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THE EFFECTS OF CEREBELLAR STIMULATION ON THE STRETCH REFLEX IN THE SPASTIC MONKEY

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SUMMARY

The effects of stimulating the cerebellar surface on abnormal segmental reflexes were examined in monkeys rendered spastic by either bilateral or unilateral decortication of areas 1, 2, 3, 4 and 6. Rectified, integrated electromyographic (EMG) activity from the biceps and triceps as well as the torque were recorded and averaged during successive flexion-extension movements of the arm produced by a displacement controlled torque motor. Two movement paradigms were employed. The first consisted of a ramp and hold paradigm with an initial rapid flexion of the forearm, a subsequent two second period during which the arm position was held constant, and a rapid extension returning the limb to the initial position. In the second paradigm, the forearm was modulated sinusoidally at several different frequencies. Cerebellar stimulating electrodes were placed over the paravermal region bilaterally. Different frequencies (10 to 300 Hz) and different charge densities (1.5 to 10 $\mu C/cm^2$) were used in each animal. In each experimental trial short periods of cerebellar stimulation (10 to 30 minutes) were interspersed between control periods. As observed in some types of clinical spasticity, flexion or extension of the extremity was capable of evoking coactivation of the biceps and triceps. Cerebellar surface stimulation reduced the amplitude of the phasic and tonic stretch reflexes recorded from the triceps during flexion and decreased the abnormal triceps response during passive shortening. The biceps response to stretch was increased by cerebellar stimulation and its abnormal response to flexion was decreased. These combined effects modified the organization of the segmental reflexes, producing a more normal reciprocal relationship of the EMG activity in the biceps and triceps. Evaluation of many different combinations of stimulus parameters revealed that not only the magnitude of the passive reflex but also the nature of the effect was dependent on stimulus parameters. Although these studies demonstrate an improvement in the abnormal reflexes present in spastic primates, they emphasize the complexities of the response evoked by cerebellar stimulation and the importance of stimulus parameters in the modifications produced by this technique.

INTRODUCTION

Cerebellar stimulation for relief of spasticity and movement disorders has now been used in a large number of patients (Cooper *et al.*, 1976, 1978; Davis *et al.*, 1977/78; Larson *et al.*, 1977/78; Whittaker, 1980; Russman *et al.*, 1979; Penn *et al.*, 1980). In

these clinical trials widely different degrees of success and failure have been reported. Most of the clinical studies (Cooper *et al.*, 1976, 1978; Davis *et al.*, 1977/78; Larson *et al.*, 1977/78; Whittaker, 1980; Ratusnik *et al.*, 1978; Penn *et al.*, 1980) have evaluated the effectiveness of cerebellar stimulation using only clinical observations and examinations of the patients. Recently two double blind studies (Whittaker, 1980; Penn *et al.*, 1980) were unable to document any consistent improvement in the clinical status of the patients by cerebellar stimulation. In an earlier study by Penn and colleagues (Ratusnik *et al.*, 1978) a blinded assessment of speech documented only slight improvements that could be correlated with cerebellar stimulation.

Studies attempting to document the effectiveness of this procedure using physiological assessments of motor system function in spastic animals or humans are limited. Upton (Upton and Cooper, 1976; Upton, 1978) reported reductions in the M1 and M2 components of the H reflex as well as reductions in somatosensory evoked potentials by cerebellar stimulation. Similar modifications in the excitability of segmental motoneuron pools were demonstrated by Fisher and Penn (1978). In spastic patients Penn and co-workers (1978) reported that cerebellar stimulation shifted the frequency at which sinusoidal displacement of the foot produced the maximal EMG response in the gastrocnemius-soleus muscle. In other series, quantitative assessment of gait using angle/angle diagrams has been studied (Milner *et al.*, 1978) and respiratory co-ordination has been evaluated (Miyasaka *et al.*, 1978; Wong *et al.*, 1979). However, correlating modifications in a physiological variable with functional gains has proved difficult (Fisher and Penn, 1978; Penn *et al.*, 1978; Wong *et al.*, 1979).

A shortcoming in almost all the blinded and unblinded clinical studies is a failure to define stimulus parameters that produce physiological changes in a given patient before the clinical trial begins. Although in a few patients stimulus parameters were adjusted to obtain a modification in the physiological variables being assessed to calibrate the patients (Upton and Cooper, 1976; Upton, 1978), the precise locations of the electrodes, stimulus frequency and charge densities of stimulation are not adequately documented in many studies, making comparisons between them impossible (Cooper *et al.*, 1978; Larson *et al.*, 1977/78; Penn and Etzel, 1977; Ratusnik *et al.*, 1978; Whittaker, 1980; Russman *et al.*, 1979). More importantly, usually no attempt was made to select stimulus parameters which produce the desired physiological or clinical effect.

Because the most appropriate way to evaluate physiologically the effects of cerebellar stimulation is not yet known, it is necessary to gain insight into how cerebellar stimulation modifies motor behaviour and to describe some of the important variables involved. Primate models of spasticity provide an excellent tool for investigations of this type because of the capability of controlling the deficit as well as the stimulus parameters and electrode locations. Despite the attractiveness of using an animal model for assessment of cerebellar stimulation, only one previous study (Hemmy *et al.*, 1977) examined the effects of this procedure in unilaterally decorticate primates. It was shown that cerebellar stimulation decreased the force

necessary passively to flex or extend the forearm. The studies reported here evaluated the effect of cerebellar stimulation on passively evoked proprioceptive reflexes in awake spastic primates. This work not only describes the changes in the stretch reflex that can be produced, but also emphasizes the importance of stimulus parameters. A preliminary report of some of these findings was recently presented (Ebner *et al.*, 1980).

METHODS

Animal Model of Spasticity

Two types of decortication procedures were used in primates to produce spasticity. In two animals a staged bilateral decortication was employed. In a Rhesus (*Macaca mulatta*) and an African green (*Cercopithecus aethiops*) monkey, decortication of areas 1, 2, 3, 4 and 6 were performed on the side ipsilateral to the extremity in which the reflexes were to be examined two to four months after decortication of the same areas in the opposite cerebral cortex. The bilaterally decorticate animals exhibited marked extensor hypertonus and hyperreflexia in all four limbs. These findings were evident both clinically and electromyographically (*see* fig. 2). In two other animals (*M. mulatta*) only unilateral decorticications were performed, encompassing areas 1, 2, 3, 4 and 6 contralateral to the side of the extremity in which reflexes were examined. These animals exhibited a flaccid paresis on the side contralateral to the lesion immediately following the operation and for a period of approximately two months. Following this period there was a slight increase in the muscle tone in the limbs of the contralateral side. The lack of overt spasticity in the unilaterally decorticate animals parallels the observations of many other investigators regarding the clinical deficit in unilaterally decorticate monkeys (Mettler, 1943; Crosby *et al.*, 1966; Tasker *et al.*, 1975). The slight increase in muscle tone that developed two months after the lesion appears similar to that observed by Gilman and associates (1974). The animals with the bilateral decortication were extremely disabled by their lesion. These animals were unable to feed or care for themselves. In contrast, the unilaterally decorticate animals were self sufficient. Three of the four animals have been sacrificed, and the extent of the cortical lesion in each was documented.

