selected for SCS as described in an earlier paper (4). They were in remission at the time of investigation but all had significant neurological deficit attributable at least in part to spinal cord lesions except one subject whose main deficit was a cerebellar ataxia.

The CSEP was recorded following stimulation of the right median nerve at the wrist with a pulse width of 0.2 msec at a strength of 3 times sensory threshold. Recording electrodes were placed at F_z (10-20 system) and over the cervical 7 vertebra (Cv7). After suitable amplification with a bandwidth of 10Hz - 10 KHz the signals were averaged and analysed by a PDP-12 computer (5). SCS was switched off during the recording periods.

The procedure for the BSEP has been described in detail elsewhere (6). Basically, broad band click stimuli are presented at a rate of 10 per second. Two recording channels using electrodes at each mastoid with a common reference (C_z) and a common earth (F_z) were used. The recording bandwidth was 100Hz to 3KHz. The data were averaged over a 30 ms window using a PDP-12 computer.

RESULTS

CSEP

Figure 1, lower trace, shows a CSEP from a normal subject with 5 negative peaks identified by their polarity and approximate latency N9, N11, N13 and N14. N9 is generated by the compound action potential in the brachial plexus (7,5) ; N11 probably has its origin in the dorsal horns (5) and N13 and N14 have their origin in more rostral structures as yet undetermined but the nucleus cuneatus and thalamus are strong candidates; N20 is the first cerebral event.

The CSEP from one patient with M.S. before SCS is shown in the upper trace. There is a clearly identified N9 potential but the other components are not distinguishable. The middle trace is the CSEP from the same patient after 4 days of SCS, its form and latency are normal and the amplitudes are within normal limits. At the time of recording the patient's clinical condition had improved considerably. The change in amplitude of the N11 component of 8 patients associated with a period of at least 4 days stimulation is shown in figure 2.

In each recording a normal amplitude N9 potential was seen indicating that a standard afferent volley was transmitted to the CNS on each occasion. From the figure it can be seen that N11 appeared or increased in amplitude in 7 our of 8 subjects and those 3 subjects who were studied on 2 or more occasions showed the same response each time. The shading covers 2 standard deviations of the mean amplitude of N11 derived from 31 normal subjects recorded under the same conditions. The N11 potential improves during SCS but tends to remain of slightly low amplitude.

The three patients in this series who showed striking clinical improvement of at least 2 points on the Kurtzke scale subsequently had permanent implants and have been studied repeatedly. The CSEP of one patient C. P. is shown in figure 3 in which the amplitudes of the four negative components of the CSEP are plotted.

Initially no cord potential was seen although a normal sized N9 potential occurred at this and all other recording sessions. A week later small and distorted cord potentials were seen. After 8 days of spinal cord stimulation, during which there had been a marked clinical improvement, a normally shaped but slightly low amplitude potential was recorded. This had deteriorated, as had his clinical state, by 28 days after stimulation but was still present 6 months later when he was readmitted for laminectomy and permanent implantation. At three months post implant

the cord potential was normal but shortly afterwards he began to deteriorate clinically so that $4\frac{1}{2}$ months after implant his clinical state was back at its initial level. Investigation showed that his stimulating electrodes had slipped. A second laminectomy was performed to replace them and 13 days later his clinical state had improved and the CSEP had returned towards its normal value.

In this case and in two others serial recordings of CSEP show improvement with each episode of stimulation which produced a clinical improvement. Clinical deterioration seemed to be accompanied by a deterioration of the CSEP.

Similar results were obtained from the BSEP data. Changes both in amplitude and in latency of the set of responses may be found but the most consistent change with M.S. is the latency of a component. All patients were stimulated at fixed levels relative to their audiometric thresholds and, in each case, the N_1 response from the cochlear nerve was within normal limits for amplitude and latency. This showed that an adequate input to the brainstem pathways was present and, as would be expected in M.S., that there was no disorder of the peripheral nerve. None of the patients had any clinically significant hearing deficiency.

Figure 4 shows the set of 5 main brainstem components for one patient both before and after SCS. Variable changes in the response amplitude and a marked decrease in the latency of response 5 occurred with SCS.

Figure 5 summarises the BSEP results for all of the patients tested. The latency of the N_5 response is expressed as a difference from the mean value for normal subjects. This difference is measured in units of standard deviations of normal subjects. Thus, a value of 2 or more is statistically significant at the 5% level. The bar represents the value before SCS and the arrowhead shows the direction of the change and the value obtained following SCS. . Out of 30 sets of results 11 showed a statistically significant improvement, 15 showed a non-significant improvement and 4 showed a non-significant worsening.

