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Co-contraction and stretch reflexes in spasticity during treatment with baclofen

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SUMMARY Surface electromyograms were recorded from the quadriceps and hamstring muscles of 11 spastic patients during cyclical flexion and extension movements of the knee. A potentiometer strapped to the knee recorded the angle of the joint, the output signal being displayed on an oscilloscope. The patient used this signal to track a sine wave target for 20 cycles. The observer then moved the patient's limb through a further 20 cycles tracking the same target. Recordings were repeated at intervals for four hours after an oral dose of baclofen. Analysis of the recordings showed that the response of a spastic muscle to lengthening is not the same during passive movement as during voluntary movement. In mild spasticity stretch reflexes appear to be suppressed by voluntary effort whereas in severe spasticity they are enhanced. Baclofen suppressed the response to passive stretch by over 30% at plasma concentrations of over 250 ng/ml and by 50% at concentrations of over 400 ng/ml, but this effect was largely extinguished during voluntary movement.

In clinical practice, spasticity denotes a characteristic syndrome of increased stretch reflexes and abnormal patterns of muscular contraction leading to impaired voluntary movement. Stretch reflexes are usually tested by gauging the strength of reflex muscular contraction during passive movement of the limb. It is often assumed that similar contraction (co-contraction) occurs during voluntary movement and thus opposes it. There are two obvious objections to this assumption. Firstly, some spastic patients have relatively flaccid limbs but nevertheless show typically 'spastic' patterns of movement. Secondly, drugs that reduce stretch reflex activity to the clinician's satisfaction are often discarded as ineffective by the patient. The present investigation was designed to assess the amount of co-contraction in a spastic muscle as it lengthens during the course of a voluntary movement, and to compare this with the contractions induced by passive movement at the same rate. Baclofen, an anti-spastic drug that suppresses spinal reflexes, was administered to the patients during the recordings in order to see whether its effects upon muscle tone were accompanied by suppression of co-contraction.

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Methods

SUBJECTS STUDIED

The patients were selected on the basis of surface electromyograms from the quadriceps and hamstring muscles during voluntary flexion and extension movements of the knee. They sat with both legs hanging over the edge of a couch for this screening procedure. Surprisingly, most patients with moderate spasticity—that is, with brisk tendon reflexes, increased muscle tone, and extensor plantar responses, but with moderate to strong voluntary power and only mild impairment of gait—showed little, if any, co-contraction under these conditions. Most patients were unable voluntarily to flex and extend the knee faster than once a second. This is slower than normal subjects (3–4 Hz) and it was also slower, in most cases, than the threshold rate at which passive movement provoked a stretch response. Thus slowing of voluntary movement could rarely be ascribed to co-contraction alone. Out of 32 subjects screened in this way, 14 were finally selected who had both co-contraction during voluntary movement and a stretch response to passive movement at the same rate. Satisfactory recordings were obtained from 11 of the patients whose clinical details are shown in the Table.

PROCEDURE

Informed consent was given by each patient, and all

Table *Clinical details of 11 spastic subjects*

Patient No.	*Sex*	*Age (yr)*	*Diagnosis*	*Troublesome clonus*	*Troublesome spasms*	*Effect of baclofen*	
						Co-contraction suppressed	*Patients opting for long-term treatment*
1	M	46	Idiopathic spastic paresis	−	++	−	*
2	M	36	Multiple sclerosis	+	+	+	
3	M	56	Idiopathic spastic paresis	--	+	++	
4	M	52	Idiopathic spastic paresis	−	+	−	
5	M	52	Idiopathic spastic paresis	+	+	++	*
6	M	37	Idiopathic spastic paresis	+	+	−	
7	M	26	Spinal cord injury	+	++	−	
8	M	20	Spinal tuberculosis	+	+	−	
9	F	36	Multiple sclerosis	−	−	−	
10	M	45	Multiple sclerosis	−	+	−	
11	M	14	Idiopathic spastic paresis	−	+	−	*

medication was stopped 48 hours before testing. Each patient was studied during the afternoon, had a light lunch of cold meat salad, dessert, with water to drink, and was then asked to empty bowel and bladder if possible. For the recordings, patients sat on a foam rubber block 6 cm thick with the back and shoulders supported and both legs hanging over the edge of a couch (Fig. 1). A linear potentiometer was strapped to the knee to record flexion and extension movements of the joint. Surface recording electrodes were applied by adhesive rings with an inside diameter of 5 mm to the skin overlying the quadriceps and hamstring muscles. The electrodes were placed 3 cm apart in the long axis of the muscle over the centre of the muscle belly. Patients were earthed *via* a strip of Velcro tape containing a lead core and soaked in physiological saline wrapped round the lower end of the thigh. The recording electrodes were fed through a standard DISA 14C 11 electromyograph, and the outputs from the two EMG channels and the potentiometer were recorded on tape for further analysis, using a 4-channel Fenlow TR4 tape recorder.

