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CORTICAL AND PERIPHERAL MODIFICATION OF CEREBELLAR CLIMBING FIBRE ACTIVITY ARISING FROM CUTANEOUS MECHANORECEPTORS

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SUMMARY

1. In cats anaesthetized with Nembutal climbing fibre (CF) responses evoked in individual cerebellar Purkyně cells by mechanical stimulation of the skin were conditioned by preceding stimuli both to the periphery and to the precruciate area of the cerebral cortex.

2. Cortical stimulation, generally subthreshold for evoking a CF response itself, induced an inhibition of cutaneous evoked CF responses in 65% of all Purkyně cells tested. The maximum inhibition ranged from 40 to 100% of the control responses at conditioning-testing intervals of 30–70 msec and the duration of the inhibition was usually 125 msec.

3. In most cases the corticofugal inhibition of cutaneously evoked CF responses was mediated by inhibitory mechanisms outside the cerebellar cortex, probably at relays within the spino-olivocerebellar pathways. Purkyně cells undergoing corticofugal inhibition were distributed widely within both the vermis and the pars intermedia of the anterior lobe.

4. In 40% of all Purkyně cells tested, there was evidence for afferent inhibition of their peripherally evoked CF responses as revealed by conditioning stimuli applied to the skin outside the receptive field. Again it was found that the inhibition was exerted at levels prior to the cerebellum.

5. It is concluded that the afferent input transmitted to Purkyně cells via climbing fibres can be modified by corticofugal and peripheral influences exerted on the relays of the CF pathways outside the cerebellar cortex.

INTRODUCTION

Individual cerebellar Purkyně cells are innervated in almost all cases by only one climbing fibre which establishes elaborate synaptic contacts

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over the dendritic surface of the cell. The climbing fibres are believed to arise perhaps entirely from the inferior olive (Szentágothai & Rajkovits, 1959; Eccles, Llinas & Sasaki, 1966; Eccles, Ito & Szentágothai, 1967), on to which several different spino-olivary pathways project (Oscarsson, 1968, 1969*a*, *b*; Larsen, Miller & Oscarsson, 1969; Miller & Oscarsson, 1970). These pathways differ in their location within the spinal cord and in the synaptic connexions made in the course of their spino-olivary projection. The possibility exists for the modification of afferent activity within these spino-olivocerebellar pathways, as part of these projections is relayed through the dorsal column nuclei (Ebbesson, 1968; Oscarsson, 1969*a*), where it known that both corticofugal and afferent inhibition operate (cf. Andersen, Eccles, Oshima & Schmidt, 1964; Andersen, Eccles, Schmidt & Yokota, 1964; Andersen, Etholm & Gordon, 1970; Schmidt, 1972). Furthermore, a hyperpolarization of inferior olive cells which project to the cerebellum has been reported following stimulation of cerebral cortex (Crill & Kennedy, 1967; Crill, 1970). Although it has been established that cerebro-cerebellar connexions terminate within the cerebellar cortex as both climbing fibres and mossy fibres, there have been no studies on the possibility that cerebral influences exerted on the spino-olivocerebellar pathways modify the climbing fibre (CF) input to Purkyně cells. Investigation of this potentiality for corticofugal and for peripheral modification of afferent activity transmitted over the CF system has been the subject of the present study. Controlled natural stimulation of cutaneous receptors was used to evoke characteristic CF responses of individual Purkyně cells located within the anterior lobe of the cerebellum, and conditioning stimuli were applied to either the cerebral cortex or to cutaneous structures. Some aspects of the results have been the subject of preliminary communications (Leicht, Rowe & Schmidt, 1972*a*, *b*).

METHODS

The experiments were performed on eighteen adult cats from the larger series employed in the previous study (Leicht *et al.* 1973), where the following procedures were described in detail: the general handling of the experimental animal, the recording and processing of unitary activity from the cerebellar cortex, histological verification of the recording sites, the electrical stimulation of limb nerves left in continuity, and the controlled natural stimulation of mechanoreceptors of the foot pads and the hairy skin.

Electrical stimulation of the right (contralateral) precruciate cortex was performed through a bipolar platinum electrode with an interpolar distance of 2 mm (diameter of the ball shaped electrode tips 0·5 mm). Stimulus currents of 50 μsec in duration and of intensities up to 10 mA were used. Usually pairs of stimuli at an interval of 5 msec were applied. The electrode was positioned for each experiment immediately anterior to the cruciate sulcus and about halfway between the mid line and the lateral extremity of this sulcus. Other areas of cortex were not tested in this

study, the precruciate region being chosen for stimulation as activity originating from the sensorimotor area is known to inhibit transmission at spinal brain stem relays (Gordon & Jukes, 1962; Andersen, Eccles, Oshima & Schmidt, 1964; Andersen, Eccles, Schmidt & Yokota, 1964).

In order to precisely evaluate the magnitude of CF responses of cerebellar Purkyně cells and the extent of their inhibition, these responses were selectively discriminated and processed in the computer as described in the preceding paper (Leicht *et al.* 1973). The magnitude of the responses could then be obtained from the cumulative frequency distributions (CFDs) by measuring the increase in number of counts above the background discharge level of CF responses. The magnitude of conditioned responses was expressed as a percentage of the control CF responses (Figs. 3, 4), or alternatively, the magnitude of both control and conditioned responses was plotted directly in terms of the increase in number of counts per stimulus over the background discharge rate.