Cerebellar Stimulation

Each animal was implanted with cerebellar stimulating electrodes on the paravermal region bilaterally. Each electrode consisted of an array of three platinum discs (7.6 mm^2/disc) embedded in a silastic strip. The three discs were orientated sagittally on the cerebellar surface. Although the electrodes were implanted primarily on the vermal region of the anterior lobe, the most posterior disc in each electrode was located on the posterior lobe. The stimuli were generally applied between the two electrode arrays. Occasionally a single array was utilized for ipsilateral stimulation (two plates anodic *versus* a cathodic plate in the same electrode strip). The effects of different frequencies (10 to 300 Hz) and different charge densities (1.5 to 10 $\mu C/cm^2$) were examined in each animal. Stimulus duration was kept constant at 0.2 ms. The upper limit of stimulation reflected charge densities below that required to produce twitching movements in the facial musculature. High charge densities in one of the bilaterally decorticate animals were noted to produce definite eye movements consisting of a fixation of the eyes with a slightly lateral left gaze. After approximately a minute of stimulation this effect on eye movements abated. Also at the higher charge densities studied in this animal, stimulation clearly reduced the marked extensor hypertonus, resulting in a change in the posture from that of extensor hypertonus to a more flexed posture in all limbs. In these studies relatively brief periods of cerebellar stimulation (10 to 30 min) were employed.

Analysis of a Passively Evoked Reflex Activity

Initially the EMG activity in the triceps and biceps was recorded by bipolar surface plate electrodes on the skin overlying these muscles. Electrodes were held in place by a tailored sleeve during the passive displacement of the extremity. In the later two animals flexible fine wire electrodes were inserted into the triceps and biceps muscle at each recording session. This procedure was employed to ensure that there was no contamination of EMG activity in the agonist with the EMG activity evoked in the antagonist (see Results).

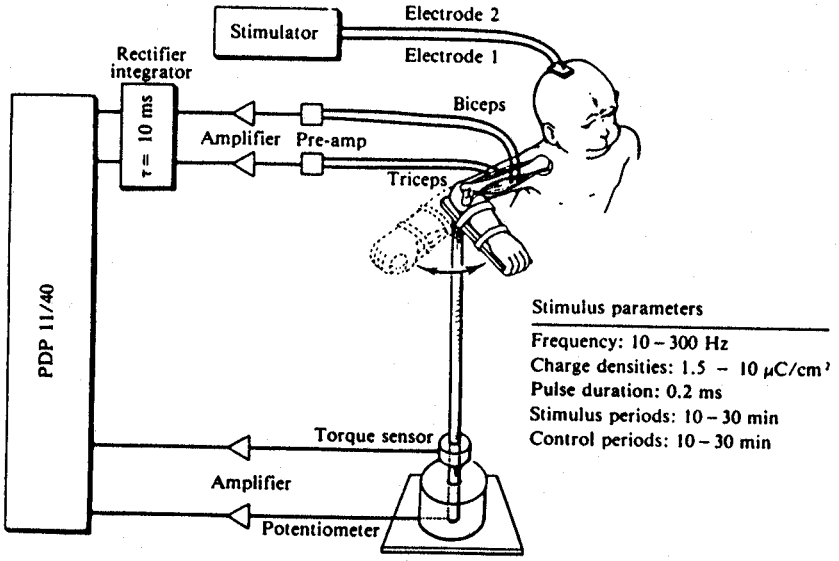

FIG. 1. Schematic diagram of the experimental paradigm. Passively evoked reflexes were recorded by fine wire EMG electrodes implanted in the biceps and triceps. The EMG activity from these muscles during passive displacement delivered by a feedback controlled torque motor was rectified and integrated (τ = 10 ms). A laboratory computer averaged the EMG responses as well as the torque and forearm displacement. Bilateral, anterior vermal cerebellar stimulating electrodes were implanted, and the range of stimulus parameters used is noted.

In a specially constructed primate chair, a displacement-controlled torque motor was used to move the forearm passively. Displacement was monitored by a precision potentiometer, and torque by a reaction torque sensor (fig. 1). Two movement paradigms were employed to evaluate the stretch reflex in these animals. The first paradigm consisted of a ramp and hold movement in which the forearm was initially positioned at 0 deg flexion (in extension) and then passively flexed (30 to 60 deg) (*see* fig. 2). The rise time of this displacement was 280 ms. After holding the arm in the new flexed position for 2 s the arm was returned to its original position. This paradigm permitted the assessment of the phasic and tonic stretch reflexes as traditionally evoked by rapid displacement of the extremity followed by the maintained stretch of the muscle. The second movement paradigm evaluated the reflex activity evoked in the biceps and triceps during the sinusoidal modulation of limb position at frequencies of 0.5 to 5 Hz. The forearm was held in flexion (15 deg) and the position modulated sinusoidally (30 deg peak to peak) about the initial position (*see* fig. 3).

The EMG activity of the triceps and biceps was rectified and integrated (τ = ms). Torque and displacement were also monitored. The average of all four of these parameters was computed as a

function of time throughout the movement. For the ramp data the average was computed through 80 presentations of the stimulus and for the sinusoidal paradigm either 50 or 100 cycles of passive movement were averaged. The time resolution of this average varied inversely with the length of the data segment analysed (1 ms for 1.0 s segment, 2 ms for 2.0 s segment).

An experimental protocol was adopted in which the reflex responses of the biceps and triceps during the two movement paradigms were examined during control and stimulation periods. Each period of stimulation was always preceded and succeeded by control periods. Control and stimulation periods were divided into smaller time epochs to study the time course of the observed changes. These smaller epochs depended on the time required to average a sufficient number of movement trials. Therefore, periods of cerebellar stimulation were longer in the ramp displacement and shorter with the high frequency sinusoidal movements.