Practice established the fastest rate at which the subject was able to continue to flex and extend the knee for 45 seconds through an arc of approximately 10–80° from full extension. The output from the goniometer was displayed on a storage oscilloscope in front of the patient. A sine-wave target was then tailored for the patient's fastest sustainable rate of accurate movement using a variable function generator (Wavetek 114), and the time base of the oscilloscope sweep was adjusted to allow approximately 10 cycles to be displayed during the course of a single sweep, using the storage mode.

This display of a series of 10 cycles was used as a target that subjects then tracked with the goniometer output, by flexing and extending the knee. They were instructed to superimpose their signal upon the target as the dot moved slowly across the screen. Thus the target was not only predictable, but was presented as a stationary display upon which the subject's signal was superimposed. After several trial

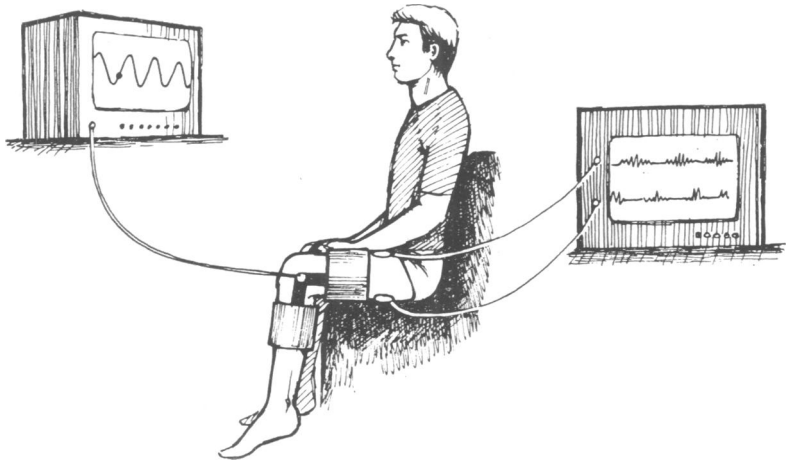

Fig. 1 *Position of subject during recording. The oscilloscope shows a sine wave target. The subject tracks the target using the output signal from the goniometer strapped to his knee.*

sessions in which a target that was too difficult could be expanded, in effect made slower, the patient's attempt to follow the target for 20 cycles was recorded. Two further control readings were obtained at five minute intervals. A clinical assessment of 'muscle tone' was made by the observer on each occasion by passive movements of the knee. In six subjects, passive movements were performed manually by the observer, one hand being placed just above the knee to steady the thigh while the other grasped the ankle and performed the movement. The observer used the same system of tracking as the subject had done to follow the same target, ensuring that both voluntary and passive movements followed the same pattern. The observer did not touch the subject's limb during the periods of voluntary movement.

After the series of control readings, an oral dose of 20 mg baclofen was given (time 0) and further recordings made at 0.5, 1.0, 1.5, 2.0, 3 and 4 hours after ingestion.

Four patients attended twice. On one of these occasions each was given two matching placebo tablets instead of baclofen. The nature of the tablets was known to the observer but not to the subject. Before tablets were given and again after each phase of the recording, 20 ml of venous blood were withdrawn into a heparinised container for estimation of the plasma baclofen concentration. The plasma was separated at once by centrifugation and the samples stored at −20°C until analysed, except for the samples obtained during placebo runs which were discarded.

Recordings were also obtained from four normal subjects aged 26–44 years who were not taking chemotherapy; the targets were set up as above and the amount of co-contraction was recorded during three sessions, each consisting of 20 cycles of voluntary movement.