RESULTS

Characteristics of climbing fibre responses evoked by cortical stimulation

In many of the Purkyně cells in which CF responses were evoked by cutaneous stimulation, the cortical stimulus itself also evoked a CF response, confirming the observations of Miller, Nezlina & Oscarsson (1969) that convergence from both peripheral and cortical inputs occurs onto individual climbing fibres. In the present study this was observed for thirty-four of the sixty-four Purkyně cells tested with both cutaneous and cortical stimulation. The mean latency and standard deviation for these cortically evoked CF responses was $16{\cdot}0 \pm 5{\cdot}6$ msec which is in good agreement with the latencies of 13–16 msec for the cortically evoked CF fields observed by Provini, Redman & Strata (1968) and Miller *et al.* (1969). Of these thirty-four Purkyně cells showing convergence of cortical and peripheral inputs, twenty-one exhibited CF responses from only one of the four peripheral nerves tested (see Methods), whereas in eleven cells CF responses were evoked from two or more of these inputs. For the remaining two cells the peripheral convergence was not fully studied.

CF responses evoked from the periphery are unable to follow high frequency stimulation (Eccles, Provini, Strata & Táboříková, 1968; Eccles, Faber, Murphy, Sabah & Táboříková, 1971*a*; Ishikawa, Kawaguchi & Rowe, 1972) due to an inhibitory period which occurs in inferior olive cells following their activation (Armstrong & Harvey, 1966; Armstrong, Eccles, Harvey & Matthews, 1968; Crill, 1970). This is confirmed in Fig. 1*D–F* where two successive vibratory stimuli were applied at a series of intervals to the pad of toe 2 of the ipsilateral hind limb. In the same cell the time course of depression of the peripherally evoked CF response following a cortically evoked CF response is illustrated in *A–C* of this Figure. There is a close resemblance in the extent and time course of the depression shown in *C* and *F*, which might be

expected from the fact that both inputs converge onto a common olivary cell. Similar phenomena appear to have been observed in the posterior lobe of the cerebellum by Freeman (1970) who reported inhibitory interactions between cortical and peripheral stimuli on Purkyně cell responses

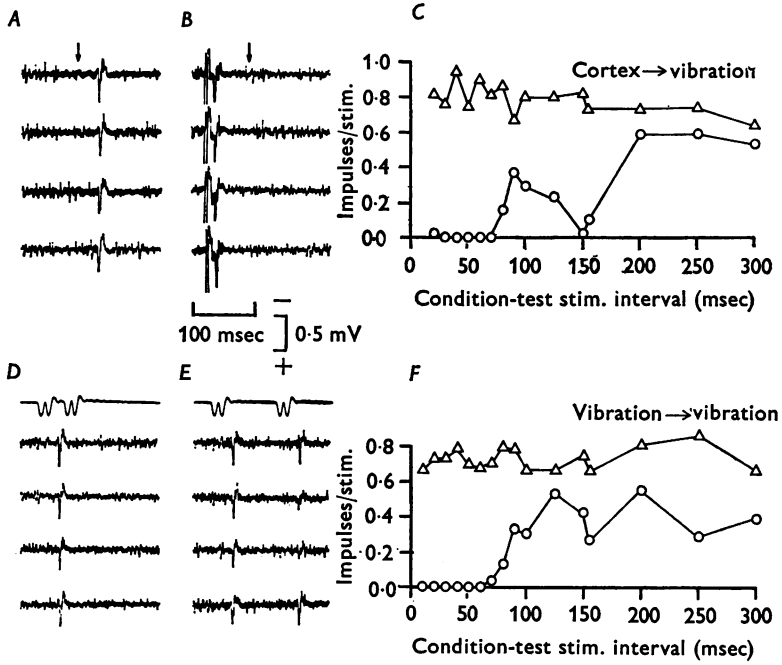


Fig. 1. Interaction of CF responses evoked from the periphery and from the cerebral cortex. Purkyně cell located in lobule III in the medial region of pars intermedia. Its cutaneous receptive field was confined to the pads of the ipsilateral hind limb. The specimen records in *A* illustrate four CF responses evoked, at a latency of 32 msec, by 2 cycles of vibration (600 μm, 85 c/s) applied to toe 2 at the time indicated by the arrow. The CF responses to vibration were abolished in *B* where CF responses were evoked, at a latency of 13 msec, following stimulation (2 pulses, 10 mA intensity) of the precruciate cortex 70 msec before the vibratory stimulus. The time course of this depression is plotted in *C*. In *D* and *E* pairs of vibratory stimuli (identical to those in *A*, *B*) were delivered at intervals of 40 msec (*D*) and 100 msec (*E*) to toe 2 to determine the time course (*F*) of depression of the second CF response.

which were not identified in terms of their CF or mossy fibre origin. In his study the depression of the test response was dependent on the conditioning stimulus itself eliciting a response from the Purkyně cell under observation.

