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GATING IN THE SPINO-OLIVOCEREBELLAR PATHWAYS TO THE c_1 ZONE OF THE CEREBELLAR CORTEX DURING LOCOMOTION IN THE CAT

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SUMMARY

1. The field potentials evoked in the cerebellar cortical c_1 zone by single-pulse, non-noxious stimulation of the superficial radial nerve have been recorded with tungsten-in-glass microelectrodes in awake cats. Responses that were due to transmission in the spino-olivocerebellar pathways (SOCPs), which terminate in the cortex as climbing fibres, were identified and studied while the cat walked on a moving belt.

2. The size of the climbing fibre-evoked potentials varied systematically during the step cycle. They were invariably largest in mid- to late swing of the ipsilateral forelimb and, at most recording sites (5/6), they were smallest during the first half of stance.

3. With low stimulus strength, the probability of evoking a measurable response also varied. The probability was greatest in mid- to late swing and least in early stance.

4. Similar variations were shown to occur when the analysis was restricted to responses evoked by a single functionally homogenous SOCP, the dorsal funiculus SOCP.

5. It is proposed that these variations reflect the operation of a gating mechanism which modulates the excitability of the SOCPs and prevents them transmitting self-generated tactile inputs to the cerebellum while facilitating transmission when unexpected inputs are most likely to arise.

6. The present data are compared with those from a similar study of the c_2 zone SOCPs (Apps, Lidierth & Armstrong, 1990) and are discussed in relation to a study of the effects of unexpected mechanical perturbations of stepping (Andersson & Armstrong, 1987).

INTRODUCTION

Climbing fibres are the terminal axons of the olivocerebellar projection and make powerful synaptic contact with Purkinje cells in which they evoke complex spikes (Eccles, Llinás & Sasaki, 1966*a*). Although complex spikes are readily discharged by tactile stimuli of the periphery in passive cats, they are not discharged by the tactile

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inputs that occur during locomotion of awake cats (Armstrong, Edgley & Lidierth, 1988). Instead, the spino-olivocerebellar pathways (SOCPs) which carry the tactile inputs are gated during active movement so that only inputs that are not self-generated are successful in evoking complex spikes (Gellman, Gibson & Houk, 1985; Andersson & Armstrong, 1987). The present report examines the properties of this gating mechanism in the SOCPs innervating the cerebellar cortical c_1 zone.

In a previous report from this laboratory, it was shown that climbing fibre-generated field potentials, which were evoked in the cerebellar cortex by electrical stimulation of cutaneous afferents, varied in amplitude over the course of the step cycle in awake, walking cats (Apps *et al.* 1990). An overall pattern emerged from these data, whereby the largest evoked potentials occurred most frequently during mid-stance and late swing in the ipsilateral forelimb step cycle. There was, nevertheless, considerable variation in the pattern of the step-related changes in excitability between recording sites and between animals. In that study, recordings were made from the cerebellar cortical c_2 zone, an area which receives climbing fibre input which is driven by tactile stimulation of widespread areas of the periphery and in which convergence of inputs occurs from both ipsilateral and contralateral forelimbs and often from both forelimbs and both hindlimbs (Larson, Miller & Oscarsson, 1969*b*). Therefore, despite an apparent correlation to the movements of the ipsilateral forelimb, the c_2 zone may be concerned with the control of movement of more than one limb, and possibly with interlimb co-ordination or with the overall postural integration required for successful locomotion.

This report presents the results of a similar study of the climbing fibre-evoked potentials in the cerebellar cortical c_1 zone which lies immediately medial to the c_2 zone in the paravermal cortex. Note that the lateral part of the c_1 zone, which has also been denoted the cx zone (Campbell & Armstrong, 1985), is included in the c_1 zone as defined here. In lobule V of the cerebellar anterior lobe, the c_1 zone receives climbing fibre-mediated peripheral input exclusively from the ipsilateral forelimb (see below). The data from this zone are therefore more readily interpreted in the context of their relationship to the movements of quadrupedal stepping because the pathways involved presumably contribute to the control principally of the ipsilateral forelimb.