For the ramp and hold paradigm (*see* fig. 2) the data was further analysed by measuring the peak of the phasic response during stretch for the triceps and biceps. The magnitude of the reflex response 1 s after initiation of the ramp for the triceps and biceps was used as a measure of the tonic reflex. Since in these animals the triceps or biceps muscles exhibited the abnormal characteristic of responding during shortening (the 'shortening' reaction) the peak amplitude of the EMG response during the shortening reaction was also determined. These values were obtained for control and cerebellar stimulation periods, and expressed as a percentage of the initial control period.

The cycle histograms obtained using the sinusoidal paradigm were analysed by a fast Fourier transform, and the power spectrum was obtained. The power present in the d.c. and fundamental component was compared between stimulation and control periods. For studies examining many different frequencies and charge densities of stimulation, the effects of these two variables on the power present in the d.c. or fundamental were displayed in a three-dimensional diagram.

RESULTS

Ramp and Hold Paradigm

The effects of cerebellar stimulation on the EMG activity of the triceps and biceps recorded throughout the ramp and hold displacement are illustrated in fig. 2. The prestimulus control (*left*) shows that during stretch of the triceps there was an initial phasic response in the triceps followed by a tonic response to the passive stretch. In addition to this very dramatic increase in the triceps response to stretch, an abnormal 'shortening' reaction was present (Westphal, 1880; Tatton *et al.*, 1979). This shortening reaction was characterized by a burst of EMG activity in the triceps when the muscle was shortened during the return of the arm to extension. Although this shortening reaction was observed in all four animals, it was more prominent in the bilaterally decorticate animals.

Bilateral stimulation of the paravermis dramatically modified the response of the triceps to the arm displacement. Fig. 2 illustrates the effects of three different charge densities at continuous 200 Hz bilateral paravermal stimulation. Both the phasic and tonic components of the stretch reflex in the triceps were reduced by cerebellar stimulation at the three stimulus intensities shown in fig. 2. In addition, the prominent shortening reaction in the triceps was attenuated. When stimulation was discontinued, the amplitude of the immediate poststimulus control of the triceps (*rightmost column*) returned to prestimulus control levels (*leftmost column*).

The effects of cerebellar stimulation on the biceps reflex activity are also illustrated in fig. 2. During the prestimulus control period (*left*) the biceps response to the passive movement was abnormal. The expected response of the biceps to its stretch was quite small, consisting of only a slight increase in the EMG activity of the biceps when the arm returned from flexion to the extended position. However, note the large shortening reaction present in the response of the biceps during the flexion phase of the movement, that is, when the biceps was shortened. This abnormal reaction in the biceps was consistently observed in the other animals of this study. It must be stressed that this biceps response to extension of the triceps was not due to contamination resulting from recording triceps EMG activity with the biceps EMG electrodes. Similar observations were made with surface as well as fine wire bipolar electrodes inserted directly into the belly of both muscles. Also, the time course of the two records differed significantly, the biceps shortening reaction actually peaking earlier than the triceps (fig. 2). In addition, the triceps shortening reaction does not appear in the control EMG responses of the biceps. These arguments suggest strongly that the abnormal shortening reaction in the biceps is not due to contamination. In fig. 2 the abnormal response of the biceps was reduced by cerebellar stimulation at all three intensities. During stimulation at the highest intensity (3.50 μC/cm^2) the response of the biceps during its stretch was actually augmented, showing an increase in both the phasic and tonic components.

These findings demonstrate that during cerebellar stimulation the modulation of the biceps and triceps EMG responses became reciprocal. Close examination of the

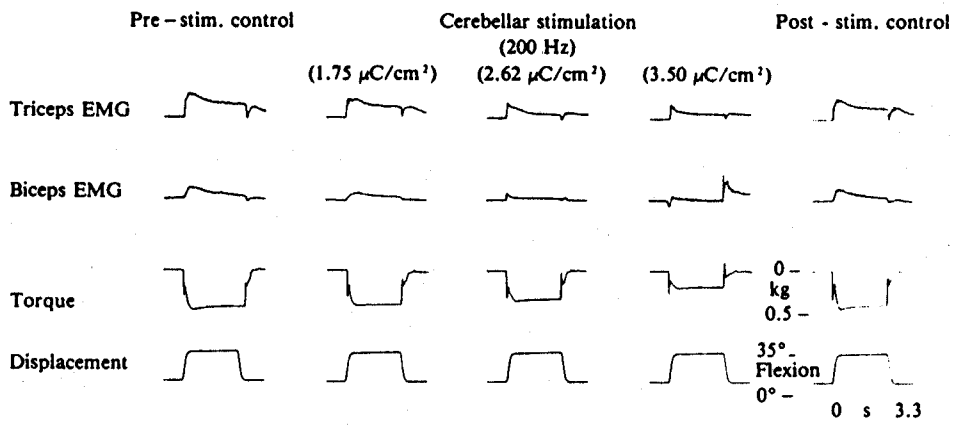

FIG. 2. Effect of cerebellar stimulation on the averaged (N = 80), rectified and integrated EMG activity of the triceps and biceps during a ramp and hold flexion of the forearm in a bilaterally decorticate monkey. The effects produced at three different intensities of stimulation at the same frequency are shown. Both the phasic and tonic components of the triceps response to stretch were decreased by paravermal stimulation. The torque required to generate the displacement was decreased by cerebellar stimulation. The response of the biceps during stretch was increased at the higher charge density (3.50 μC/cm^2). Note that the abnormal activation of the biceps and triceps during their respective shortening (i.e. shortening reaction) was reduced by cerebellar stimulation. The EMG traces are all displayed at equal gains for control and stimulation periods.

records at 3.50 μC/cm^2 reveals that there was also a reciprocal reduction in the EMG of a muscle during stretch of its antagonist. For example, in fig. 2 stimulation at 3.50 μC/cm^2 decreased the triceps EMG activity below baseline during the return of the arm to extension, coincident with the large increase in biceps activity during its stretch. Similarly, there was a reduction in EMG activity of the biceps below background when the arm was passively flexed. This reduction in the biceps EMG activity was coincident with the large phasic triceps EMG response. Thus, cerebellar stimulation at this combination of charge densities and stimulus frequencies produced a reciprocal pattern of excitation and inhibition in the responses of this agonist and antagonist pair, an effect which disappeared when cerebellar stimulation was discontinued.

