J. Physiol. (1987), **386**, *pp.* 311–331
With 12 text-figures
Printed in Great Britain

INTEGRATIVE PROCESSING OF VIBRATORY INFORMATION IN CAT DORSAL COLUMN NUCLEI NEURONES DRIVEN BY IDENTIFIED SENSORY FIBRES

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(*Received 25 March 1986*)

SUMMARY

1. In decerebrate or anaesthetized cats, the vibration-induced responses of dorsal column nuclei neurones were examined, first, when their input came from simultaneously recorded pairs or other combinations of identified Pacinian corpuscle (P.c.) afferent fibres of the interosseous nerve, and secondly, when different convergent sets of P.c. fibres were engaged by footpad vibration.

2. Suprathreshold actions were observed on individual dorsal column nuclei neurones from two or more identified P.c. fibres. Recruitment of these convergent fibres usually led to summation in the dorsal column nuclei neurone as reflected in higher response levels compared with those evoked by single-fibre inputs.

3. When the input was increased from one to two or more identified P.c. fibres the dorsal column nuclei neurones could retain a single, dominant phase of response to high-frequency (> 100 Hz) vibration even though these fibres, in isolation, evoked responses in the target neurone at substantially different latencies. However, on average, phase locking was significantly tighter in response to single-fibre input than to multiple P.c.-fibre input.

4. Dorsal column nuclei neurones were also able to retain phase-locked responses to high-frequency vibration when phase differences between different convergent inputs were systematically introduced to alter the degree of synchrony in the activity arriving over convergent, identified P.c. fibres.

5. When the input to dorsal column nuclei neurones came from the skin it was found that with the recruitment of two converging sets of P.c. fibres the dorsal column nuclei neurones were able to retain phase-locked responses to high-frequency vibration even when phase shifts were introduced between the two sets of P.c. inputs.

6. In conclusion, the observed integrative processing by dorsal column nuclei neurones of vibration-induced inputs arriving over identified, convergent P.c. fibres, or sets of P.c. fibres, is consistent with our hypothesis that the retention of phase-locked responses to vibration at frequencies $\geqslant 100$ Hz may reflect the functional domination of the target neurone by just one or a few of its convergent input fibres.

INTRODUCTION

Within the dorsal column nuclei of the cat there is a prominent representation of inputs from vibration-sensitive receptors in the skin (Perl, Whitlock & Gentry, 1962; Gordon & Jukes, 1964; Bystrzycka, Nail & Rowe, 1977; Douglas, Ferrington & Rowe, 1978; Ferrington & Rowe, 1982; Connor, Ferrington & Rowe, 1984; Ferrington, Horniblow & Rowe, 1987*a*). The dorsal column nuclei neurones that respond to vibration applied to the footpads form two major classes: one most sensitive to high frequencies (> 100 Hz) and deriving its input from Pacinian corpuscle (P.c.) receptors, the other most sensitive at 10–60 Hz and appearing to derive its input from Krause corpuscles and their associated r.a. class of sensory fibres (Bystrzycka *et al.* 1977; Douglas *et al.* 1978; Ferrington & Rowe, 1982; Connor *et al.* 1984; Ferrington *et al.* 1987*a*). The pathway through the dorsal column nuclei probably represents the major signalling system for information about cutaneous vibration from the distal glabrous skin of the limbs as other somatosensory pathways, the spinocervical and spinothalamic systems, receive little or no input from P.c. and r.a. fibres (Brown & Franz, 1969; Willis, Maunz, Foreman & Coulter, 1975).

One way in which information about vibration frequency may be represented in the responses of dorsal column nuclei neurones is in an impulse pattern code with the responses phase locked so that the pattern replicates the periodicity of the vibration. Such phase locking is found in dorsal column nuclei neurones up to 400–500 Hz but its presence is puzzling as the P.c. input fibres show considerable dispersion from fibre to fibre in the preferred phase of their responses at frequencies of $\geqslant$ 100 Hz (Douglas *et al.* 1978; Greenstein, Kavanagh & Rowe, 1987; Ferrington *et al.* 1987*a*).

One mechanism that would allow phase locking of responses to vibration would be for each central neurone to receive and process input from only a single P.c. fibre. However, there is much evidence for convergence upon dorsal column nuclei neurones (Perl *et al.* 1962; Gordon & Jukes, 1964; Anderson, Eccles, Oshima & Schmidt, 1964; Winter, 1965; Pubols & Warren, 1985; Ferrington *et al.* 1987*a*) and it is unlikely that the neurones involved in processing P.c. inputs represent an exception in this respect (see Discussion). We therefore suggested in earlier papers that the phase-locked responses to vibration at frequencies of $\geqslant$ 100 Hz may reflect the functional domination of the central neurone by just one or a few of its convergent P.c. input fibres (Greenstein *et al.* 1987; Ferrington *et al.* 1987*a*; Ferrington, Rowe & Tarvin, 1987*b*). Our previous observation (Ferrington *et al.* 1987*b*), that individual P.c. fibres exert powerful synaptic actions on their central target neurones appears consistent with this hypothesis.

In the present study we have investigated the hypothesis of functional domination of the central neurone by a single input fibre by examining the integrative processing of vibratory information by dorsal column nuclei neurones when their input is derived from identified, convergent sources of P.c. fibres. We have employed P.c. fibres of the interosseous nerve (Ferrington *et al.* 1987*b*) as it is possible to identify and monitor in the intact nerve the activity of each fibre recruited by vibration applied to the region of the interosseous membrane.

METHODS

Experiments involving interosseous P.c. inputs were carried out on cats from the earlier series (Ferrington *et al.* 1987*b*) and all procedures with the exception of those outlined below were described in that paper. Five additional experiments were performed in adult cats, to investigate whether convergent P.c. inputs carrying vibration information from the footpads are processed by dorsal column nuclei neurones in similar ways to those observed for identified interosseous P.c. inputs. In these experiments vibratory stimulation of the forelimb footpads was employed to activate cutaneous P.c. inputs to the cuneate division of the dorsal column nuclei. Apart from the procedures outlined below for reducing the spread of vibration in the distal limb the techniques for the study of footpad inputs were the same as those described earlier (Ferrington *et al.* 1987*a*).

Two mechanical stimulators, each fitted with 0·2 mm diameter probes, were used to activate separate P.c. fibres of the interosseous region. Vibration amplitude and frequency were controlled independently on each stimulator, but where frequency needed to be identical the two stimulators were driven by a common function-generator. This was essential in examining phase locking and temporal processing of convergent P.c. inputs because even small discrepancies in frequency between the two vibrators could, over a 1 s period of vibration, introduce significant shifts in the temporal relations of the spike activity coming over the two P.c. fibres. When the phase relations of the convergent inputs were systematically varied, the function-generator output was fed directly to one mechanical stimulator unit and to the second stimulator via a phase-delay unit that permitted precise phase differences to be introduced between the two vibration wave forms. It was then possible to determine whether the target neurone's capacity for phase-locked responses was affected by the introduced phase shifts in the convergent inputs and whether its phase of response was locked to one or other of those inputs.

Similar procedures were employed for studying the processing in dorsal column nuclei neurones of different sets of P.c. inputs from the footpad, in this case using two vibrators, fitted with 2 mm diameter probes, that were positioned on different foot- or toe-pads of the same limb. In these experiments it was necessary to establish that the two vibrators were recruiting separate sets of P.c. inputs that converged on the central neurone under study. In the intact limb there is considerable spread of high-frequency mechanical disturbances from the point of application on the footpads to adjacent digits. In order to minimize this spread of vibration, 4–5 mm segments of the distal or proximal phalangeal bone in each digit of the forelimb were surgically removed while preserving the neural and vascular supplies to the digit. Removal of this rigid, bony linkage appeared to substantially reduce the spread of vibration between the footpads.

Other procedures for recording, stimulation and analysis of phase locking are described in the earlier papers (Ferrington *et al.* 1987*a*, *b*). For comparisons of the tightness of phase locking, a factorial analysis of variance for unequally replicated data was employed (Searle, 1971; Walpole & Myers, 1972). This adaptation of the usual analysis of variance was necessary because some neurones were studied in more detail than others, on account of the normal difficulties associated with extended periods of recording from central neurones. The variance analysis enabled total variance in measures of phase locking to be compartmentalized into its different components. These included, first, a component related to the different groups being compared, for example, gracile neurones being driven by single P.c. fibres *versus* gracile neurones driven by multiple P.c. fibre inputs; secondly, a component related to vibration frequency; thirdly, a component related to interactions between the first and second components, and fourthly, the residual random variation contributing to the total variance in measures of phase locking.