The c_1 zone receives input from climbing fibres which may be activated by several ascending pathways. The most direct path is the short-latency dorsal funiculus spino-olivocerebellar pathway (DF-SOCP) which relays in the dorsal column nuclei. In barbiturate-anaesthetized cats, the DF-SOCP generates climbing fibre-evoked field potentials on the surface of the c_1 zone at latencies of 9–12 ms (Oscarrson, 1969) or 10–15 ms (Ekerot & Larson, 1979) in response to high strength ($20 \times T$) electrical stimulation of the ipsilateral superficial radial nerve. These latencies have been interpreted as indicating a monosynaptic (Oscarsson, 1969) or disynaptic (Ekerot & Larson, 1979) relay in the cuneate nucleus. In addition Oscarsson (1969) noted an inflexion on the falling edge of the short-latency response which may indicate the presence of a more complex pathway and, in chloralose-anaesthetized cats, Ekerot & Larson (1979) reported the presence of longer latency responses (*ca* 19 ms). In both of these series of experiments, the spinal cord was sectioned sparing only the ipsilateral dorsal funiculus so all responses must have been mediated by pathways in

the dorsal columns. A pathway in the dorsolateral funiculus (the DLF-SOCP) has also been described (Larson, Miller & Oscarsson, 1969*a*) and evokes responses at 15–20 ms latencies in the cerebellar cortex following electrical stimulation of the ipsilateral superficial radial nerve. None of the SOCPs that innervate the c_1 zone has been shown to be activated by contralateral nerve stimulation.

The present study examines the gating of transmission of cutaneous input through the SOCPs to the cerebellar cortical c_1 zone during locomotion in awake cats.

METHODS

Methods of animal training, preparatory surgery, recording and data analysis were described fully in earlier publications (Edgley & Lidierth, 1988; Apps *et al.* 1990) and are given here only briefly. At an initial aseptic operation under full pentobarbitone anaesthesia, a small craniotomy was made over the cerebellum and a chamber for receiving a micro-manipulator was secured over it with dental acrylic cement. In addition, bipolar intramuscular electrodes were implanted for recording of electromyographic activity in selected limb muscles (among which the lateral or the long head of the ipsilateral triceps brachii, an elbow extensor, was always included). Leads for electrically stimulating the superficial radial nerves and for recording the resulting nerve compound action potentials were also implanted. The stimulus strengths used were non-noxious and no signs of stimulus aversion were evident; on the contrary, such stimuli usually exerted a mildly somnolent effect. Field potentials evoked by such stimuli were recorded from the cerebellar cortex using tungsten-in-glass microelectrodes which were advanced into the cerebellum during each recording session. The cerebellar field potentials, nerve compound action potentials and electromyograms were stored on analog tape and analysed off-line. The data were filtered (bandpass 30 or 40 Hz to 1 kHz and 10 Hz–10 kHz respectively for the cerebellar fields and the nerve compound action potentials) and digitized using a PDP 11/34 minicomputer. The amplitudes of the cerebellar evoked potentials and the corresponding nerve compound action potentials were measured using the computer and later correlated with the phase of the step cycle in which the stimulus was delivered.

RESULTS

General remarks

Field potentials evoked by single-pulse, non-noxious electrical stimulation of the superficial radial nerve were recorded in the cerebellar cortical c_1 zone in lobule V of the anterior lobe in three awake, walking cats. Data recorded from the c_2 zone in one of these cats have been presented elsewhere (Apps *et al.* 1990).

Field potentials were attributed to activation of Purkinje cells by climbing fibres using the criteria described previously (Apps *et al.* 1990), i.e. that the amplitude of the responses exhibited substantial variation between stimuli, even in the resting cat, and that the amplitude of the response to the second of a pair of stimuli delivered within an interval of less than 100 ms was depressed when compared to the response evoked by the first stimulus. Responses that were due to the climbing fibre-mediated activation of Purkinje cells in the c_1 zone of the cortex were identified by their shorter latency to electrical stimulation of the ipsilateral superficial radial nerve when compared to the fields evoked in neighbouring zones and by the failure of electrical stimuli to the contralateral superficial radial nerve to evoke responses.

