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SPINAL MECHANISMS IN MAN CONTRIBUTING TO RECIPROCAL INHIBITION DURING VOLUNTARY DORSIFLEXION OF THE FOOT

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SUMMARY

1. The inhibition of the soleus Hoffmann reflex (H reflex) during voluntary dorsiflexion of the foot – henceforth referred to as 'natural' reciprocal inhibition – was found to be initiated 50 ms before the onset of the EMG activity in the tibialis anterior muscle and to increase gradually during a ramp-and-hold dorsiflexion. There was a positive correlation between strength of tonic dorsiflexion and amount of 'natural' reciprocal inhibition.

2. The change of activity in the disynaptic and a long-latency group Ia inhibitory pathway and the change in presynaptic inhibition of the Ia fibres mediating the soleus H reflex were tested separately during ramp-and-hold dorsiflexion as well as during tonic dorsiflexion of the foot, and the results were compared with the development of the 'natural' reciprocal inhibition of the unconditioned soleus H reflex.

3. The disynaptic group I inhibition of soleus motoneurones was increased, as compared to rest, during the dynamic phase of a ramp-and-hold dorsiflexion movement, but the inhibition generally did not increase during tonic dorsiflexion of the foot.

4. The long-latency group I inhibition was seen only during dorsiflexion of the foot. It appeared around 50 ms before tibial anterior EMG activity and there was a positive correlation between strength of tonic dorsiflexion and amount of this long-latency inhibition.

5. Presynaptic inhibition of Ia afferents terminating on soleus motoneurones was estimated by an indirect method. The increase of presynaptic inhibition started soon after the onset of the ramp-and-hold dorsiflexion, and gradually became more pronounced during the ramp phase. The amount of presynaptic inhibition was positively correlated with strength of tonic dorsiflexion.

6. It is concluded that all investigated mechanisms may contribute to the 'natural' reciprocal inhibition and it seems that the different pathways are used differentially during different types of movement.

INTRODUCTION

Poul Hoffmann showed in 1918 that the soleus H reflex is inhibited, as compared to rest, during tonic dorsiflexion of the foot. This finding has later been confirmed by several other groups (mainly Paillard, 1955; Gottlieb, Agarwal & Stark, 1970; Tanaka, 1974).

The inhibition of the soleus H reflex during voluntary dorsiflexion of the foot – henceforth referred to as 'natural' reciprocal inhibition – may be evoked by several different spinal mechanisms. The aim of the present study was to establish in man the contribution of some defined spinal pathways to this 'natural' reciprocal inhibition.

The activity in the disynaptic Ia inhibitory pathway projecting from the tibial anterior muscle to the soleus motoneurones has previously been studied in man during tonic dorsiflexion of the foot. Thus Tanaka (1974) and Shindo, Harayama, Kondo, Yanagisawa & Tanaka (1984) reported that the disynaptic reciprocal Ia inhibition of soleus motoneurones (evoked by stimulation of the common peroneal nerve and assessed by a soleus test H reflex) was increased during dorsiflexion of the foot. Crone, Hultborn, Jespersen & Nielsen (1987) later confirmed that this disynaptic inhibition was increased at the onset, and during the dynamic phase of an isometric ramp-and-hold dorsiflexion of the foot, but, contrary to Tanaka (1974) and Shindo *et al.* (1984), they failed to see any increase during tonic contraction (see also Crone, Hultborn & Jespersen, 1985). Therefore the decrease of the soleus H reflex during tonic dorsiflexion of the foot can hardly be explained by an inhibition of soleus motoneurones via the disynaptic Ia inhibitory pathway.

In the present study we have determined the contribution from three defined spinal mechanisms (disynaptic reciprocal Ia inhibition, long-latency group I inhibition and presynaptic inhibition of soleus Ia afferents) to the 'natural' inhibition of the soleus H reflex during isometric ramp-and-hold dorsiflexion of the foot. It is concluded that each of them contribute to the inhibition, but at different phases of the movement.

METHODS

General experimental arrangement

The work presented here may be regarded as a continuation of an earlier paper (Crone *et al.* 1987). Some results obtained from the sixty subjects of that study have been used here as reference material. However, the new results which are presented in the present paper were obtained from six healthy subjects aged 23–44 years. These subjects were tested several times in order to ensure reproducibility of results, and because they took part in several experiments with different aims. All the subjects gave informed consent to the experimental procedure which was approved by the local Ethical Committee.

The experimental method and the design of the experiments have been for the main part described in detail in a preceding paper (Crone *et al.* 1987) and will only be summarized briefly here.

The subjects were seated in a reclining armchair with the examined leg semiflexed in the hip (120 deg), the knee flexed to 160 deg and the ankle in 110 deg plantarflexion. The foot was mounted to a torquemeter, and the torque was displayed on an oscilloscope placed in front of the subject. This allowed a careful examination of the voluntary contractions performed by the subject. During experiments involving dynamic contraction, the subject initiated the movement in relation to an auditory start signal and the conditioning and test stimuli were pre-set in relation either to the start signal or to the start of the EMG activity in the contracting muscle.

Test reflexes

The soleus H reflex was evoked by stimulating the tibial nerve through a monopolar stimulating electrode. The stimuli were 1 ms rectangular pulses. The reflex response was measured as the area below the full-wave-rectified H reflex recorded by a non-polarizable disc electrode placed over the soleus muscle. At the beginning of each experiment the maximum motor response (M_{max}) was measured. During the experiment the stimulus strength was adjusted to give an H reflex of 15–25% of this value at rest as well as during movement. This adjustment is important since the susceptibility of the H reflex to excitatory and inhibitory effects increases dramatically with decreasing size of the test reflex (Meinck, 1980; Mazieres, 1982; Crone *et al.* 1985).

Experiments concerning 'natural' inhibition were complicated by the finding (Schieppati & Crenna, 1984; C. Crone & J. Nielsen, unpublished results) that a voluntary dorsiflexion has a long-lasting (up to 8 s) inhibitory effect upon the following soleus H reflex. Hence the onset of any inhibitory effect, caused by a dorsiflexion movement, must be assessed *either* when the stimulus interval is longer than 8 s *or* with reference to the size of the H reflex elicited at the time of the start signal (the beep). The latter possibility was used in the present experiments.

Particular effort was made to ensure that the recorded changes in the size of H reflexes during movement do reflect excitability changes at the spinal level. It was thus ensured that the stimulating and recorded electrodes did not change their positions during movement. Hence, at the beginning of every experiment the maximal soleus M response was measured at rest and during dorsiflexion to ensure that the positions of the recording electrodes were stable. During the experiment a small M response was evoked randomly between the test reflexes in order to ensure that the stimulating electrode position was stable. Data were only retained when the size of this M response did not change during movement.