Corticofugal inhibition of peripherally evoked CF responses

The specimen records in Fig. 2*A* illustrate the responses of a Purkyně cell to brief taps (arrow) applied to the pad of toe 4 of the ipsilateral hind limb. In this cell there was no discriminable simple spike activity and the CF responses were recorded under conditions of partial impalement of the cell. Each stimulus evoked a CF response. With stimulation of the precruciate cortex 60 msec before tapping of the toe pad (*B*) CF responses were completely abolished. The magnitudes of control and conditioned CF responses are plotted in *C* for a variety of conditioning-testing intervals.

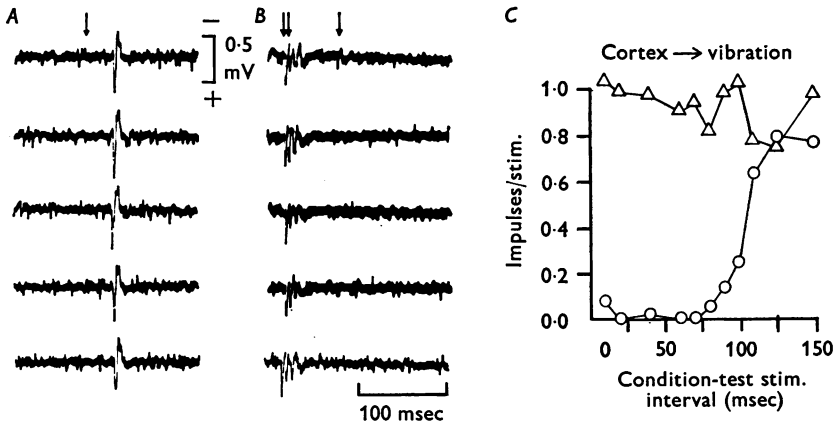


Fig. 2. Inhibition of CF responses by stimulation of the precruciate cortex. Purkyně cell located in the pars intermedia of lobule III. Its cutaneous receptive field was confined to the distal area of the ipsilateral hind limb. *A*, CF responses evoked by a tap (550 μm, 100 c/s) applied to toe 4. *B*, inhibition of these responses by stimulation (2 pulses, 10 mA intensity) of the precruciate cortex 60 msec before tapping. Arrows in *A* and *B* indicate the times of stimulus application. *C*, time course of inhibition of the CF response.

It is seen that the inhibition is complete at intervals of 30–70 msec and that full recovery occurs after approximately 125 msec. Of fifty-one Purkyně cells tested in this way thirty-three displayed a cortically induced inhibition of their CF responses evoked by mechanical stimulation of the skin. In the majority of these cells the maximum inhibition ranged from 40 to 100 % of their control responses. The duration of the inhibition was usually about 125 msec, but ranged from 100 to 200 msec.

Direct cortically evoked CF responses were observed in eighteen of the thirty-three Purkyně cells which displayed corticofugal inhibition, and in nine of the eighteen Purkyně cells in which no corticofugal inhibition was

seen. In almost all cases the threshold for corticofugal inhibition of peripherally evoked CF responses was lower than the threshold strength required for the cortically evoked CF responses. Consequently it was possible to investigate the effects of corticofugal inhibition in the absence of any direct cortically evoked CF response.

Of the thirty-three Purkyně cells displaying corticofugal inhibition, twenty-three had CF responses to stimulation of only one of the testing nerves, whereas seven were activated from two or more of these nerves. The cutaneous receptive fields for twenty-five of these Purkyně cells did not extend beyond one limb, and in fact in most cases were confined to small areas on the distal regions of the limb. Five Purkyně cells had cutaneous receptive fields which included two or more limbs and in one case most of the body. In the remaining three Purkyně cells the extent of the receptive field was not satisfactorily evaluated. There was no apparent difference in the latencies of peripherally evoked CF responses between those Purkyně cells which displayed corticofugal inhibition and those in which there was no evidence of inhibition. From the fifty-one Purkyně cells tested for corticofugal inhibition, the mean latency $\pm$ S.D. of CF responses evoked from ipsilateral sciatic nerve was $20{\cdot}9 \pm 5{\cdot}5$ msec, and from the ipsilateral superficial radial nerve was $14{\cdot}8 \pm 4{\cdot}4$ msec. In general the latencies of CF responses evoked by vibratory stimulation of the foot pads were 10–12 msec longer than those evoked by nerve stimulation, the values being $33{\cdot}1 \pm 4{\cdot}8$ msec for hind limb stimulation and $25{\cdot}7 \pm 4{\cdot}8$ msec for fore limb stimulation.