RESULTS

Convergence of identified interosseous P.c. fibres on gracile neurones: effects on responsiveness

Recruitment of two identified P.c. fibres that converged on a gracile neurone usually produced an elevation in response (Fig. 1). P.c. fibre A, responding in a 1 : 1 pattern to 200 Hz vibration (Fig. 1*A*) elicited at the outset a pair of spikes in the target neurone but few subsequent spikes. Recruitment of a second fibre that

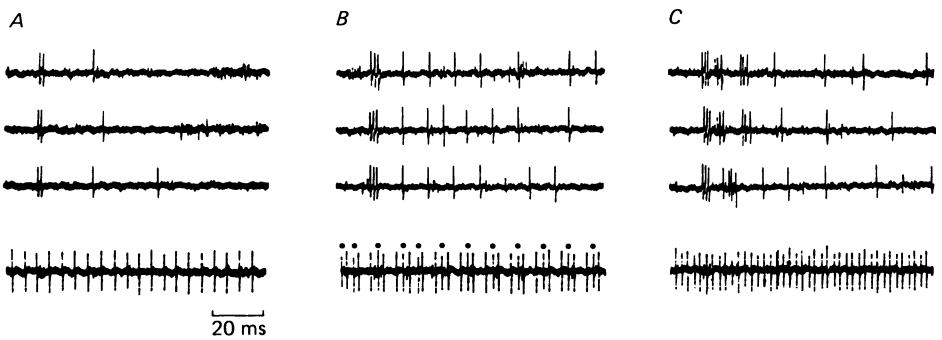

Fig. 1. Effect of recruitment of convergent P.c. fibres on responsiveness of a gracile target neurone. Each group of records shows three response traces for a gracile neurone (uppermost traces) and P.c. fibre responses (lowest trace). In *A* the input to the gracile neurone came from a single P.c. fibre responding at a 1 : 1 level to 200 Hz vibration. A substantial enhancement of response occurred in the gracile neurone with the recruitment of a second P.c. fibre (whose responses are indicated in *B* by the dots) that responded at a 0·5 : 1 level in *B*, but little further increase occurred when this fibre was activated at the higher, 1 : 1 level in *C*.

responded with a spike on approximately every second vibration cycle (a 0·5 : 1 level in fibre B, Fig. 1*B*) produced an elevated response in the neurone with little further increase when both fibres responded at a 1 : 1 level (Fig. 1*C*).

The enhanced response of the central neurone with recruitment of dual or multiple P.c.-fibre input was quantified by averaging the spike output for successive vibration cycles (Fig. 2*D*). In Fig. 2*A* and *B*, the first spike coming over P.c. fibre A or B, when each was activated in isolation, elicited a double-spike output from the gracile neurone on almost every occasion. However, the gracile neurone output, in response to subsequent spikes in the single-fibre spike trains, was lower for the fibre B input than for fibre A, in particular for the second, third and fourth cycles, where it appears (Fig. 2*D*) that the neurone underwent a period of inhibition or post-excitatory depression. When both P.c. fibres were recruited there was a response in the target neurone on most vibration cycles in the segment shown in Fig. 2*C* and *D*. Furthermore, even in the impulse-trace replicas of Fig. 2*C* it is apparent that the neurone's response occurs with a particular phase preference.

Effect of convergent input from identified P.c. fibres on phase locking in gracile neurone responses to vibration

The capacity of gracile neurones to retain phase-locked responses to vibration at $\geqslant$ 100 Hz in the face of convergence from identified pairs, triplets or multiple P.c. fibres was examined and quantified by constructing post-stimulus time histograms and cycle histograms from a series of successive responses. The upper post-stimulus time histograms in Fig. 3 were constructed from responses of a gracile neurone to 200 Hz vibration when the input came from a single P.c. fibre in *A*, a pair of fibres in *B* and from three fibres in *C*. In each case the fibres were responding at an approximately 1 : 1 level to the vibration. In the lower series in Fig. 3 the post-stimulus time histograms were constructed from the P.c. fibre responses recorded in

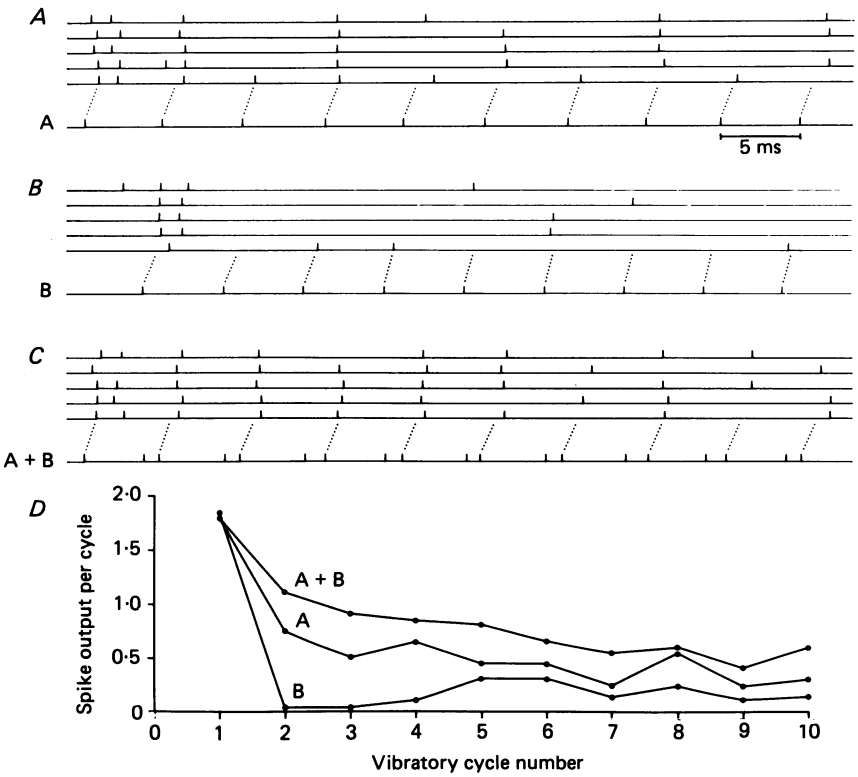

Fig. 2. Quantified estimates of the change in security and responsiveness in the linkage between P.c. fibres and their gracile target neurone with the recruitment of convergent P.c. fibres. Each set of impulse trace replicas in *A–C* shows five records of gracile neurone responses (upper five traces) to single P.c. fibres (lowest trace) responding at a 1 : 1 level to 200 Hz vibration (*A* and *B*) and to both fibres recruited simultaneously in *C*. The mean response of the gracile neurone to successive cycles of vibration was obtained from twenty traces of the kind shown in *A–C* and plotted in *D* for the first ten cycles of the vibration train. The graphs show that with simultaneous recruitment of the two fibres (A + B) there is, on each cycle after the first, an elevated level of response in comparison with that to fibre A or B alone. All the gracile neurone response traces have been displaced to the left by about 8 ms to align the P.c. fibre–gracile neurone responses more easily.

the interosseous nerve. In *A*, the lower histogram shows the very tight grouping of impulses in the responses of P.c. fibre A_1, with the separation of peaks reflecting the vibration cycle period of 5 ms. The gracile neurone's response to fibre A_1 was sporadic as seen in the upper histogram in *A*. When a second P.c. fibre was recruited (fibre A_2 in Fig. 3*B*), the primary-fibre histogram displayed two discrete peaks for each vibration cycle and the gracile neurone response increased markedly. In addition, however, the response peaks for the gracile neurone in the upper histogram in Fig. 3*B* are grouped at intervals corresponding to the vibration cycle period and are therefore tightly phase locked to the vibration.