Conditioning stimuli

When studying disynaptic reciprocal Ia inhibition and the long-latency group I inhibition the conditioning stimulus (a rectangular 1 ms pulse) was applied to the common peroneal nerve. The stimulus was applied through a bipolar surface electrode at the level of the caput fibula. The conditioning stimulus strength was expressed in multiples of the M (motor) threshold.

In experiments investigating presynaptic inhibition of soleus Ia fibres we employed a new method, recently described by Hultborn, Meunier, Morin & Pierrot-Deseilligny (1987; see that paper for a full description). The method is based on the measurement of the amount of facilitation of the soleus H reflex produced by a heteronymous Ia volley from the femoral nerve. A constant conditioning stimulation, activating the same Ia fibres in the femoral nerve, will elicit a monosynaptic EPSP of constant size in soleus motoneurones, provided that there is no change in presynaptic inhibition of femoral Ia fibres. Under these conditions a change in the amount of H reflex facilitation, which indicates a change in the size of the conditioning EPSP, must be ascribed to a change in presynaptic inhibition of femoral nerve Ia fibres terminating on soleus motoneurones. Why this change may be interpreted as being parallel to a simultaneous change in presynaptic inhibition of soleus Ia afferent fibres is described in the Results section. The conditioning stimulus was applied to the branches of the femoral nerve which innervate the quadriceps muscle. The stimulus was delivered through a monopolar stimulating electrode (a ball electrode, diameter 2 cm), which was placed in the femoral triangle where stimulation caused a visible contraction of the lateral vastus muscle. The anode was placed at the back of the upper aspect of the thigh. Conditioning stimulus strength was around 1·5 × motor threshold.

If the afferent volleys, following the conditioning stimuli (to the femoral nerve), and the test stimuli (tibial nerve) are to arrive at the spinal cord simultaneously, the test shock has to be delivered before the conditioning shock, as the distance from the site of femoral nerve stimulation to the spinal cord is shorter than the distance from the popliteal fossa to the spinal cord. Negative conditioning–test values indicate that the test stimulus is applied before the conditioning stimulus.

Stimulus protocol and analysis of results

In each experimental run (at rest, tonic contraction; before or during dynamic contractions) unconditioned and conditioned H reflexes were randomly presented (cf. Fournier, Katz & Pierrot-Deseilligny 1984). Usually about forty responses of each alternative (unconditioned and conditioned test reflexes) were collected for statistical analysis (mean, standard error of the mean and differences between groups by Student's t test).

RESULTS

'Natural' reciprocal inhibition of the soleus H reflex during dorsiflexion of the foot

The unconditioned soleus H reflex is inhibited, as compared to its size at rest, during dorsiflexion of the foot; this inhibition will be referred to as the 'natural'

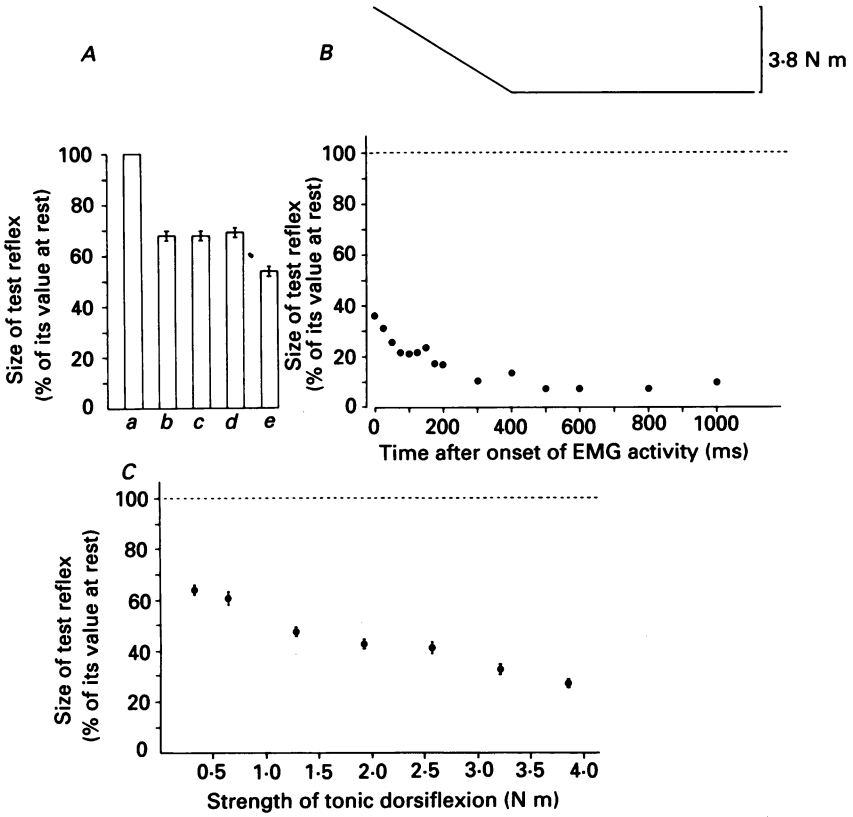

Fig. 1. Size of the unconditioned soleus H reflex (expressed as a percentage of its value at rest) before and during a ramp-and-hold dorsiflexion of the foot (reaching 3·8 N m in 400 ms) and during different strengths of tonic dorsiflexion. *A*, the test stimulus was delivered at rest (*a*), 50 ms before the start signal (*b*), at the time of the start signal (*c*), and 50–100 and 20–50 ms before appearance of the first tibialis anterior EMG activity (*d* and *e*). Repetition frequency was 1 stimulus per 5 s. *B*, the size of the soleus H reflex at different delays during a ramp-and-hold dorsiflexion. The upper part represents the ramp which the subject was asked to follow. *C*, the reflex is elicited during different strengths of tonic dorsiflexion of the foot. Each bar represents one standard error of the mean. All data are from the same subject.

reciprocal inhibition. In order to investigate which inhibitory mechanisms contribute to the 'natural' inhibition it is necessary to know the full time course of this inhibition during a ramp-and-hold movement as well as the relation between the amount of 'natural inhibition' and the strength of tonic dorsiflexion. Experiments were thus performed with the aim of establishing the onset of the 'natural' inhibition in relation to start of the dorsiflexion movement.