The corticofugal inhibition of peripherally evoked CF responses of the type illustrated in Fig. 2 could be mediated by inhibitory mechanisms within the cerebellar cortex as a result of the activation of mossy and CF inputs following stimulation of the cerebral cortex (Provini *et al.* 1968), or at relays within the spino-olivo-cerebellar pathways. In the former case the inhibition should be reflected in a temporary depression of the simple spike activity of the Purkyně cell, particularly in those cases where the spontaneous simple spike activity is of a suitably high level. Fig. 3*C* illustrates the time course of corticofugal inhibition of CF responses evoked in a Purkyně cell by displacement of the hairs in the vicinity of the central pad of the ipsilateral hind limb. For this cell, in which there was a high level of spontaneous simple spike activity, it can be seen in the specimen records of *A* and the post-stimulus time histogram, PSTH, and cumulative frequency distribution, CFD, in *B* that cortical stimulation, identical with that producing the depression of the CF responses illustrated in *C*, was without effect on the background simple spike discharge of the cell. In all, for seventeen of the thirty-three Purkyně cells displaying corticofugal inhibition of their peripherally evoked CF responses it was possible

to evaluate the effect of the cortical stimulation on the cell's simple spike activity as was done in Fig. 3. Ten cells of the seventeen examined were of the type illustrated in Fig. 3, in that there was no evidence for a depression of their simple spike activity concomitant with the cerebral-evoked depression of the CF responses. For these Purkyně cells it can be concluded that the inhibition of peripherally evoked CF responses was mediated at levels prior to the cerebellum, thus establishing that there is cerebral modification of afferent activity transmitted to Purkyně cells via the CF system.

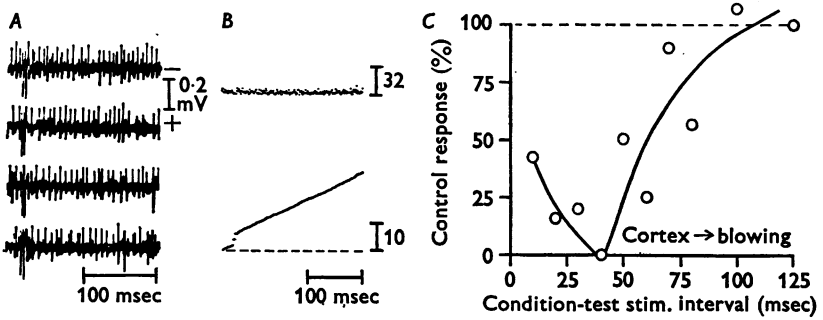


Fig. 3. Cerebral-evoked inhibition of CF responses without concomitant inhibition of simple spike activity. Purkyně cell located in pars intermedia of lobule IV b. Its cutaneous receptive field was confined to the hairy skin immediately surrounding the pads on the ipsilateral hind limb. *A*, background simple spike activity recorded during cortical stimulation (2 pulses, 5 mA intensity). *B*, the PSTH and CFD constructed from 50 successive traces of impulse activity as in *A*. Except for the sharp jumps in the CFD associated with the cortical stimulus artifacts there is no change in slope indicative of any simple spike inhibition. Stimulation of the hairs between toes 4 and 5 evoked from this cell CF responses which could be selectively discriminated and counted. Prior stimulation of the precruciate cortex, as in *A*, produced an inhibition of the peripherally evoked CF responses with the time course plotted in *C*. The scale next to the PSTH in this and subsequent figures provides a calibration for the total number of counts in each address at the completion of 50 sweeps; those next to the CFDs provide a calibration for the average number of impulses counted per sweep.

In the remaining seven Purkyně cells an inhibition of simple spike activity was produced in association with the cerebrally evoked depression of their CF responses. However, in only one of these cells (Fig. 4*A–C*) was the duration of simple spike inhibition (see specimen records in *A* and the computer records in *B*) of a similar time course to that of the CF depression (approximately 200 msec) plotted in *C*. The other six Purkyně cells which displayed simple spike inhibition in association with the cerebrally evoked depression of their CF responses were of the type illustrated by the cell in Fig. 4*D* and *E*. The time course of the depression of the CF response

in this cell was approximately 100 msec (plotted in *E*), whereas the duration of the concomitant cerebrally induced simple spike inhibition, indicated by the arrows in *D*, was approximately 25 msec.

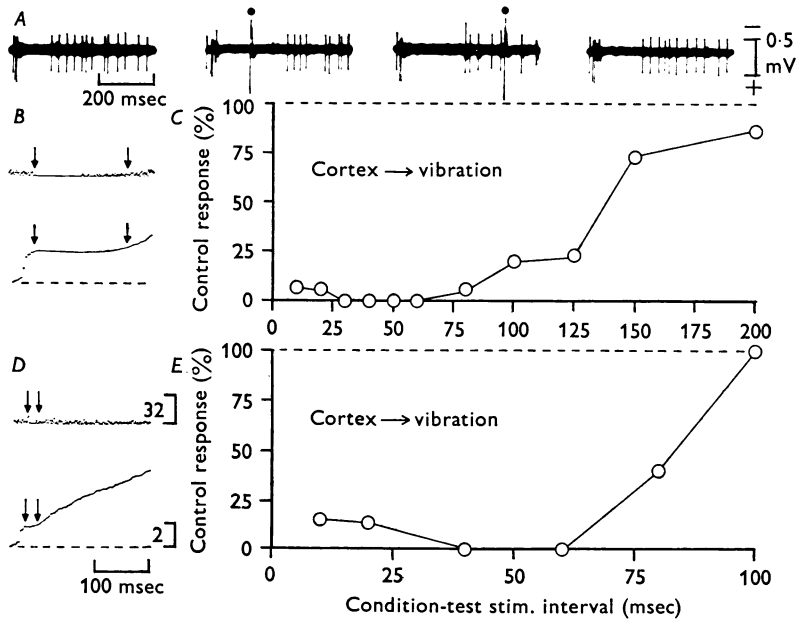
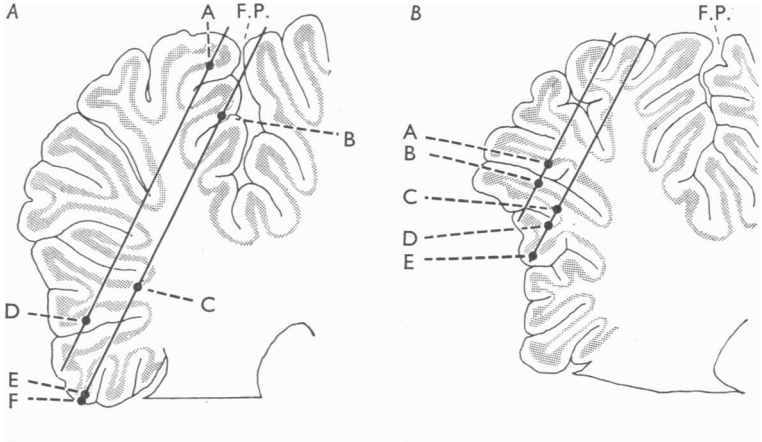


