Journal of Physiology (1992), **449**, *pp.* 673–687
With 6 figures
Printed in Great Britain

CHANGES IN PRESYNAPTIC INHIBITION OF AFFERENTS TO PROPRIOSPINAL-LIKE NEURONES IN MAN DURING VOLUNTARY CONTRACTIONS

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(*Received 5 July 1991*)

SUMMARY

1. The possibility was investigated that the facilitation of the transmission in the propriospinal-like system during voluntary contraction, documented in the companion paper (Burke, Gracies, Mazevet, Meunier & Pierrot-Deseilligny, 1992), is due to a decrease in presynaptic inhibition of afferents projecting to propriospinal-like neurones.

2. The radial nerve was stimulated to evoke presynaptic inhibition of the monosynaptic Ia projections to forearm flexor motoneurones (Berardelli, Day, Marsden & Rothwell, 1987) and, hopefully, of the afferent input to propriospinal-like neurones projecting to these motoneurones.

3. The propriospinal-like excitation of forearm motoneurones evoked from mixed afferent inputs was depressed by radial nerve stimulation, and this depression was long-lasting (200 ms). Despite the convergence of mixed nerve and cutaneous afferents onto common propriospinal-like neurones, the radial stimulation did not depress the cutaneous-induced excitation. This differential effect and the time course of the depression suggest that it results from presynaptic inhibition of mixed nerve afferents (presumably large muscle afferents) projecting to propriospinal-like neurones.

4. With voluntary contractions, phasic or tonic, the radial-induced depression of the propriospinal-like excitation evoked by mixed nerve afferents was much greater than at rest, but the cutaneous-evoked excitation was unchanged. Thus, with voluntary contractions, there was no evidence of decreased gating of the afferent input to propriospinal-like neurones whether the input was of muscle or cutaneous origin and it is concluded that changes in presynaptic inhibition cannot account for the facilitation of the transmission in the propriospinal-like system during voluntary contraction.

5. By contrast, presynaptic inhibition of the monosynaptic Ia projections to

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motoneurones was consistently reduced at the onset of contraction, and to a much lesser extent during a weak tonic contraction.

INTRODUCTION

Transmission of propriospinal-like excitation to motoneurones of forearm flexor muscles is facilitated by various forms of voluntary contraction (Burke *et al.* 1992). The question arises whether this facilitation results from excitation of propriospinal-like neurones or a decrease in presynaptic inhibition of primary afferents projecting to these neurones. Changes in presynaptic inhibition of afferents synapsing with propriospinal neurones have never been investigated in the cat. Nevertheless the possibility must be considered because, in the human lower limb, there is a decrease in presynaptic inhibition of monosynaptic Ia projections to motoneurones at the onset of voluntary contractions (Hultborn, Meunier, Pierrot-Deseilligny & Shindo, 1987*b*; Meunier & Pierrot-Deseilligny, 1989). The present study was therefore undertaken to determine whether primary afferents projecting to propriospinal-like neurones are subject to presynaptic inhibition and whether changes in presynaptic inhibition contribute to the increase in excitability of the propriospinal-like system associated with a voluntary contraction.

METHODS

Experiments were performed on ten normal subjects, using essentially the same methodology as in the companion paper (Burke *et al.* 1992). Only those methods specific to the present study are described below.

Presynaptic inhibition of the monosynaptic Ia pathway projecting to flexor carpi radialis (FCR) motoneurones was evoked using the protocol developed by Day, Marsden, Obeso & Rothwell (1984) and Berardelli *et al.* (1987). Conditioning stimuli of 0·5 ms duration were delivered at 0·95 × MT (motor threshold) to the radial nerve in the spiral groove using conditioning–test intervals of 10–300 ms. In most of the cases the cutaneous sensation evoked by these stimuli was purely local. The effect of the radial nerve stimuli on the facilitation of the FCR H reflex produced by different mixed nerve and cutaneous afferent volleys was studied in the same experimental sequences. To ensure that the radial-induced effects were not specific to afferents from a particular source (i.e. afferents from extensor muscles of the forearm), the effects of musculo-cutaneous nerve stimulation at 0·95 × MT on the FCR H reflex and on its facilitation by different afferent volleys were studied using an otherwise identical experimental protocol. These experiments were performed at rest and then during the two forms of FCR voluntary contraction described in the accompanying paper (Burke *et al.* 1992): onset of a phasic wrist flexion and weak (one-motor-unit) tonic contraction.

The present experiments required at least four combinations of stimuli: A, test alone; B, first conditioning (mixed nerve stimulation evoking propriospinal-like excitation) + test; C, second conditioning (radial nerve stimulation) + test; D, first and second conditioning + test. This protocol was necessary to determine the effect of radial nerve stimuli on the facilitation of the H reflex produced by mixed nerve afferent volleys. Sometimes a third conditioning stimulus (cutaneous stimulation evoking propriospinal-like excitation) was added and six combinations used: the preceding four, plus E (third conditioning + test) and F (second and third conditioning + test). This protocol was necessary to compare the effects of radial nerve stimuli on the facilitation of the H reflex produced by ulnar volleys and by cutaneous volleys. In each sequence twenty stimuli were randomly presented for each stimulus combination, and usually each sequence was repeated 2–10 times to ensure reproducibility. The amounts of facilitation or inhibition evoked by separate conditioning stimuli, B − A, C − A and E − A, and by the combined stimuli, D − A and F − A, were calculated from the size of the different kinds of reflexes. Amounts of propriospinal-like excitation

evoked in the absence (B − A and E − A) and in the presence (D − C and F − C) of radial nerve stimulation were then compared. Variance analysis was used to test the statistical significance of these different values (F test).