Figure 1*A* illustrates the onset of reciprocal inhibition before the start of the

movement. Column *a* in Fig. 1*A* shows the size of the soleus H reflex at rest and this value was designated 100%. The ramp-and-hold movement (sketched above in Fig. 1*B*) was repeated every 5 s. The tibialis anterior EMG was initiated between 200 and 400 ms after the start signal. Columns *b* and *c* show the size of the H reflex elicited 50 ms before (*b*) and at the time of (*c*) the start signal. The difference between column *a* and columns *b* and *c* thus reflects the long-lasting inhibitory effect evoked by the *preceding* dorsiflexion. The sizes of the H reflex measured 50–100 and 20–50 ms before the first tibialis anterior EMG activity are shown in columns *d* and *e*, respectively. The values of the reflex seen in columns *b* and *c* can be regarded as the 'reference values' and it is concluded that the 'natural' reciprocal inhibition of the soleus H reflex starts between 20 and 50 ms (column *e*) before the first tibialis anterior EMG spike appears. This time of onset was found in all three subjects tested in this way. It thus seems that the 'natural' inhibition is initiated by a supraspinal mechanism since no peripheral activity can yet have been evoked by the 'future' dorsiflexion movement. Figure 1*B* shows the size of the unconditioned soleus H reflex during a ramp-and-hold dorsiflexion movement of the foot. It is seen that the H reflex is further inhibited during the ramp phase of the movement. The inhibition reaches a maximum towards the end of the dynamic phase (in this case around 300 ms after start of the movement; this was also the case when the duration of the ramp phase was 200, 400 and 600 ms).

In order to establish if the 'natural' inhibition of the soleus H reflex was directly correlated with the degree of tonic dorsiflexion, the test reflex was also measured at different strengths of tonic dorsiflexion of the foot. (The results are shown in Fig. 1*C*.) Already during a very weak contraction, when only a few motor units are active, there was a pronounced inhibition of the soleus H reflex (down to around 60% of its value at rest). The inhibition increases gradually with increasing strength of dorsiflexion. The amount of 'natural' inhibition during dynamic and tonic dorsiflexion of the foot differs from one subject to another, but the relative change of inhibition was similar for all six subjects tested this way.

Long-latency group I inhibition

The filled circles in Fig. 2 show the time course of the inhibition, evoked by a single conditioning peroneal nerve stimulus (1·0 × motor threshold) in a subject at rest. The effect of the same conditioning stimulus was also investigated during tonic dorsiflexion of the foot (open circles). It is seen that at rest the maximal inhibition is reached at a conditioning–test interval of 2 ms and that this value is not increased during tonic dorsiflexion of the foot. However, at longer conditioning–test intervals, the inhibition is markedly increased during tonic dorsiflexion. The maximum difference between values obtained at rest and during tonic dorsiflexion is seen at conditioning–test intervals of between 3 and 5 ms. The inhibition then decreases and almost reaches the values obtained at rest at a conditioning–test interval of 6 ms. Similar time courses at rest and during tonic dorsiflexion of the foot were obtained in fifteen subjects.

The inhibition evoked by a peroneal nerve stimulation was also measured during the dynamic phase of a ramp-and-hold dorsiflexion (triangles) where a dorsiflexion strength of 3·4 N m was reached in 600 ms. The reflex was elicited 400 ms after start

of tibialis anterior EMG activity. In this case the inhibition is increased, as compared to rest, both at the short conditioning–test interval of 2·0 ms and at longer intervals (see also Crone *et al.* 1987). Similar time courses of the inhibition, which is evoked by a conditioning peroneal nerve stimulation during dynamic dorsiflexion of the foot, were obtained in five subjects.

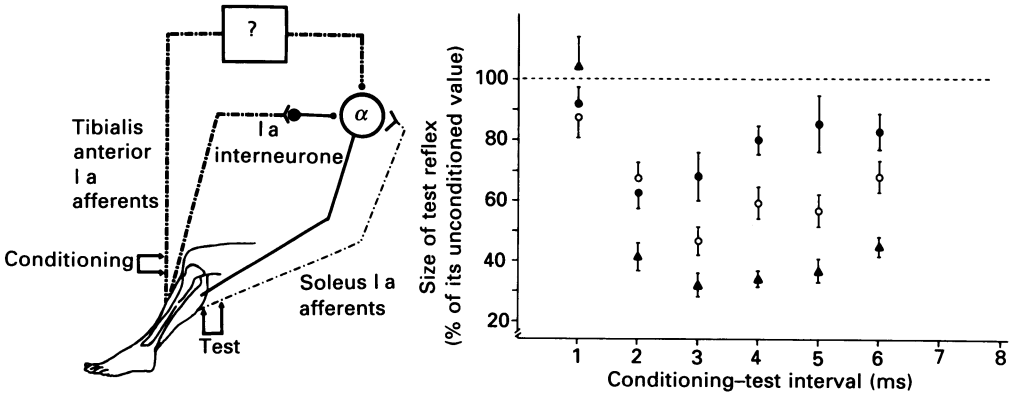

Fig. 2. The time course of the inhibition of the soleus H reflex, evoked by a single conditioning stimulus to the common peroneal nerve (1 ms duration, 1·0 × motor threshold), at rest (●), during tonic dorsiflexion of the foot (3·4 N m, ○) and during the dynamic phase of a ramp-and-hold movement, reaching 3·4 N m in 600 ms and the reflex being elicited 400 ms after start of movement (▲). The size of the conditioned reflex is expressed as a percentage of its unconditioned value. Each bar represents one standard error of the mean. The diagram to the left schematically shows the possible pathways mediating the reciprocal inhibition of the soleus α-motoneurones.

The stimulus strength of the conditioning stimulation was graded while the resulting inhibition was measured at a conditioning–test interval of 1·5–2 and 3–6 ms, in order to establish which afferent fibre groups most likely mediate the long-latency inhibition. The interval between the conditioning peroneal nerve stimulation and the test stimulus was 5 ms in the experiment illustrated in Fig. 3*B*. Closed and open circles represent values measured at rest and during tonic dorsiflexion of the foot, respectively. It is possible that the small inhibition, which is seen at rest in Fig. 3*B*, mainly represents the decay phase of the disynaptic reciprocal Ia inhibition. When judging the afferent fibre group, which is responsible for the long-latency inhibition, by grading the strength of the conditioning stimulus, it is thus necessary to consider the increase in inhibition with tonic dorsiflexion (i.e. the difference between closed and open circles). The difference appears already at 0·6 × motor threshold and then increases up to around 1·0 × motor threshold. It is important to note that this relation between the strength of conditioning stimulation and the amount of inhibition is virtually the same for the long-latency inhibition (the *difference* between filled and open circles in Fig. 3*B*) and the disynaptic reciprocal Ia inhibition (Fig. 3*A*; note that there is no significant difference between rest and tonic contraction in the case of the short-latency inhibition). A similar threshold for the long-latency inhibition during tonic dorsiflexion of the foot was obtained in three other subjects. The very low threshold at which the long-latency inhibition is evoked strongly suggests that low-threshold group I fibres (probably Ia afferents) are responsible for the observed inhibition. The possibility that activation of cutaneous

fibres contributes to the inhibition was ruled out by testing that a pure cutaneous stimulation of the skin surrounding the effective electrode position did not evoke any inhibitory effect on the soleus H reflex. An additional contribution from group Ib fibres cannot, however, be excluded (cf. Burke, Gandevia & McKeon, 1983, and Discussion).