Fig. 4. Inhibition in two different Purkyně cells of both simple spike activity and peripherally evoked CF responses by cerebral stimulation. Data for *A*, *B*, *C* from a Purkyně cell located on the lateral border of vermis in lobule Vb. Its cutaneous receptive field was on the pads of the ipsilateral fore limb. Data for *D* and *E* from a Purkyně cell located in the vermis of lobule Vd. Its cutaneous receptive field was also on the pads of the ipsilateral fore limb. *A*, simple spike inhibition induced by cortical stimulation (2 pulses, 6 mA intensity). Two spontaneously occurring CF responses are indicated by the black dots. *B*, on the PSTH and CFD the approximate duration of this simple spike inhibition is indicated by the arrows. *C*, the time course of inhibition, following cerebral stimulation as in *A* and *B*, of CF responses evoked by vibration (550 μm, 2 cycles, 100 c/s) applied to the central pad. *D*, PSTH and CFD illustrate simple spike inhibition (following brief excitation) by cortical stimulation (1 pulse, 5 mA intensity) for a second Purkyně cell. *E*, the time course of inhibition of CF responses evoked by vibration (600 μm, 1 cycle, 90 c/s) following cortical stimulation as in *D*. The PSTHs and CFDs of both *B* and *D* were constructed from fifty successive responses. The sharp jumps in the CFDs are due to the cortical stimulus artifacts. The scales on the computer records in *D* apply to the corresponding records in *B*.

Distribution within the anterior lobe of Purkyně cells displaying corticofugal inhibition

Purkyně cells which underwent corticofugal inhibition of their peripherally evoked CF responses were distributed widely within both the vermis and the pars intermedia of the anterior lobe. These cells did not differ in their location from those which did not display a corticofugal



C

P-cell	Peripheral stimulus	Site of stimulation	Inhibition
A	Hair stim.	i H Medial thigh	100%
B	Pad vibr.	i F Toe 4	100%
C	Pad vibr.	i H Toe 5	100%
D	Pad vibr.	i H Toe 2	18%
E	Hair stim.	i F Between toes	90%
F	Pad vibr.	i H Toe 2	42%

D

P-cell	Peripheral stimulus	Site of stimulation	Inhibition
A	Pad vibr..	i H Toe 2	31%
B	Pad vibr.	i H Toe 5	30%
C	Hair stim. .	i H Between toes	100%
D	Pad vibr.	i H Toe 4	34%
E	Pad vibr..	i H Toe 2	94%

Fig. 5. Distribution within the anterior lobe of the cerebellum of Purkyně cells which displayed inhibition of their peripherally evoked CF responses following stimulation of the precruciate cortex. *A*, parasagittal section in the vermis showing the paths of 2 electrode penetrations. The location of cell *F* was marked by the ejection of fast green FCF dye from the electrode. *B*, parasagittal section in pars intermeda showing the path of two electrode penetrations in a different experiment. *C* and *D*, the tables indicate the type and site of peripheral stimulation employed for eliciting CF responses from each cell, and the extent of the inhibition, determined as described in Methods, of these responses by precruciate stimulation. iH, ispsilateral hind limb; iF, ipsilateral forelimb.