In the example shown in fig. 2, the torque required to generate the arm displacement was also reduced by cerebellar stimulation. In spite of the rather complex changes in EMG activity of the biceps and triceps, the stiffness of the forearm was substantially reduced by cerebellar stimulation. The magnitude of the reduction was dependent on the charge density of stimulation: the greater the intensity of stimulation, the greater the amount of reduction.

Sinusoidal Paradigm

The sinusoidal displacement of the forearm was also used to evaluate the effects of cerebellar stimulation on the reflex activity of the triceps and biceps. A typical control-stimulation-control sequence is illustrated in fig. 3 in a bilaterally decorticate animal. The EMG activity of the triceps was characterized by considerable background activity and was extensively modulated by the stretch. During the prestimulus control (*left panel*), the triceps EMG response was modulated in phase with the displacement, the response being maximal at peak flexion. During cerebellar stimulation (*centre panel*), the modulation present in the EMG activity of the triceps was reduced, and there was a large reduction in the background activity. In the immediate poststimulus control (*right panel*), the characteristics of the triceps EMG activity returned to prestimulus control levels.

The EMG activity of the biceps during the sinusoidal displacement was markedly abnormal. As shown for the control periods the peak EMG response of the biceps occurred in phase with the stretch and the maximal response of the triceps, the inverse of the expected reciprocal relationship between an agonist and antagonist. Stimulation of the anterior lobe dramatically altered the characteristics of the biceps response. In addition to reducing the background EMG activity in this muscle, the phase of the biceps response was shifted. As a consequence, biceps EMG activity was maximal during stretch, and the triceps and biceps responses were out of phase. During cerebellar stimulation the biceps and triceps responded to the sinusoidal displacement reciprocally instead of cocontracting, as observed during the control period. The peak-to-peak amplitude of the torque resulting from the sinusoidal movement was also reduced (40 per cent) by cerebellar stimulation.

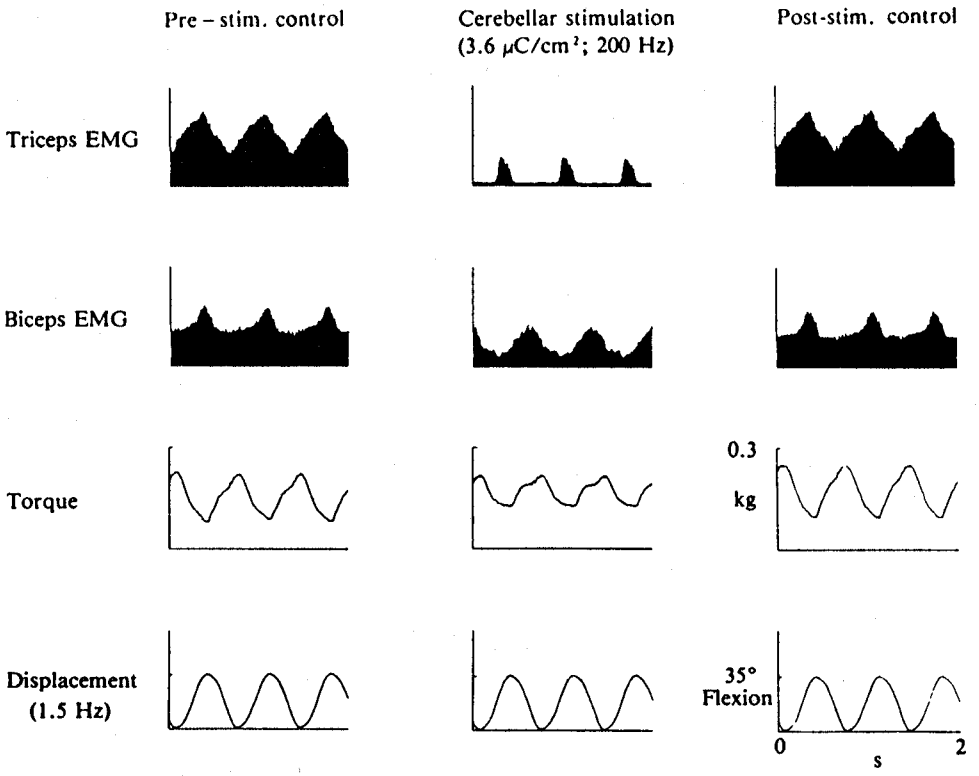

FIG. 3. Effects of cerebellar stimulation on the EMG activity of the triceps and biceps during sinusoidal displacement of the forearm in a bilaterally decorticate monkey. Both the tonic and sinusoidally modulated components of the triceps EMG activity were dramatically reduced by bilateral anterior lobe stimulation. Although the tonic activity in the biceps was reduced by stimulation, the sinusoidally modulated component was accentuated. The cocontraction of the triceps and biceps during the control periods was replaced by reciprocal activation during cerebellar stimulation. The torque was also reduced by this procedure.

Effects of Different Charge Densities at Constant Frequency

The measurements obtained from responses evoked using the ramp and hold paradigm during cerebellar stimulation at different frequencies and intensities revealed the importance of these parameters in determining the effect produced by this procedure on the reflex EMG activity. The importance of charge density is illustrated in fig. 4 for each of the different components of the triceps EMG response as well as the torque required to generate the ramp displacement. In this study, stimuli were applied bilaterally to the anterior lobe at a frequency of 200 Hz using three different charge densities. These plots show that the magnitude of the reduction in the phasic (A) and tonic (C) components of the triceps response to stretch was dependent on the intensity of stimulation. Lower charge densities of stimulation resulted in less reduction in the phasic and tonic components of the

triceps response than at the two higher charge densities. Similarly the peak of the triceps shortening reaction (B) was also dependent on charge density. Fig. 4D illustrates that the reduction in torque necessary to produce the forearm displacement could be graded as the charge density of cerebellar stimulation increased. At the lowest charge density used (1.75 μC/cm^2) there was only a slight reduction in the torque. As the charge density was increased to 3.5 μC/cm^2, the torque was reduced to 50 per cent of control levels. Notice that for all the components of the triceps response (A, B, C) as well as the torque (D), there was a return to prestimulus control levels in the immediate poststimulus control period.