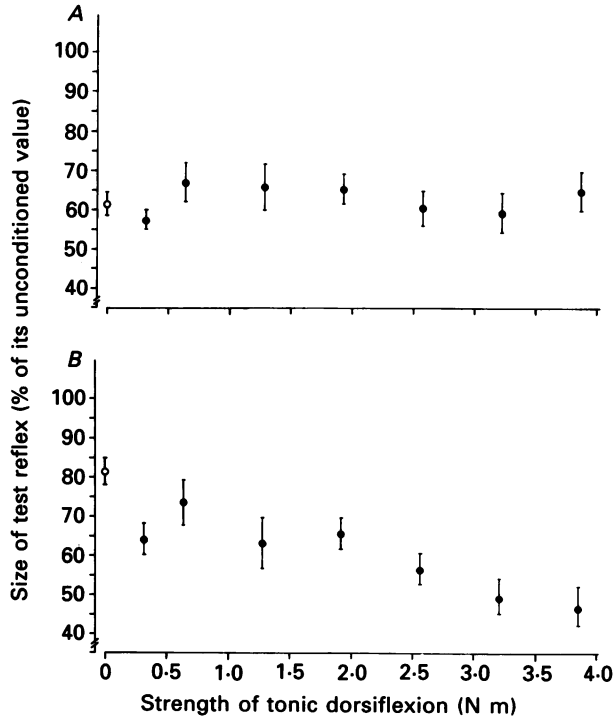

Fig. 3. Size of the conditioned H reflex (expressed as a percentage of its unconditioned value) as a function of the conditioning stimulus strength (expressed in multiples of the motor threshold) at rest (●), and during tonic dorsiflexion of the foot (3·4 N m, ○). The conditioning–test intervals in *A* and *B* are 2 and 5 ms, respectively. Each bar represents one standard error of the mean.

There are basically two possible mechanisms by which the long-latency inhibition can be evoked: (1) a *postsynaptic* mechanism, mediated either via a polysynaptic or a propriospinal pathway or (2) an increase of *presynaptic* inhibition of soleus Ia afferent fibres mediating the test reflex. In order to test the possibility of presynaptic inhibition of soleus Ia afferent fibre terminals, we adopted a new method for assessing the degree of presynaptic inhibition, recently introduced by Hultborn *et al.* (1987*a*). In short it can be said (cf. the graph in Fig. 4) that a conditioning stimulation of the femoral nerve produces a monosynaptic Ia EPSP in the soleus motoneurones, which is seen as a facilitation of the soleus H reflex. A change in the size of this facilitation must reflect a change in the size of the EPSP, i.e. a change in presynaptic inhibition of the heteronymous Ia afferent terminals from the femoral nerve onto soleus motoneurones.

In the experiment illustrated in Fig. 4 it was tested whether the amount of presynaptic inhibition of the heteronymous Ia afferents was changed by a

conditioning stimulation of the common peroneal nerve. All results represented in Fig. 4 were obtained during tonic dorsiflexion of the foot (3·4 N m). Column *a* shows the size of the unconditioned soleus test reflex at rest (set to 100%) and column *b* shows the amount of facilitation evoked by femoral nerve stimulation. The

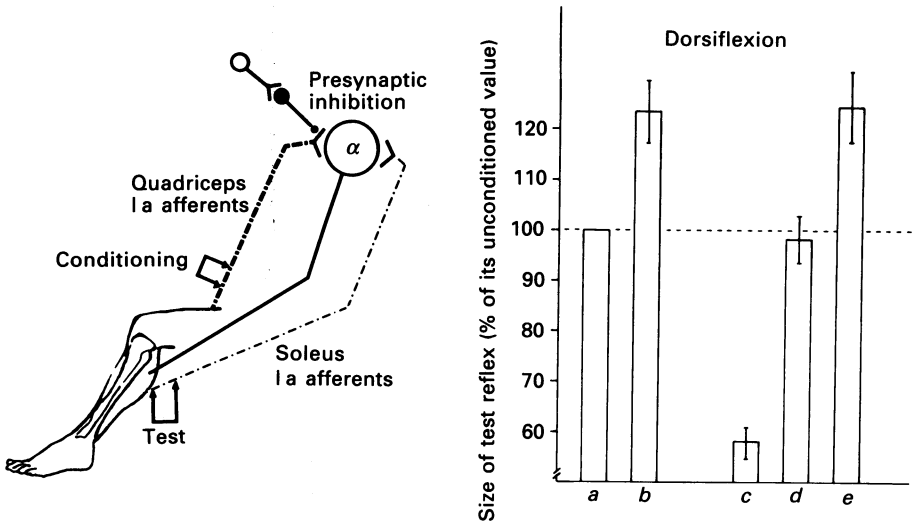

Fig. 4. Heteronymous Ia facilitation of the soleus H reflex was elicited by a femoral nerve stimulation (1·5 × motor threshold; conditioning–test interval −5·5 ms). *a* = size of the unconditioned reflex. *b* = size of the conditioned reflex as a percentage of its unconditioned value. *c* = size of the soleus H reflex, which has been conditioned by a stimulus to the common peroneal nerve (1·0 × motor threshold) at a conditioning–test interval of 5 ms. *d* = the compensated conditioned test reflex, i.e. the test stimulus strength has been increased to make the size of the test reflex equal to the control reflex. *e* = size of the compensated test reflex, which has been preceded by a conditioning femoral nerve stimulation. All values were measured during tonic dorsiflexion of the foot (3·4 N m). Each bar represents one standard error of the mean.

conditioning–test interval was kept as short as possible to ensure that the monosynaptic Ia EPSP was not contaminated by polysynaptic actions (cf. Methods). Column *c* shows the inhibition of the soleus H reflex, evoked by stimulation of the common peroneal nerve at a conditioning–test interval of 5 ms, i.e. corresponding to the long-latency inhibition. In column *d* the test stimulus strength is increased so that the inhibited reflex attains the same value as the unconditioned test reflex (100%). As described before, this compensation is necessary since the susceptibility of an H reflex to inhibition/facilitation changes with the size of the test reflex (Meinck, 1980; Mazieres, 1982; Crone *et al.* 1985). Finally, column *e* shows the compensated inhibited soleus H reflex, when preceded by a femoral nerve stimulation. The size of the reflexes in columns *b* and *e* are the same, i.e. the femoral nerve stimulation evoked the same amount of Ia facilitation in the two situations. Therefore it is concluded that the conditioning common peroneal nerve stimulation does not evoke presynaptic inhibition of heteronymous quadriceps Ia afferent terminals on soleus motoneurones at the conditioning–test interval of 5 ms. The

