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# PATTERN OF PROPRIOSPINAL-LIKE EXCITATION TO DIFFERENT SPECIES OF HUMAN UPPER LIMB MOTONEURONES

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SUMMARY

1. The pattern of distribution of non-monosynaptic (propriospinal-like) excitation to various motor nuclei (deltoid, extensors and flexors of the elbow, the wrist and the fingers) was investigated.

2. Changes in the firing probability of individual voluntarily activated motor units were studied following conditioning stimuli. Conditioning volleys were evoked by weak electrical stimuli applied to various mixed nerves (circumflex, musculocutaneous, median, radial, ulnar) and to the skin.

3. In all investigated nuclei stimulation of the 'homonymous' nerve evoked a peak of increased firing probability with a latency which was 2–7 ms longer than the monosynaptic Ia latency. The average central delay of the late excitation, measured from monosynaptic latency, seems to depend only on the segmental level of the motor nucleus: the more caudal the nucleus the longer the latency. This strongly suggests a transmission through neurones located above the cervical enlargement, as are C3–C4 propriospinal neurones in the cat.

4. Both group I muscle and cutaneous afferents were shown to contribute to propriospinal-like excitation. It is argued that a spatial facilitation of the effects evoked by these two inputs might explain why the threshold of late excitation is always below that of the monosynaptic Ia excitation in motoneurones.

5. The pattern of distribution of propriospinal-like excitation was diffuse: stimulation of each mixed nerve was able to evoke excitation in all investigated motor nuclei. Similarly, stimulation of a given skin field could produce excitation of biceps and wrist flexor and extensor units.

6. Each motor nucleus therefore receives excitation from a multimodal and wide range peripheral input. However, it is argued that what appears as a diffuse pattern might simply reflect connections which are not used in each movement but appropriately selected by higher centres.

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## INTRODUCTION

In man stimulation of low-threshold afferents in the median and ulnar nerves has recently been shown to evoke non-monosynaptic excitation of wrist flexor motoneurones (Malmgren & Pierrot-Deseilligny, 1988*a*), and neurones mediating it seem to receive a descending facilitation at the onset of voluntary movement (Baldissera & Pierrot-Deseilligny, 1989). Parallels have been drawn (Malmgren & Pierrot-Deseilligny, 1988*a*) with a system of C3–C4 propriospinal neurones in the cat (for references see Lundberg, 1979) which mediates the descending command for target-reaching (Alstermark, Lundberg, Norrsell & Sybirska, 1981). Accordingly, the neurones mediating the excitation are strongly inhibited by low-threshold cutaneous afferents from the upper limb (Malmgren & Pierrot-Deseilligny, 1988*b*: Nielsen & Pierrot-Deseilligny, 1991), as are C3–C4 propriospinal neurones by cutaneous afferents from the forelimb in the cat.

Electrophysiological analysis has revealed that, in the cat, all investigated forelimb motor nuclei receive monosynaptic excitation from C3–C4 propriospinal neurones (Alstermark & Sasaki, 1986). The present study was therefore undertaken to investigate whether propriospinal-like excitation could also be found in motoneurones supplying various shoulder, elbow, wrist and finger muscles in man, and, if so, what was the pattern of this excitation. The latter point is of particular interest since, in the cat, peripheral excitation of C3–C4 propriospinal neurones has only been sought from the radial nerve (Illert, Lundberg, Padel & Tanaka, 1978), and the pattern of distribution of propriospinal excitation has not been established.

## METHODS

The experiments were carried out in seven healthy subjects (including the four authors), aged 26–55 years, all of whom gave informed consent to the experimental procedure which was approved by the local ethical committee. They were comfortably seated in an armchair. The elbow was semi-flexed (100–120 deg) and the forearm was supported by the arm of the chair.

Post-stimulus time histograms (PSTHs) of a voluntarily activated motor unit were constructed for the period following a conditioning stimulation. This process extracts from the naturally occurring spike train only those changes in firing probability which are time-locked to the stimulus (Stephens, Usherwood & Garnett, 1976).

A detailed description of the particular method with the PSTH technique used in this study is given elsewhere (Fournier, Meunier, Pierrot-Deseilligny & Shindo, 1986), so it will be only summarized here. PSTHs of motor units from various upper limb muscles (see below) were constructed for the 10–50 ms following a conditioning stimulation (bin width 1 ms). The contraction strength was below 5% of maximal voluntary power. The motor units studied were therefore all in the low-threshold range. The electromyogram (EMG) was recorded by surface electrodes placed over the corresponding muscle belly. After a few training sessions it proved possible for all subjects, with the aid of visual and auditory feedback, to isolate one motor unit and to fire it at more or less ($\pm$10 ms) constant frequency (80–160 ms intervals). The EMG potentials of single motor units were converted into standard pulses by a discriminator with variable trigger levels and were used to trigger first a computer and then the stimulator delivering the conditioning stimulation.

Motor units were recorded from various muscles: deltoid, biceps brachii, triceps brachii, flexor carpi radialis and flexor carpi ulnaris, extensor carpi radialis, flexor digitorum superficialis and extensor digitorum. Because the forearm muscles are close to each other it was carefully checked that motor units were selectively activated by the movement corresponding to the function of a

given muscle, e.g. motor units of the flexor carpi radialis have to be activated by a slight wrist flexion combined with radial deviation, and not by a pure finger flexion nor by a pure pronation; inversely, it was checked that motor units of the flexor digitorum superficialis activated during finger flexion remained activated during associated wrist extension, and vice versa for units of the extensor digitorum.

Conditioning stimuli were 1 ms duration electrical pulses delivered at a mean rate of 0·7/s through bipolar surface electrodes (1·5 $cm^2$ silver electrodes placed 2 cm apart). The median nerve was stimulated in the cubital fossa a few centimetres above elbow level. The radial nerve was stimulated at two points: at the upper part of the arm to involve the triceps brachii branches, and a few centimetres below the elbow so that the stimulation did not involve the brachio-radialis muscle branch. The ulnar nerve was stimulated at the ulnar groove. The musculo-cutaneous nerve was stimulated 10–15 cm above elbow level on the anterior and medial aspect of the arm. The circumflex nerve was stimulated at Erb's point: it was always possible to find a position of the stimulation electrode where the deltoid was the muscle activated with the lowest threshold. In each case the site of stimulation was chosen such that increasing the stimulation strength above motor threshold resulted in a steep increase in the motor response of the corresponding muscle. The current delivered by constant current stimulators was measured by a current probe (Tektronix, 6021) and the stimulus intensity was expressed in multiples of the threshold intensity of the motor wave ($\times$ motor threshold, $\times$ MT). The stimulation was always subthreshold for the compound H reflex.