inhibition, or from those where the corticofugal influence was not tested (Eccles *et al.* 1971*a*; Eccles, Sabah, Schmidt & Táboříková, 1972; Leicht *et al.* 1973), i.e. cells which received peripheral input from the forelimb

were located predominantly within lobule V, whereas those receiving hind limb imputs were generally more widely distributed within lobules II to IV of the anterior lobe. In Fig. 5 the location of eleven Purkyně cells undergoing corticofugal inhibition is illustrated from two experiments. In *A* the electrode penetrations were made in the vermis half way between the mid line and the paravermal vein, while in *B* the electrode penetrations were made in pars intermedia approximately 0·5 mm lateral to the paravermal vein. For the section illustrated in *A*, cells *B* and *E* had cutaneous receptive fields on the ipsilateral forelimb, cell *E* thus being exceptionally located for a Purkyně cells receiving forelimb input. Cells *D* and *F* had cutaneous receptive fields on the ipsilateral hind limb, while those of *A* and *C* included both ipsilateral limbs. In the section illustrated in *B* all five Purkyně cells had cutaneous receptive fields confined to the ipsilateral hind limb. It can be seen from these two experiments that cells undergoing corticofugal inhibition were widely distributed in the various lobules of the anterior lobe, and furthermore, as tabulated in *C* and *D*, that there was no particular distribution of those Purkyně cells in which the inhibition was most pronounced (cells *A*, *B*, *C*, *E* in section *A* and cells *C*, *E* in section *B*).

Afferent inhibition of peripherally evoked CF responses

Fig. 6*A*, *B* illustrates the time course of inhibition of vibratory evoked CF responses following conditioning cutaneous stimulation with a brief jet of air applied to the hairs beyond the excitatory receptive fields of the two cells. For the cell whose time course of inhibition is illustrated in *A* the cutaneous receptive field was confined to a small lateral area of the distal limb (*D*), whereas for the cell whose time course of inhibition is plotted in *B*, the cutaneous receptive field was small but discontinuous, being confined only to the pads of toes 3–5 and to the central pad (*E*). It was seen, as illustrated by the PSTH and CFD in *C*, that the conditioning stimulus which produced the CF inhibition shown in *B* was without direct effect on the simple spike activity of this Purkyně cell which indicates that this afferent inhibition, in agreement with the observations on the cortically evoked inhibition of CF responses, was exerted at levels prior to the cerebellum.

In six of fifteen Purkyně cells tested, conditioning stimulation of the skin beyond the excitatory receptive field of the Purkyně cell inhibited CF responses evoked by natural stimulation within the excitatory cutaneous receptive field. This has been termed afferent inhibition. In three of these cells the peripherally evoked CF response was also inhibited by stimulation of the precruciate cortex, and for these cells there was a close correspondence between the duration of the corticofugal and the afferent

inhibition. In contrast, however, to the complete inhibition of peripherally evoked CF responses frequently observed following conditioning stimulation of the cerebral cortex, the afferent inhibition was usually not as profound, as can be seen in Fig. 6*A*, *B*.

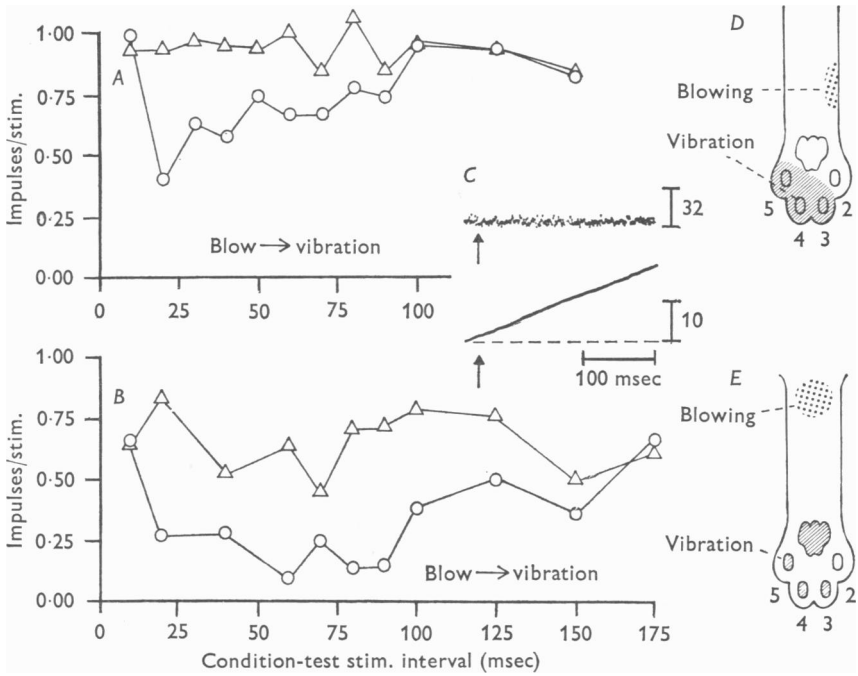


Fig. 6. Afferent inhibition of CF responses evoked by natural stimulation. The data for *A* and *D* are for a Purkyně cell located within lobule II in the medial region of pars intermedia. Those for *B*, *C* and *E* are for a Purkyně cell located in the pars intermedia of lobule III. The cutaneous receptive fields for each of these cells are indicated by the shaded areas in *D* and *E* respectively. The sites of application of the vibratory test stimuli (520 μm, 1 cycle, 100 c/s in D; 600 μm, 1 cycle, 100 c/s in *E*) and conditioning hair stimuli (blowing) are also indicated in *D* and *E* for each of these cells. *A* and *B* illustrate the time courses of inhibition of vibratory evoked CF responses for the two cells. The conditioning hair stimulus in *E* was without effect on the background simple spike activity of the cell as indicated by the PSTH and CFD of *C* which were constructed from 50 sweeps during hair stimulation alone.