results by Hultborn *et al.* (1987*a*) and Hultborn, Meunier, Pierrot-Deseilligny & Shindo (1987*b*) showed that presynaptic inhibition of heteronymous quadriceps Ia afferents and homonymous soleus Ia afferents terminating on soleus motoneurones is evoked in parallel at the onset of a quadriceps muscle contraction. This indicates that the descending control of presynaptic inhibition of Ia afferents during movement is related to the target motoneurones rather than their muscle origin. The lack of presynaptic inhibition of heteronymous quadriceps Ia fibres projecting to soleus motoneurones, following peroneal nerve stimulation (Fig. 4), therefore suggests a similar absence of change in presynaptic inhibition of the homonymous soleus Ia fibres at this conditioning–test interval. The inhibition of the soleus H reflex evoked by a peroneal nerve stimulation at a conditioning–test interval of 5 ms is then most likely due to a postsynaptic inhibition of the soleus motoneurones rather than to a presynaptic inhibition of the Ia afferents mediating the test reflex.

It was now of interest to determine the onset and time course of the increase in the long-latency inhibition during the standard ramp-and-hold contraction. In Fig. 5*C* the onset of the soleus inhibition, seen at a conditioning–test interval of 5 ms, is established. It is seen that there is a slight increase of inhibition (in relation to column *a*) already at 50–100 ms before the start of tibialis anterior contraction (column *c*), but the inhibition does not become pronounced until between 0 and 50 ms before start of the movement (column *d*). This is interpreted as the facilitation of the long-latency inhibition having an onset of around 50 ms before the appearance of the first tibialis anterior EMG spike.

Figure 5*D* illustrates how the long-latency inhibition develops during the ramp-and-hold contraction (reaching a force of 3·4 N m in 400 ms). It is seen that the inhibition increases during the dynamic phase of the contraction, and reaches a maximum at the end of the ramp, 400 ms after start of the movement. During the following 'holding' phase the inhibition decreases slowly to reach a steady level around 1800 ms after the start of contraction (not shown here), which corresponds to the value measured during tonic dorsiflexion of the foot (open triangle). In order to be able to demonstrate a significant and gradual change of polysynaptic inhibition during dynamic dorsiflexion of the foot, the subjects must (1) exhibit a rather pronounced long-latency inhibition and (2) have relatively large soleus H reflexes (around 20 % of M_{max}) also during dorsiflexion of the foot. This is rarely the case since most subjects only have a long-latency inhibition of around 10–15 % (see Crone *et al.* 1987, Fig. 8*D*) and since, in many subjects, the soleus H reflex is nearly abolished already 100–200 ms after the start of tibialis anterior EMG activity. Therefore a gradual change of long-latency reciprocal inhibition during dynamic dorsiflexion of the foot has so far only been demonstrated in two subjects, namely the only two subjects which had a sizeable polysynaptic inhibition as well as relatively large soleus H reflexes during dynamic dorsiflexion of the foot. Figure 5 *A* and *B* illustrates results (from the same subject and experiment) which were obtained at a shorter conditioning–test interval, in order to evaluate the change in the amount of disynaptic reciprocal Ia inhibition. This figure will be commented on in the next section.

The long-latency inhibition was also correlated with different degrees of tonic dorsiflexion of the foot. This is shown in Fig. 6*B*. At each dorsiflexion force the

strength of the test stimulus was adjusted to obtain the same size of the unconditioned test reflex as at rest. It is seen that the long-latency inhibition increases with increasing strength of tonic dorsiflexion.

To summarize, the facilitation of the inhibition of soleus motoneurones, evoked

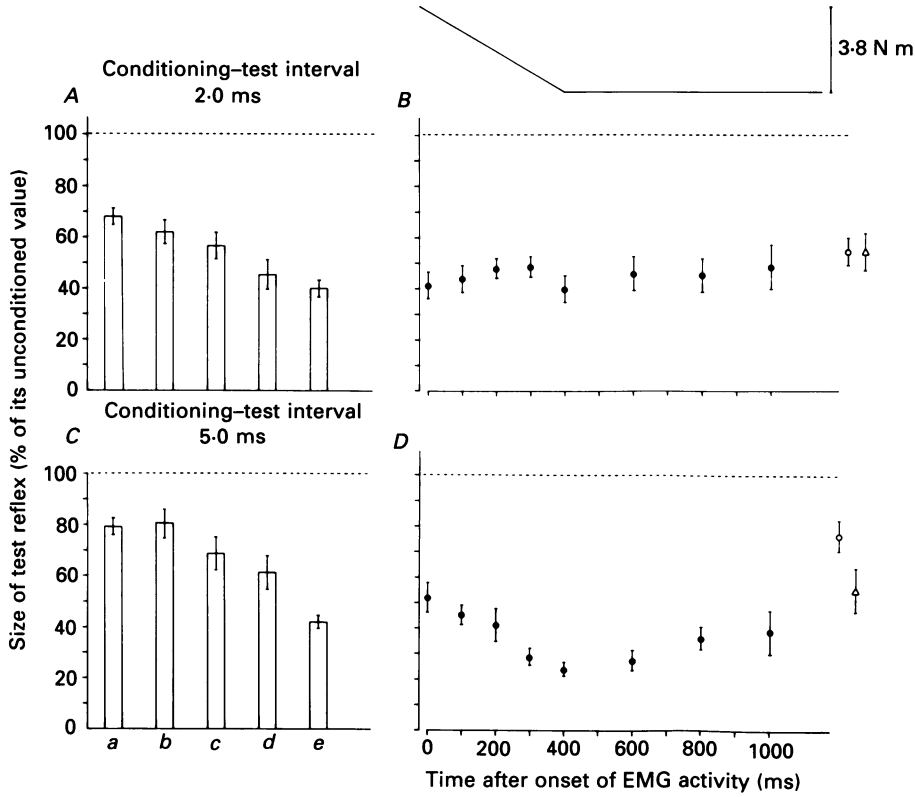

Fig. 5. The size of the conditioned soleus H reflex (expressed as a percentage of its unconditioned value) before and during a ramp-and-hold dorsiflexion of the foot (reaching 3·4 N m in 400 ms). Conditioning stimulus was a single stimulus to the common peroneal nerve (1·0 × motor threshold) elicited 2 and 5 ms before the test stimulus (*A* and *B*) before the test stimulus (*C* and *D*). *A* and *C*, the size of the conditioned test reflex when elicited at the time of the start signal (the beep; (*a*); 100–150 ms before the tibialis anterior EMG (*b*); 50–100 ms before the EMG onset (*c*); 10–50 ms before the EMG onset (*d*); at the time of the tibialis anterior EMG onset (*e*). *B* and *D*, size of the conditioned test reflex, elicited at different delays after start of tibialis anterior EMG activity (●); size of the conditioned test reflex at rest (○), and during tonic dorsiflexion of the foot (3·4 N m, △). Each bar represents one standard error of the mean.

from the peroneal nerve at a conditioning–test interval of 5 ms, has the same onset and time course as the development of the 'natural' reciprocal inhibition. Furthermore, both the inhibition seen at a conditioning–test interval of 5 ms and the 'natural' reciprocal inhibition increase with increasing strength of tonic dorsiflexion (cf. Fig. 1).