The cutaneous sensation (locally light and/or weak paraesthesiae irradiating along the nerve to the fingers) evoked by mixed nerve stimulation was mimicked by pure cutaneous stimuli. The local sensation was reproduced by electrodes (plates or clips pinching the skin) placed 3–5 cm more laterally (or more medially) than the nerve trajectory. The stimulus intensity was adjusted to evoke the same sensation as that produced by the mixed nerve stimulus, and it was checked that at that intensity muscular afferents contained in the muscle beneath the skin were not activated (the current passage was always below 0·2 $\times$ MT). To mimic the irradiating paraesthesiae plate electrodes were placed over the nerve projection area on the skin of the fingers (after accounting for the extra peripheral conduction time). Here, also, the stimulus intensity was adjusted to imitate the sensation evoked by mixed nerve stimulation.

When a conditioning stimulus causes a monosynaptic discharge in the recorded motor unit, the subsequent refractoriness prevents any polysynaptic excitatory postsynaptic potential (EPSP) from firing it. For the purpose of this study it was therefore necessary to hinder the monosynaptic discharge. This was achieved both by reducing the stimulus intensity and by applying the stimulation at an optimal delay (*D*) with respect to the previous motoneurone discharge, when the resulting after-hyperpolarization would reduce the probability of firing due to the monosynaptic EPSP evoked by the stimulation, but would have less effect on any polysynaptic EPSPs since they would occur later when the after-hyperpolarization had decayed further.

Stimulation at a fixed interval after the previous discharge implies that the probability of discharge in the PSTH depends not only on the postsynaptic potentials evoked by the stimulation but also on the motoneurone membrane trajectory during the interspike interval. To take account of the latter a histogram was constructed in a control situation without stimulation. Thus, in the control situation the 'spontaneous' firing (shaded columns in Figs 1–4) often increased with time intervals (Fig. 1*G* and *O*, Fig. 3*C*), reflecting the post-spike trajectory of the motoneurone membrane potential (see Fournier *et al.* 1986). Sometimes, however, the after-hyperpolarization had completely waned at the time of the stimulation-evoked postsynaptic potentials and the spontaneous firing was level (Figs 1*K* and 2*G*). The control and different conditioned situations were randomly alternated (same number of triggers) within a sequence. The PSTHs obtained after nerve or skin stimulation (open columns on the left of each pair in Figs 1–4) were compared to the background firing probability. To clarify the differences between the results obtained in the two situations, the control value in each 1 ms bin was subtracted from that obtained after stimulation to give the open columns on the right of each pair.

The statistical analysis of changes in firing probability was confined to the first 10 ms after the onset of monosynaptic Ia excitation to avoid contamination by the long-latency M2 response (see Marsden, Rothwell & Day, 1983; Matthews, 1984). Within each 1 ms bin a $\chi^2$ test was used to determine the extent to which the distribution of firing probability after stimulation differed from that in the control situation. This was also examined for groups of consecutive bins

exhibiting an increase in firing probability. Such an analysis was only performed after having checked that a change in the firing probability within the window of analysis of the control sequence was not responsible for the differences seen between the two situations (control and after stimulation). A non-monosynaptic peak was accepted if there was a significant increase in firing probability in two or more adjacent bins within this 10 ms period occurring at a longer latency than that of the monosynaptic peak. The latency of the first bin of the increased firing probability was taken to be the latency of the non-monosynaptic excitation provided that the onset was abrupt, as was usually the case (see Figs 1–4), and that the probability was significantly increased in the first group of 2–3 bins (probability was often significantly increased even in the first bin by itself: Figs 1*H*, *L*, *P* and 2*H*, *L*). The duration of the non-monosynaptic excitation was measured as the interval between the first and last bin of an uninterrupted sequence of increased firing probability, and the statistical significance of the peak was measured over the whole duration.

## RESULTS

### *EPSPs evoked in homonymous pathways*

Changes in the firing probability of motor units following stimulation of the nerve containing the afferents from the explored muscle (referred to as the 'homonymous' nerve in the following) are illustrated in Figs 1 and 2. Stimulation of the 'homonymous' nerve at motor threshold (1 × MT) evoked an early increase in firing probability (upper row of each subset). In the examples shown in Figs 1 and 2, the latency of this peak (before correction for the trigger delay) was 11 ms (deltoid, Fig. 1*A–B*) 20 ms (biceps, Fig. 1*E–F*; flexor carpi ulnaris, Fig. 1*I–J*; flexor digitorum superficialis, Fig. 1*M–N*; triceps, Fig. 2*A–B*; extensor digitorum, Fig. 2*E–F*) and 28 ms (extensor carpi radialis, Fig. 2*I–J*). Data concerning the flexor carpi radialis are not illustrated here (see Malmgren & Pierrot-Deseilligny, 1988*a*). After correction for the trigger delay, the actual latency of the early peak was identical to that of the corresponding H reflex either evoked at rest (flexor and extensor carpi radialis) or revealed by an averaging technique (Nicolet 370) during sustained voluntary contraction. This early peak can therefore be attributed to the monosynaptic Ia EPSP (Mao, Ashby, Wang & McCrea, 1984).

When the stimulus intensity was reduced to 0·4–0·6 × MT the monosynaptic peak disappeared more or less completely whereas a second peak appeared, as shown in the lower row of each subset. This peak was statistically significant (at least $P < 0·05$) and often highly significant ($P < 0·001$; Figs 1*G–H*, *K–L*, *O–P* and 2*K–L*). In the examples illustrated in Figs 1 and 2 the latencies of the second peak were 2 (Fig. 1*C–D*), 3 (Fig. 1*G–H*), 4 (Fig. 2*K–L*), 5 (Figs 1*K–L* and 2*C–D*) and 6 (Figs 1*O–P* and 2*G–H*) ms longer than that of the corresponding monosynaptic peak. Whatever the afferents responsible for this late increase in firing probability (see Discussion), its threshold was regularly lower than that of the monosynaptic homonymous Ia excitation. This indicates that these afferents do not have a smaller diameter, and thus a slower conduction velocity, than Ia afferents. Under these conditions the longer latency of the late excitation cannot be attributed to a longer peripheral conduction time, but reflects the central delay of this effect. Hence, in each homonymous pathway, the latency difference between the late and monosynaptic peaks represents the central delay of the late excitation. Table 1 shows that the *average* central delay found in each motor nucleus seems to depend only on its segmental level: 3·5 and 3·68 ms for the biceps and deltoid located in C5–C6; 4·24, 4·20 and 4·24 ms for the flexor carpi radialis, extensor carpi radialis and extensor digitorum located in C6–C7–C8; 4·54 and 4·61 ms for the flexor carpi ulnaris and