The different components of the EMG activity of the biceps were also dependent on the charge density of stimulation, as illustrated in fig. 5. The plots in fig. 5 were obtained by measuring the responses of the biceps during the same control and stimulation periods used for the data presented in fig. 4. As illustrated in A and B the phasic and tonic components of the biceps response to stretch were increased at the highest charge density (3.50 μC/cm^2) of cerebellar stimulation. Notice, however, that at the two lower charge densities, there was actually a slight reduction in these

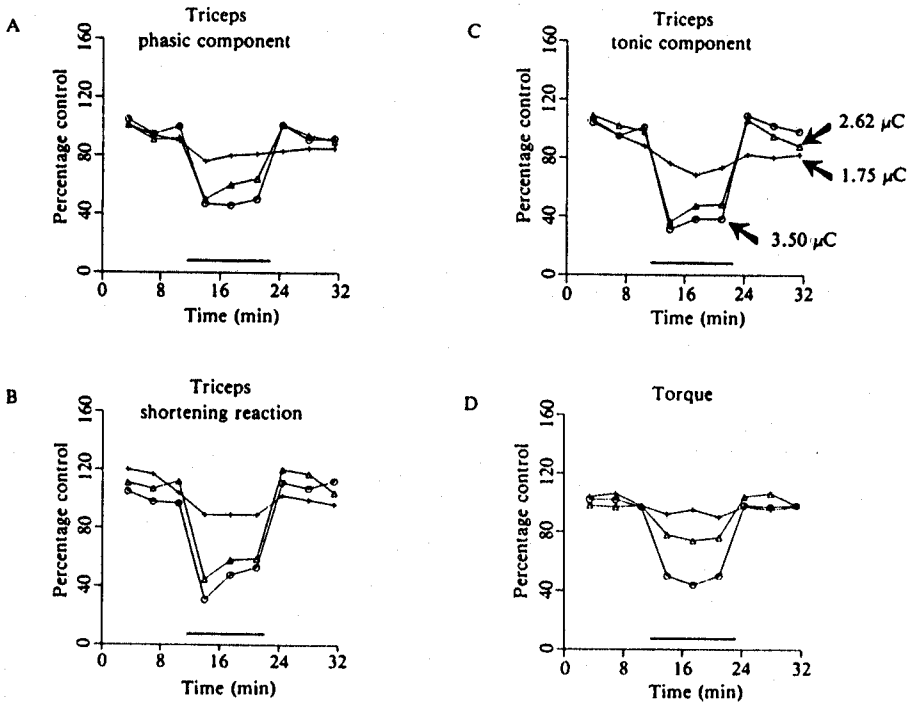

FIG. 4. The effects of three different charge densities on the different components of the triceps EMG response to the ramp and hold displacement to cerebellar stimulation at 250 Hz. As the charge density increased, all three components of the triceps response, the shortening reaction (B), and the phasic (A) and tonic (C) components of the stretch reflex were progressively decreased. The torque (D) decreased gradually as the intensity of cerebellar stimulation increased. The black bar denotes the period of bilateral anterior lobe stimulation, which occurs between two control periods. All values are expressed as a percentage of each measurement obtained during the initial control period. Charge densities in C are per cm^2.

two components. Similarly, the biceps shortening reaction could either be increased or decreased with cerebellar stimulation (c) depending on the level of charge density employed. These findings illustrate that the relationship between charge density and the responses in the biceps is not simply monotonic, in which greater charge densities produce greater effects.

Effects of Different Stimulus Frequencies at Constant Charge Density

In general the lower frequencies (10 to 50 Hz) of cerebellar stimulation were less effective in modifying the reflex activity of the triceps and biceps than higher frequency stimuli (100 to 300 Hz). The dependence of the EMG responses on the frequency of cerebellar stimulation is illustrated in fig. 6. In this experiment the peak EMG response of the triceps phasic component evoked by the ramp and hold stimulus was measured during the application of cerebellar stimulation at three different stimulus frequencies when the charge density was held constant. For the triceps, 100 Hz stimulation was less effective in reducing the peak mean phasic EMG response than either 200 or 300 Hz cerebellar stimulation. At the two highest stimulus frequencies the peak mean response was reduced to 15 to 20 per cent of the control, while at 100 Hz stimulation this response was reduced to only 50 per cent of

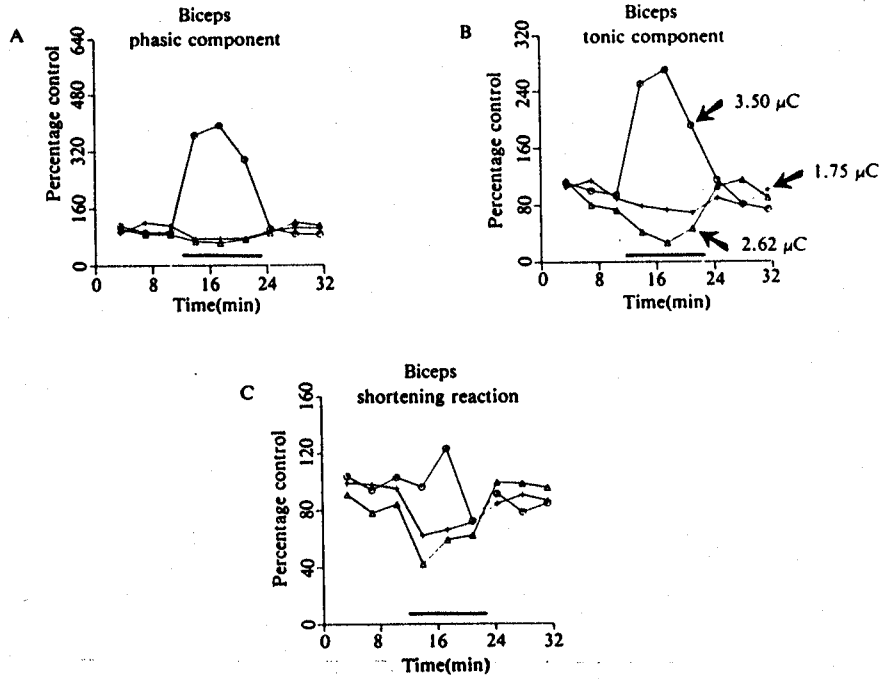

FIG. 5. Sensitivity of the different components of the biceps response to the ramp and hold displacement to changes in charge density. Low charge density stimulation (1.7 μC and 2.62 μC/cm²) decreased the phasic component (A), tonic component (B), and the shortening reaction (C) of the biceps. As the charge density was increased to 3.5 μC/cm², the phasic and tonic components of the biceps as well as the shortening reaction were increased by the stimulation. The period of bilateral anterior stimulation at 250 Hz is denoted by the black bar.

control. This figure also illustrates the reproducibility of these observations over a period of twenty-three days. The data from the control and stimulation periods obtained on three different days are superimposed on the same graph. Stimuli were applied with the same charge densities and stimulus frequencies on each day. On all three days the peak mean EMG response of the phasic component of the triceps was affected similarly with cerebellar stimulation.