Disynaptic reciprocal Ia inhibition

The change of transmission in the pathway of the disynaptic reciprocal Ia inhibition during ramp-and-hold contractions and tonic contractions has been described in detail in two earlier reports by Crone *et al.* (1985, 1987). The upper part

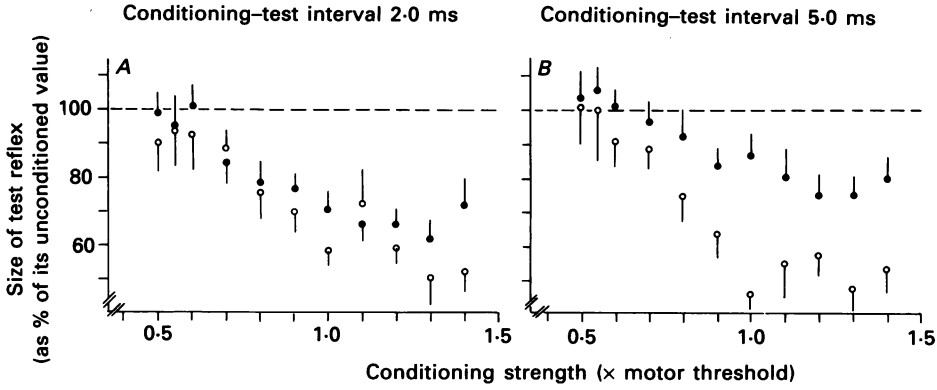

Fig. 6. Size of the conditioned soleus H reflex (expressed as a percentage of its unconditioned value) measured during different strengths of tonic dorsiflexion (●) and at rest (○). Conditioning stimulus was a single stimulus to the common peroneal nerve at 1·0 × motor threshold. The conditioning–test intervals were 2 and 5 ms in *A* and *B*, respectively. Each bar represents one standard error of the mean.

of Fig. 5*A* and *B* shows that the disynaptic Ia inhibition is increasing before the movement (*A*) much as the long-latency inhibition (*C*), but it is also seen that the disynaptic Ia inhibition does not increase further during the dynamic part of the ramp-and-hold contraction (*B*). This was shown in all seven subjects tested this way. In accordance with our previous experiments (Crone *et al.* 1987) we confirmed that the disynaptic Ia inhibition was not increased during tonic contraction of any force (Fig. 6*A*), while the long-latency inhibition was increased with the force during the same session (Fig. 6*B*).

Presynaptic inhibition of homonymous soleus Ia afferent fibres

The 'natural' reciprocal inhibition of the soleus H reflex during dorsiflexion of the foot could possibly be explained by presynaptic inhibition of the Ia afferents mediating the H reflex. It is, however, difficult to obtain a selective measure of the amount of presynaptic inhibition of the homonymous Ia fibres terminating on the soleus motoneurones (see further below). On the other hand a recently introduced method (Hultborn *et al.* 1987*a*) permits an accurate estimation of the presynaptic inhibition of the heteronymous Ia fibres (from quadriceps) terminating on the soleus motoneurones. Since presynaptic inhibition, evoked from sensory afferents and descending tracts, seems to act in parallel on homonymous and heteronymous Ia fibres projecting to soleus motoneurones (Hultborn *et al.* 1987*a*, *b*), it may be assumed that recorded changes in presynaptic inhibition of the heteronymous fibres during dorsiflexion also apply to the homonymous Ia fibres.

Figure 7 illustrates the increase in presynaptic inhibition of the heteronymous Ia fibres terminating on soleus motoneurones during a ramp-and-hold dorsiflexion (*A*) and at increasing strength of tonic dorsiflexion (*B*).

In the experiment illustrated in Fig. 7*A* the conditioning femoral nerve stimulation

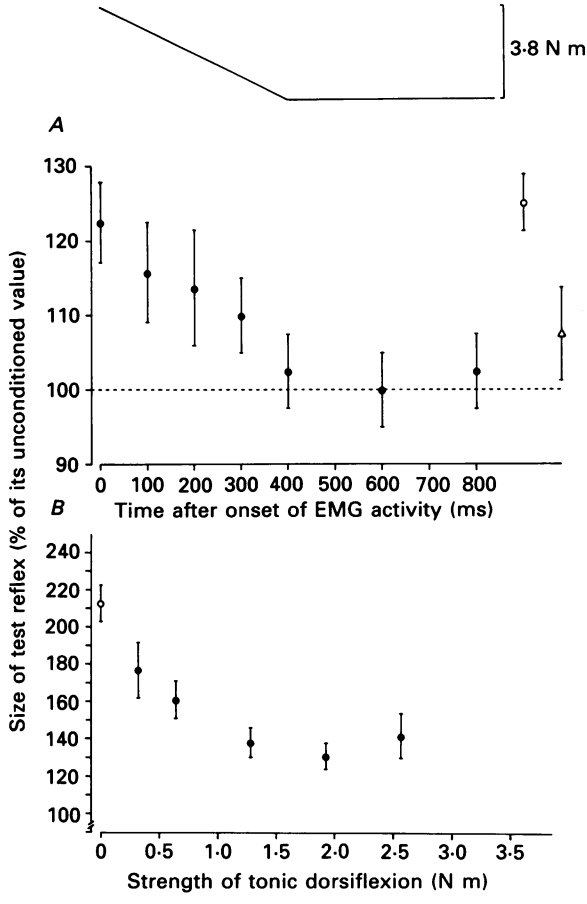

Fig. 7. *A*, size of the conditioned soleus H reflex (expressed as a percentage of its unconditioned value) measured at different time intervals after start of tibialis anterior EMG activity (●), at rest (○), and during tonic dorsiflexion of the foot (△). *B*, size of the conditioned soleus H reflex during different strengths of tonic dorsiflexion of the foot (●) and at rest (○). Conditioning stimulus was a single 1 ms stimulus applied to the femoral nerve (1·0 × motor threshold) at a conditioning–test interval of −7·0 ms. Each bar represents one standard error of the mean. *A* and *B* represent results from two different subjects.