RESULTS

Evidence for presynaptic inhibition

Depression of the flexor carpi radialis H reflex by stimulation of the radial nerve

Stimulation of the radial nerve inhibits the FCR H reflex (Day *et al.* 1984), and the available evidence favours the view that the phase of inhibition at conditioning–test intervals of 10–30 ms is due to presynaptic inhibition of the Ia afferent projection to FCR motoneurones responsible for the test reflex (Berardelli *et al.* 1987; Nakashima, Rothwell, Day, Thompson & Marsden, 1990). Accordingly, it was confirmed that single radial nerve stimuli at 0·95 × MT significantly depress the FCR H reflex at conditioning–test intervals of 10–30 ms (Fig. 1*C*) and this was found in all fifty-two experiments. At conditioning–test intervals of 40–50 ms the radial-induced depression was less, and often completely absent, probably due to a superimposed long-latency facilitation of FCR neurones, as revealed by parallel experiments using post-stimulus time histograms of voluntarily activated motor units in FCR. At intervals of around 100 ms there was sometimes a second phase of facilitation (Fig. 1*H*), as has also been observed in the course of the soleus H reflex inhibition after vibration of the tibialis anterior tendon (Hultborn, Meunier, Morin & Pierrot-Deseilligny, 1987*a*).

Depression of mixed nerve-induced propriospinal-like excitation by stimulation of the radial nerve

In Fig. 1*A–G*, the comparison is drawn between the reflex facilitation evoked by ulnar nerve stimulation (0·7 × MT, 5 ms conditioning–test interval) when not preceded (*B*) and when preceded (*D*) by a stimulus to the radial nerve (0·95 × MT, 10 ms before the ulnar stimulus). The ulnar-induced facilitation has been shown to be produced through the propriospinal-like system (Malmgren & Pierrot-Deseilligny, 1988; Burke *et al.* 1992), and the amount of facilitation was smaller after radial nerve stimulation (*D minus C*, displayed in *F*) than in the control situation (*B minus A*, displayed in *E*). The depression of the ulnar-induced facilitation (i.e. *F minus E*) is shown in *G*. A similar depression was found in all eight subjects who exhibited a sizeable ulnar-induced facilitation and was present in twenty-one of twenty-four experiments. Although this depression was usually small, its mean value (−5·8% of the control H reflex, $n = 24$) was highly significant ($P < 0·001$).

The time course of the depression is shown in Fig. 1*I*, in which the abscissa represents the time interval between radial and ulnar stimulations. Maximal depression occurred at the 10–60 ms intervals and then progressively subsided over the subsequent 150 ms. A similar time course for the depression of the ulnar-induced facilitation was found in three other subjects. In a further three subjects, the full time course was not tested, but similar radial-induced depression was seen using conditioning–test intervals of 10–20 ms and more than 50 ms. This long time course is similar to that described for presynaptic inhibition of Ia fibres projecting monosynaptically onto motoneurones in the cat hindlimb (Eccles, 1964) and in the human lower limb (Hultborn *et al.* 1987*a*).

As seen in the companion paper (Burke *et al.* 1992), musculo-cutaneous-induced facilitation of the FCR H reflex was rarely seen. However, in two of three experiments (three subjects) in which a trend to facilitation was observed it was similarly depressed by radial nerve stimulation.