ANALYSIS OF ELECTROMYOGRAMS

The surface electromyograms were displayed on an oscilloscope and on a loudspeaker during analysis in order to detect possible artefacts. The signal from each muscle was half-wave rectified and then integrated electronically in two ways. First, a summing integrator was used to sum the area of the signal during specified phases of the movement. The goniometer output was used to trigger the integrator so that the extremes of flexion and extension were ignored: only the signals generated while the knee moved through the middle 45° of its arc were summed. The signals from flexion and extension were analysed separately for each muscle. Data of voluntary movement were available for 11 patients and of corresponding passive movement for six patients.

The second system of integration used a smoothing time constant of 100 ms that gave a continuous indication of the amount or profile of electromyographic activity during the course of each cycle. The goniometer output and the rectified smoothed EMG from quadriceps and hamstring muscles were fed into a Biomac 1000 computer operating in the averaging mode. It was found that 250 data points per channel were adequate to cover a sweep time of 2.56 seconds or less, but if doubt remained about the timing of the peak EMG activity, the tapes were reanalysed using 500 data points per channel. The computer was triggered by the goniometer output and the analysis time chosen to include slightly more than one cycle of movement. Thus alternate cycles were accepted by the averager and a second run through the tape was necessary to include the others until 16 cycles had been analysed. The system was similar in principle to that devised by Burke *et al.* (1971). The averaged goniometer and integrated EMG signals were written out on an X–Y plotter, allowing identification of the timing of the peak EMG and its relationship to muscle length and the rate of change of length.

ESTIMATION OF PLASMA BACLOFEN CONCENTRATION

The samples were stored at −20°C as above and analysed by the Department of Pharmacological Chemistry, Ciba-Geigy Ltd., Basle, using a gas-liquid chromatographic assay procedure (Degen and Riess, 1976).

Results

PLASMA BACLOFEN CONCENTRATIONS

No baclofen was detected in any of the control samples. By half an hour all except subject 8 had detectable concentrations of baclofen in the plasma, and the concentration increased rapidly, reaching a peak between one and two hours after ingestion. The pooled data from the 11 subjects are shown in Fig. 2.

VOLUNTARY MOVEMENT—INDEX OF CO-CONTRACTION

In order to avoid the problems inherent in comparing EMG amplitudes in different subjects, and in the same subjects at different times, EMG activity was expressed as a ratio. The ratio was derived from the records of the same muscle undergoing similar displacements under different conditions, with intervals of less than four minutes between recordings. The amount of co-contraction—that is, the amount of contraction of the antagonist during voluntary movement—was expressed as the ratio:

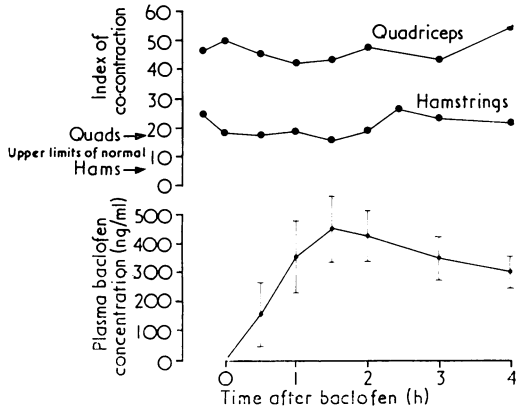

Fig. 2 *Data from 11 spastic patients showing time course of changes in the mean index of co-contraction in quadriceps and hamstring muscles, and in plasma baclofen concentration, after an oral dose of 20 mg baclofen. Arrows indicate upper limit of co-contraction recorded from four normal subjects. ±1 SD shown for baclofen levels.*

$$\frac{\text{Sum of EMG during lengthening of muscle}}{\text{Sum of EMG during shortening of muscle}} \% = \text{index of co-contraction}$$

In normal subjects under the particular conditions of these recordings, the greatest index of co-contraction recorded from the quadriceps was 17% and the greatest index recorded from the hamstrings was 5%. The patients were able to perform the movements at less than half the speed of normal subjects.

The pooled data from the spastic patients show little change in the indices of co-contraction for either muscle during the course of the afternoon's recording (Fig. 2), there being no significant difference between the effects of baclofen and the effects of placebo (Fig. 3). Analysis of individual data did, however, show that patients differed in their response to baclofen (Fig. 4). The patients showing a definite effect tended to suffer from spontaneous clonus and obvious spasms during voluntary movement, pronounced suppression of co-contraction being found in patients 2, 3, and 5 (see Table). Patients who responded in this way had similar baclofen concentrations to those who did not.