With recruitment of a third P.c. fibre (fibre A_3 in Fig. 3*C*) there are no longer discrete peaks recognizable for the three primary fibres as the responses of fibre A_3 overlap those of fibres A_1 and A_2. Once again there is a marked elevation in the

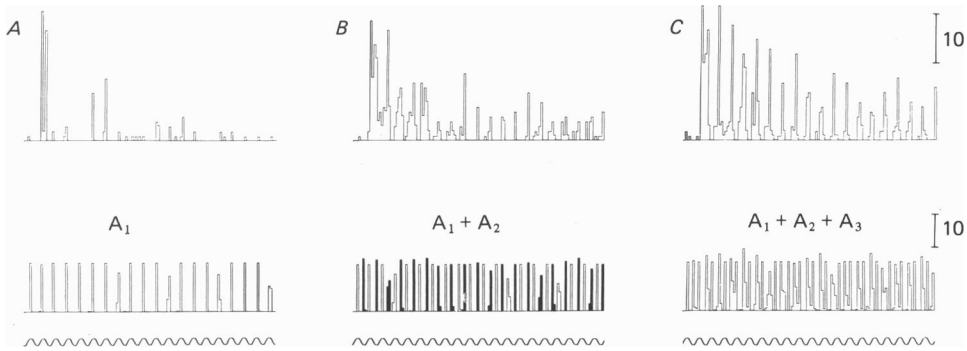

Fig. 3. Effect of recruitment of identified P.c. fibres on response level and phase locking in gracile neurone responses to vibration. The pairs of post-stimulus time histograms in *A–C* were constructed from successive responses of a gracile neurone (upper histograms) and from P.c. fibre activity recorded from the interosseous nerve (lower histograms). The analysis period covers the first 100 ms segment of the 200 Hz vibration train which is represented beneath the histograms to provide a time marker. In *A*, one P.c. fibre (A_1) was activated at a 1 : 1 response level. Recruitment of a second P.c. fibre (A_2 in *B*) and then a third (A_3 in *C*) led to marked increases in the response level in the gracile neurone. In *B* and *C* the separation of major peaks in the upper histograms by 5 ms demonstrates that the responses of the gracile neurone were well phase locked to the 200 Hz vibration. The vertical scale bars represent 10 impulse counts. In the lower histogram in *C*, fewer counts have been registered than should be the case for three fibres responding at a 1 : 1 level at 200 Hz. This is because the discriminator unit failed to resolve some of the superimposed or overlapping impulses recorded from the three fibres over the one recording channel.

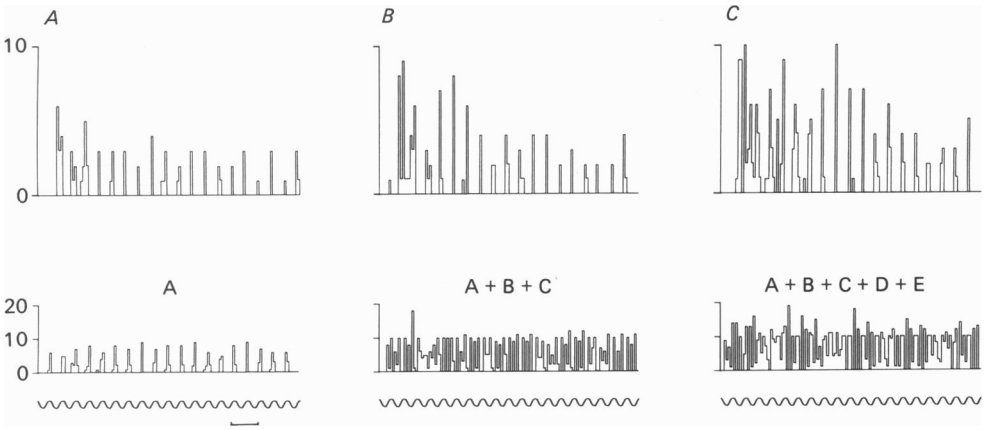

Fig. 4. Retention of phase-locked responses to vibration by a gracile neurone driven by multiple, identified P.c. fibres. The post-stimulus time histograms were constructed from ten successive responses of the gracile neurone (upper histograms) and the P.c. activity recorded from the interosseous nerve (lower histograms). The analysis time covers the first 100 ms segment of the 200 Hz vibration train which is represented beneath each set to provide a time marker. In *A* a single P.c. fibre was activated at an approximately 1 : 1 level of response and in *B* and *C*, three and five P.c. fibres, respectively, were recruited. The 5 ms separation of major peaks in the histograms for the gracile neurone demonstrates a tight phase locking of responses despite the lack of phase synchrony in the activity of the responses of the convergent P.c. fibres. The vertical scale refers to impulse counts accumulated in each column of the histograms.

response of the gracile neurone, as reflected in the greater height of the histogram columns, but, despite the lack of phase synchrony in the P.c. fibre responses, there was no apparent degradation in the tightness of phase locking as the gracile responses remained tightly grouped at intervals corresponding to the 5 ms cycle period.

This capacity to respond on a single preferred phase of the vibration wave form with the progressive recruitment of multiple P.c. fibre inputs is seen for a different gracile neurone in Fig. 4 where the central neurone's response is generated by only one P.c. fibre in *A*, three fibres in *B*, and five fibres in *C*. Fibre D, which was recruited before fibre E, elicited little or no increment in response over that evoked by fibres A, B and C (Fig. 4*B*). However, recruitment of fibre E caused a substantial further increase in response (Fig. 4*C*). Furthermore, despite the lack of phase synchrony in the responses of the five recruited P.c. fibres the target neurone's responses remained tightly phase locked to the vibration wave form (Fig. 4*C*).

Quantitative evaluation of phase locking

Changes in the tightness of phase locking and in the phase angle of response with the recruitment of convergent P.c. fibres were quantified for gracile responses by constructing cycle histograms (Talbot, Darian-Smith, Kornhuber & Mountcastle, 1968; Ferrington & Rowe, 1980*a*; Ferrington *et al.* 1987*a*, *b*).

The three sets of paired cycle histograms in Fig. 5*A–C* display the distribution of impulse activity in response to 200 Hz vibration for the P.c. input fibres (left-hand side) and for their gracile target neurone (right-hand side). With the input derived from a single fibre (Fig. 5*A*) the gracile responses were phase locked as indicated by the peak in the early segment of the histogram. The percentage entrainment value of 93 % represents the highest percentage of impulses that fall within any continuous half-cycle segment of the vibration cycle period. When two P.c. fibres were recruited (Fig. 5*B*) there was a marked shift in the dominant phase of response in the gracile neurone, but the phase locking remained tight with a percentage entrainment value of 84 %. The drop from over 90 % occurs because of a small subsidiary grouping whose peak is out of phase with the major peak in the response.

With the recruitment of a third P.c. fibre (Fig. 5*C*) the gracile neurone response level was elevated. However, the neurone retained a single dominant phase of response, at the same angle and with a percentage entrainment value of 89 %, despite the activation of three convergent P.c. fibres that displayed phase-discrepant responses to the vibration.

Temporal asynchrony between inputs from convergent P.c. fibres

When identified pairs or larger numbers of P.c. fibres were recruited it can be seen (Figs. 2–5) that even at the peripheral recording site in the interosseous nerve there are substantial differences between fibres in their phase of response, as found earlier for P.c. fibres arising in the footpads (Greenstein *et al.* 1987). This phase discrepancy is seen most clearly in the primary-fibre cycle histograms of Fig. 5*B* where the responses of fibres A and B are approximately 170 deg out of phase. It is most improbable that the known conduction-velocity variations in different P.c. fibres (Greenstein *et al.* 1987; Ferrington *et al.* 1987*a*) will compensate for these phase discrepancies observable at the periphery in a way that would ensure synchronous