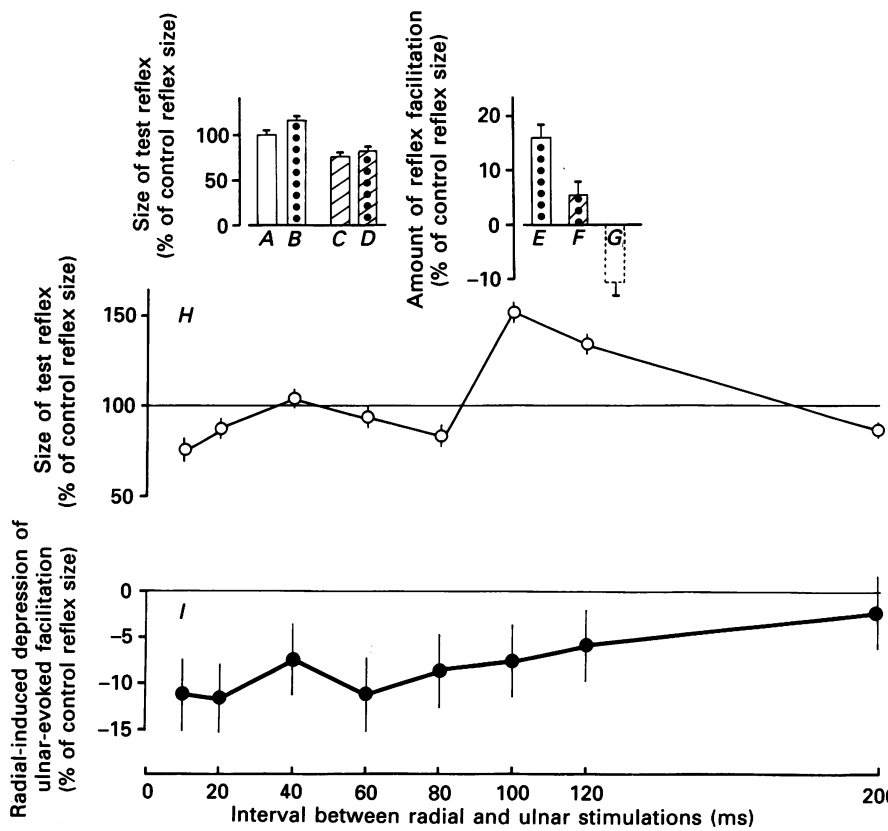

Fig. 1. Radial-induced depression of the FCR H reflex and of the ulnar-evoked facilitation. The comparison is drawn between the test reflex size (expressed as a percentage of the control reflex size) when not facilitated (*A* and *C*) and facilitated (dotted columns, *B* and *D*) by ulnar nerve stimulation (0·7 × MT, 5 ms conditioning–test interval), and when not preceded (*A* and *B*) and preceded (*C* and *D*, hatched columns) by radial stimulation (0·95 × MT, 15 ms before test stimulation). *E* and *F*, amount of ulnar-evoked facilitation when not preceded (*E* = *B minus A*) and preceded (*F* = *D minus C*) by radial stimulation. *G*, depression by radial stimulation of the ulnar-evoked facilitation (i.e. *F minus E*). This depression (*I*) and the size of the reflex conditioned by radial nerve stimulation (*H*) (expressed as a percentage of the control reflex size) are plotted against the time interval between radial and ulnar (or test) stimulations. Each point represents the mean of forty measurements. Each column represents the mean of 200 measurements for one subject. Vertical bars, one standard error of the mean.

Homonymous facilitation of the FCR H reflex is the net result of monosynaptic Ia and propriospinal-like excitations (Malmgren & Pierrot-Deseilligny, 1988). Temporal facilitation was therefore used to explore the latter selectively. Two conditioning

shocks (0·5 × MT) were delivered 5 and 10 ms before the test shock. Figure 2*A* and *B* shows the amount of reflex facilitation when the two shocks were delivered separately and Fig. 2*C* the algebraic sum of the two facilitations. On combined stimulation (Fig. 2*D*) the facilitation was much larger than the algebraic sum. The

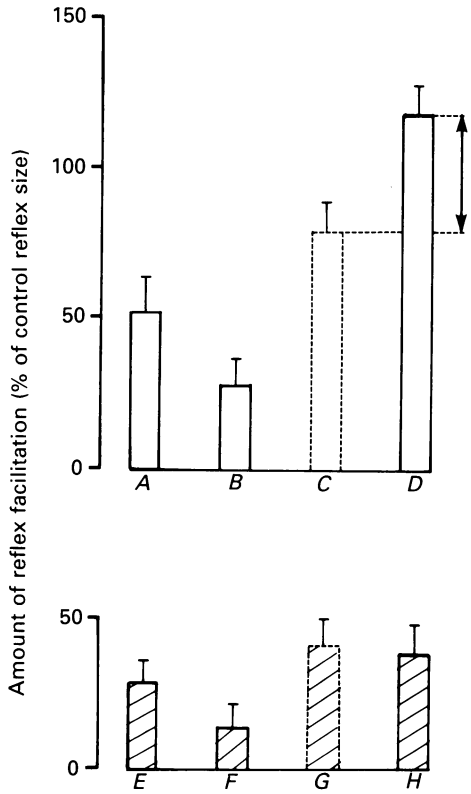

Fig. 2. Radial-induced depression of the homonymous propriospinal-like excitation. The FCR H reflex was conditioned by two conditioning stimuli applied to the median nerve (0·5 × MT, 5 and 10 ms before the test shock). The comparison is drawn between the amount of reflex facilitation (conditioned reflex *minus* unconditioned reflex), expressed as a percentage of the control reflex size, when the conditioning stimuli were applied separately (*A* and *E*, *B* and *F*) or together (*D* and *H*), when not preceded (*A–D*) or preceded (*E–H*, hatched columns) by radial stimulation (0·95 × MT, 10 and 15 ms before the two conditioning shocks). The third (interrupted) columns in each subset (*C* and *G*) represents the algebraic sum of the effects of separate stimuli. The double-headed arrow in *D* represents the difference between the facilitation on combined stimulation and the sum of effects of separate stimuli, i.e. the extra facilitation on combined stimulation (which was highly significant, $P < 0·001$). Each column represents the mean of eighty measurements for one subject. Vertical bars, one standard error of the mean.

resulting extra facilitation of the reflex (double-headed arrow in Fig. 2*D*) has been shown to be produced at the level of propriospinal-like neurones (Malmgren & Pierrot-Deseilligny, 1988). The same experiment was repeated after radial nerve stimulation (0·95 × MT, 10 and 15 ms before the two conditioning shocks): the

facilitations evoked by the individual median nerve stimuli were reduced (Fig. 2*E* and *F*), but the extra facilitation on combined stimulation, i.e. the propriospinal-like facilitation, was suppressed completely (Fig. 2*H*). The same result was obtained in a second subject.