For example, the patient (C.P.) whose CSEP results were considered in detail during periods of improvement and deterioration gave BSEP results (left side) shown in table 1.

Results similar to these were found in the other cases in which serial studies were carried out.

TABLE 1

Changes in the N_5 BSEP. Values are the N_5 latency difference from normal expressed as multiples of the standard deviation of normal subjects. Ninety five per cent of normal subjects would give a value of less than 2.

Initial	7.21
1st trial SCS	3.35
On Readmission	7.75
After 1st laminectomy	2.42
Clinical deterioration	2.81
After 2nd laminectomy	1.30

DISCUSSION

If the N11 component above is considered, it was improved in amplitude in 7 out of 8 cases undergoing SCS and on each occasion when SCS was applied. However only 3 of the 8 cases had a worthwhile clinical improvement so it must be concluded that a change in N11 with SCS does not predict a good clinical response.

Evidence has been given (5) indicating that N11 is generated by dorsal horn neurones which are activated by low threshold cutaneous afferent volleys. In these M.S. patients this mechanism is suppressed but recovers partially after a period of SCS. The effect of SCS on this dorsal horn mechanism would appear to be one of increasing their excitability. Such a change however did not result in clinical improvement of most of the patients.

For the BSEP, taking a change of 2 standard deviations as significant, 3 of these 8 cases showed a significant improvement. Two of these were considered to have made a worthwhile clinical improvement. The third patient who showed a significant improvement of the BSEP showed no significant clinical improvement. The case that showed clear clinical improvement but only a non-significant (1.55) change in N_5 latency did in fact show significant improvements in the latencies of some of the earlier responses (N_3 and N_4) which is not apparent in figure 5 as it summarises only the N_5 data.

More data are needed to evaluate the degree to which CSEP and BSEP data correlate with clinical findings.

It has been found that both CSEP and BSEP techniques can detect clinically silent lesions when used diagnostically. It is reasonable therefore to expect that evoked potential changes associated with SCS would not all reflect a significant clinical change.

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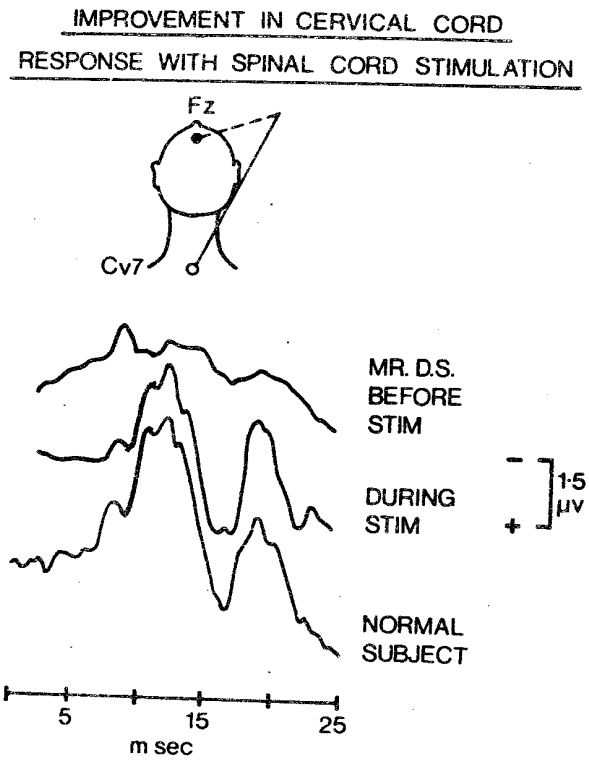

Figure 1 . The cervical somatosensory evoked potential from a normal subject is shown in the lower trace. The potential peaks N9, N11, N13 and N14 can be seen before the positive peak which preceeds N20. The upper trace is from a patient with M.S. before spinal cord stimulation. N9 is clearly visible but the remaining potentials are absent or of very low amplitude. The centre trace is from the same patient after a 4 day period of spinal cord stimulation, the CSEP is now within normal limits. The montage indicates the recording derivation from cervical 7 - F_z (10 - 20 system) such that a negativity at the active (Cv7) electrode produces an upward deflection on the trace.