For the Purkyně cell whose peripheral receptive field and time course of afferent inhibition are illustrated in Fig. 6*A*, *D*, a study was made of the effectiveness of different sites on the limb for inducing inhibition of the CF responses evoked by vibratory stimuli to the pad of toe 4 (Fig. 7). In Fig. 7*G* the different areas where the conditioning stimuli were applied to

the hairs are indicated by the shaded and finely stippled patches proximal to the excitatory receptive field of the cell. Conditioning stimulation at the four shaded locations was effective in inhibiting the CF responses, as can be seen by comparison of the control cumulative frequency distributions for three of these sites (upper records in Fig. 7*D*, *E*, *F*) with those constructed during conditioning stimulation (lower records in *D*, *E*, *F*). Conditioning stimulation at the three more proximal locations (finely stippled areas) was without inhibitory influence on the CF responses as seen in *C*

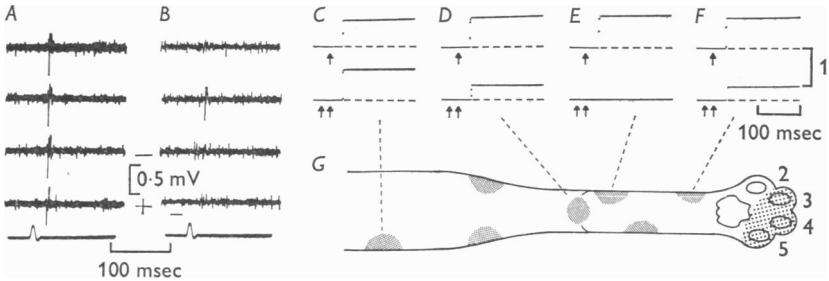


Fig. 7. Afferent inhibition of peripherally evoked CF responses from a restricted area surrounding the excitatory receptive field of the cell. Same Purkyně cell as in Fig. 6*A*, *D*. *A*, CF responses evoked by vibration (520 μm, 1 cycle, 100 c/s) applied to toe 4. *B*, hair stimulation (indicated by the bar) 20 msec before the vibration, abolished the CF response in 3 out of 4 sweeps. *C*, *D*, *E* and *F* shows CFDs for control responses to the vibratory stimulus (upper records) and for the conditioned responses (lower records) obtained when hair stimulation was applied at the indicated sites. Inhibition was observed by conditioning at the shaded locations but not at the finely stippled sites. The arrows below the CFDs in *C*, *D*, *E* and *F* indicate the times of applications of conditioning and testing stimuli.

for one of these sites. The specimen records in *A*, in all four traces show CF responses to the control vibratory stimulus, whereas in *B*, when conditioning stimulation was applied at one of the effective inhibitory sites, the CF response is suppressed in three of the four traces. The observations on this Purkyně cell indicate that the cutaneous area from which afferent inhibition could be produced was limited to the region immediately surrounding the excitatory receptive field of the cell.

In the few Purkyně cells tested for afferent inhibition by natural stimulation at sites remote from the excitatory receptive fields of the cells, no evidence of inhibition was found. However, in two Purkyně cells whose cutaneous receptive fields were located on distal areas of the ipsilateral hind limb it was observed that electrical stimulation of the ipsilateral superficial radial nerve effectively inhibited CF responses evoked by vibration applied to the toe pads of the hind limb. In Fig. 8*A* the time course

of this type of inhibition is illustrated for one of these cells. This cell also displayed corticofugal inhibition of the CF responses evoked from the pad of toe 4 on the ipsilateral hind limb, but neither stimulation of the hairs on the ipsilateral hind limb (Fig. 8*B*) nor electrical stimulation of the contralateral sciatic nerve had any influence on the CF responses.