A typical result is shown in Fig. 1*A* which shows the responses evoked by four pairs of stimuli delivered every 1·5 s with an interstimulus interval of 30 ms and at

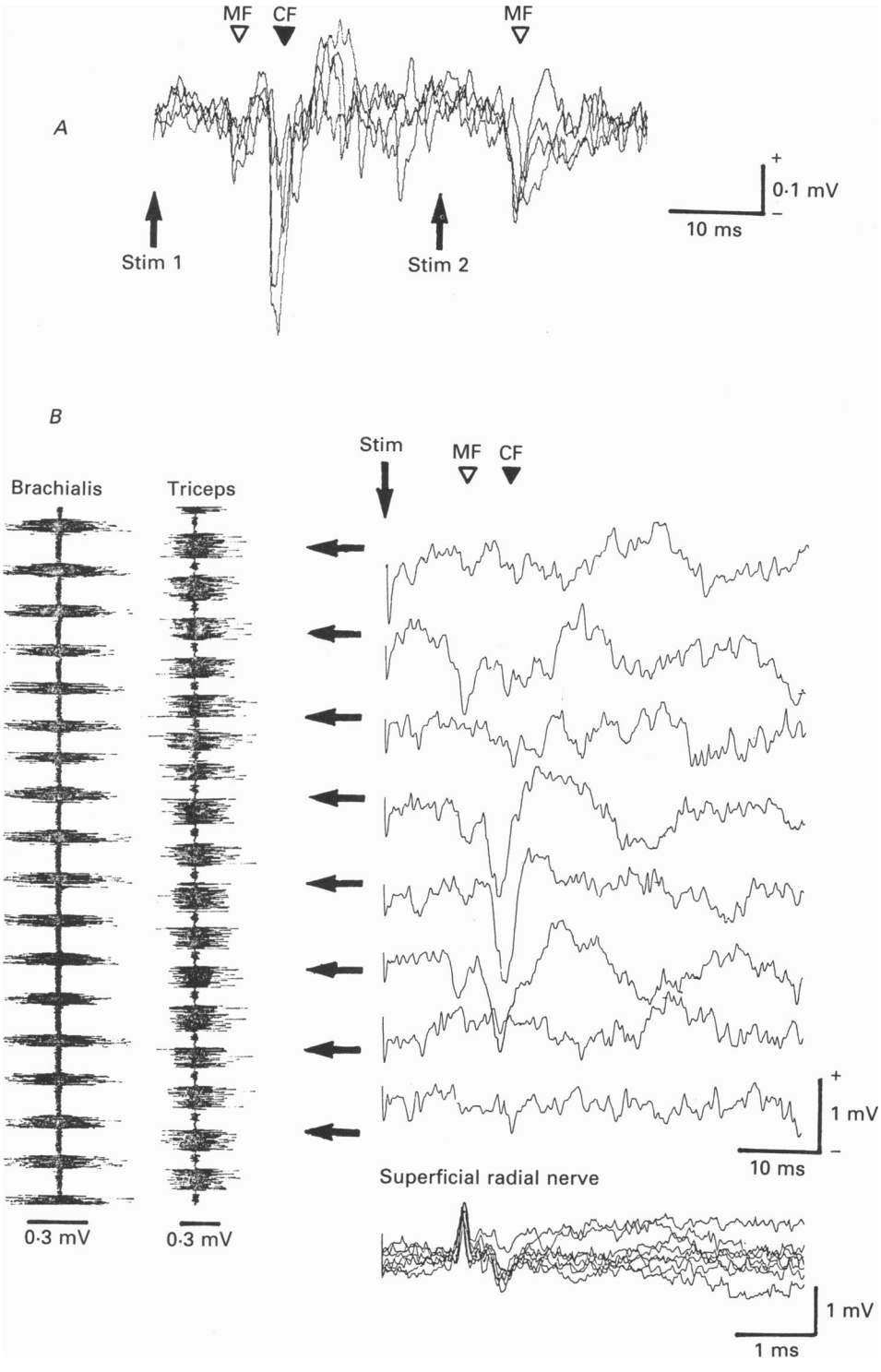

Fig. 1. For legend see facing page.

a strength of $1{\cdot}7 \times T$ for evoking a just-detectable compound action potential in the ipsilateral superficial radial nerve (stimuli marked by arrows). The evoked responses are biphasic, negative–positive potentials which indicates that the electrode tip was between the level of the climbing fibre synapses and the Purkinje cell bodies (Eccles *et al.* 1966*a*). An initial short-latency response (marked MF) to the first stimulus of the pair is seen which is due to activation of mossy fibre inputs to the cortex because its latency is shorter than that of any known climbing fibre-mediated pathway from the periphery. The second response (marked CF) is the climbing fibre-evoked potential as is evident from its variable amplitude and its failure to appear in response to the second of the pair of stimuli. Note that the second stimulus clearly evokes a mossy fibre response which in this example is facilitated. The latency to onset of the climbing fibre-evoked response (12 ms) indicates that its early phase was evoked through the DF-SOCP which innervates the c_1 zone although other pathways may have contributed to its later part (e.g. the DLF-SOCP, see Introduction). Its latency is some 5 ms shorter than that of climbing fibre-evoked potentials in the c_2 zone when stimuli of comparable strength are used (e.g. Apps *et al.* 1990).