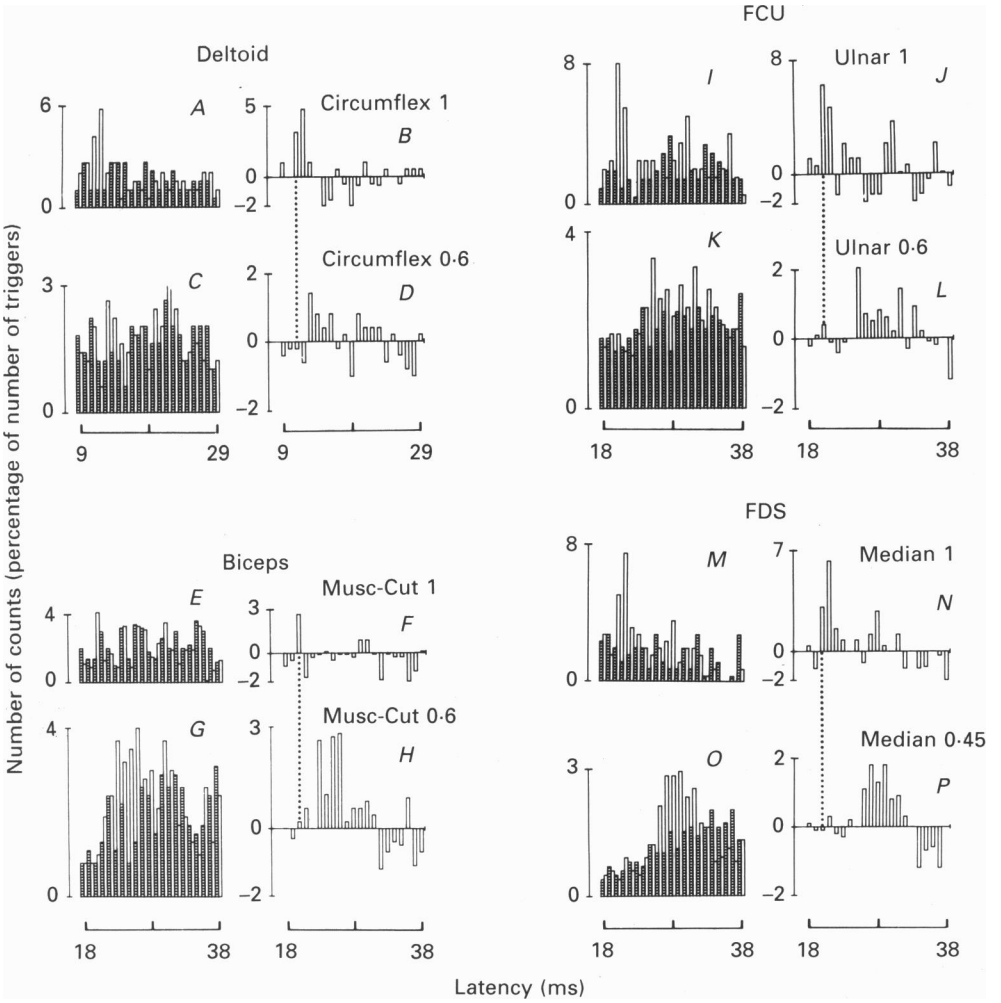


Fig. 1. Mono- and non-monosynaptic excitation in motor units from various muscles after stimulation of the 'homonymous' nerve. Time histograms of the discharge of voluntarily activated motor units in control conditions (shaded columns) and in response to stimulation (open columns), and differences between these two histograms (open columns on the right in each pair). The number of counts, expressed as a percentage of the number of triggers (*A–B* 200, *C–H* 500, *I–J* 200, *K–L* 1000, *M–N* 250, *O–P* 1500), is plotted against the latency from the stimulation. The vertical dotted line in each subset indicates the monosynaptic latency. *A–D*, response of a deltoid unit to stimulation of the circumflex nerve (*A–B* 1 × MT, *C–D* 0·6 × MT). *E–H*, response of a biceps unit to stimulation of the musculo-cutaneous (Musc-Cut) nerve (*E–F* 1 × MT, *G–H* 0·6 × MT). *I–L*, response of a flexor carpi ulnaris (FCU) unit to stimulation of the ulnar nerve (*I–J* 1 × MT, *K–L* 0·6 × MT). *M–P*, response of a flexor digitorum superficialis (FDS) unit to stimulation of the median nerve (*M–N* 1 × MT, *O–P* 0·45 × MT).

flexor digitorum superficialis located in C7–C8–Th1 and 4·66 ms for the triceps which is located in (C6)–C7–C8–Th1 (Kendall, Kendall & Wadsworth, 1971). This will be considered further in the Discussion.

The frequency of occurrence of the homonymous late excitation was about the

same (59–68 % of the motor units tested) in five out of the eight muscles tested, but significantly lower in the flexor carpi ulnaris and extensor digitorum and higher in the flexor digitorum superficialis.

*EPSPs evoked in heteronymous pathways*

The latency of the late excitation can also be directly compared to that of the monosynaptic Ia excitation in those heteronymous pathways where Ia fibres have