Effects of Different Charge Densities and Frequencies Varied Simultaneously

The use of the sinusoidal movement paradigm allowed a rapid assessment of the effects of different charge densities and stimulus frequencies on the magnitude and nature of the effect produced by cerebellar stimulation on passively evoked reflex behaviour. This was undertaken by evaluating the cycle histograms using a power spectral density analysis. Initially the power in the d.c. and the fundamental components was evaluated. These two components of the cycle histogram were computed and compared with those obtained during pre- and poststimulation control periods using many different combinations of stimulus frequency and charge density. In addition, the importance of stimulus location was preliminarily

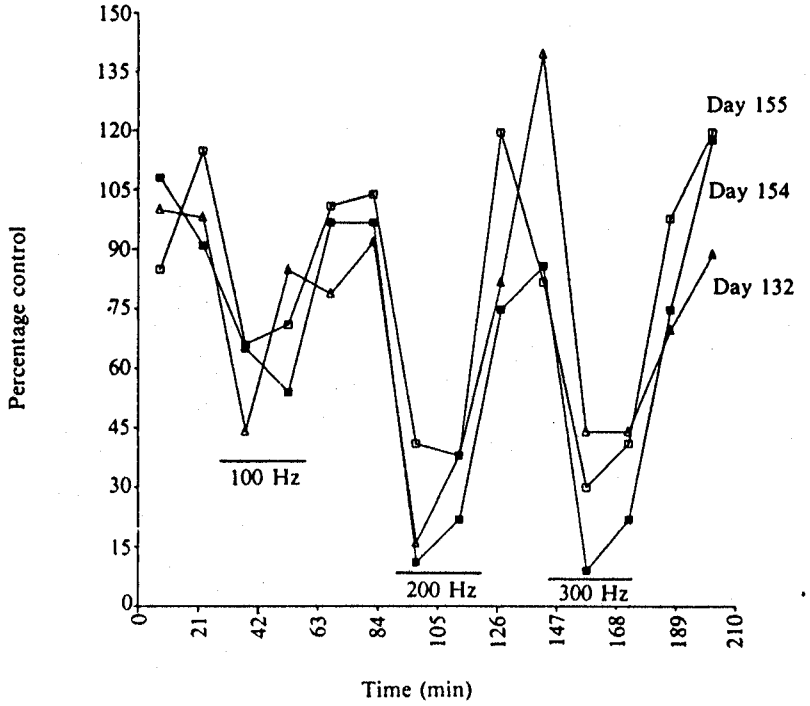

FIG. 6. Effect of stimulus frequency on the peak EMG response of the triceps. Bilateral paravermal stimulation was applied at a current density of 6.5 $\mu C/cm^2$ in a unilaterally decorticate animal. Three different stimulation periods at 100, 200 and 300 Hz are denoted by the black bars. As the stimulus frequency increased from 100 to 200 and 300 Hz there was a greater reduction in the response. Furthermore, the figure illustrates the reproducibility of the effects produced using the same stimulus parameters on three different days.

evaluated by comparing the effects of stimulating ipsilaterally, contralaterally and bilaterally with the two electrode strips located in the paravermal region. Fig. 7 presents the data from one experiment showing the power present in the d.c. component at different intensities and frequencies of stimuli applied ipsilaterally, contralaterally and bilaterally. With ipsilateral stimulation the d.c. power in the triceps was reduced as the frequency of stimulation and charge density increased. In contrast, with contralateral stimulation the mid-range current intensities (1.0 to 2.0 mA) applied at the higher frequencies produced large reductions in the d.c. component. As the stimulus intensities were increased further (2.5 to 3.0 mA) using

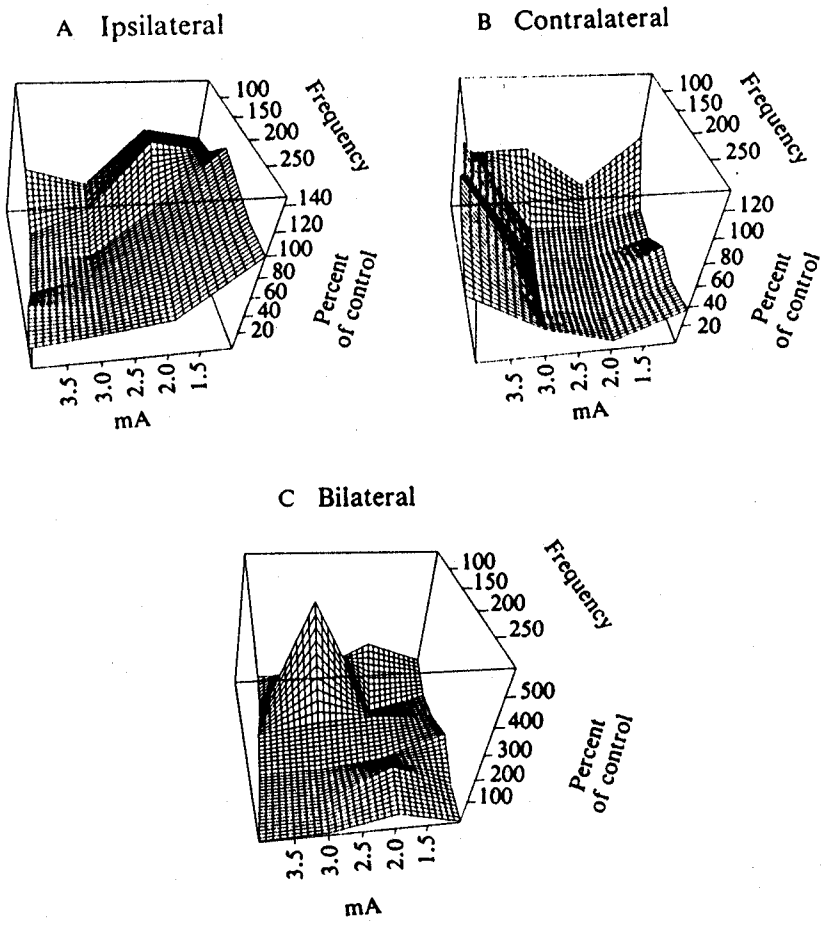

FIG. 7. Effects of varying the frequency and intensity of stimulation on the power present in the d.c. component of the triceps response to sinusoidal forelimb displacement. Ipsilateral (A), contralateral (B) and bilateral (C) anterior lobe stimulation at different frequencies and stimulus parameters are plotted. The change in the magnitude of the power present in the d.c. component is shown as a percentage of pre- and poststimulus control. With ipsilateral or bilateral stimulation, an increase in the frequency and charge density was associated with a progressive reduction in the d.c. power. Notice that for contralateral stimulation the most effective parameters for reducing the d.c. power were in the 2.0 to 3.0 mA range. In figs. 7, 8 and 9, 1 mA converts to 0.85 $\mu C/cm^2$ with the electrode arrays used in these experiments.

contralateral stimulation the d.c. power in the triceps returned toward control levels. The surface describing the effects of bilateral stimulation was quite different. The combination of the largest stimulus frequencies and charge densities (2.0 to 3.0 mA, 200 to 300 Hz) produced a dramatic reduction in the d.c. power. Notice, however, that increases in d.c. power occurred using 100 Hz stimulation at 2.0 to 2.5 mA.