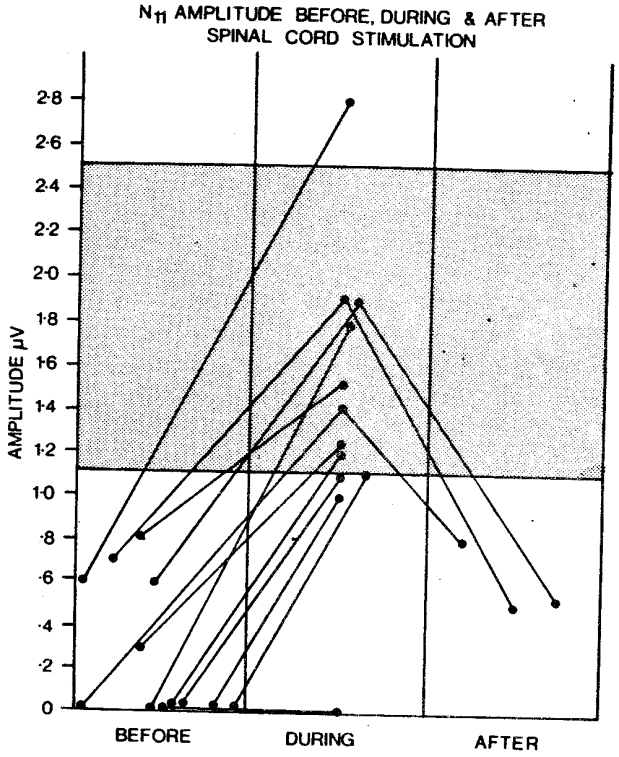

Figure 2. The amplitude of the N11 peak from 8 patients is plotted before and after a period of at least 4 days of spinal cord stimulation. Three patients were studied 3-7 months after stimulation. Some patients were studied on more than one occasion. The stippled area represents 2 standard deviations of the N11 amplitude of 31 normal subjects.

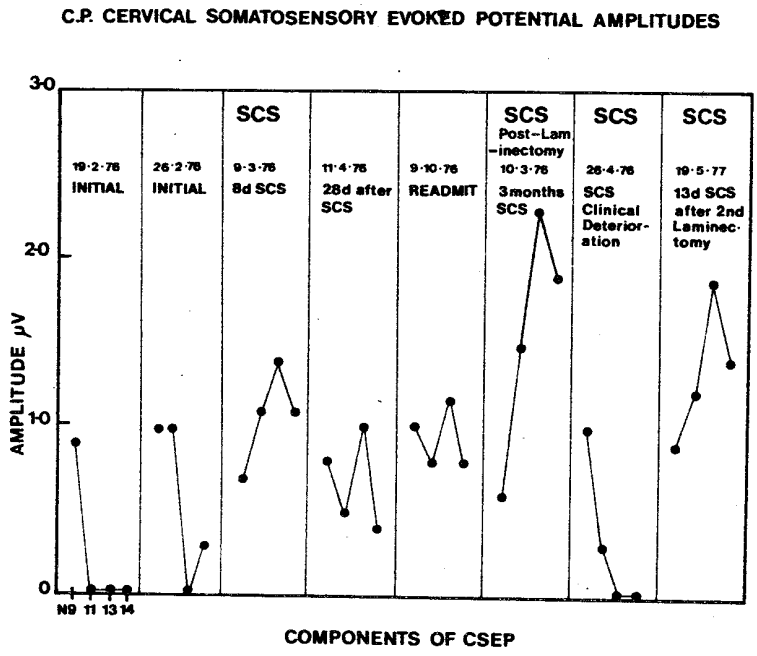

Figure 3. Changes in the N9, N11, N13 and N14 components of CSEP in one patient undergoing spinal cord stimulation. The amplitudes of each component are plotted beginning with N9.
The normal amplitudes are N9 0.8 μV : N11 1.8 μV : N13 2.2 μV : N14 1.3 μV.
Note that a normal amplitude N9 is present on each occasion.