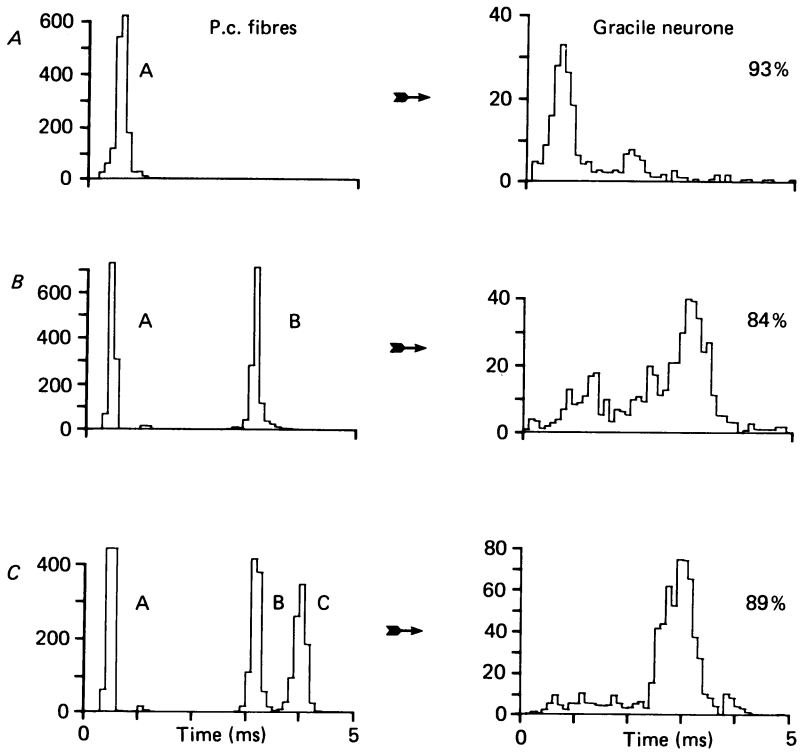

Fig. 5. Quantitative measures of the tightness of phase locking in the vibration-induced responses of a gracile neurone driven by a single P.c. fibre (*A*), a pair of P.c. fibres (*B*) and by three P.c. fibres (*C*). In each pair of cycle histograms in *A–C* the left-hand histogram was constructed from the responses of the P.c. fibre(s) and the right-hand histogram from the responses of the gracile neurone to the 200 Hz vibration. The percentage entrainment values indicated on the gracile neurone's histograms indicate the highest percentage of impulse occurrences falling within any continuous half-cycle of the vibration cycle period. The analysis period for the histograms corresponds to the vibration cycle period of 5 ms. The vertical scales refer to the number of accumulated impulse counts in each column of the cycle histograms. The three sets of histograms in *A–C* were constructed from responses to 1000–1600 cycles of vibration at 200 Hz. To prevent the fibre A peak in the primary-fibre histograms straddling the ends of the distribution these histograms were rotated. For illustrative purposes this adjustment was made so that the fibre A peak was positioned at the same point as its related gracile response peak in *A*. It is coincidence that the shift in gracile response phase going from *A* to *B* is approximately the same as the separation of the fibre A and fibre B peaks in the P.c.-fibre histogram in *B*.

arrival of activity centrally and therefore account for the tight phase locking observable in the gracile neurone responses (Figs. 2–5). Indeed, conduction velocity discrepancies are likely to exacerbate phase dispersion in the responses of incoming afferents. In fact, evidence for asynchronous actions of different converging fibres on a common target neurone comes from the discrepancies found in the response latencies of the neurone to different P.c. fibres. For example, in one neurone, the latencies of response to three identified converging fibres were 8·5, 9·5 and 11·3 ms from the time of occurrence of their recorded spikes in the interosseous nerve.

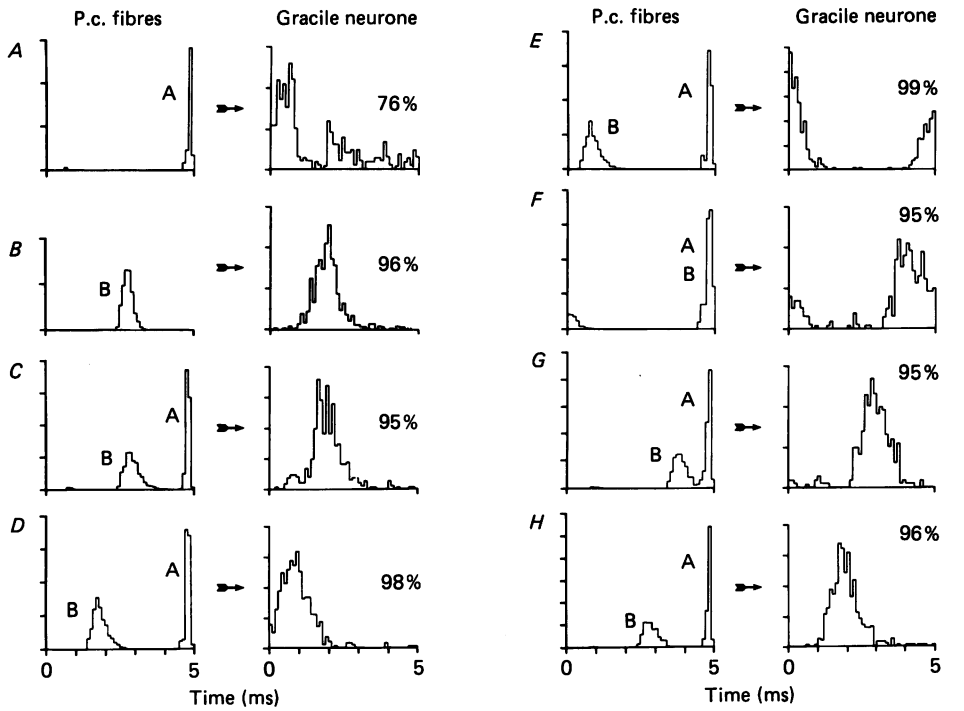

Fig. 6 Effects on phase locking of systematic changes in the phase relations of input activity coming over convergent P.c. fibre inputs. The pairs of cycle histograms in *A–H* show the distribution of impulse activity within the vibration cycle period for gracile neurone responses (right-hand histograms) and for the identified P.c. fibre(s) providing the input to the neurone (left-hand histograms). In *A* and *B* the gracile neurone was driven by single P.c. fibres, A and B, each responding to the 200 Hz vibration with an approximately 1 : 1 level of activity. In *C–H* the two P.c. fibres were recruited simultaneously using two separate vibrators, and the phase relations between their responses systematically varied by 1 ms (or 72 deg) steps as reflected in the progressive change in the separation of their response distributions in the left-hand histograms. In *F* their distributions coincide. In this histogram and in those for the gracile neurone in *E* and *F* the impulse counts on the left-hand end of this histogram are continuous with those on the right-hand end because 0 and 360 deg are coincident; that is, the cycle histogram distributions represent a circular distribution. The histograms were constructed from responses accumulated from up to 800 cycles of vibration at 200 Hz. The vertical scale divisions represent 100 impulse counts for the P.c. fibre histograms and 10 counts for the gracile neurone histograms.

Introduced phase shifts in the input activity of convergent P.c. fibres: effects on phase locking of gracile neurone responses

In order to vary systematically the degree of synchrony in the activity arriving over convergent P.c. fibres at the gracile nucleus we varied the response phase relations between pairs of P.c. fibres converging onto a common target neurone. This was done by activating each fibre of the pair with a different mechanical stimulator and varying the temporal relations between the two sets of impulse trains (see Figs. 6, 7 and 10). In Fig. 6 the cycle histograms on the right-hand side in *A* and *B* show the distribution of impulse activity and associated entrainment values for gracile

neurone responses to 200 Hz vibration when the neurone was driven singly by P.c. fibres A and B. The associated cycle histograms on the left-hand side display the distribution of activity recorded from each of these P.c. fibres which responded at an approximately 1 : 1 level. In response to fibre A the target neurone has a percentage entrainment value of 76 %. It has one major response phase at approximately 50 deg from the left-hand border of the plotted histogram in Fig. 6*A* and a smaller subsidiary peak approximately 120 deg away. The neurone's responses to fibre B occurred (Fig. 6*B*) in a tight unimodal distribution (percentage entrainment value, 96 %) at a phase angle of about 170 deg from the left-hand border of the histogram.

When both fibres, A and B, were activated by vibration trains delivered simultaneously and with an identical onset phase there were two peaks in the primary-fibre cycle histogram (Fig. 6*C*), reflecting the activity of the two P.c. fibres, but the responses of the target neurone remained grouped around a single, preferred segment of the vibration cycle with the percentage entrainment value (95 %) essentially unchanged from that seen in response to fibre B alone. Phase relations for the activity in the two P.c. fibres were varied systematically in Fig. 6*D–H* by delaying one vibration train in relation to the other by a series of five 1 ms steps which, at 200 Hz, represent a series of 72 deg phase shifts. In each case, from the 72 deg delay in *D* to the 360 deg, or one-cycle delay in *H*, the target neurone displayed a single peak in its response distribution and its tightness of phase locking remained remarkably constant with percentage entrainment values in the range 95–99 %.