PASSIVE MOVEMENT—LENGTHENING INDEX

Passive movement was analysed in six of the patients. It did not produce contraction in normal subjects, nor in the majority of mildly spastic patients initially considered for study. For the reasons given above, the amount of EMG in the passively stretched muscle was given as the ratio:

$$\frac{\text{EMG in lengthening muscle during passive stretch}}{\text{EMG in lengthening muscle during voluntary movement}} \% = \text{lengthening index}$$

As the co-contraction index was usually constant,

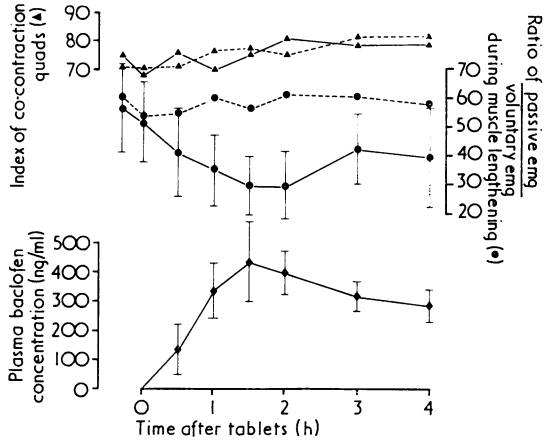

Fig. 3 *Mean data from six spastic patients showing time course of changes in quadriceps co-contraction (x), quadriceps response to passive stretch (•), and plasma baclofen concentration after an oral dose of baclofen (——) and placebo (– – – –, four patients only). The appearance of baclofen in plasma is accompanied by a reduction in response to passive stretch, but co-contraction during voluntary movement is unchanged. ±1 SD shown for lengthening index and baclofen levels.*

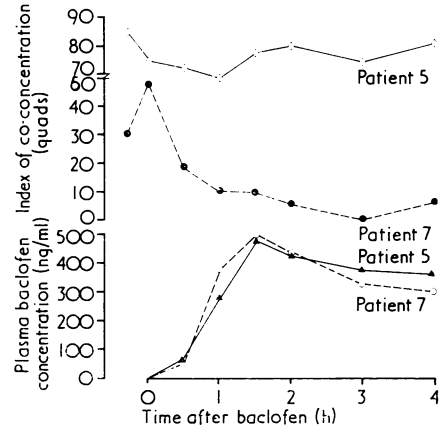

Fig. 4 *Data from two spastic patients, showing time course of changes in the amount of co-contraction of quadriceps muscles and in plasma baclofen concentrations. Plasma levels of baclofen were similar in both subjects. Patient 7 suffered spontaneous clonus and spasms which were suppressed by baclofen, but co-contraction was not suppressed in patient 5.*

this lengthening index principally reflected the amount of activity induced by passive stretch. If co-contraction were to be suppressed, the lengthening index would tend to underestimate the amount by which the response to passive stretch had declined.

Responses to passive stretch of the quadriceps muscle were reduced by baclofen in all six subjects but placebo tablets had no effect (Fig. 3). The lengthening index at one and 1½ hours after baclofen was significantly different from the control values ($P < 0.02$ using the paired t test), and was significantly different also from the values obtained in the same subjects at one and 1½ hours after placebo ($P < 0.05$). Placebo tablets caused no significant change in the lengthening index of the quadriceps. The response to stretch declined by more than 30% once the plasma baclofen concentration reached 250 ng/ml, being almost halved at concentrations of over 400 ng/ml (Fig. 4). That this change was due to baclofen is further indicated by the delay in suppression occurring in patient 8, the only subject in whom baclofen was still undetected in the plasma half an hour after ingestion (Fig. 5). Despite a pronounced effect upon passive stretch, co-contraction was virtually unchanged (Figs. 3 and 5).