The effect of cerebellar stimulation on the power present in the fundamental of the triceps was also extremely dependent on stimulus parameters and stimulus location (fig. 8). With bilateral stimulation the greater charge densities and stimulus

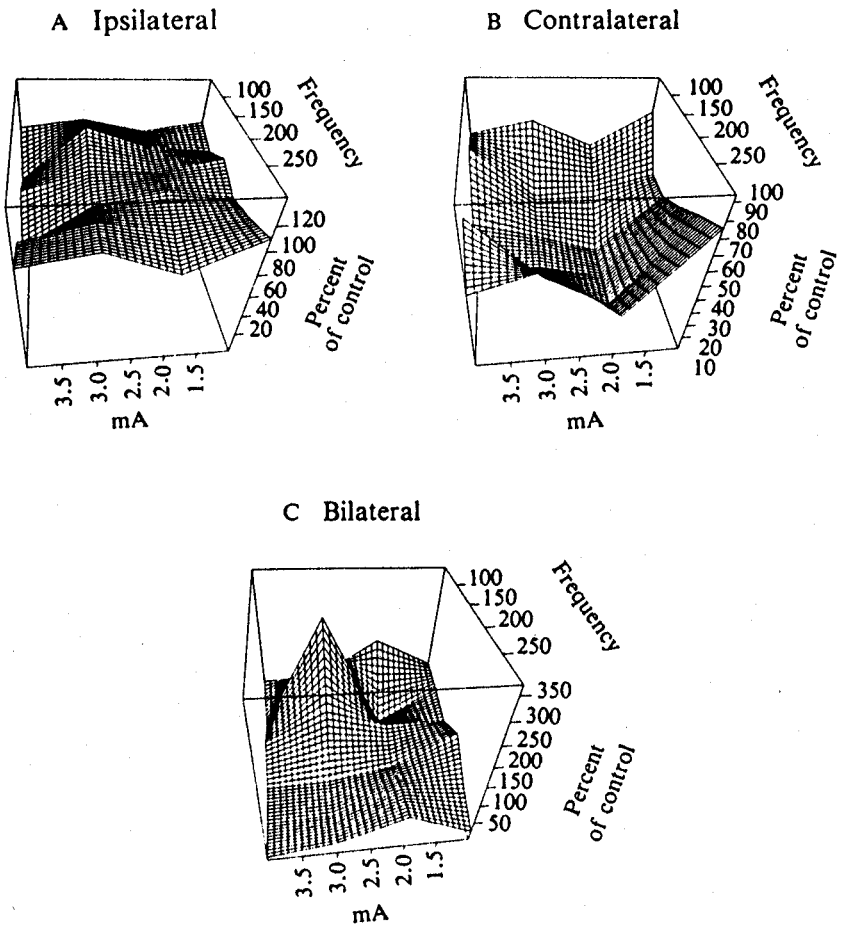

FIG. 8. Effects of different charge densities and stimulus frequencies on the power in the fundamental of the triceps response to sinusoidal displacement. Ipsilateral stimulation (A) in this animal had little effect on the fundamental component of the triceps response. B, contralateral stimulation produced a complex change in the triceps power in the fundamental which was maximally reduced at the mid-range of frequencies and charge densities of stimulation (2.0 to 3.0 mA, and 150 to 200 Hz). C, bilateral stimulation resulted in a large reduction in the power present in the fundamental of the triceps at the highest charge densities and frequencies. Notice also that an increase in the power in the triceps fundamental was produced at 100 Hz and 3.0 mA.