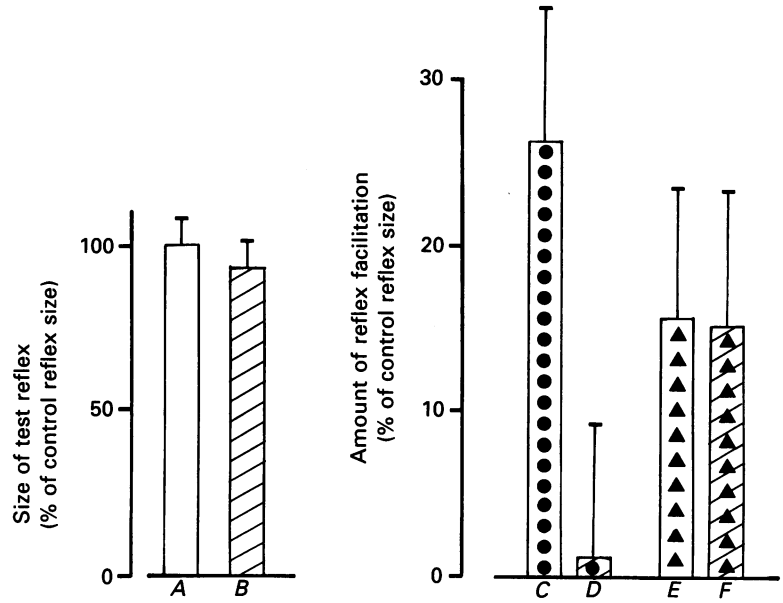

Fig. 3. Comparison between the effects of radial nerve stimulation on ulnar- and cutaneous-induced facilitation of the FCR H reflex. *A* and *B*, size of the test reflex (as a % of its control value) when not preceded (*A*) and preceded (*B*, shaded column) by radial nerve stimulation (0·95 × MT, 15 ms before the test stimulus). *C–F*, amount of reflex facilitation (see Fig. 1) evoked by ulnar nerve (*C* and *D*, dotted columns) and cutaneous (*E* and *F*, columns with triangles) stimulations when not preceded (*C* and *E*) and preceded by radial stimulation (shaded columns, *D* and *F*). Each column presents the mean of forty measurements for one subject. Vertical bars, one standard error of the mean.

Hence in relaxed subjects, the propriospinal-like excitation of FCR motoneurones evoked by various mixed nerves (ulnar, musculo-cutaneous, median) was decreased by radial nerve stimuli at conditioning–test intervals appropriate for presynaptic inhibition.

Lack of depression of cutaneous facilitation by stimulation of the radial nerve

Cutaneous volleys from both sides of the hand have been shown to elicit propriospinal-like excitation of FCR motoneurones (Burke *et al.* 1992), and the effect of radial nerve stimulation on this cutaneous-induced excitation was investigated. In the same sequence, ulnar (0·7 × MT) and superficial radial (2 × PT) volleys were randomly alternated and timed so that both reached the spinal level 5 ms before the test volley. In the experiment illustrated in Fig. 3 the test reflex was only slightly inhibited by the radial nerve stimulation at 0·95 × MT (*B*). The ulnar nerve-induced propriospinal-like excitation, which was large in the control situation (*C*), was markedly

depressed by radial nerve stimulation (*D*) but the cutaneous-induced propriospinal-like excitation (*E*) was not modified by the same stimulation (*F*). A similar absence of depression of the cutaneous-induced excitation was found in ten of eleven experiments (seven subjects) so performed, and the mean difference between the amount of facilitation with and without radial nerve stimulation was −0·3 % of the control reflex value. In these subjects, the ulnar and superficial radial volleys were shown to have a strong convergence on the same population of propriospinal-like neurones (Burke *et al.* 1992), suggesting that the selective depression of the ulnar-evoked facilitation involves the afferent input to propriospinal-like neurones and not the neurones themselves (see Discussion).

Similar results were obtained when the cutaneous volley was evoked by stimulating the palmar side of the last four fingers: in eight of the ten experiments (seven subjects), the cutaneous-induced propriospinal-like excitation was not depressed by radial nerve stimulation.

Changes in presynaptic inhibition during voluntary contraction

Changes in the radial-induced depression of the flexor carpi radialis monosynaptic reflex

At the onset of voluntary wrist flexion the depression of the FCR H reflex by stimulation of the radial nerve (0·95 × MT, 15–25 ms conditioning–test interval) was consistently reduced in the thirty experiments so performed. In the example illustrated in Fig. 4*A–F*, the radial nerve stimulation decreased the size of the test reflex to 72 % of its control value at rest (*B*) but only to 88 % at the onset of phasic contractions of FCR (*F*), a difference of 16 % which was highly significant ($P < 0·001$). By contrast, the reduction in the effect of radial stimulation was usually small during a weak tonic contraction (6 % of the control reflex size, not significant, in the example illustrated in Fig. 4*I–N*) and was sometimes absent.

Changes in the radial nerve-induced depression of propriospinal-like excitation evoked by mixed nerves

As seen in the companion paper (Burke *et al.* 1992), voluntary contraction usually enhanced the ulnar nerve-evoked propriospinal-like excitation, whether studied at the onset of a phasic contraction or during weak tonic contraction of FCR. Figure 4*C* & *D* and *G* & *H* illustrate the radial-evoked changes in the ulnar-induced facilitation at rest (*C* & *D*) and at the onset of FCR contraction (*G* & *H*). At rest the amount of facilitation evoked by ulnar nerve stimulation (0·7 × MT, 5 ms conditioning–test interval) was reduced by radial nerve stimulation. At the onset of a phasic contraction, although the ulnar nerve-induced facilitation was significantly increased with regard to rest (*G*), it was almost completely abolished by radial nerve stimulation (*H*). Figure 4*K* & *L* (rest) and *O* & *P* (contraction) illustrate that during weak tonic contraction of FCR the depression of the ulnar-evoked facilitation by radial stimulation was also greater during contraction than at rest. A similar enhanced radial depression of the propriospinal-like excitation evoked by ulnar nerve stimulation was found in all six subjects so explored (ten of thirteen experiments at the onset of contraction and seven of nine during weak tonic contraction).