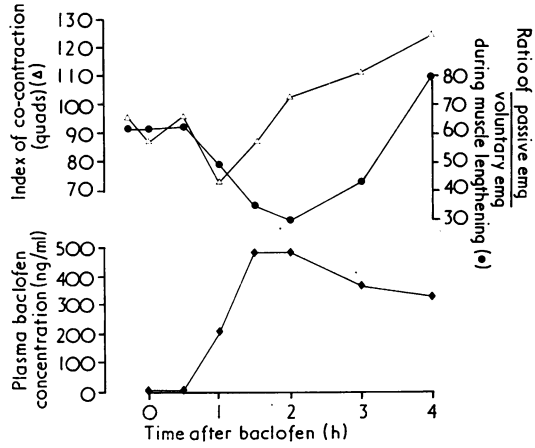

Fig. 5 *Effect of baclofen in patient 8. Suppression of response to passive stretch, and possibly of co-contraction, is delayed until plasma baclofen concentration belatedly starts to rise.*

The responses obtained from the hamstrings muscle during passive stretch fluctuated widely during the course of the recording session, despite reasonably consistent levels of hamstring co-contraction. The lengthening ratio sometimes varied from 20% to 500% from one half hour to the next. Thus the amount of contraction during passive stretch was sometimes much less than the amount of co-contraction of the hamstrings, and at other times greatly exceeded it. By contrast, the amount of EMG during passive stretch of the quadriceps was always less than the EMG during co-contraction. This may have reflected partly a greater instability in hamstring stretch responses, and partly a restraining action of the quadriceps as it helped to track the target during the flexion phase, when gravity was assisting the movement. It was to minimise such artefacts that the patient's *fastest* rate of movement was used in setting up the target. The hamstring response to passive stretch was too variable for useful quantitative analysis.

PROFILES OF CONTRACTION IN LENGTHENING MUSCLE—PASSIVE MOVEMENT

The characteristic response of the quadriceps is shown in Fig. 6. If one complete cycle of the knee movement is regarded as containing 360°, each phase of movement—that is, flexion and extension—of the knee contains 180°. The quadriceps EMG activity starts about 45° after extension of the knee and the peak activity leads the most stretched point of the muscle by 90°. This type of phase relationship was found in spastic quadriceps muscles by Burke *et al.* (1971) and was considered to reflect an interplay of motor neurone facilitation by spindle primary endings with inhibition by spindle secondary endings. Figure 6 shows progressive abolition and then recovery of the stretch response in patient 11. As the stretch response declines, its starting point is delayed but its peak does not shift phase.

The hamstring responses are shown in Fig. 7. No significant change is seen.

PROFILES OF CONTRACTION DURING VOLUNTARY MOVEMENT

Normal subjects Figure 8 shows a typical profile of EMG activity during voluntary movement by a normal subject. The activity in each muscle starts after the limb has reached maximum velocity, deceleration resulting from declining contraction in the agonist followed by increasing contraction of the antagonist.

Spastic patients Figure 9 shows profiles of voluntary movement, again from patient no. 11. Neither muscle is silent at any stage. Quadriceps contraction starts to build up much earlier than in a normal subject, at about 45° rather than 130° from full extension of the knee. This is the point at which contraction is induced by passive stretch (Fig. 6). The peak of the passive stretch response coincides precisely with the peak of co-contraction (Fig. 10) Activation of the hamstrings is similarly advanced, occurring at about the same time as the passive

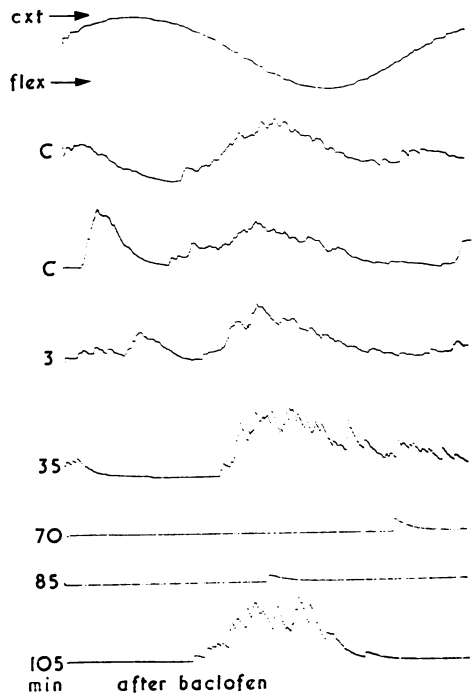

Fig. 6 *Integrated EMG from quadriceps muscle of patient 11 during passive movement (16 cycles averaged). The target repeats every 2.44 second; sweep time shown is 2.56 s. Top trace indicates position of knee joint (10°–80° from full extension). The other traces show EMG activity during the cycle before baclofen (C) and at various times after baclofen. The stretch response is completely suppressed at 70 min, reappearing at 105 min. The peak EMG leads the most stretched point by 90°. This phase lead does not alter as the amplitude of response diminishes. (Note that the gain is increased in later traces to allow satisfactory identification of position of EMG peak.)*