was applied 7 ms before the test stimulus; the facilitation began at −7·4 ms and the interval used should thus guarantee that the facilitation is caused by a monosynaptic Ia EPSP without contamination of polysynaptic effects (see Methods and Hultborn *et al.* 1987*a*). The open circle in *A* shows the facilitation (about 125%) at rest. The amount of femoral nerve facilitation was not changed at the onset of the tibialis anterior EMG, but was decreased at 100 ms after the start of the movement. This

decrease becomes more pronounced during the dynamic phase. In the illustrated case the facilitation evoked by the femoral nerve stimulation virtually disappeared at the end of the dynamic phase and it is thus difficult to judge the changes during the holding phase. In some experiments (two subjects) the time course of the presynaptic inhibition during the ramp-and-hold dorsiflexion looked similar to the one illustrated, although the femoral nerve facilitation was not abolished. In the subjects tested in this type of experiment the soleus test reflex was only diminished to between 40 and 60% of its size at rest, and the prerequisite for using the method was thus fulfilled (Hultborn *et al.* 1987*a*). It can thus be concluded that the decrease of femoral nerve facilitation (i.e. the increase of presynaptic inhibition) on the whole follows the development of force during a ramp-and-hold dorsiflexion. The finding that the decrease of femoral nerve facilitation starts after the onset of movement (seen in four out of four subjects tested this way) suggests that the increase of presynaptic inhibition is caused mainly by afferent feedback, following the contraction, rather than by direct supraspinal control. Some contribution from a descending mechanism cannot, however, be completely ruled out with the described experiments. Meunier & Morin (1989) have reported that the femoral nerve facilitation of the soleus H reflex is diminished already at the start of a dorsiflexion movement. However, this was only the case when the movement was very strong (around 50% of the maximal possible dorsiflexion force). When the tibial anterior contraction was moderate (as in the present study) Meunier & Morin (1989) found that the femoral nerve facilitation was not decreased until 50–100 ms after initiation of the dorsiflexion movement, which is in good accordance with our experiments.

Despite the fact that the 'natural' inhibition is probably initiated by a supraspinal mechanism and the presynaptic inhibition most likely by a peripheral mechanism, the increase of presynaptic inhibition could still contribute to the change of 'natural' inhibition seen *after* start of the movement. Hence it was of interest to correlate the change of presynaptic inhibition with the strength of tonic dorsiflexion. In Fig. 7*B* it is seen that the facilitation by the femoral nerve stimulation decreases gradually with increasing strength of tonic dorsiflexion of the foot until the force reaches 1·3 N m, after which the level of inhibition is constant. The same increase of presynaptic inhibition was seen in two other subjects, i.e. there is a positive correlation between degree of presynaptic inhibition and contraction force, but the maximal inhibition is reached at rather small contraction forces.

DISCUSSION

In this investigation we have described the 'natural' inhibition of the soleus H reflex during an isometric ramp-and-hold dorsiflexion of the foot. The inhibition starts to develop around 50 ms before the onset of EMG activity in the pretibial flexors, increases during the ramp phase and stabilizes during the holding phase. Moreover there is a positive correlation between the strength of tonic dorsiflexion and the amount of 'natural' inhibition. Before approaching the functional role of 'natural' reciprocal inhibition the possible responsible segmental mechanisms must be specified.

The different phases in the development of reciprocal inhibition of the soleus H reflex during dorsiflexion of the foot suggest that several spinal mechanisms are involved. However, the pathway of the disynaptic reciprocal Ia inhibition was the first inhibitory spinal pathway to be thoroughly analysed and most findings on the convergence onto the interposed interneurone fitted so well with what could be expected of a mechanism involved in reciprocal inhibition during active movement (for references see Lundberg, 1970; Baldissera, Hultborn & Illert, 1981), that it was more or less assumed that this particular pathway was the main mechanism underlying 'natural' reciprocal inhibition. Hence other possible pathways escaped thorough attention for a considerable time, although the evidence for reciprocal inhibition, mediated via other interneurones than the 'Ia inhibitory interneurones', has been emphasized several times (see e.g. Lundberg, 1970; Fedina & Hultborn, 1972; Hultborn & Udo, 1972).

The first evidence that Ia inhibitory interneurones contribute to the 'natural' reciprocal inhibition during voluntary dorsiflexion of the foot was given by Kots & Zhukov (1971) and Simoyama & Tanaka (1974); both described a facilitation of disynaptic Ia inhibition from the peroneal nerve even before the onset of movement. Tanaka (1974) and Shindo *et al.* (1984) also claimed that the disynaptic Ia inhibition was facilitated during tonic dorsiflexion, but our own work (Crone *et al.* 1985, 1987; see also Iles, 1986) strongly suggests that the Ia inhibitory interneurones are not facilitated during the tonic phase; possible explanations for this disagreement have been discussed in detail by Crone *et al.* (1985). According to our findings the Ia inhibitory interneurones are selectively used in the dynamic phase of the movement, including the preparatory period.

With the newly introduced method which can be used to assess presynaptic inhibition in man (Hultborn *et al.* 1987*a*), we have provided indirect evidence that presynaptic inhibition contributes to the 'natural' reciprocal inhibition seen during dorsiflexion of the foot. However, the results indicate that there is no increase of presynaptic inhibition of Ia fibres at (or before) the onset of foot dorsiflexion. The increase is seen 100 ms after the onset, and later the increase in presynaptic inhibition largely parallels the development of torque (cf. Fig. 7). The late onset in relation to the start of movement suggests that presynaptic inhibition is not controlled primarily from the brain during this type of movement, but by the sensory feedback arising from the contracting pretibial flexors.

This does not exclude the possibility that presynaptic inhibition is initiated from the brain during the preparatory period of other types of movement. Indeed Hultborn *et al.* (1987*b*) have recently demonstrated large changes at the onset of contraction of the tested muscle and its synergists.

Of the three spinal mechanisms investigated in this study the long-latency inhibition from the peroneal nerve shows the best correlation with the 'natural' reciprocal inhibition. As seen in Figs 1 and 5 they both start before the movement, they are both maintained during the holding phase and both increase with the strength of tonic dorsiflexion. The long-latency inhibition also seems to increase, like the natural inhibition, during the dynamic phase of the ramp-and-hold dorsiflexion movement. This has so far, due to technical reasons mentioned in the Results section, only been possible to investigate in two subjects, but the increase of polysynaptic

inhibition during the dynamic phase of the movement was quite clear in these two subjects. These positive correlations suggest that the long-latency peroneal inhibition of soleus motoneurones is essential for the 'natural' inhibition, but the qualitative matching does not allow one to evaluate the quantitative importance of this mechanism in relation to other inhibitory pathways.