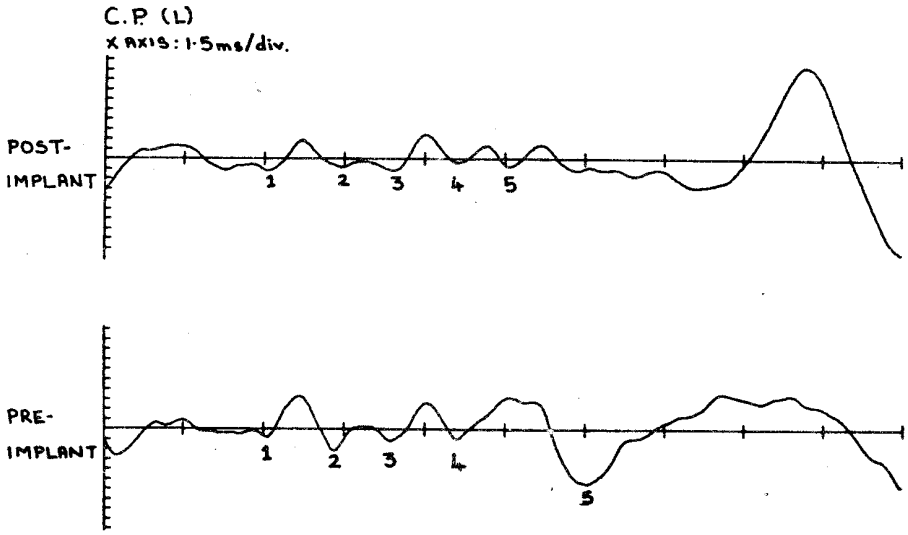

Figure 4. Auditory evoked cochlear and brainstem responses recorded before (lower trace) and after (upper trace) SCS.

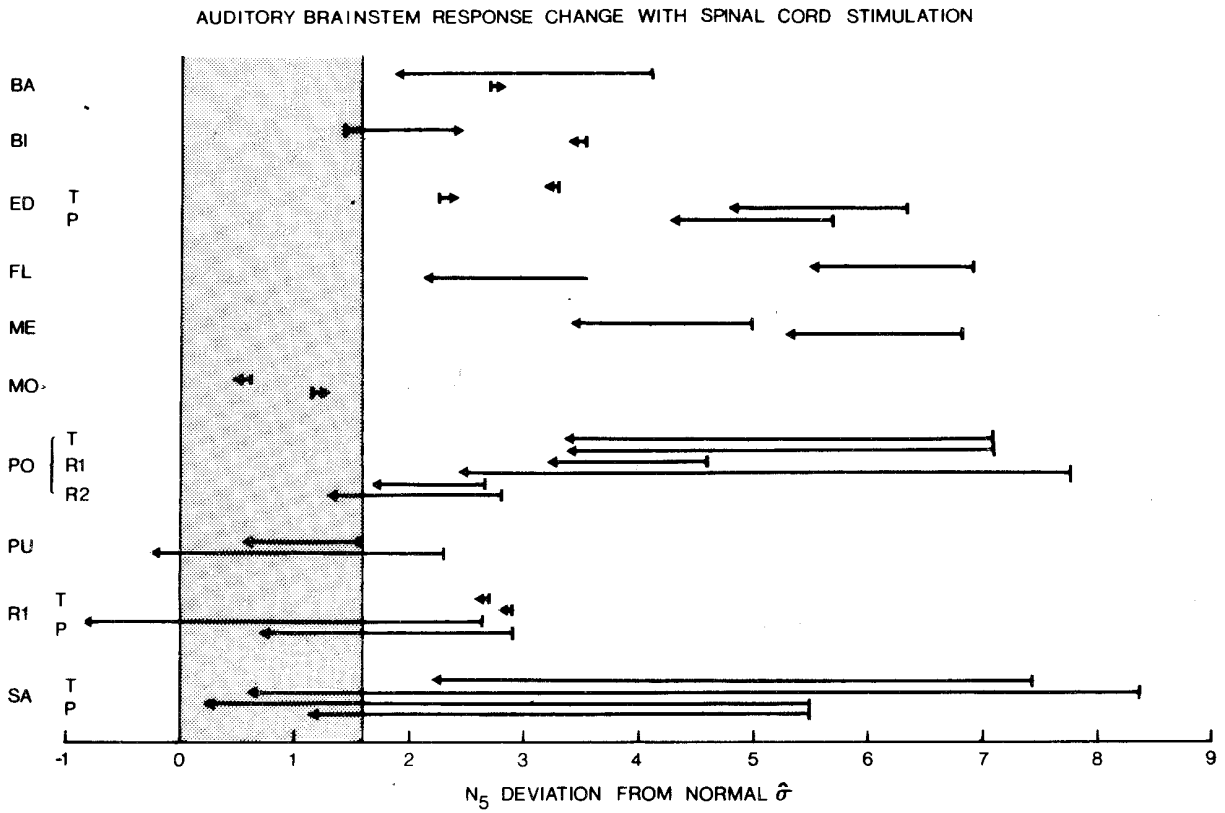

Figure 5. Summary of the BSEP data. The horizontal axis shows the latency difference of N5 from its normal value expressed as a multiple of the normal standard deriation. The change occurring with each SCS treatment is shown by a bar at the pre-treatment value and an arrowhead indicating the post-treatment value and the direction of the change. For each patient two results are given which are for the left (upper line) and right (lower line) sides. Values lying within 0 to 1.6 may be considered as normal (90% confidence limit) as shown by the shaded region.