Phase-dependent variation in the size of climbing fibre-evoked potentials

Single, non-noxious electrical stimuli were presented to the ipsilateral superficial radial nerve at intervals of 1·5 s while the cats walked steadily on a belt moving at 0·4–0·5 m/s. Only periods of recording in which the size of the compound action potential evoked in the superficial radial nerve showed no step-related variation were included in the analysis (see below).

Figure 1*B* shows a typical recording from the same site illustrated in Fig. 1*A*. To the left, the electromyograms of the ipsilateral triceps brachii and brachialis muscles are shown. The arrows mark the time of delivery of stimuli at $1{\cdot}7 \times T$ to the ipsilateral superficial radial nerve and the records to the right show the potentials evoked in the c_1 zone of the cerebellar cortex in response to the stimuli. It is clear from the records illustrated in Fig. 1*B* that the size of the climbing fibre-evoked field potentials varied between stimuli and that for several of the records shown no detectable field potential was evoked. The potentials were largest when evoked during the period of activity of the brachialis muscle and smaller or absent during triceps activity. It is important to note that, for this and all other samples included in the analysis, the compound action potentials in the superficial radial nerve remained relatively constant while the cat was walking (lower right of Fig. 1*B*) which shows that the effectiveness of the stimulus current on the nerve did not vary because of limb

Fig. 1. *A* shows the identification of a c_1 zone climbing fibre-mediated evoked potential. Four traces are shown superimposed, in each of which two stimuli separated by 30 ms were given to the ipsilateral superficial radial nerve. The first stimulus of the pair evokes a short-latency mossy fibre-mediated potential (MF) and a subsequent climbing fibre-mediated response (CF) with a latency of 12 ms. The second stimulus evokes only a mossy fibre-mediated response. Positivity is upwards in this and all other records. *B* shows the responses evoked by single stimuli of $1{\cdot}7 \times T$ delivered during locomotion. To the left are the electromyograms of the ipsilateral brachialis and triceps brachii muscles. Stimuli (marked by arrows) were delivered at 1·5 s intervals. The records to the right show the evoked potentials recorded in the cerebellar cortex. The lowest trace shows the compound action potential recorded in the superficial radial nerve in response to the same stimuli.

movement. As a consequence, variations in the size of the cerebellar evoked potentials must have arisen centrally and were not due to variation in the efficacy of the peripheral nerve stimulus.

The potentials evoked by each stimulus were filtered and digitized (see Methods) and those evoked by stimuli delivered in each tenth of the step were separately