The possibility that the inhibition seen at a conditioning–test interval of 5 ms (during dorsiflexion) is due to activity in the disynaptic inhibitory pathway cannot be ruled out in the present experiments, since a group Ia-mediated EPSP can have a duration of up to 15 ms (Araki, Eccles & Ito, 1960). It does, however, seem unlikely for several reasons. (1) One is that this would imply the unlikely possibility that only the 'decay phase' of the disynaptic inhibition is facilitated during tonic dorsiflexion of the foot, while the inhibition, seen before and during the period of maximum inhibition, is not facilitated (see Fig. 2*B*). (2) Furthermore, several subjects have no or only a negligible reciprocal inhibition at a conditioning–test interval of 2 ms, while they do show a pronounced inhibition at a conditioning–test interval of 5 ms (cf. Fig. 8 in Crone *et al.* 1987). (3) Thirdly some subjects have a distinctive two-peaked reciprocal group I inhibition with the first peak at a conditioning–test interval of around 5–7 ms. These observations would be difficult to explain if the same (disynaptic) spinal pathway was responsible at both conditioning–test intervals.

Also the possibility that the late inhibition simply reflects a double firing (or repetitive firing) of the Ia inhibitory interneurones following a single group I volley must be dealt with. The pathway underlying the long-latency inhibition is unknown and has no established counterpart in the cat spinal cord. In cat such a volley only triggers a single spike in this interneurone (Hultborn, Jankowska & Lindström, 1971); this is related to a very synchronized afferent volley causing a short-lasting peak in the resulting monosynaptic EPSP. In man the afferent volley is much less synchronized (cf. Burke *et al.* 1983) and therefore a double firing of the 'Ia inhibitory interneurones' cannot be refuted (in cat the firing of these interneurones can reach 500 impulses/s on *repetitive* afferent stimulation, Hultborn *et al.* 1971). However, this explanation is unlikely for two reasons. Firstly, the double-firing hypothesis would imply that the long-latency inhibition would always be preceded by a disynaptic inhibition. This is not the case: the disynaptic inhibition is absent in some subjects (see Fig. 2 in Crone *et al.* 1987) who exhibit a pronounced late inhibition (during contraction; cf. Fig. 8 in Crone *et al.* 1987). Secondly, the control of the two phases of inhibition during a ramp-and-hold contraction is different: although both are facilitated before the movement, only the long-lasting inhibition increases further during the ramp phase; and during the holding phase only the long-lasting inhibition is facilitated as compared to rest. These observations are difficult to reconcile with the hypothesis of double firing of Ia inhibitory interneurones as a cause of the long-latency inhibition.

Another possible explanation for the increased inhibition seen at a conditioning–test interval of 5 ms could be a decreased Ib excitation of soleus motoneurones, which may also be evoked by the low-threshold stimulation of the common peroneal nerve. This is, however, not very likely since at conditioning–test intervals of both 2 and 5 ms there is a steady increase of inhibition with increasing conditioning stimulus strength at rest (C. Crone & J. Nielsen, unpublished observations). If Ib

excitation contributed significantly to the excitability level of the soleus motoneurones at a conditioning–test interval of 5 ms, a decrease of inhibition would be expected after the initial increase.

Which are then the possible pathways mediating the long-latency inhibition? In

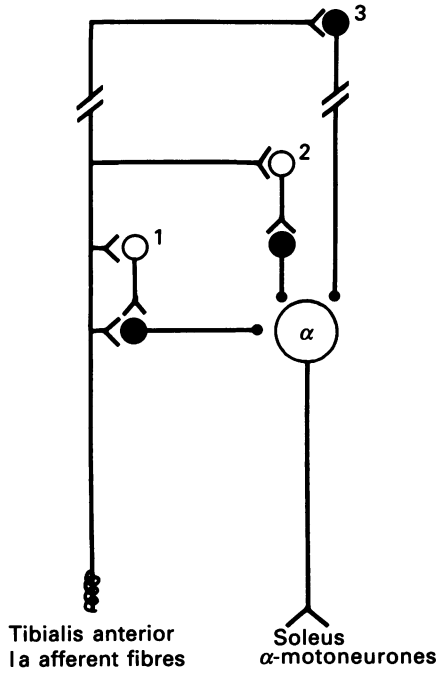

Fig. 8. Possible spinal pathways subserving the long-latency reciprocal inhibition. ○—≺, excitatory interneurones; ●—● inhibitory interneurones. For further details see text.

the Results section we described experiments which suggested that the inhibition is postsynaptic rather than presynaptic. This postsynaptic inhibition could be mediated by a trisynaptic pathway (alternative 1 in Fig. 8) where the first interneurone excites the 'classical' disynaptic Ia inhibitory pathways. Our results cannot rule out this possibility, but there is no support from animal experiments for such connections. The possibility of a fully separate di- or trisynaptic pathway therefore seems more likely.

The long latencies (2–3 ms in addition to the disynaptic Ia inhibition, cf. Fig. 2 and Crone *et al.* 1987) have to be explained either by slower conducting fibres or a longer pathway. Since both the disynaptic and long-latency inhibition (cf. Fig. 3) has the same low threshold it seems likely that the fastest afferent fibres are responsible in both cases. The remaining possibility – the longer pathway – would include either additional interneurones at the segmental level (alternative 2 in Fig. 8) or a more distant localization of the interposed interneurone in a disynaptic pathway (alternative 3 in Fig. 8).

Since the long-latency inhibition is evoked by very weak stimuli, it must be assumed that the synaptic coupling in the pathway is strong. This is most easily realized in a disynaptic pathway with the interneurones localized a few segments

rostral to the main hindlimb segments (propriospinal neurones). Such groups of propriospinal neurones, localized rostral to the limb semgents and projecting down to the proper limb segments, have been described in the cat both for forelimb and hindlimb segments (for references see Baldissera *et al.* 1981). These propriospinal neurones usually receive strong excitation from supraspinal centres and mediate the command signals to segmental interneurones and motoneurones (Illert, Lundberg & Tanaka, 1977). However, to different degrees they also receive an afferent feedback from the controlled limb. Although most of these propriospinal neurones may mediate excitation, there is also evidence of inhibitory propriospinal neurones (Alstermark, Lundberg & Sasaki, 1984).

In man it has recently been demonstrated that Ia volleys produce both mono- and oligosynaptic excitation (with a latency difference of 3–5 ms; lower limb, Fournier, Meunier, Pierrot-Deseilligny & Shindo, 1986; upper limb, Malmgren & Pierrot-Deseilligny, 1988). It was suggested that the pathway of the oligosynaptic excitation may correspond to the propriospinal systems referred to above. In keeping with that hypothesis Hultborn, Meunier, Pierrot-Deseilligny & Shindo (1986) demonstrated a larger facilitation of the oligosynaptic excitation during voluntary activation of the muscle. The long-latency group I inhibition described here may represent the inhibitory counterpart of this oligosynaptic excitation. However, the exact identification of the pathway mediating long-latency reciprocal inhibition needs further study.

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