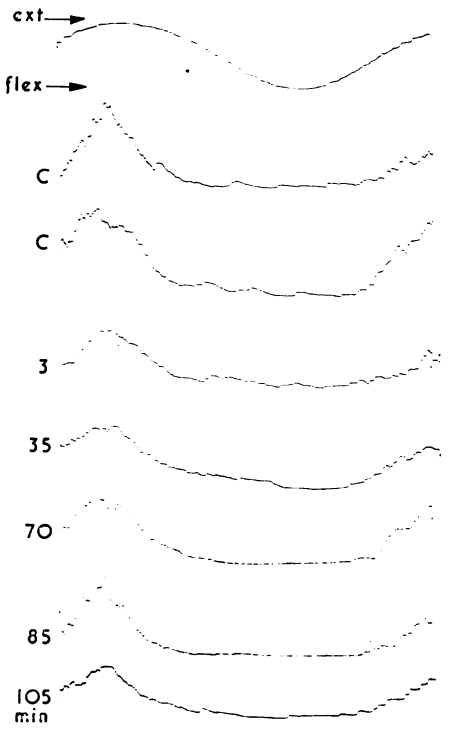

Fig. 7 *Integrated EMG from hamstrings muscle of patient 11 during passive movement. Format in this and subsequent figures is similar to Fig. 6. The peak EMG response occurs as muscle reaches its most stretched point, and its timing is unaffected by baclofen.*

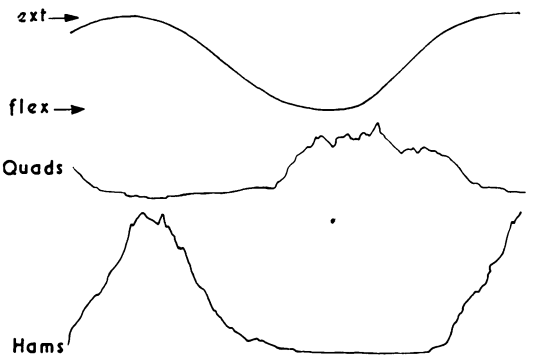

Fig. 8 *Integrated EMG from quadriceps and hamstrings muscles during voluntary tracking of a target by a normal subject. The target repeats every 0.9 s.*

stretch response (Fig. 7), well ahead of normal voluntary contraction (Fig. 8). Moreover a second burst of hamstring contraction is necessary to overcome the abnormal quadriceps activity (Figs. 9 and 11).

After baclofen, activation of the quadriceps is delayed, though it does not become normal; the hamstrings are unaffected (Fig. 9).

Discussion

Symptomatic treatment of spasticity at the present time is mainly in the hands of physiotherapists who encourage the patient to develop more useful patterns of muscular activity. Little is known about the mechanisms that allow this to be achieved. In patients with acquired spasticity, especially those with stroke, loss of sensation contributes considerably to their inability to move, so that in practice it is impossible to improve movement without retraining sensory function at the same time.

The importance of stretch reflexes in spasticity

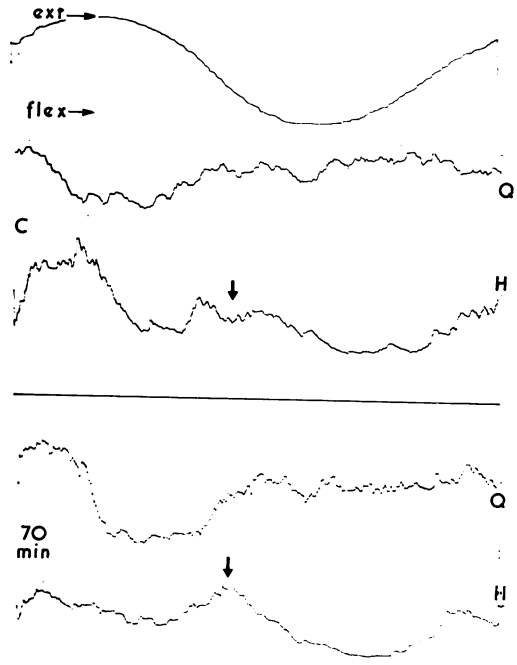

Fig. 9 *Integrated EMG from spastic quadriceps (Q) and hamstrings (H) muscles during voluntary movement (patient 11). Cycle time as Fig. 6. Upper pair of EMG traces before baclofen (C). Lower pair 70 min after baclofen, showing delayed take-off of quadriceps activity. The profiles are otherwise unchanged by treatment.*