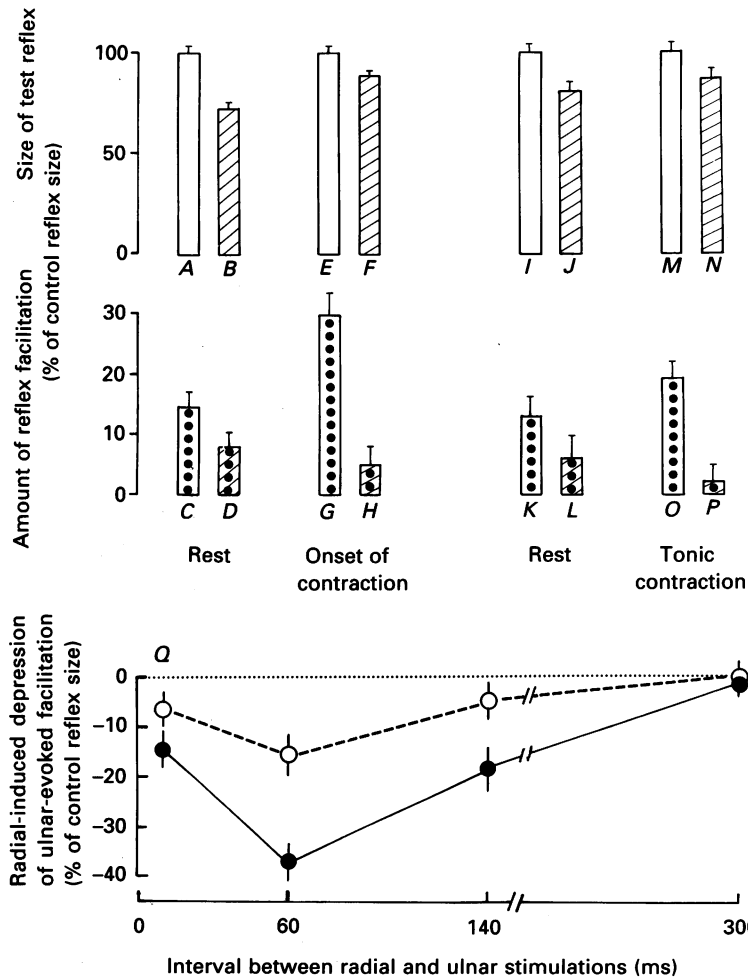

Fig. 4. Comparison between the radial-induced depression of the FCR H reflex and that of the ulnar-evoked facilitation at rest (*A–D* and *I–L*), at the onset of voluntary wrist flexion (*E–H*) and during a weak tonic FCR contraction (*M–P*). Hatched columns *B*, *F*, *J* and *N* show the test reflex size (expressed as a percentage of the control reflex size) when preceded by radial nerve stimulation (0·95 × MT, 15 ms before the test stimulus). *C* & *D*, *G* & *H*, *K* & *L* and *O* & *P*, amount of ulnar-evoked facilitation (conditioning–test interval 5 ms, see Fig. 1) when not preceded or when preceded (hatched columns, *D*, *H*, *L*, *P*) by radial nerve stimulation (radial–ulnar interval 10 ms). *Q*, the radial depression of the ulnar-evoked facilitation (calculated as in Fig. 1*G* and *I*) is plotted against the time interval between radial and ulnar nerve stimulation at rest (○) and during tonic FCR contraction (●). The first interval was 10 ms, i.e. the same as in *A–H* and *I–P*. Data in *A–H* and *Q* are from separate experiments in one subject. Data in *I–P* are from a second subject. Each column or point represents the mean of 360 (*A–H*), 100 (*I–P*) or sixty (*Q*) measurements. Vertical bars, one standard error of the mean.

In Fig. 4*Q* the comparison is drawn between the time course of the radial depression of propriospinal-like excitation (the amount of which was calculated as in Fig. 1*G*) at rest (○) and during weak tonic contraction (●): any depression at rest

was increased during contraction, but neither the depression nor its enhancement lasted longer than the 300 ms interval. A similar time course for the contraction-associated increase in the effects of radial stimulation was found in the three other subjects so explored (one during weak tonic contraction, two at the onset of