For constructing the cycle histograms in Fig. 6 the timing pulse was, in all cases, associated with the vibration wave form used to activate P.c. fibre A. This is reflected in the fixed position of the fibre A response distribution near the right-hand border of the cycle histograms for the P.c. fibres. With both P.c. fibres activated (*C–H*) it can be seen that the phase of response of the gracile neurone shifted in a way that correlated with the timing of the fibre B response rather than that of fibre A. The changes for the gracile neurone in mean phase of response (in degrees) have been plotted in Fig. 7 in relation to the timing of the vibration stimulus for P.c. fibre A (continuous line) and fibre B (interrupted line). The two relations were plotted by setting the mean phase of response of the neurone to 0 deg when it responded to the two P.c. fibres (Fig. 6*C*) prior to introducing the progressive series of phase rotations (Fig. 6*D–H*). The relations in Fig. 7 demonstrate that the phase of response of the central neurone is dominated by fibre B.

Processing by dorsal column nuclei neurones of convergent P.c. fibre inputs from the footpads

By employing the interosseous nerve preparation it was possible to investigate the processing of vibration information by dorsal column nuclei neurones when their input came from *identified* single, paired, or multiple P.c. fibres. We were unable to achieve this for P.c. inputs from the footpads. However, additional experiments were performed to establish whether vibration-induced inputs from the footpads might be processed in dorsal column nuclei along the same lines we have observed for the identified P.c. fibre inputs from the interosseous nerve.

In these experiments, two sets of P.c. fibres, each with multiple, but indeterminate numbers of fibres, were engaged by footpad vibration and the effect of their con-

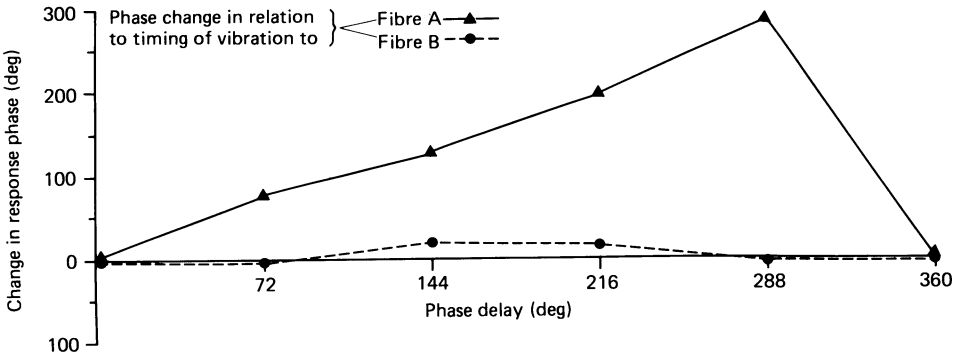

Fig. 7. Effect of varying the phase relations between inputs from two convergent P.c. fibres on the phase of response of a gracile neurone (data from Fig. 6). The mean phase of response of the gracile neurone to the convergent inputs from P.c. fibres A and B was set to 0 deg when the two fibres were activated by synchronous vibratory stimuli at 200 Hz (from Fig. 6*C*). Changes in mean response phase in the gracile neurone (based on cycle histogram data in Fig. 6*D–H*) have been plotted on the ordinate as the phase relations between fibre A and B inputs were systematically altered by 72 deg phase increments (abscissa). The phase of response in the gracile neurone is locked to fibre B.

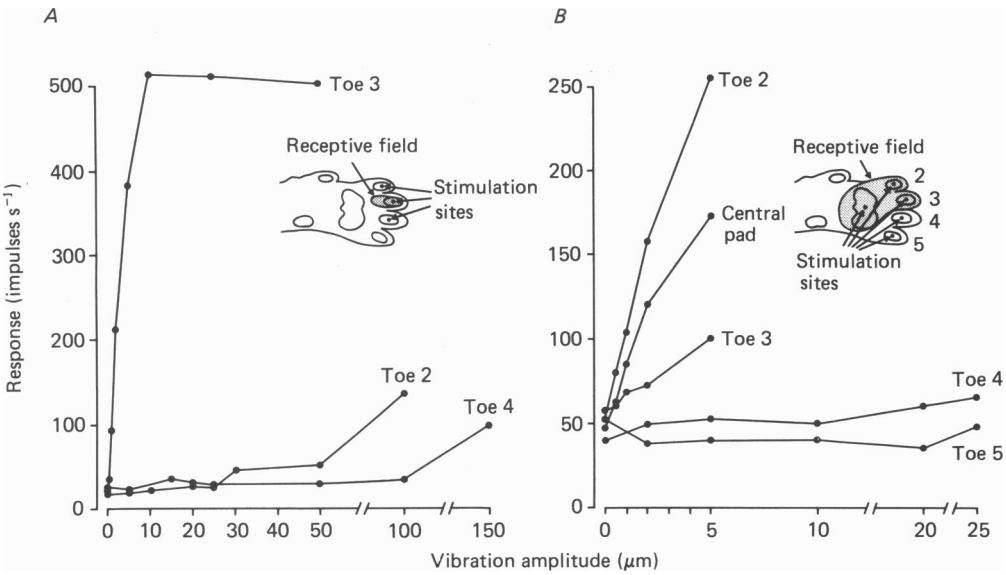

Fig. 8. Stimulus–response relations constructed from the responses to 300 Hz vibration for two neurones of dorsal column nuclei activated by P.c. inputs from the footpads. In *A*, the receptive field of the neurone was confined to the pad of toe 3 and an area immediately proximal to the pad. The neurone was unaffected by 300 Hz vibration applied to toes 2 and 4 at amplitudes of $\leqslant 50\ \mu$m peak-to-peak. In *B*, the neurone had a low threshold to vibration ($< 1{\cdot}0\ \mu$m) from the central pad and toes 2 and 3 but was unaffected by 300 Hz vibration delivered to toes 4 and 5 at amplitudes up to 25 μm. Each point in the stimulus–response relations represents the mean of five to ten responses to a 1 s train of vibration.

vergent input examined on phase locking in vibration-induced responses of dorsal column nuclei neurones, in this case within the cuneate division as the forelimb footpads were used. The aim was to determine whether the response phase in the central neurone was dominated by one source of the P.c. input. As a first stage of

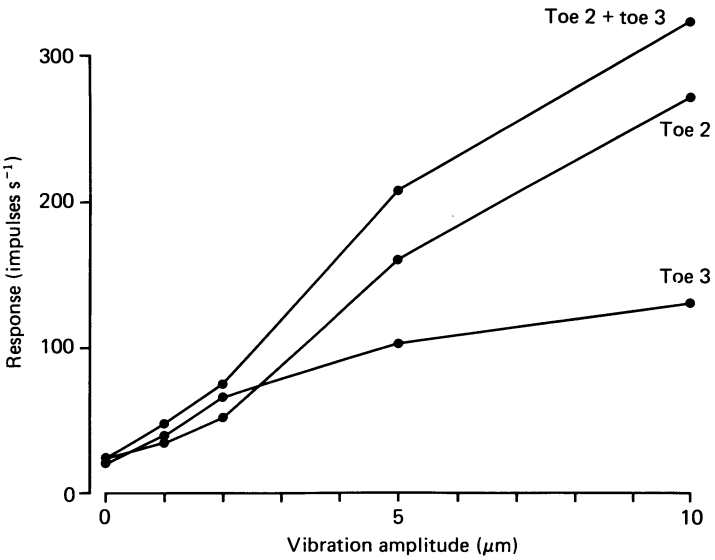

Fig. 9. The effect of recruitment of different sets of P.c. fibres from the footpads on the response of a central neurone of dorsal column nuclei. The three stimulus–response relations were constructed from the mean of five to ten responses to 1 s trains of vibration at 200 Hz when the input came separately from toe 2 or toe 3 and when these sites were stimulated simultaneously.

these experiments it was necessary to verify that convergence occurred from P.c. fibres of the footpads onto individual dorsal column nuclei neurones. Although conclusive evidence already exists for convergence of sensory fibres onto dorsal column nuclei neurones (Ferrington *et al.* 1987*a*) such evidence has not been established specifically for this class of input fibres from the footpads. In order to resolve this issue we made precise measurements of vibration thresholds at different points on the toes and central footpads after using procedures (see Methods) to minimize the spread of vibration from the point of application on the footpads to adjacent digits. Once this was carried out some P.c. neurones appeared to receive P.c. input from the region of only one digit (Fig. 8*A*) while for others there was evidence for convergence from more than one toe-pad (Fig. 8*B*).