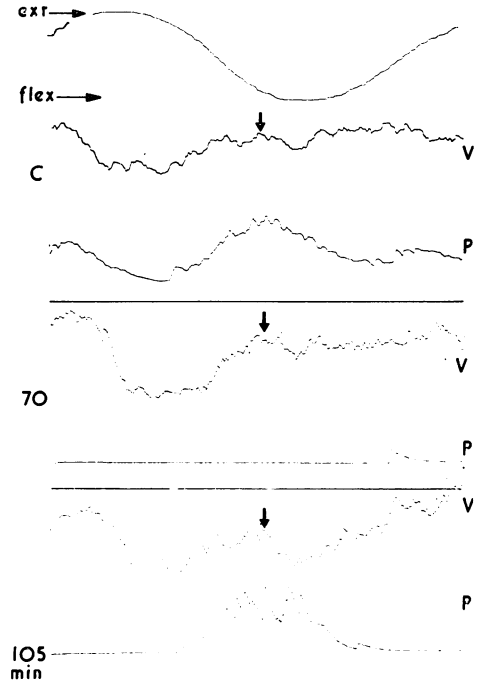

Fig. 10 *Comparison of quadriceps activity during voluntary (V) and passive (P) movement. Same patient and cycle times as Fig. 6. A peak of activity (arrowed) can be discerned during voluntary movement corresponding to peak of passive stretch response. This peak can still be seen during voluntary movement 70 min after baclofen, when response to passive stretch has disappeared.*

is traditionally emphasised by physicians. This emphasis derives partly from the long tradition of physiological work on the subject of reflexes, and partly on their usefulness in arriving at a diagnosis. It does not follow that abnormal stretch reflexes are necessarily an important cause of disability.

The flexion-extension movement studied in the present paper is admittedly of little significance to the patient except as an indication of how well he can perform a simple movement when he is fully concentrating on it. The patterns of reflex activity that occur when the knee flexes and extends during a co-ordinated movement of the whole limb, or of both lower limbs in sequence, may well differ from the patterns reported here. Semi-voluntary movement, such as walking, may involve still further modifications of reflex activity. It would be imprudent to assume that the present conclusions necessarily apply to more complex motor acts. Nevertheless, they do underline the fact that even a damaged nervous system can modulate stretch reflex activity in response to different circumstances, and that the onset of voluntary movement may either increase or diminish stretch responses compared with the resting state. In mild spasticity, stretch responses elicited by passive stretch tend to be inhibited during simple flexion-extension movement whereas in more severely spastic patients they may become accentuated, particularly during vigorous effort.

Voluntary and passive movements cannot be fully congruent. For example, the pressure of the observer's restraining hand upon the subject's knee was sometimes sufficient to induce a spasm in the muscles of the limb. Although this spasm was allowed to die down before passive movements began, the continued cutaneous stimulus might have altered reflex activity and thus have contributed to the difference between voluntary and passive movement. Furthermore, passive movement could be performed on a subject whose other muscles were relatively relaxed, while the onset of voluntary movement was necessarily accompanied by contraction of muscles maintaining the posture of the hips and trunk. This kind of objection applies equally to the clinical use of muscle tone as an index of the 'severity of spasticity'.