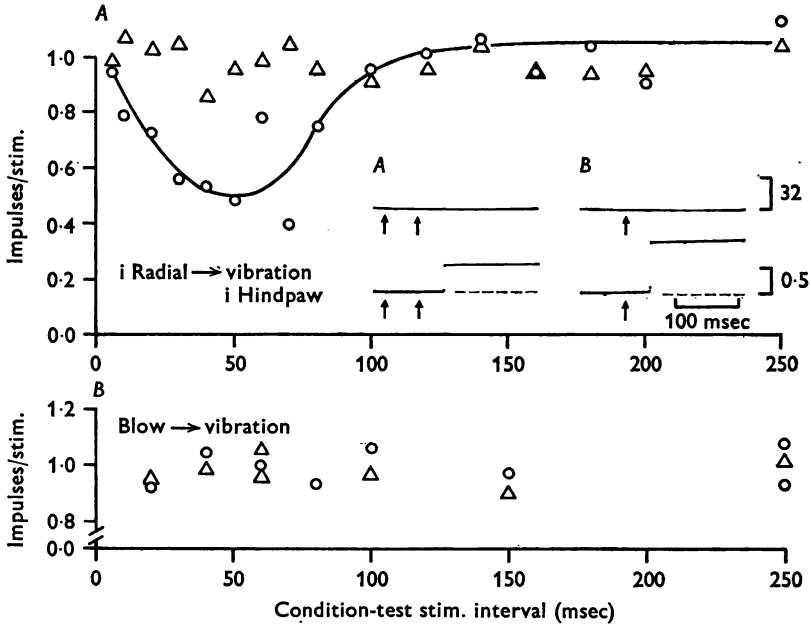


Fig. 8. Inhibition of peripherally evoked CF responses by conditioning stimulation of the ipsilateral superficial radial nerve. Purkyně cell located near the medial border of pars intermedia in lobule II. Its cutaneous receptive field was confined to the toe pads of the ipsilateral hind limb. *A*, time course of inhibition of CF responses by conditioning stimulation of ipsilateral superficial radial nerve (1 pulse, 5 times threshold); Δ = control responses (see example PSTH and CFD shown in inset *B*) evoked by vibration (600 μm, 2 cycles, 90 c/s) applied to toe 4 of the ipsilateral hind limb; ○ = conditioned responses (see example PSTH and CFD in inset *A* for a conditioning-testing interval of 50 msec). *B*, there was no inhibition with conditioning stimulation of the hairs on the area proximal to the central pad of the ipsilateral hind limb.

DISCUSSION

The observation of a convergence from both peripheral and cortical inputs onto individual climbing fibres confirms the finding of Miller *et al.* (1969). In the present study this was observed for 54% of the Purkyně cells, whereas such convergence was found in almost all Purkyně cells (94%) studied by Miller *et al.* (1969). This difference is probably explained

by the fact that the site of cortical stimulation was fixed in the present experiments whereas Miller *et al.* (1969) stimulated areas of the sensorimotor cortex extending from the mid line to the coronal sulcus.

Purkyně cells which underwent corticofugal inhibition of their cutaneously evoked CF responses had cutaneous receptive fields, latencies to peripheral stimulation and cerebellar locations which were representative of the general population of Purkyně cells responsive to cutaneous input (Leicht *et al.* 1973). The occurrence of corticofugal inhibition was not confined to Purkyně cells which had restricted cutaneous receptive fields as approximately 17% of those studied had cutaneous receptive fields extending onto two or more limbs.

It was usually observed that higher stimulus thresholds pertained for the cortically evoked CF responses than for the corticofugal inhibition of cutaneously evoked CF responses. This may indicate that different groups of cortical descending fibres are involved in evoking these two effects. In this connexion it has been reported by Oshima, Provini, Tsukahara & Kitai (1968) that the cortical projection to the inferior olive is composed of the slower conducting pyramidal tract fibres. The latencies for cortically evoked CF responses observed in the present study (mean 16·0 msec) are certainly consistent with their being mediated via this pathway. In regard to the lower threshold of the corticofugal inhibition of cutaneously evoked CF responses it may be noted that part at least of the corticofugal inhibitory influences on brain stem nuclei is mediated via the fast conducting pyramidal tract fibres, as Oshima (1969) has reported that these fibres are responsible for the corticofugal post-synaptic inhibitory effects in the cuneate nucleus. Although part of the spino-olivary projection is relayed through the dorsal column nuclei (Oscarsson, 1969*b*) it is not possible to say from the present study at what levels of the pathways to the cerebellar climbing fibres the observed corticofugal inhibition is mediated.

The observation that in association with corticofugal inhibition of cutaneously evoked CF responses there was usually none or only a very brief concomitant inhibition of the cell's simple spike activity indicates that the observed inhibition of CF responses was not due to the activation of inhibitory mechanisms within the cerebellar cortex by the cerebrocerebellar projections. This is consistent first, with the finding of Latham & Paul (1971) that CF responses evoked by stimulation in the juxtafastigial region were not inhibited by inputs to the cerebellar cortex from the periphery, and secondly, with the observation of Eccles, Llinas, Sasaki & Voorhoeve (1966) that even with powerful activation of the inhibitory interneurones within the cerebellar cortex by parallel fibre stimulation, there was never a complete suppression of CF responses

evoked in nearby Purkyně cells. Consequently, the observed inhibition of cutaneously evoked CF responses in the present study, must be mediated at levels prior to the cerebellum. It may, for example, be mediated on the cells of origin of the climbing fibres, or by presynaptic inhibition of primary afferent fibres. However, as indicated above, it is not possible from the present study to specify the relevant site or sites.

Afferent inhibition of cutaneously evoked CF responses was observed somewhat less frequently (40% of cells tested) than the corticofugal inhibition (65% of cells tested), and this afferent inhibition was less pronounced. However, a close correspondence was found in their time courses which may suggest a common site at which these inhibitory influences were mediated. The presence of a restricted surround arrangement of the afferent inhibition was observed for the Purkyně cell in Fig. 7. However, there have been insufficient observations to comment on the generality of this, particularly since with nerve stimulation more remote afferent inhibition has also been seen (cf. Fig. 8).

It has long been considered that the elaborate interconnexions between the cerebral cortex and the cerebellum are important in the regulation of motor functions. In addition to these direct interconnexions, evidence has now been obtained for an enlarged facility for cerebral influences on cerebellar activity by modification of the afferent inputs transmitted to the Purkyně cells via the climbing fibres.

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