For the dorsal column nuclei neurone whose stimulus–response relations are plotted in Fig. 8*A* vibration thresholds at 200 Hz were $< 0{\cdot}5$ μm from the pad of toe 3 but were $>$ 30–50 μm from the two adjacent toes. In Fig. 8*B*, for another neurone, vibration thresholds were $< 1{\cdot}0$ μm from the central pad and toes 2 and 3 but were > 25 μm from toes 4 and 5. We infer that dorsal column nuclei neurones with this latter pattern of vibration sensitivity received convergent P.c. inputs from two or more toe-pads, whereas those of the type shown in Fig. 8*A* did not, although they may receive convergent P.c. inputs from within the one toe.

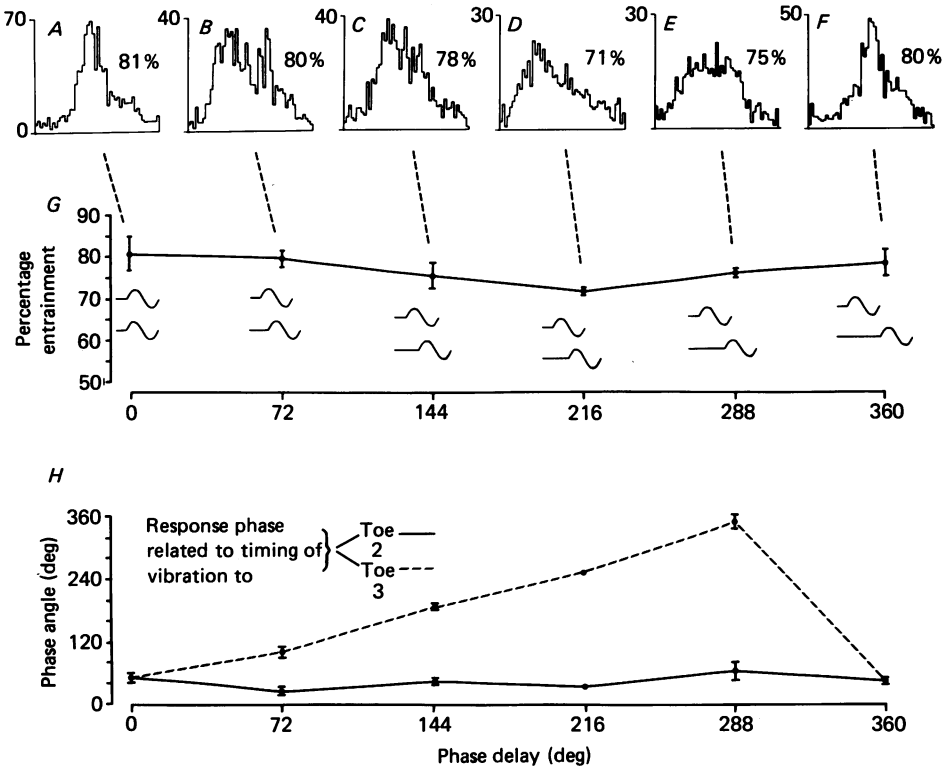

Fig. 10. Phase locking and phase angle of dorsal column nuclei neurone responses to 200 Hz cutaneous vibration: effect of phase rotation between inputs from separate sets of convergent P.c. fibres. The cycle histograms in *A–F* were constructed from the responses of the central neurone to stimulation of toe-pads 2 and 3 with 200 Hz vibration (5 μm) using two separate vibrators. In each cycle histogram the length of the abscissa corresponds to the vibration cycle period of 5 ms. The ordinate axis provides a calibration for the number of impulse counts accumulated in individual columns of the cycle histogram. In *A*, the vibration trains delivered to the two toes were coincident in time but from *B–F* a series of 1 ms (or 72 deg) phase delays was introduced between the two vibration trains as indicated by the wave form relations in the insets in *G*. Despite these introduced phase shifts in the relations between the two sets of inputs the dorsal column nuclei neurone retained a predominantly unimodal, phase-locked distribution in its reponses to vibration. Each distribution in *A–F* was centred to enable easier visual comparison of the tightness of phase locking. The percentage entrainment value as a measure of phase locking is indicated on each histogram. The mean ($\pm$S.D.) of two to three percentage entrainment values obtained at each phase rotation step was calculated and plotted in *G* against the magnitude of the introduced phase delay. In *H*, the mean phase of response, calculated as the mean phase angle for the cycle histogram distribution (prior to any rotation to centre the distributions as in *A–F*) is plotted in relation to the timing of the vibration delivered to toes 2 and 3. The graph shows that with each 72 deg phase delay introduced between the stimuli to toes 2 and 3 (abscissa) the phase angle of response (ordinate) shifts by approximately 72 deg in relation to the toe 3 input but remains locked to the toe 2 input.

For dorsal column nuclei neurones receiving convergent P.c. input from two or more toes it was found that simultaneous stimulation of two toes could enhance the response of the neurone compared with its response to stimulation of the individual toes (Fig. 9). Recruitment of two sources of convergent P.c. fibre input by simultaneous vibratory stimulation of two separate toes was also used to perform the phase-rotation experiments of the kind outlined for identified pairs of interosseous P.c. fibres in Fig. 5. This is shown in Fig. 10 for a dorsal column nuclei neurone receiving convergent P.c. inputs from toes 2 and 3. When both sources of input were recruited simultaneously using two vibrators and the same vibration parameters (200 Hz, 5 μm), the responses of the target neurone were phase locked as seen in Fig. 10*A*. Furthermore, when a series of phase shifts, each of 72 deg (that is, 1 ms at 200 Hz) was introduced between the two inputs (Fig. 10*B–F*) the cycle histograms retained an essentially unimodal, phase-locked impulse distribution with percentage entrainment measures (Fig. 10*A–G*) remaining within the range 71–81 %.

In Fig. 10*A–F* the cycle histogram distributions were rotated to approximately centre the distributions in order that the tightness of phase locking could be more easily visualized. However, for each distribution the actual phase of the original response was evaluated statistically by determining the position, or phase angle, for the mean of the distribution. This was obtained by an iterative analysis on the cycle histogram distribution that specifies the minimum S.D. for the distribution (Bennett, Ferrington & Rowe, 1980; Ferrington & Rowe, 1980*a*, *b*), and, as well, identifies the location of the mean of the distribution which becomes a precise index of the phase angle of the response. When the mean phase angles for the responses were assessed in relation to the timing of the vibratory stimulus to toes 2 and 3 respectively (Fig. 10*H*) it is seen that as the timing between the stimuli to toes 2 and 3 is changed in 72 deg steps (abscissa Fig. 10*H*), the phase angle of the target neurone response retains an approximately constant position in relation to the timing of the vibration stimulus to toe 2, but shifts markedly in relation to the timing of the vibration stimulus to toe 3. The response phase is therefore dictated by the set of P.c. inputs from toe 2. In this circumstance the toe 2 input may be said to functionally dominate the phase of response in the target neurone.