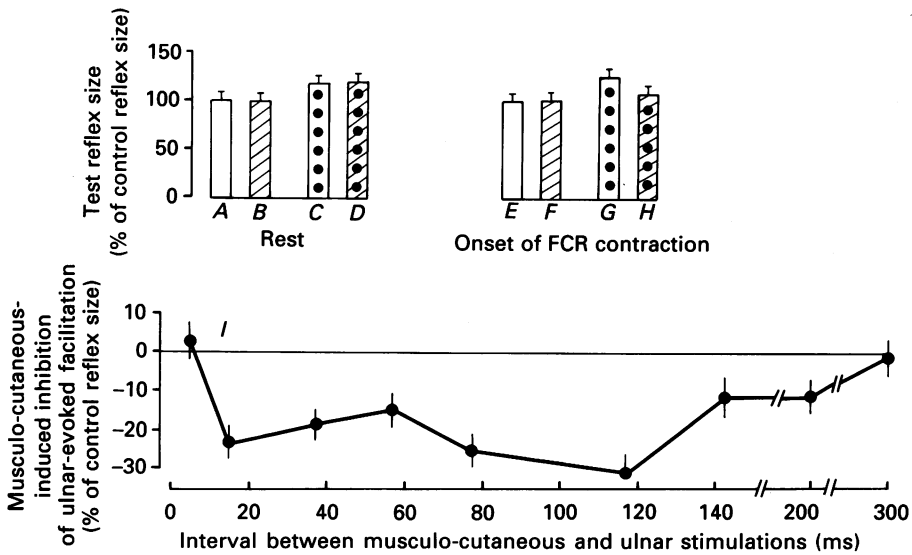

Fig. 5. Effects of the musculo-cutaneous stimulation on the FCR H reflex and on the ulnar-evoked facilitation. *A–H*, the comparison is drawn between the size of the reflex (expressed as a % of the control reflex size) when not preceded (*A* and *C*, *E* and *G*) and preceded (hatched columns, *B* and *D*, *F* and *H*) by musculo-cutaneous stimulation (0·95 × MT, 35 ms before the test stimulus), when not facilitated (*A* & *B* and *E* & *F*) and facilitated (dotted columns, *C* & *D* and *G* & *H*) by ulnar nerve stimulation (0·7 × MT, 4 ms conditioning–test interval), at rest (*A–D*) and at the onset of FCR contraction (*E–H*). *I*, the depression of the ulnar-evoked facilitation at the onset of contraction (calculated as in Fig. 1*G* and *I*) is plotted against the time interval between musculo-cutaneous and ulnar nerve stimulation. Each column or point represents the mean of sixty (or forty) measurements for a single subject. Vertical bars, one standard error of the mean.

contraction). Again this time course is consistent with presynaptic inhibition of ulnar afferents projecting onto propriospinal-like neurones.

A similar increase in the radial-induced depression of the propriospinal-like excitation evoked by musculo-cutaneous nerve stimulation was observed in two of three experiments performed during weak tonic contraction of the FCR.

In the case of the homonymous facilitation of the FCR H reflex it is more difficult to interpret changes in the radial-induced depression of the facilitation because monosynaptic Ia excitation also contributes to the homonymous facilitation. However, during weak tonic contractions, there was, in three experiments (three subjects), an increase in facilitation evoked by median nerve stimulation at latencies appropriate for propriospinal-like excitation (4–6 ms but neither earlier nor later) but no change in the radial nerve-induced depression of the FCR H reflex. In these three experiments, the increase in median-evoked facilitation during contraction therefore cannot reflect increased monosynaptic Ia excitation due to a decrease in presynaptic inhibition and, accordingly, it can be attributed to facilitation of transmission in the propriospinal-like system. During this

weak tonic contraction the radial-induced depression of the facilitation was greater than at rest, a finding which is consistent with results obtained using either the ulnar or the musculo-cutaneous nerve to produce the propriospinal-like excitation.

Musculo-cutaneous nerve-induced depression of propriospinal-like excitation

To explore whether presynaptic inhibition could be evoked from another afferent source, conditioning stimuli (one shock, 0·95 × MT) were applied to the musculo-

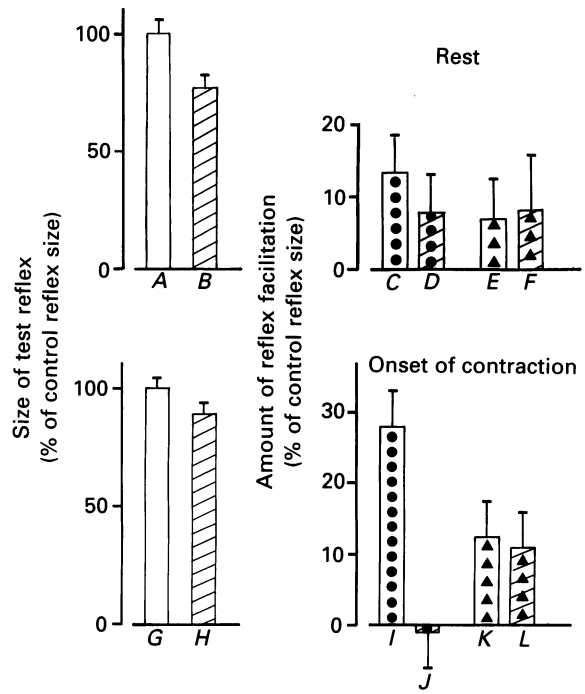

Fig. 6. Comparison between the effects of radial nerve stimulation on ulnar- and cutaneous-induced facilitations of the FCR H reflex, at rest (*A–F*) and at the onset of FCR contraction (*G–L*). *A* & *B* and *G* & *H*, size of the test reflex when not preceded (*A* and *G*) and preceded (*B* and *H*, hatched columns) by radial nerve stimulation (0·95 × MT, 15 ms before the test stimulus). *C–F* and *I–L*, amount of reflex facilitation (see Fig. 1) evoked by ulnar (dotted columns) and cutaneous (columns with triangles) stimulation when not preceded (*C*, *E*, *I* and *K*) and preceded (hatched columns, *D*, *F*, *J* and *L*) by radial nerve stimulation. Each column represents the mean of 100 measurements for a single subject. Vertical bars, one standard error of the mean.

cutaneous nerve instead of the radial nerve. Figure 5*A* and *B* shows that when the musculo-cutaneous stimulation preceded the test reflex (35 ms) the test reflex size was altered little either at rest (*A* and *B*) or at the onset of contraction (*E* and *F*). The musculo-cutaneous stimulation did not depress the ulnar nerve-induced facilitation at rest (compare *D* to *C*) but depressed it at the onset of FCR contraction (compare *H* to *G*). The time course of this depression during contraction (Fig. 5*I*) was prolonged (200–300 ms) as in the case of the radial-induced depression (Figs 1 and 4). Similar results, i.e. a depression of the ulnar-induced facilitation during contraction,

were observed in two other subjects using both short (10–20 ms) and long (80–120 ms) intervals between the musculo-cutaneous and ulnar stimuli. However, in a further two subjects the depression was small and only seen at short (10–40 ms) intervals.