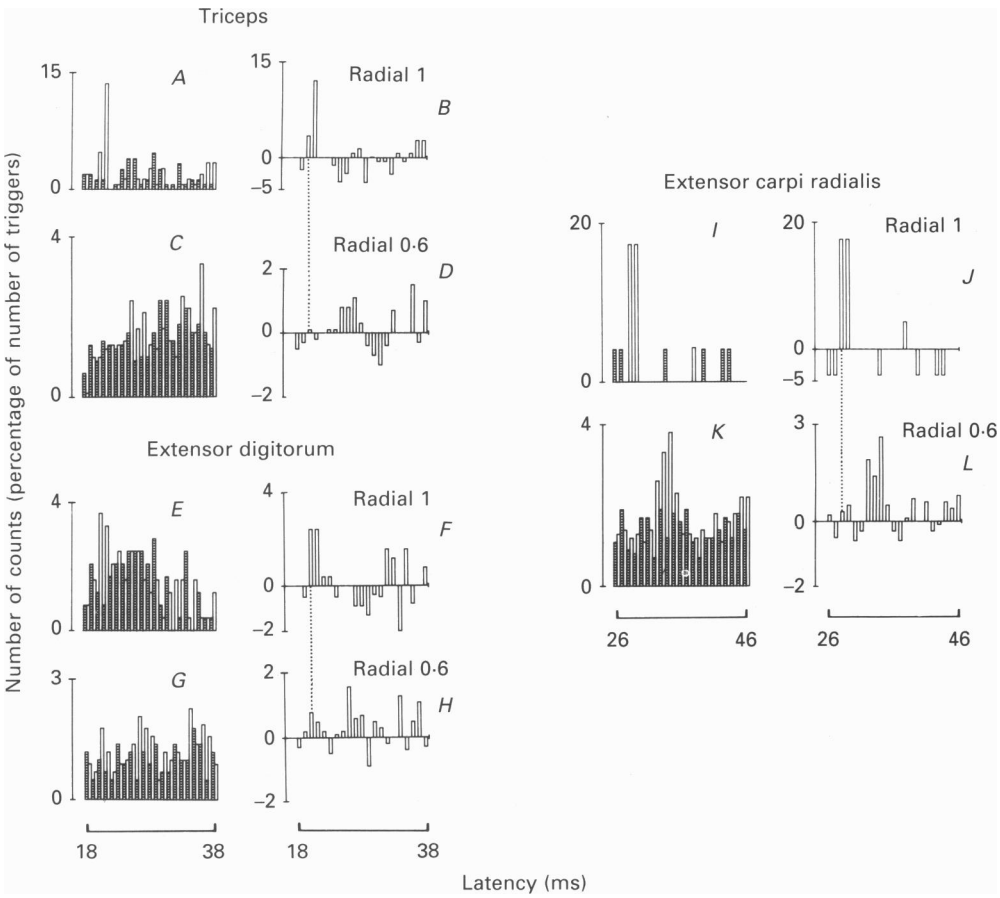


Fig. 2. Mono- and non-monosynaptic excitation in extensor motor units. Left and right in each pair, abscissa and ordinate, same legend as in Fig. 1. Responses of a triceps (*A–D*), an extensor digitorum (*E–H*) and an extensor carpi radialis (*I–L*) unit after stimulation of the radial nerve at 1 × MT (*A–B*, *E–F*, *I–J*) and 0·6 × MT (*C–D*, *G–H*, *K–L*). The radial nerve was stimulated either at the upper part of the arm (*A–D*) or a few centimetres below the elbow (*E–L*). The vertical dotted line in each subset indicates the monosynaptic latency. Number of triggers: *A–B* 150, *C–D* 750, *E–F* 250, *G–H* 550, *I–J* 50, *K–L* 450.

monosynaptic projections onto motoneurones, as previously described for Ia fibres contained in the median nerve onto flexor carpi ulnaris (Malmgren & Pierrot-Deseilligny, 1988*a*) and biceps (Cavallari & Katz, 1989) motoneurones. In the experiments illustrated in Fig. 3 the median nerve stimulus intensity was adjusted

to evoke both monosynaptic and late excitations in heteronymous (biceps, *A–B*; flexor carpi ulnaris, *E–F*) and homonymous (flexor carpi radialis, *C–D*; flexor digitorum superficialis *G–H*) motoneurones. The central delay, i.e. the difference between late and monosynaptic latencies, was calculated in homonymous and heteronymous (fifteen biceps, fifty-three flexor carpi ulnaris) pathways. Average

TABLE 1. Non-monosynaptic excitation in 'homonymous' pathways

| Motor unit | Segmental level | Homonymous nerve | Non-monosynaptic excitation | Average central delay (ms) |
|---|---|---|---|---|
| Deltoid | C5–C6 | Circumflex | 6/10 (60%) | 3·5±0·5 |
| Biceps | C5–C6 | Musculo-cutaneous | 16/27 (59%) | 3·68±0·29 |
| Flexor carpi radialis | C6–C7–C8 | Median | 33/50 (66%) | 4·24±0·22 |
| Extensor carpi radialis | C6–C7–C8 | Radial | 15/22 (68%) | 4·20±0·33 |
| Extensor digitorum | C6–C7–C8 | Radial | 7/22 (32%) | 4·24±0·37 |
| Triceps | (C6)–C7–C8–Th1 | Radial | 6/9 (66%) | 4·66±0·31 |
| Flexor carpi ulnaris | C7–C8–Th1 | Ulnar | 26/66 (39%) | 4·54±0·21 |
| Flexor digitorum superficialis | C7–C8–Th1 | Median | 21/25 (84%) | 4·61±0·28 |

Explored muscles are listed from top to bottom. Second column, segmental location of the motor nucleus (Kendall *et al.* 1971). Third column, 'homonymous' nerve. Fourth column, frequency of occurrence of the non-monosynaptic excitation with the number of units where it was statistically significant (numerator), the number of explored units (divisor) and the former as a percentage of the latter (in parentheses). Last column, average central delay of the 'homonymous' non-monosynaptic excitation (±S.E.M.), i.e. the difference between non-monosynaptic and monosynaptic latencies.

values on the right of Fig. 3, all obtained with median nerve volleys, confirm that the more caudal the motoneurone pool the longer the central delay.

The central delay of the late excitation cannot be measured with precision in those heteronymous pathways where there are no monosynaptic Ia connections. An estimate of the central delay can, however, be obtained by comparing the latency of the effects elicited by heteronymous stimulation to the homonymous monosynaptic latency after correction for the difference in the afferent conduction times of the homonymous and heteronymous Ia volleys. Afferent conduction times of Ia volleys can be estimated from both the length of the afferent pathway and the conduction velocity of Ia fibres. Conduction velocity of Ia afferents in the ulnar (Malmgren & Pierrot-Deseilligny, 1988*b*) and the radial (Cavallari & Katz, 1989) has been shown to be identical to that in the median nerve. In all subjects conduction velocity of Ia fibres in the median and musculo-cutaneous nerves was measured using the method proposed by Hultborn, Meunier, Morin & Pierrot-Deseilligny (1987): it was calculated from the latency of the monosynaptic peaks evoked in the same unit by stimulation of the homonymous nerve at two sites. As already mentioned (Cavallari & Katz, 1989) the conduction velocity of Ia fibres in the musculo-cutaneous nerve (46–60 m/s) was slower than that in the median nerve (60–70 m/s). Heteronymous stimulations were then timed so that the afferent conduction time of the heteronymous Ia volleys was the same as that of the homonymous one.

For technical reasons (inability to find two stimulation sites sufficiently far apart) it was