Comparison of phase locking in responses of dorsal column nuclei neurones to single and multiple P.c.-fibre inputs

The extent of phase locking in gracile neurone responses to vibration when the input was conducted over a single, interosseous P.c. fibre is plotted in Fig. 11*E*, using the percentage entrainment index, for six neurones studied at multiple frequencies in the range 100–600 Hz. At each frequency the vibration amplitude was adjusted to achieve a 1 : 1 level of response in the P.c. input fibre. Phase locking was tightest over the range 100–300 Hz and fell thereafter, a trend confirmed in Fig. 11*F* where the mean percentage entrainment values obtained for all gracile neurones driven by a single P.c. fibre are plotted (continuous line) against vibration frequency. To permit direct comparison, the mean percentage entrainment values are plotted as the interrupted line in Fig. 8*F* for gracile neurone responses to vibration of the hind-limb footpads where the input is assumed to come over multiple P.c. fibres (data from Ferrington *et al.* 1987*a*). The same trend is seen, but at all frequencies the entrainment

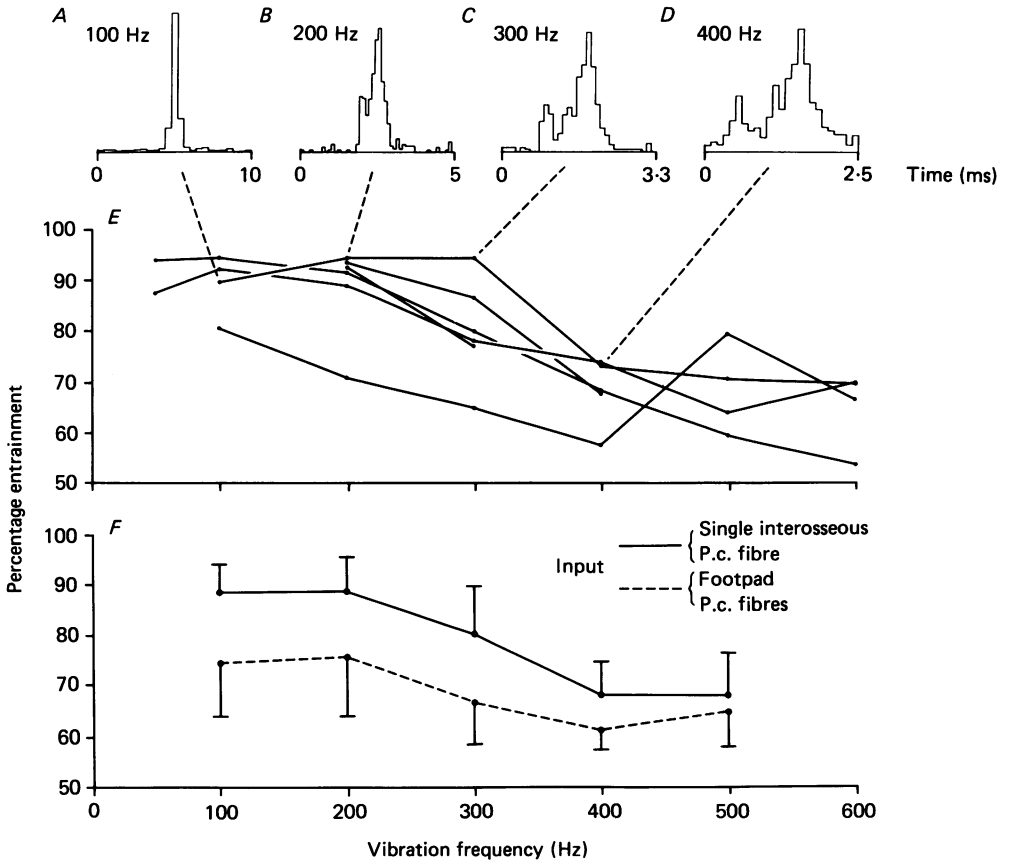

Fig. 11. Quantitative measures of phase locking in the vibration-induced responses of gracile neurones to single P.c. fibre inputs. *A–D*: cycle histograms and percentage entrainment values for the response of a representative gracile neurone when driven by a single P.c. fibre that was responding at a 1:1 level to each of the four vibration frequencies (from 100 to 400 Hz). The percentage entrainment measures obtained for these distributions are plotted as indicated in *E* along with values for five other gracile neurones when each was driven by a single P.c. fibre responding at a 1:1 level to a series of vibration frequencies (from 50 to 600 Hz). The mean (±S.D.) percentage entrainment values for these six neurones activated by single P.c. fibres are plotted in *F* (continuous line) and can be compared with the mean (±S.D.) percentage entrainment values (interrupted line) for sixteen target neurones that were activated by multiple P.c. fibres from the footpad of the cat. The latter data points came from Ferrington *et al.* (1987*a*).

is higher for the responses to the single-fibre inputs. Two-sample t testing on the means at each frequency indicated that phase locking was significantly tighter at all frequencies, except 500 Hz, when the input came from a single fibre. The P values were $< 0{\cdot}01$ at 100, 200 and 400 Hz, $< 0{\cdot}05$ at 300 Hz and $> 0{\cdot}05$ at 500 Hz. A factorial analysis of variance for unequally replicated data confirmed that differences were significantly related, first, to vibration frequency, and secondly, to whether the input came from single or multiple P.c.-fibre sources; that is, gracile neurone responses to single-fibre input were more tightly phase locked ($P < 0{\cdot}05$) than those to miltiple-fibre footpad input.

Sources of phase dispersion in vibration-induced responses of gracile neurones

Even when gracile neurone responses to vibration are generated by single P.c. fibre inputs their observed phase dispersion is considerably greater than that in primary-P.c.-fibre responses (Ferrington *et al.* 1987*b*). Quantitative comparison of the two sets

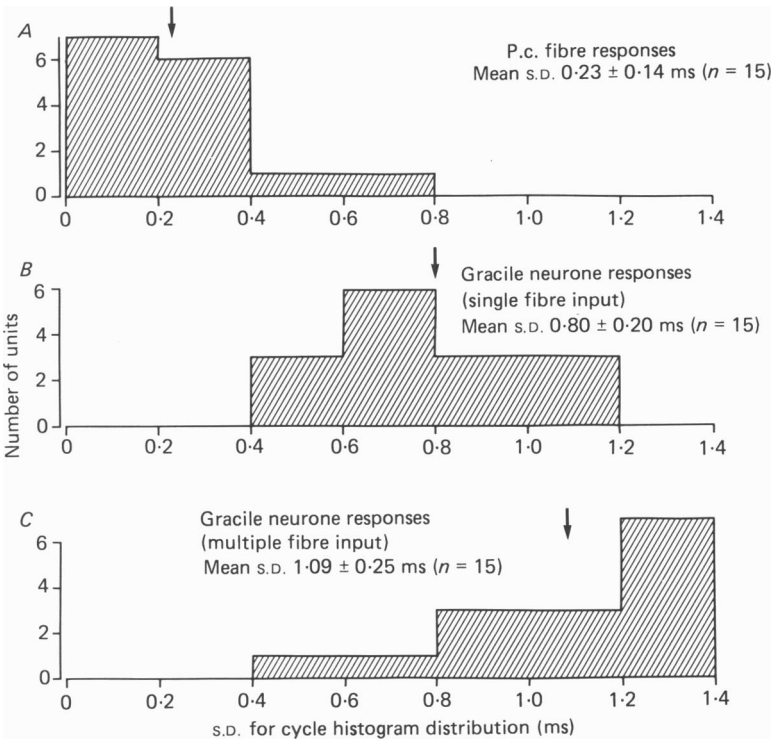

Fig. 12. Distributions comparing the tightness of phase locking in the responses to 200 Hz vibration of three groups: single interosseous P.c. fibres (*A*), gracile neurones when activated by single interosseous P.c. fibres (*B*), and gracile neurones activated by multiple P.c. fibre inputs from the hind-limb footpads (*C*). The measure of tightness of phase locking in the response of each fibre or central neurone was the S.D. (abscissa) derived as a measure of scatter from the cycle histogram distribution for each unit. The tightness of phase locking is inversely related to the S.D. values obtained. Thus the responses of P.c. fibres are most tightly phase locked with a mean S.D. value of $0{\cdot}23 \pm 0{\cdot}14$ ms (S.D.) while mean S.D. values were 0·80 and 1·09 ms for gracile neurone responses to single and multiple P.c.-fibre inputs respectively. The differences in tightness of phase locking for the three groups were significant ($P < 0{\cdot}001$) using a one-way analysis of variance. The arrow above each distribution indicates the mean S.D. value for that distribution.

is, however, unsatisfactory using the *percentage entrainment* measure as this attains a maximum of 100 % for any cycle histogram distribution that is confined within half the vibration cycle period. It therefore provides an insensitive measure of phase locking for responses of P.c. fibres. To overcome this difficulty, an alternative measure of scatter in the cycle histogram distribution (Ferrington & Rowe, 1980*a*, *b*), the S.D. (in milliseconds) for the distribution, has been used to compare the phase locking of

vibration-induced responses in all three groups: first, the P.c. fibres; secondly, gracile neurones responding to single P.c.-fibre input; and thirdly, gracile neurones responding to multiple P.c.-fibre input from the footpads. These S.D. values have been plotted in Fig. 12 for responses to 200 Hz vibration with the mean S.D. value indicated for each of the three groups. This dispersion measure in gracile neurone responses to single P.c. inputs (0·8 ms) is 3–4 times that for P.c. fibres themselves (0·23 ms), while that for gracile neurone responses to multiple P.c.-fibre input (1·09 ms) is approximately five times that for the P.c. fibres. Thus, the major component of the phase dispersion in the vibration-induced responses of these central neurones is attributable to the properties of the synaptic linkage between an individual input fibre and its target neurone. Convergence effects contribute, on average, only a small additional component to degrading the fidelity of impulse patterning.