Lack of depression by radial stimulation of the cutaneous-induced propriospinal-like excitation during contraction

In the experiment illustrated in Fig. 6 the comparison is drawn between the effects of radial nerve stimulation on the test reflex (*B* and *H*) and on the amount of reflex facilitation evoked by ulnar nerve and by cutaneous stimulation (superficial radial) at rest (*A–F*) and at the onset of FCR contractions (*G–L*). At rest the amount of ulnar-evoked reflex facilitation was reduced by half by radial stimulation (*C* and *D*). At the onset of phasic wrist flexion the facilitation was increased (*I*), only to be suppressed completely by radial stimulation (*J*). By contrast the cutaneous-induced facilitation was not modified by radial stimulation either at rest (*E* and *F*) or at the onset of contraction (*K* and *L*). Similar results (depression of the ulnar-induced excitation with unchanged or minimally changed cutaneous excitation) were observed in the twelve experiments (seven subjects) so performed at the onset of contraction (six) or during weak tonic contractions (six). Similarly the propriospinal-like excitation evoked by cutaneous afferents from the palmar side of the hand was not depressed by radial nerve stimulation in all nine experiments performed at the onset of contraction.

DISCUSSION

Radial nerve stimulation was used to evoke presynaptic inhibition of the monosynaptic pathway to motoneurones (see Berardelli *et al.* 1987; Nakashima *et al.* 1990) and, hopefully, of the afferent input to propriospinal-like neurones. Propriospinal-like excitation evoked by mixed nerve volleys was markedly depressed while that evoked by cutaneous afferents was unchanged. In addition, during contraction, the radial-induced inhibition of propriospinal-like excitation was increased whereas that of the monosynaptic reflex was decreased.

Evidence for presynaptic inhibition of afferents to propriospinal-like neurones

Radial nerve stimulation decreases the ulnar-evoked propriospinal-like excitation, and the time course of this depression has a long duration (Fig. 1*I*), much as has been described for presynaptic inhibition of Ia fibres in the cat hindlimb (see Eccles, 1964) and in the human lower limb (Hultborn *et al.* 1987*a*). This suggests that the depression is not due to postsynaptic inhibition of propriospinal-like neurones but to presynaptic inhibition of afferents projecting to them. The absence of a similar depression of the propriospinal-like excitation of cutaneous origin strongly supports this view, since cutaneous afferents from the dorsal side of the hand and mixed afferents in the ulnar nerve have a readily demonstrable convergence onto common propriospinal-like neurones (Burke *et al.* 1992). Under these conditions it appears unlikely that complete or near-complete abolition of the mixed nerve-evoked facilitation, as was seen sometimes at rest (Fig. 3*D*) and often during contraction (Fig. 6*J*), could occur postsynaptically at the propriospinal-like neurone level

without a significant reduction in the cutaneous facilitation. Hence, it appears likely that the radial-induced depression of the propriospinal-like excitation evoked by mixed nerve afferents reflects presynaptic inhibition of those afferents. Given the absence of depression of the excitation evoked by cutaneous afferents from both sides of the hand, it may be assumed that this presynaptic inhibition is exerted on muscle afferents (large muscle afferents when considering the weak stimuli used).

An alternative possibility would be radial-induced postsynaptic inhibition of an additional interneurone interpolated in the pathway for the mixed nerve afferent input, with no convergence of cutaneous and mixed nerve inputs on this interneurone. However the time course of the depression does not favour postsynaptic inhibition. In addition there is no such additional interneurone in the analogous pathway in the cat (see Lundberg, 1979), and it is unlikely to exist in man because of the abrupt onset and very low threshold of the propriospinal-like excitation (Malmgren & Pierrot-Deseilligny, 1988; Gracies, Meunier, Pierrot-Deseilligny & Simonetta, 1991; Burke *et al.* 1992).

Changes in presynaptic inhibition accompanying voluntary contraction

Propriospinal-like excitation evoked by mixed nerve volleys is more depressed by radial (and musculo-cutaneous) stimulation during voluntary contraction than at rest, and this implies that at least some inputs to propriospinal-like neurones are gated during contraction. This finding is not compatible with the possibility that the facilitation of the transmission in the pathway of propriospinal-like excitation during voluntary movement (Burke *et al.* 1992) is due to a decrease in presynaptic inhibition of afferents to propriospinal-like neurones. Hence, this facilitation reflects an increased excitation of these neurones and, at the onset of contraction, this is purely descending in origin (see Burke *et al.* 1992).

Radial nerve stimulation did not depress the cutaneous afferent excitation of propriospinal-like neurones during contraction. This implies that the increased radial-induced presynaptic inhibition of mixed nerve afferents specifically involves muscle afferents. It could also be taken to indicate that there is no gating of cutaneous afferent inputs to propriospinal-like neurones during contraction. However, there was no radial-induced depression of cutaneous excitation at rest either, and this absence of effect suggests that radial stimuli do not evoke presynaptic inhibition of cutaneous fibres. Thus, no conclusion can be drawn from the present experiments concerning the level of presynaptic inhibition of cutaneous afferents to propriospinal-like neurones during contraction.