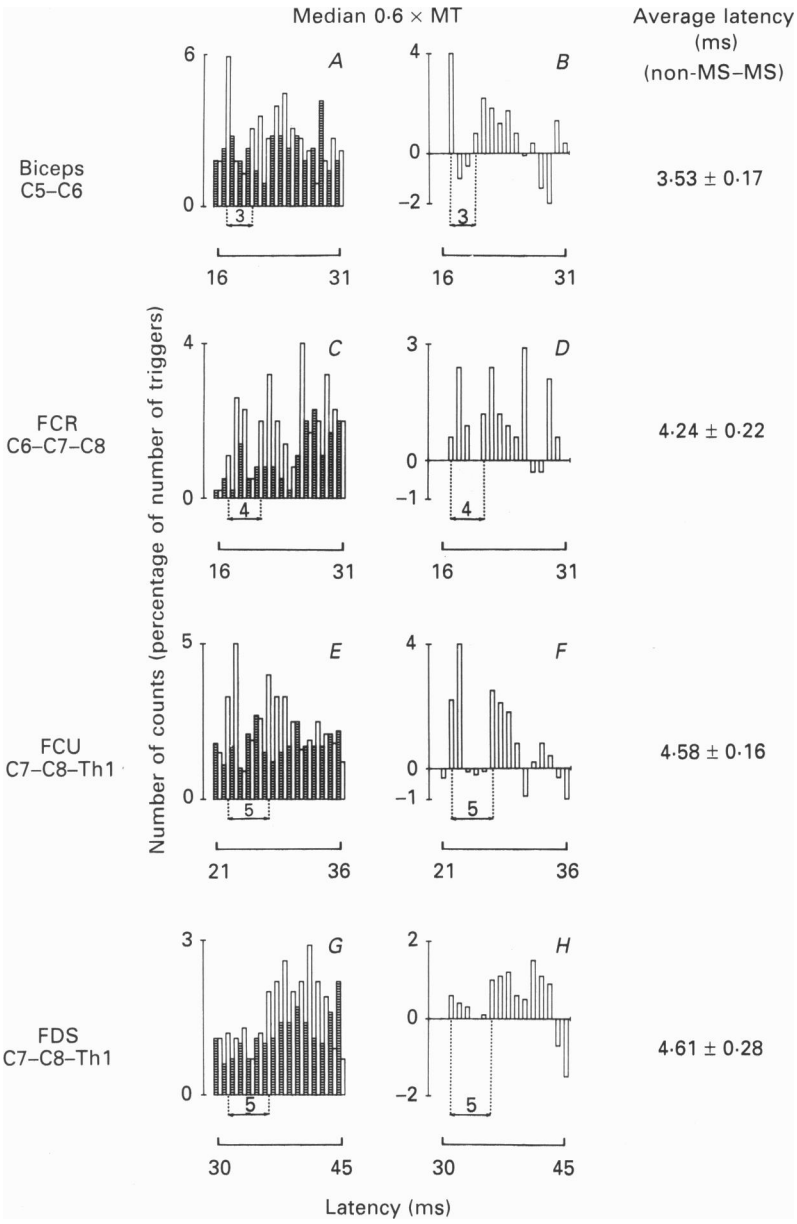


Fig. 3. Mono- and non-monosynaptic excitation evoked in a biceps (*A–B*), a flexor carpi radialis (FCR; *C–D*), a flexor carpi ulnaris (FCU; *E–F*) and a flexor digitorum superficialis (FDS; *G–H*) unit by median nerve stimulation (0·6 × MT). Left and right histograms, abscissa and ordinate same legend as in Fig. 1. Vertical dotted lines show the onset of the mono- and non-monosynaptic excitations and the difference between the latencies of the mono- and non-monosynaptic peaks is indicated. The segmental location of the explored motor nuclei is indicated on the left and the average central latency of the non-monosynaptic excitation (measured from the monosynaptic latency, non-MS − MS) is on the right. Number of triggers: *A–B* 200, *C–D* 350, *E–F* 700, *G–H* 900.

impossible to measure the conduction velocity of the Ia fibres from the triceps and deltoid muscles. The central delay of the heteronymous effects to these motor nuclei therefore could not be estimated and they were not retained for further analysis. However, musculo-cutaneous nerve stimulation at 1 × MT evoked an early peak in deltoid units, the latency of which was compatible with a monosynaptic excitation. Reducing the stimulus intensity made this early peak disappear and a later peak appeared in four out of the fourteen units so explored.

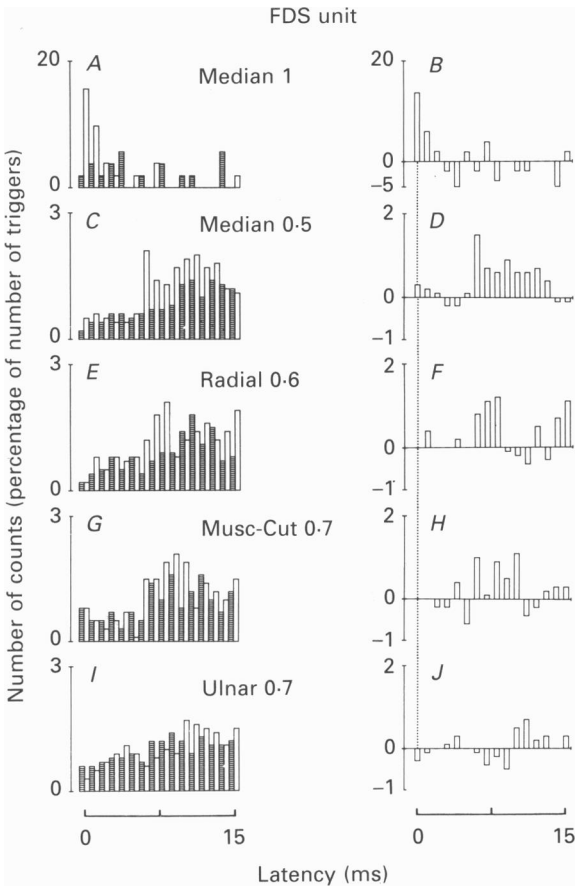


Fig. 4. Changes in firing probability evoked in the same flexor digitorum superficialis (FDS) unit by stimulation of various nerves: median (1 × MT, *A–B* and 0·5 × MT, *C–D*), radial (0·6 × MT, *E–F*), musculo-cutaneous (Musc-Cut; 0·7 × MT, *G–H*) and ulnar (0·7 × MT, *I–J*). Left and right, ordinate as in Fig. 1. Abscissa, latency measured from the monosynaptic latency (indicated by the vertical dotted line below the monosynaptic peak evoked by median nerve stimulation at 1 × MT). Number of triggers: *A–B* 50, *C–D* 1150, *E–F* 700, *G–H* 550, *I–J* 1300.

Most often a given motor unit received late excitation from different nerves. This is exemplified in Fig. 4 (a flexor digitorum superficialis unit), where the zero of the abscissa corresponds to the latency of the monosynaptic peak evoked by stimulation of the median nerve at 1 × MT (*A–B*). Stimulation of the median nerve at 0·5 × MT (*C–D*) evoked a highly significant ($P < 0·001$) late excitation at the 6 ms latency. Stimulation of the radial (*E–F*) nerve evoked a significant ($P < 0·01$) excitation at

the same latency, when allowance was made for the difference in peripheral afferent times. Stimulation of the musculo-cutaneous nerve (*G–H*) also induced a significant ($P < 0.05$) late excitation, whereas, ulnar nerve stimulation did not modify significantly the firing probability of the unit.