DISCUSSION

Convergence of P.c. fibres on neurones of dorsal column nuclei

Convergence of P.c. fibres onto individual dorsal column nuclei neurones was established by identifying and monitoring the inputs from P.c. fibres of the interosseous nerve where it was found that two or more of the identified, convergent P.c. fibres were capable of suprathreshold actions on individual neurones. Evidence for convergence of P.c. fibre inputs from the footpads onto central neurones was also obtained using procedures that limited the spread of vibration in the distal limb (Figs. 8 and 9). These observations reinforce earlier indirect evidence for convergence based on comparison of the stimulus–response relations of central P.c. neurones and primary P.c. fibres (Ferrington *et al.* 1987*a*).

Convergence of P.c. fibres on dorsal column nuclei neurones and the retention of phase-locked responses to vibration

The representation of information about vibration may constitute a form of somatosensory signalling based upon an impulse pattern code (Talbot *et al.* 1968; Mountcastle, Talbot, Sakata & Hyvärinen, 1969; Ferrington & Rowe, 1980*a*; Rowe, Ferrington, Fisher & Freeman, 1985). Thus, information about vibration frequency may depend on impulse activity being phase locked to the vibration wave form so that the impulse pattern reflects the periodicity inherent in the stimulus.

The present investigation demonstrates that even where dorsal column nuclei neurones receive convergent P.c. inputs they can retain phase-locked responses to high-frequency vibration ($\geqslant$ 300 Hz). Indeed, there is only a small decline in the tightness of phase locking when the gracile responses are mediated by multiple rather than single P.c.-fibre inputs (Figs. 11 and 12). Furthermore, the responses remain phase locked even when there is asynchrony in the convergent input activity, either from latency differences among these inputs or as a result of introduced phase differences (Figs. 5, 6, 7 and 10). These observations are consistent with our hypothesis (Greenstein *et al.* 1987; Ferrington *et al.* 1987*a*) that the target neurone's response to vibration may be functionally dominated by one of its converging input sources thereby allowing these neurones to retain reliable phase locking of responses at least up to vibration frequencies of about 400 Hz.

The observation of functional domination of the target neurone is reminiscent of the manner in which auditory nerve fibres or neurones of the anteroventral cochlear nucleus may be dominated by one of two simultaneously delivered tone frequencies, each of which in isolation is a very effective stimulus (Rose, 1980). When the two tones are delivered together there is no significant summation of the individual responses; instead the phase locking of response in the neurone is determined by the cycle time of just one of the two tones. However, the explanation for this masking, or domination of one tone's response by another appears to reside in the mechanics of the cochlea (Rose, 1980) rather than in synaptic mechanisms. In contrast, synaptic mechanisms probably account for the dorsal column nuclei responses to vibration being functionally dominated by one of the convergent P.c. input fibres.

Phase locking of vibration-induced responses in dorsal column nuclei neurones at low vibration frequencies

We have not investigated whether at low vibration frequencies (< 100 Hz) the preferred phase of response in the central neurone is determined by just one or a few of its convergent inputs. However, at these frequencies such a scheme would be unnecessary for retaining phase-locked responses because the cycle period is long in relation to the known phase disperson in the vibratory responses of the afferent fibre population (see Ferrington *et al.* 1987*a*). In a study of median nerve responses to cutaneous vibration at 40 Hz, Johnson (1974) found that there was synchronization of activity among the fibres sampled. He concluded that the near synchrony of discharge in somatotopically adjacent fibres would provide a highly synchronous drive on central neurones.

Even at a vibration frequency of 100 Hz the dispersion in conduction times to dorsal column nuclei, for 67 % of fibres (that is, for those with conduction times within ± 1 S.D. of the mean conduction time), is less than a quarter of the vibration cycle period of 10 ms for inputs to the cuneate nucleus, and less than half for gracile inputs (Ferrington *et al.* 1987*a*). Although additional phase dispersion among different fibres may arise from differences in the phase of spike initiation (Greenstein *et al.* 1987), it is probable that at frequencies below 100 Hz there is enough coherence in the vibration-induced inputs to ensure phase locking of target neurone responses even without any mechanisms for functional domination by one or few of the input fibres.

Limitations at high vibration frequencies on phase locking of responses in dorsal column nuclei neurones

The responses of P.c. neurones display tightest phase locking to vibration at 100–200 Hz but by 400–500 Hz they occur randomly in relation to the vibration wave form (Fig. 11 and Douglas *et al.* 1978; Ferrington *et al.* 1987*a*, *b*). The disappearance of phase-locked responses above 400–500 Hz occurs even when the input comes from a single P.c. fibre (Fig. 11 and Ferrington *et al.* 1987*b*). Presumably timing fluctuations introduced in synaptic transmission preclude phase locking at these high frequencies (Ferrington *et al.* 1987*b*). Thus, above 400–500 Hz, no further signal of vibration frequency can be transmitted in a simple, phase-locked, impulse pattern code in the output from dorsal column nuclei.

Neural and psychophysical correlations in the processing of information about vibration frequency

Although the decline and disappearance of phase locking in the vibration-induced responses of dorsal column nuclei neurones contrasts with the extremely tight phase locking and metronome-like regularity of discharge seen in the responses of primary P.c. fibres up to 800–1000 Hz (Hunt, 1961; Talbot *et al.* 1968; Ferrington & Rowe, 1980*b*; Ferrington, Hora & Rowe, 1984), the behaviour of the dorsal column nuclei neurones nevertheless parallels the steep decline observed in the subjective capacity for vibration frequency discrimination (von Bekesy, 1962; Goff, 1967; Rothenberg, Verrillo, Zahorian, Brachman & Bolanowski, 1977). The Weber fraction, $\Delta f/f$, for frequency discrimination increases steeply above 100–200 Hz, its value being about 0·3–0·4 at 200 Hz (Goff, 1967; Rothenberg *et al.* 1977) whereas in the range 350–450 Hz, von Bekesy (1962) reported that doubling the vibration frequency no longer raised the pitch, a finding that implies a Weber fraction > 1.

Summary of vibratory information processing in dorsal column nuclei neurones

In conclusion, we propose that information about vibration frequency may be transmitted through the dorsal column nuclei relay in an impulse pattern code up to vibration frequencies of about 400–500 Hz. Over the low segment of this range, < 100 Hz, the phase-locked responses in the central neurones may reflect temporal coherence in the convergent inputs. However, because there are marked phase discrepancies in the vibration-induced inputs over the broader part of this frequency range, from 100 to 400–500 Hz, the phase-locking of responses in this range must have another explanation. Our findings in the present paper support the hypothesis (Greenstein *et al.* 1987; Ferrington *et al.* 1987*a*) that phase-locking in this range is based on the target neurone output, in particular its phase of response, being dominated by one or a few of its convergent P.c. fibres.

At frequencies above the range of phase-locked responses in dorsal column nuclei neurones ($>$ 400–500 Hz) the vibratory character of the stimulus can still be sensed up to 800–1000 Hz (Newman, Doupe & Wilkins, 1939; Verrillo, 1962; Goff, 1967). This suggests that an impulse pattern code is not required for the recognition of vibration of these highest frequencies. Perhaps the sense of vibration at frequencies above 300–400 Hz where frequency discrimination is poor or non-existent, depends simply upon the occurrence of central activity, whether patterned or non-patterned, arising from P.c. fibre inputs.

We wish to thank Dr John Eccleston for guidance with statistical procedures and C. Riordan for technical assistance. Grant support came from the Australian Research Grants Scheme and the National Health & Medical Research Council of Australia.

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