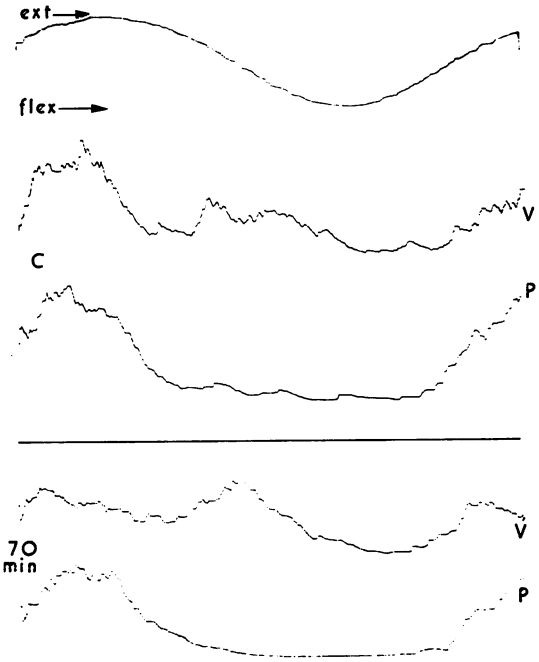

Fig. 11 *Comparison of hamstrings activity during voluntary (V) and passive (P) movement. Same patient and cycle time as Fig. 6. Passive stretch of hamstrings induces a contraction slightly before the point at which voluntary contraction would be expected to occur (Fig. 8). Voluntary movement in this spastic subject is characterised by an additional peak of activity during flexion of knee (arrowed). Presumably this is necessary to overcome the abnormal peak of quadriceps contraction arrowed in Fig. 10.*

Under the conditions stated, co-contraction in quadriceps and hamstring muscle was reasonably consistent throughout an afternoon's recording session. The response of the quadriceps muscle to passive stretch was similarly stable but the hamstring response was variable.

This type of electromyographic technique was first used to measure the effect of baclofen upon passive stretch reflexes by Burke *et al.* (1971). They found that baclofen increased the threshold velocity at which muscle contraction was first induced, which corresponds to the present findings of delayed initiation of the stretch response (Fig. 6). After baclofen, the rate of sinusoidal movement that they had chosen was insufficient to elicit a stretch response, so that the timing of the peak activity could not be compared directly with the untreated state. The present findings show that, provided the rate of stretch remains constant, the peak activity in the quadriceps occurs at the same phase of the cycle after baclofen, even though the onset of contraction is delayed. The effects of speeding up the stretch cycle were not recorded in the present study.

Baclofen reduces the amplitude of tendon jerks, H responses and slow passive stretch responses in spasticity (Birkmayer *et al.*, 1967; Burke *et al.*, 1971; McLellan, 1973). Patients whose stretch responses can be diminished by cooling the limb respond better to baclofen than those in whom cooling has no effect (Knutson *et al.*, 1973). Baclofen suppresses a number of spinal cord functions but its net effect is to suppress the motor neurone facilitation that is generated by afferent input from the limb and from the muscle in particular (Pedersen *et al.*, 1970; Knutson *et al.*, 1973).

Baclofen appeared in the blood within half an hour of ingestion in 10 of the 11 patients, reaching a peak between one and two hours. The response to passive stretch was reduced by 30% at plasma concentrations of over 250 ng/ml and by 50% at concentrations of over 400 ng/ml (Fig. 4). Co-contraction during voluntary movement, while the quadriceps was being stretched by the same amount and at the same rate as during passive movement, was unaltered by baclofen in most patients even when the plasma concentration exceeded 400 ng/ml.

This marked difference between the effect of baclofen upon passive stretch responses and its effect on co-contraction suggests that different physiological mechanisms are involved. Reciprocal innervation is a basic mechanism that operates not only on a segmental level, but can be controlled from the brain. It is not clear whether co-contraction occurs as a direct result of inappropriate supraspinal drive on antagonist motor neurones, or whether it reflects unsuppressed segmental stretch responses in the antagonist. The latter possibility is supported by the similarity in the EMG profile of co-contraction with the EMG of the stretch response (Fig. 10) but it is probable that both mechanisms are involved. It remains to be proved that the observed peak in the co-contraction profile depends upon an input from the stretched muscle. It would be interesting to observe the effect of blocking the muscle afferent nerve fibres.

Drugs that suppress passive stretch reflexes are prescribed for spasticity on the assumption that stretch reflexes impede voluntary movement. The present study shows that co-contraction may be unaffected even in patients whose passive stretch responses have been halved by treatment. As in the studies of Hedley *et al.* (1975) and Duncan *et al.* (1976), the patients who derived most benefit from baclofen were those whose voluntary movement was impeded by spasms. Further work is needed to

establish the physiological basis of co-contraction so that it can be manipulated more effectively.

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