The pattern of distribution of homonymous and heteronymous late excitations is summarized in Table 2 which shows the frequency of occurrence of excitation in

TABLE 2. Frequency of occurrence of non-monosynaptic excitation

| | | Nerve | | | | |
|---|---|---|---|---|---|---|
| | Motor unit | Musculo-cutaneous | Median | Radial | Ulnar | 'Sum' |
| Elbow | Biceps | 16/27 (59%) | 26/35 (74%) | 3/17 (18%) | 4/12 (33%) | 54% |
| Wrist | FCR | 18/21 (86%) | 33/50 (66%) | 9/14 (63%) | 4/15 (27%) | 65% |
| | FCU | 14/19 (74%) | 65/94 (69%) | 5/18 (28%) | 26/66 (39%) | 56% |
| | ECR | 13/23 (56%) | 4/18 (22%) | 15/22 (68%) | 5/16 (31%) | 47% |
| Fingers | FDS | 7/16 (44%) | 21/25 (84%) | 10/17 (59%) | 8/15 (53%) | 63% |
| | ED | 8/23 (35%) | 7/25 (28%) | 7/22 (32%) | 2/15 (13%) | 28% |

The motor nuclei are listed from top to bottom: biceps, flexor carpi radialis (FCR), flexor carpi ulnaris (FCU), extensor carpi radialis (ECR), flexor digitorum superficialis (FDS), extensor digitorum (ED). The stimulated nerves are listed from left to right. In each case the number of units where there was a statistically non-monosynaptic excitation (numerator), the number of explored units (divisor), and the former as a percentage of the latter (in parentheses) are given. Last column, sum of the non-monosynaptic excitations evoked in a given motor nucleus by the different nerves as a percentage of the number of units explored.

motor units from six muscles (biceps, wrist and finger flexors and extensors) after stimulation of four nerves (musculo-cutaneous, median, radial and ulnar). In most cases the different nerve stimulations (0·5–0·7 × MT), or two or three of them, were randomly alternated within the same sequence so that it was valid to compare the results. The number of units in which a significant ($P < 0.05$ at least) late excitation was evoked and the number of units tested (raw values, and the former as a percentage of the latter) are indicated for each nerve–nucleus combination. It must be pointed out that in each combination there was a good correlation between the frequency of the excitation and its statistical significance for individual units (presumably reflecting the size of the propriospinal-like EPSP in those motoneurones). For example, in the flexor carpi ulnaris both the frequency of the excitation and the proportion of highly significant ($P < 0.01$ and 0·001) increases in firing probability were much higher after median (69 and 60%) than after ulnar (39 and 33%) nerve stimulation. Similarly, in the flexor digitorum superficialis the more frequent occurrence of the excitation after median (84%) than after musculo-cutaneous (44%) nerve stimulation was accompanied by a much larger proportion of highly significant excitation (76 *versus* 17%).

Several points concerning the distribution of the non-monosynaptic excitation deserve to be noted: (1) late excitation was found in all nerve–motor nucleus combinations. (2) The homonymous nerve was often not the most efficient in eliciting non-monosynaptic excitation, e.g. excitation of biceps units was more often found after median than after musculo-cutaneous nerve stimulation; similarly, the

musculo-cutaneous nerve was the most efficient in evoking excitation of wrist flexor units. (3) The frequency of the excitation was less when stimulating the nerve supplying the antagonists of the nucleus tested (e.g. the median nerve in the case of extensor carpi radialis units). This frequency was, however, probably underestimated since an early inhibition (probably reciprocal Ia inhibition) often prevented the excitation from manifesting itself. (4) Whatever the motor nucleus (except the flexor digitorum superficialis), the efficiency of the ulnar nerve in eliciting excitation was poor. (5) The sum of the effects evoked by median, radial, ulnar, and musculo-cutaneous nerve stimulation in each nucleus (last column in Table 2) shows that the frequency of excitation was higher in wrist and finger flexors than in wrist and finger extensors.

This smaller frequency of excitation in wrist and finger extensors was not due to a smaller number of trials. Indeed, the number of recordings in extensor digitorum units was larger than in finger flexor units and the number of triggers was on average the same for the extensors as for the flexors.

*Afferents responsible for the non-monosynaptic excitation*

Nerves stimulated here contain both muscle and cutaneous afferents (and the skin beneath the electrodes was usually stimulated). An attempt was made to estimate the relative contribution of these two kinds of afferents to the late excitation.

It was sometimes possible (particularly when stimulating the musculo-cutaneous nerve) to find a position of the electrodes such that the threshold for activation of muscle afferents (0·5–0·6 × MT) was significantly lower than that of cutaneous afferents. Thus, in the extensor carpi radialis unit illustrated in Fig. 5*A* the musculo-cutaneous nerve stimulation evoked an excitation while the stimulus intensity (0·6 × MT) was 0·7 × perception threshold (PT) for any cutaneous sensation. According to Burke, Mackenzie, Skuse & Lethlean (1975), it is unlikely that such a stimulation activates any cutaneous afferents. Similar results were obtained in three wrist flexor units while stimulating the musculo-cutaneous nerve below the PT, confirming that muscle afferents are able to evoke the late excitation.

The contribution of cutaneous afferents to the late excitation was also investigated. To this end, the effects of mixed nerve stimulation were compared to those of pure cutaneous stimulation (see Methods). With the weak intensities of stimulation used, the musculo-cutaneous (usually), the ulnar (sometimes) and the median (rarely) nerve stimulations only produced a local sensation. This sensation was mimicked by placing two electrodes on the skin of the anterior (upper part, musculo-cutaneous; lower part, median) or the posterior (lower part, ulnar) aspect of the arm. Effects of a mixed nerve stimulation (eighteen musculo-cutaneous, five ulnar, three median) evoking a late excitation were compared to those of an equivalent local cutaneous stimulation in twenty-six units (eight biceps, ten flexor carpi radialis, seven flexor carpi ulnaris, one extensor carpi radialis). In nine cases (35%) the pure cutaneous stimulation did not evoke any significant excitation. In ten other units it produced an excitation which was weaker and/or occurred later than that evoked by the mixed nerve stimulation (Fig. 5*C–D*; see also Malmgren & Pierrot-Deseilligny, 1988*a*). In five units the cutaneous-induced excitation had both the same latency and the same size as that evoked by the mixed nerve stimulation. In two biceps units the

excitation was even larger after cutaneous stimulation (Fig. 5*E–F*). Thus, in 25% of the cases, the efficiency of such cutaneous stimulations in eliciting excitation was equal or superior to that of mixed nerve stimulation. Finally, Fig. 5*A–B* (an extensor carpi radialis unit) shows that a pure cutaneous stimulation (Fig. 5*B*) could be as