It is possible that during tonic contraction the contraction-induced afferent discharge contributes to the changes in presynaptic inhibition described above. With the onset-of-movement protocol the radial stimulation was triggered by the initial EMG potential and the conditioning and test stimuli were delivered at variable intervals after the onset of contraction. With long intervals, the test volley samples spinal circuitry that could have been affected by afferent feedback associated with the initiation of the contraction. However, a significant fusimotor-induced increase in Ia discharge is unlikely to occur during the first 50 ms of the contraction (Vallbo, 1971), and an increased Ib discharge will occur with a delay after EMG of 12–24 ms (Binder, Kroin, Moore & Stuart, 1977). This implies that, when the conditioning–test interval was less than 20 ms, changes in the efficacy of the radial stimulus in eliciting presynaptic inhibition at the onset of contraction are unlikely to be due to peripheral

feedback and presumably reflect changes in the descending control of 'presynaptic interneurones'.

The inhibition of the FCR H reflex during the 10–30 ms following radial stimulation is thought to reflect presynaptic inhibition of monosynaptic Ia projections to FCR motoneurones (Berardelli *et al.* 1987; Nakashima *et al.* 1990), and was markedly reduced at the onset of contractions and, to a much lesser extent, during tonic contractions. This indicates a decrease in presynaptic inhibition of Ia terminals on motoneurones of the contracting muscle and confirms previous results in the lower limb (Hultborn *et al.* 1987b; Meunier & Pierrot-Deseilligny, 1989). Hence, at the onset of contraction, presynaptic inhibition of large muscle afferents to propriospinal-like neurones is increased whereas it is decreased on Ia terminals on motoneurones.

If propriospinal-like excitation is evoked predominantly from Ia fibres such a differential control of presynaptic inhibition of Ia afferents to motoneurones and to propriospinal-like neurones may seem surprising. In fact, in the cat, cortical stimulation effectively removes presynaptic inhibition of monosynaptic Ia projections to motoneurones (Lundberg & Vyklický, 1963) but this depression could conceal an opposite, facilitatory, effect from the cortex to 'presynaptic interneurones' (as discussed by Hongo, Jankowska & Lundberg, 1972). It is likely that the dominant, depressive effect from cortex on presynaptic inhibition of Ia terminals is exerted by activation of interneurones in the FRA (flexion reflex afferent) pathway (Lund, Lundberg & Vyklický, 1965; Hongo *et al.* 1972), and this could account for the decreased presynaptic inhibition of Ia terminals on motoneurones at the onset of movement. It is likely that FRA interneurones only have a segmental projection. Under these conditions interneurones mediating presynaptic inhibition of Ia afferents to propriospinal-like neurones (located in C3–C4) would not receive the depressive cortical effect but only the facilitatory one, and this could account for the increased presynaptic inhibition of this projection at the onset of movement.

However, it must be pointed out that the relative contribution of Ia and Ib afferents to propriospinal-like excitation is unknown (Gracies *et al.* 1991). If there was a significant excitatory contribution from Ib afferents, the present results (presynaptic inhibition decreased on monosynaptic Ia projections to motoneurones but increased on muscle afferents to propriospinal-like neurones during movement) would be quite consistent with results obtained in the cat after cortical stimulation: presynaptic inhibition is then decreased on Ia afferents (Lundberg & Vyklický, 1963) but increased on Ib terminals (Carpenter, Lundberg & Norrsell, 1963).

Functional significance

As already discussed (Meunier & Pierrot-Deseilligny, 1989) the decrease in presynaptic inhibition of monosynaptic Ia projections to motoneurones would increase the gain of the stretch reflex at the onset of movement, and this could be functionally important: at that moment, the load is not yet precisely known, and a high gain would allow the stretch reflex to contribute to rapid compensation for deviations from the expected load.

During voluntary contraction propriospinal-like neurones receive descending excitation (see above), presumably part of the descending command to motoneurones

(J. M. Gracies, D. Mazevet, S. Meunier & E. Pierrot-Deseilligny, unpublished). It is probable that the voluntary contractions studied in the present experiments do not require excitatory feedback from muscles. Under these conditions the gating of this input would allow descending impulses easier access to propriospinal-like neurones in order to maximize the transmission of the descending command. It is possible that during the course of less-stereotyped movements, requiring more feedback from muscle, the muscular input might be less gated.

It has been suggested that the major role of the peripheral feedback would be to inhibit the descending command at the level of propriospinal neurones, thus contributing to an appropriately timed termination of the movement (Alstermark, Lundberg & Sasaki, 1984). The present experiments were not designed to evaluate the gating of afferents mediating inhibition of propriospinal-like neurones. However, it has been shown (Nielsen & Pierrot-Deseilligny, 1991) that, during one-motor-unit contractions, cutaneous afferents can depress propriospinal-like excitation during contraction quite efficiently. This suggests that the gating of peripheral inhibitory feedback is not major during such contractions.

The authors wish to express their gratitude to Dr B. Alstermark and Professor A. Lundberg for reading and commenting upon the manuscript. Our thanks are also due to Annie Rigaudie and Michèle Dodo for excellent technical assistance. This work was supported by grants from the Pierre and Marie Curie University (Paris VI), from INSERM (89 60 12) and from IRME.

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