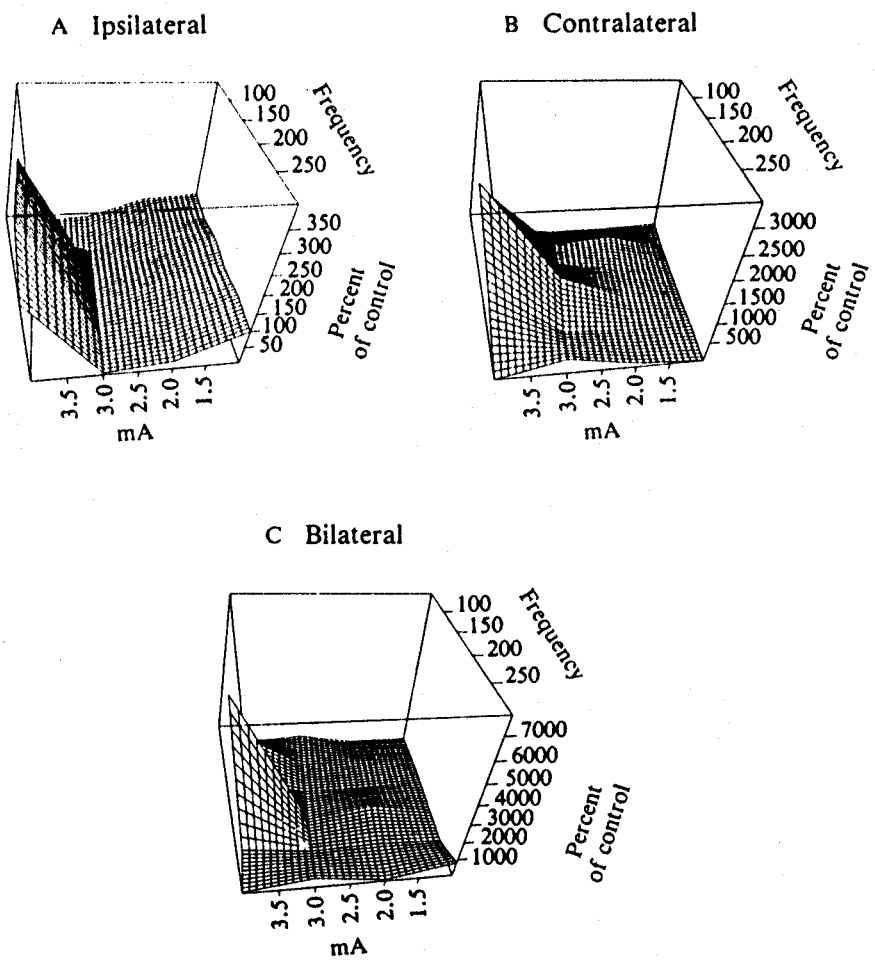

FIG. 9. Effects of different frequencies and stimulus intensities on the power present in the fundamental of the biceps. Ipsilateral stimulation (A) increased or decreased the power present in the fundamental depending on the charge densities. At an intensity of 3.0 mA and a frequency of 150 to 300 Hz there was a large reduction in the power present in the fundamental. In contrast, the power present in the fundamental increased at 4.0 mA, 150 to 200 Hz stimulation. Contralateral (B) and bilateral (C) stimulation produced similar effects.

frequencies reduced the power in the fundamental of the triceps. In contrast, ipsilateral stimulation had minimal effect on the power in the fundamental despite its dramatic effect on the d.c. power in the triceps response (compare figs. 7 and 8). Contralateral stimulation was maximally effective in reducing the power in the fundamental at the midrange of the frequencies and current intensities.

The power in the fundamental of the biceps response was also very sensitive to stimulus frequency and charge density (fig. 9). Ipsilateral stimulation (A) at 2.0 mA and frequencies ranging from 100 to 300 Hz produced a large reduction in the power present in the fundamental. However, as the stimulus intensity increased to 3 mA,

the stimulus frequencies between 100 and 300 Hz actually increased the power present in this component. Similar effects were produced by stimulating with the contralateral (B) or bilateral (C) electrode arrays. Therefore, stimuli applied in these locations could increase or decrease the biceps EMG response to stretch dramatically, depending on the particular combination of stimulus parameters used. These observations extend those made using the ramp and hold paradigm (*see* fig. 5) in which the peak response of the biceps could be increased or decreased depending on the charge density of stimulation. Thus, various combinations of stimulus intensities and frequencies will produce qualitatively different effects on the amplitude of these reflexes which cannot be predicted *a priori* based on the magnitude of the parameters.

DISCUSSION

A precise universally accepted definition of spasticity in neurophysiological or clinical terms is not available. As pointed out by Landau (1974), there are at least six definitions of spasticity in the literature. However, certain features of motor reflex behaviour are usually considered important elements of this condition. Hyperreflexia, particularly in the antigravity muscles, is a crucial feature of spasticity (Nathan, 1973; Dietrichson, 1971*a*, *b*; Burke *et al.*, 1970, 1971). Recently abnormal patterns of reflex behaviour, particularly those associated with cocontraction of an agonist-antagonist muscle group, are also viewed as an important element (Penn *et al.*, 1978; Andrews *et al.*, 1973; Penn and Etzel, 1977; Milner-Brown and Penn, 1979). It is important to point out that the primate model of spasticity employed in our studies, the decorticate monkey, possessed both of these features, the hyperreflexia in the antigravity muscles as well as marked cocontraction (*see* figs. 2 and 5).

In these experiments cerebellar stimulation had four principal effects upon different aspects of the evoked proprioceptive reflex behaviour: (i) reduction of the phasic and tonic reflex response of the triceps during passive flexion; (ii) decreased cocontraction and increased reciprocal activation of the muscles in an agonist-antagonist pair; (iii) an increased responsiveness of the biceps to extension; and (iv) decreased torque required to displace the limb. Thus cerebellar stimulation not only can decrease the abnormal amplitude of stretch reflexes but it can also improve an abnormal pattern of stretch reflex activity in a spastic animal. The marked cocontraction and lack of reciprocal activity seen in these animals was improved by this procedure. A more reciprocal pattern of reflex activation of the agonist-antagonist pair was produced by surface stimulation. Furthermore, the apparently abnormal hyporeflexia present in the flexor (biceps) could be reversed by cerebellar stimulation.

Although these studies clearly demonstrate that surface stimulation can modify passive reflex behaviour in the decorticate primate, the results do not show

unambiguously that these effects are confined to cerebellar structures. However, certain observations and inferences suggest that current spread to the brainstem is unlikely. First, stimulation was always between electrode plates at modest charge densities, reducing the likelihood of current spread to deeper structures. Secondly, although some motor effects were observed at the greater charge densities, there were no clinically evident changes in the state of consciousness or arousal during stimulation. Lastly the reduction in extensor tone is similar to that observed with surface stimulation in acute animal studies in which undercutting of the cerebellar surface abolished the effect (for review, *see* Dow and Moruzzi, 1958). For these reasons it is felt that the spread of current to the brainstem was not a contributing factor to the effects reported in these studies.

A primary focus of this investigation was to assess the importance of stimulus parameters on qualitative as well as quantitative effects produced by cerebellar stimulation. Not only was the magnitude of the passive reflex activity a function of the stimulus parameters, but the nature of the effect on a segmental reflex behaviour was also dependent on the stimulus parameters. For example, the fundamental component of the biceps response during sinusoidal movements could be increased or decreased with cerebellar stimulation depending on stimulus parameters (*see* fig. 9). As shown in fig. 9, bilateral stimulation could increase the power present in the fundamental of the biceps response to 6000 per cent of control or decrease it to 20 per cent of control by manipulating stimulus parameters. Furthermore different components of the reflex activity could be differentially affected by a given set of stimulus parameters. For example, in fig. 3 the biceps background activity was decreased during stimulation, but the sinusoidally modulated component was increased. These studies have also begun to demonstrate the importance of stimulus location. Ipsilateral *versus* contralateral stimulation produced quite different effects on the power present in the fundamental component of the triceps (fig. 8).

In conclusion, these results suggest that with the appropriate stimulus parameters and location, surface stimulation can 'improve' the abnormal reflex patterns in spastic primates. The next step is to explore the effects of stimulation on voluntary motor behaviour in spastic animals (Robertson *et al.*, 1979). However, these studies have also begun to indicate the complexities of the motor effects which can be evoked by cerebellar stimulation. Significant therapeutic benefits are not likely to be forthcoming unless these complexities are seriously addressed in the clinical trials.

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