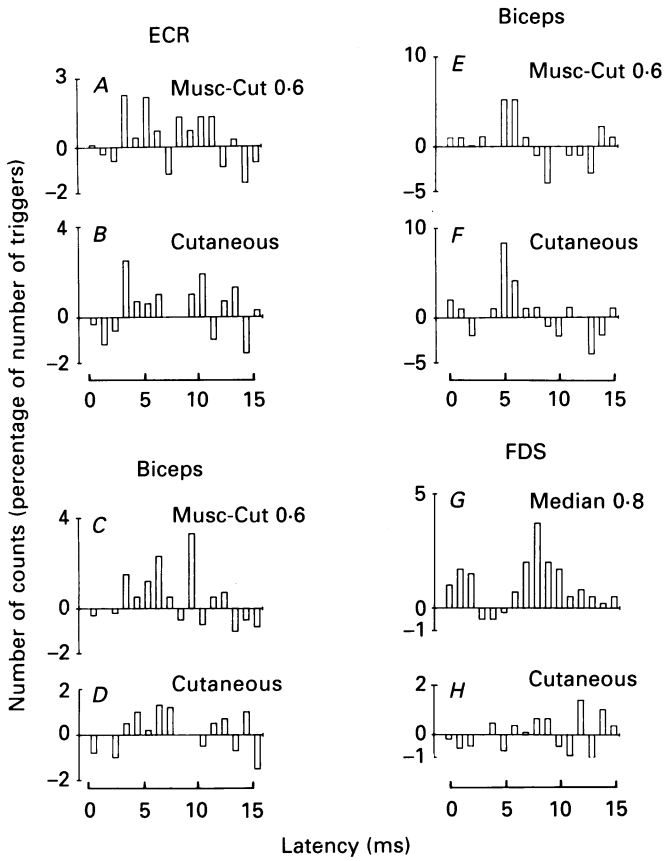


Fig. 5. Relative contribution of group I and cutaneous afferents to non-monosynaptic excitation. Time histograms of the discharge of one extensor carpi radialis (ECR; *A–B*), two biceps (*C–D* and *E–F*) and one flexor digitorum superficialis (FDS; *G–H*) units were obtained in the control situation and after stimulation, and each column represents the difference between these two histograms (like the columns on the right in Figs 1–4). *A–B*, the effects of a musculo-cutaneous (Musc-Cut) nerve stimulation below the threshold for any cutaneous sensation (*A*) and those of a weak stimulation of the skin of the arm (*B*) are compared. *C–F*, the effects of a musculo-cutaneous stimulation (0·6 × MT; *C* and *E*) and those of a pure cutaneous stimulation mimicking the local sensation evoked by the mixed nerve stimulation (*D* and *F*) are compared. *G–H*, the effects of a median nerve stimulation (0·8 × MT) evoking both mono- and non-monosynaptic excitations (*G*) and those of a cutaneous stimulation mimicking the median nerve-induced paraesthesia to the fingers (*H*) are compared. Number of triggers: *A–B* 250, *C–D* 600, *E–F* 100, *G–H* 400.

efficient as a pure group I stimulation (Fig. 5*A*) in eliciting non-monosynaptic excitation.

Mixed nerve stimulation also often evoked weak paraesthesiae irradiating along the nerve to the fingers (at least when using relatively high stimulus intensities:

0·6–0·7 × MT). Cutaneous stimuli applied to the palmar or the dorsal side of the fingers were used to reproduce the irradiating paraesthesiae evoked by stimulation of the median, ulnar and radial nerves (see Methods). Effects of mixed nerve and cutaneous stimulations were compared in sixty-one units (nine biceps, ten flexor carpi radialis, twenty-four flexor carpi ulnaris, nine extensor carpi radialis, nine flexor digitorum superficialis) in which nerve stimulation evoked a significant non-monosynaptic excitation. As exemplified in Fig. 5*G–H* (a flexor digitorum superficialis unit), in most cases (fifty-one units, 84 %) cutaneous stimulation did not induce any significant increase in firing probability at the latency of the mixed nerve-induced late excitation. Cutaneous stimulation evoked a significant ($P < 0·05$) increase in firing probability only in ten units (16 %) distributed in the different muscles. This effect was always weaker than that induced by mixed nerve stimulation and in seven cases it occurred later (2–5 ms, after allowance for the extra peripheral conduction time). In seven out of these ten units the excitation observed on combined stimulation (cutaneous + mixed nerve stimulation) was clearly smaller than that evoked by separate cutaneous stimulation. Thus, cutaneous-induced excitation, as that evoked by mixed nerve stimulation (Malmgren & Pierrot-Deseilligny, 1988*b*), is depressed when the afferent input is increased.

There was no particular pattern of cutaneous excitation since biceps, wrist flexor and extensor units could receive excitation from the palmar as well as from the dorsal side of the fingers, or from the skin of the anterior aspect of the arm.

## DISCUSSION

### *Further evidence for a propriospinal-like excitation*

As shown in Figs 1 and 2 stimulation of low-threshold afferents in different nerves of the human upper limb evokes a late excitation of homonymous motoneurones in all explored motor nuclei. This excitation occurs with a latency 2–7 ms longer than that of the homonymous monosynaptic peak, and, as seen above, this longer latency cannot be attributed to a longer peripheral conduction time, but reflects the central delay of this effect.

It has already been argued (Malmgren & Pierrot-Deseilligny, 1988*a*) that a shift of several milliseconds in latency cannot be ascribed to a decrease (due to the low intensities used) in the monosynaptic Ia EPSP since, in the cat, decreasing the size of the EPSP only delays the corresponding increase in firing probability by a maximum of 0·35 ms (Fetz & Gustafsson, 1983). In addition, experimental evidence that the monosynaptic Ia EPSP is not responsible for the late excitation is presented here since it was observed in all heteronymous pathways (Table 2), despite the absence of monosynaptic Ia connections in most of them. This confirms that the late excitation is interneuronally mediated.

Differences in the average central delay of the homonymous non-monosynaptic excitation seem to be related to the segmental level of the motor nuclei (Table 1). However, other factors could play a role: (1) the after-hyperpolarization following the previous spike, which, if marked, would prevent the motoneurone from firing at an earlier delay; in fact, the same proportions of recordings with (Fig. 1*K–L*) and without (Fig. 1*G–H*) wane of the after-hyperpolarization were found while exploring the different motor nuclei. (2) The strength of the 'homonymous' afferent input,

which, if weak, would require temporal summation at the interneuronal level with the consequent lengthening of the latency of the excitation; however, the average values of the central delay of the excitation evoked in flexor carpi ulnaris units by stimulation of the ulnar (weak input) and median (strong input) nerves were almost identical (4·55 and 4·58 ms). Thus, the location of the motor nucleus appears to be the relevant factor: the more caudal the nucleus location the longer the central delay. This relation suggests that the excitation is mediated through a system of neurones located above the cervical enlargement, and reinforces the view that this system could be similar to the C3–C4 propriospinal system in the cat (for references, see Lundberg, 1979). Accordingly, in the following this excitation is denoted propriospinal-like excitation.

### *Pattern of propriospinal-like excitation*

*Afferent input*

In the cat, stimulation of both cutaneous and group I afferents may evoke EPSPs in C3–C4 propriospinal neurones. It is shown here that a pure stimulation of either muscle (Fig. 5*A*) or cutaneous (Fig. 5*B*) afferents is able to evoke the late excitation.

With the low stimulus intensities used here (0·5–0·6 × MT), it is very probable that group I fibres were the only muscle afferents activated. If there is the same overlap for thresholds and conduction velocities for Ia and Ib afferents in the human upper limb as in the cat forelimb (Rosén & Sjölund, 1973), it is impossible from the present results to know the receptor origin of the afferents responsible for the propriospinal-like excitation. However, in the case of the flexor carpi radialis a contribution from Ia afferents has been demonstrated while conditioning the H reflex of this muscle by very weak tendon taps (Malmgren & Pierrot-Deseilligny, 1988*a*).

The finding that the cutaneous-induced excitation has a latency longer than the monosynaptic latency cannot be attributed to a slower conduction velocity of cutaneous afferents, since conduction velocities of Ia and cutaneous fibres are of the same order of magnitude in the human upper limb (Buchthal & Rosenfalk, 1966; Nielsen & Pierrot-Deseilligny, 1991). In those experiments where cutaneous- and group I-induced propriospinal-like excitations have the same latency (Fig. 5*A–B*) a similar central delay appears therefore to be likely. The question then arises whether the two excitations are mediated through the same spinal pathway. The finding that the transmission of these two kinds of excitation is similarly depressed by another peripheral volley suggests a transmission through similar neurones. In addition, it is shown in the companion paper (Nielsen & Pierrot-Deseilligny, 1991) that cutaneous stimulation of the side of the hand which does not evoke cutaneous inhibition may increase the mixed nerve-induced excitation. This might be due to a convergence of cutaneous and mixed nerve afferents onto common propriospinal-like neurones (Nielsen & Pierrot-Deseilligny, 1991).

In the cat, convergence from group I muscle afferents in the deep radial nerve and from cutaneous afferents in the superficial radial nerve onto propriospinal neurones has not been found (Illert *et al.* 1978). However, it is shown in the companion paper (Nielsen & Pierrot-Deseilligny, 1991) that in man the radial nerve-induced excitation is specifically depressed by a cutaneous stimulation applied to the dorsal side of the hand (i.e. the cutaneous field supplied by the superficial radial nerve). If there is the same pattern of cutaneous inhibition in the cat, the resulting inhibition of propriospinal neurones could prevent spatial facilitation between excitatory effects due to deep and superficial radial nerves from manifesting itself.

Cutaneous-induced excitation is generally weaker and occurs later than that evoked by stimulation of the corresponding mixed nerve. This could be taken to entail that the cutaneous input to propriospinal-like neurones is weaker than the group I input. In fact, in the rare cases where it was possible to compare the effects of a pure cutaneous and a pure muscular input, the excitation of the motoneurone was similar (Fig. 5*A–B*). If one admits that cutaneous and group I muscle afferents converge onto common propriospinal-like neurones (see above), an alternative explanation would be that the earlier and more significant excitation evoked by mixed nerve stimulation is due to a spatial facilitation of the effects produced by the two inputs. Such a convergence might also explain why in 'homonymous' pathways the threshold of the propriospinal-like excitation is regularly below that of the monosynaptic Ia excitation in motoneurones, a finding which has been considered surprising (Fetz, 1989).

To explain this very low threshold it was previously argued (Malmgren & Pierrot-Deseilligny, 1988*a*) that the Ia fibres activated by weak median nerve stimuli could be heteronymous and lack monosynaptic projections onto wrist flexor motoneurones, whilst projecting onto propriospinal-like neurones. Given the large number of muscles supplied by the median nerve, this appeared plausible, and the efficiency of heteronymous afferents in eliciting non-monosynaptic excitation is largely confirmed here (see Table 2). However, it is more difficult for this explanation to account for the musculo-cutaneous nerve-induced excitation of biceps units, since the musculo-cutaneous nerve only supplies two muscles, the biceps and the brachialis.

*Pattern of distribution*

The differences in the frequency of occurrence of the non-monosynaptic excitation between motor nuclei found here can have several causes: (1) the organization of the propriospinal-like projections onto various species of motoneurones. (2) The organization of the afferent input from different nerves to different subsets of propriospinal-like neurones. (3) The fact that excitation observed at the motoneuronal level is likely to be the net result of a mixture of excitation and inhibition evoked in propriospinal-like neurones by the same upper limb afferents (Malmgren & Pierrot-Deseilligny, 1988*b*).

In the cat, the strength of the excitatory projections from C3–C4 propriospinal neurones onto various species of forelimb motoneurones has been investigated while applying an antidromic volley to the ascending collaterals of the axons of propriospinal neurones (Alstermark & Sasaki, 1986), which allows a selective stimulation of the whole pool of C3–C4 propriospinal neurones. The data so obtained in the cat have been compared to the 'global' results observed in human experiments, i.e. the sum of the excitations evoked in each motor nucleus by the different nerves (last column in Table 2). Despite obvious differences between cat experiments (motoneuronal EPSPs only depend on the projections from propriospinal neurones) and human experiments (non-monosynaptic excitation depends on the three factors listed above), some common features were observed: (1) propriospinal (cat) and propriospinal-like (man) excitations are observed in all investigated motor nuclei. (2) In wrist and finger (digit) motor nuclei the excitation is significantly stronger in physiological flexors. This suggests that, when considering the differences in the sum of excitations evoked by the four nerves between motor nuclei, the relevant factor could be the organization of the projections from propriospinal-like neurones onto motoneurones.

The pattern of distribution of the propriospinally mediated excitation from different peripheral sources onto various nuclei has not been investigatd in the cat, probably because the peripheral excitatory input of propriospinal neurones is too weak (only a minority of these neurones receive excitatory projections from forelimb afferents, Illert *et al.* 1978). If these connections are equally weak in mean, the non-monosynaptic excitation of motoneurones found here could be due to a descending facilitation of propriospinal-like neurones during the one motor unit contraction required by the PSTH method.

It was a striking finding that there was a wide range input and a diffuse pattern of distribution of the excitation: each nerve was able to evoke propriospinal-like excitation at least in some motor units of all investigated motor nuclei. It could be argued that the effects evoked in different motor nuclei when stimulating a nerve supplying many muscles (like the median nerve) are due to stimulation of afferents from different muscles (having different functions). However, the same diffuse distribution of the excitation was found when stimulating the musculo-cutaneous nerve, which supplies only two muscles having the same function. Similarly, stimulation of a limited skin field evoked a diffuse excitation, which contrasts with the very specific pattern of cutaneous inhibition (Nielsen & Pierrot-Deseilligny, 1991).

The wide range input and diffuse distribution of excitation would imply that the afferent activity resulting from any muscle contraction raises the excitability of propriospinal-like neurones projecting onto every motor nucleus. This might seem purposeful if, as with the C3–C4 propriospinal system in the cat (Alstermark *et al.* 1981), the propriospinal-like system governs multi-joint target-reaching movements (i.e. movements involving many motor nuclei). Yet this does not mean that all the connections described here are necessarily operative in all movements, and the seemingly diffuse pattern of excitation could be partly the product of the method used. During voluntary contraction, propriospinal-like neurones projecting onto motoneurones activated in the contraction receive a descending excitation (Baldissera & Pierrot-Deseilligny, 1989). Thus, with this method, transmission through the whole population of propriospinal-like neurones projecting onto the motor unit explored may be facilitated, with the consequent disclosure of an excitation from various peripheral nerves. However, this population is not homogeneous and consists of subsets of neurones having different peripheral input (see Nielsen & Pierrot-Deseilligny, 1991), and higher centres might select them according to the requirements of each movement.

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