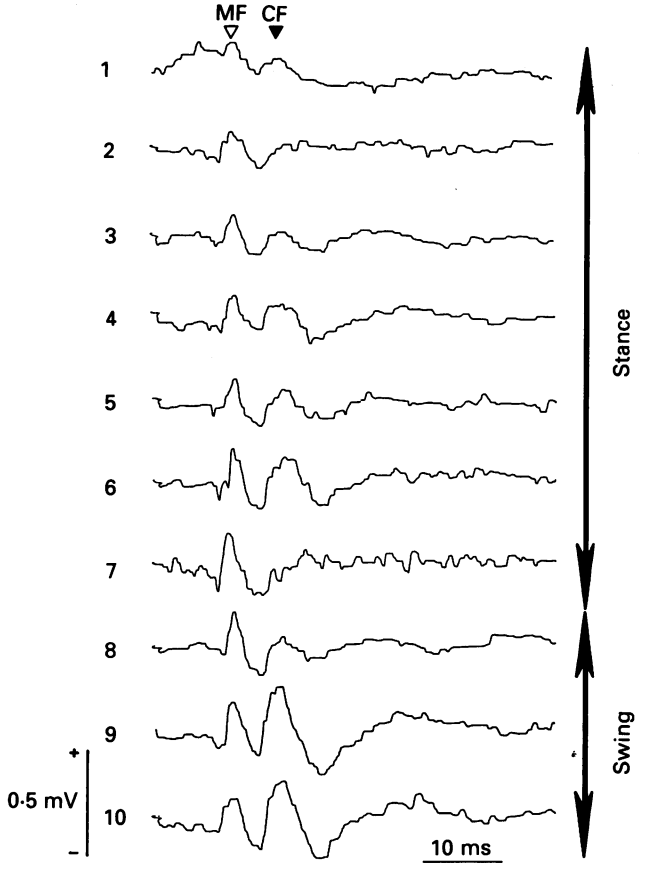

Fig. 2. Individual responses such as those in Fig. 1*B* were sorted and averaged according to the tenth of the step cycle in which the stimulus was delivered. The resulting averaged trials for each tenth (marked to the left) for a different recording site are shown in this figure. As in Fig. 1, both mossy (MF) and climbing fibre- (CF) mediated responses were evoked. The approximate timing of the periods of the stance and swing phases of the step are shown to the right. Note that these potentials were of positive polarity.

pooled and averaged to see if the variation in the size of the climbing fibre-evoked potentials was correlated with the phase of the step in which the stimulus was presented. For this purpose, the onset of electromyographic activity in the ipsilateral triceps brachii muscle was taken as the arbitrary start of each step cycle. This precedes the time of paw contact and the onset of the stance phase of the step cycle in the ipsilateral forelimb by 30–40 ms at the speeds of locomotion used in this study (Drew, 1981).

Figure 2 shows the averaged traces for each tenth of the step from one recording site and demonstrates that there was variation in the amplitude of the climbing fibre-evoked potentials (marked CF) which was related to the phase of the step. Note that these responses are positive-going which indicates that the electrode tip was close to the Purkinje cell bodies (Eccles *et al.* 1966*a*). During the early part of the stance phase (1st trace), the responses were reduced in amplitude but during the middle and late part of stance their size increased; a further reduction occurred at the onset of swing (7th trace) but the responses grew to reach a maximum towards the end of the swing phase. Note that the mossy fibre responses shown in Fig. 2 (marked MF) also exhibited some step-related variation in amplitude.

This pattern of modulation in the size of the climbing fibre-evoked potentials during locomotion was consistently observed in the c_1 zone and is illustrated further in Fig. 3, each column of which shows a quantitative analysis of the data for one recording site in each of the three cats. The sites chosen for this illustration were those at which the largest data sample was obtained at the lowest strengths of nerve stimulation which were consistent with evoking individual field potentials of sufficient amplitude for them to be reliably measured. The upper row of graphs in Fig. 3*A–C* shows the mean areas (±S.E.M.) under the climbing fibre field potentials evoked by stimuli delivered in each tenth of the step cycle (●——●). The data are based on measurements of individual responses to each nerve stimulus such as those illustrated in Fig. 1*B*. The data in Fig. 3*A* and *B* are from the same recording site as the records shown in Figs 1 and 2 respectively (but those in Fig. 3*B* are derived from a different period of locomotion to those in Fig. 2). Examination of each of the curves reveals that the mean size of the climbing fibre-evoked potentials varied during the course of the step cycle and that there were common features to the pattern of that variation in each of the cats. In Fig. 3*A* and *B* the mean area of the responses is reduced during the middle or early part of the stance phase but rises during the later part of stance. This effect is not as clear in Fig. 3*C*, although for this and all other samples from the same cat the evoked responses were smallest during the second tenth of the step. In all three cats the responses showed a progressive increase in amplitude during the swing phase to reach a maximum in the final tenth of the step cycle (or in the 9th tenth in some unillustrated samples, see below). In the cats for which data are shown in Fig. 3*A* and *B* this increase was preceded by a reduction in the response amplitude during the transition between the stance and swing phases.

Not every nerve stimulus was successful in generating a discriminable climbing fibre-evoked potential in the cerebellum. The lowest row of graphs in Fig. 3 shows the probability of evoking a discriminable potential by stimuli delivered in each tenth of the step and in Fig. 3*A* and *B* this clearly fluctuates in parallel with the variations in the mean size of the evoked responses and will therefore contribute to, and may be the cause of, that variation. For this reason, the mean areas of the responses were recalculated after excluding the stimuli which were unsuccessful in evoking climbing fibre-mediated responses. The resulting areas (mean±S.E.M.) are also shown in the upper row of Fig. 3 (○···○). The pattern of modulation when the unsuccessful stimuli were excluded from the analysis was similar to that when they were included. Thus changes in the probability of evoking a response do not account fully for the

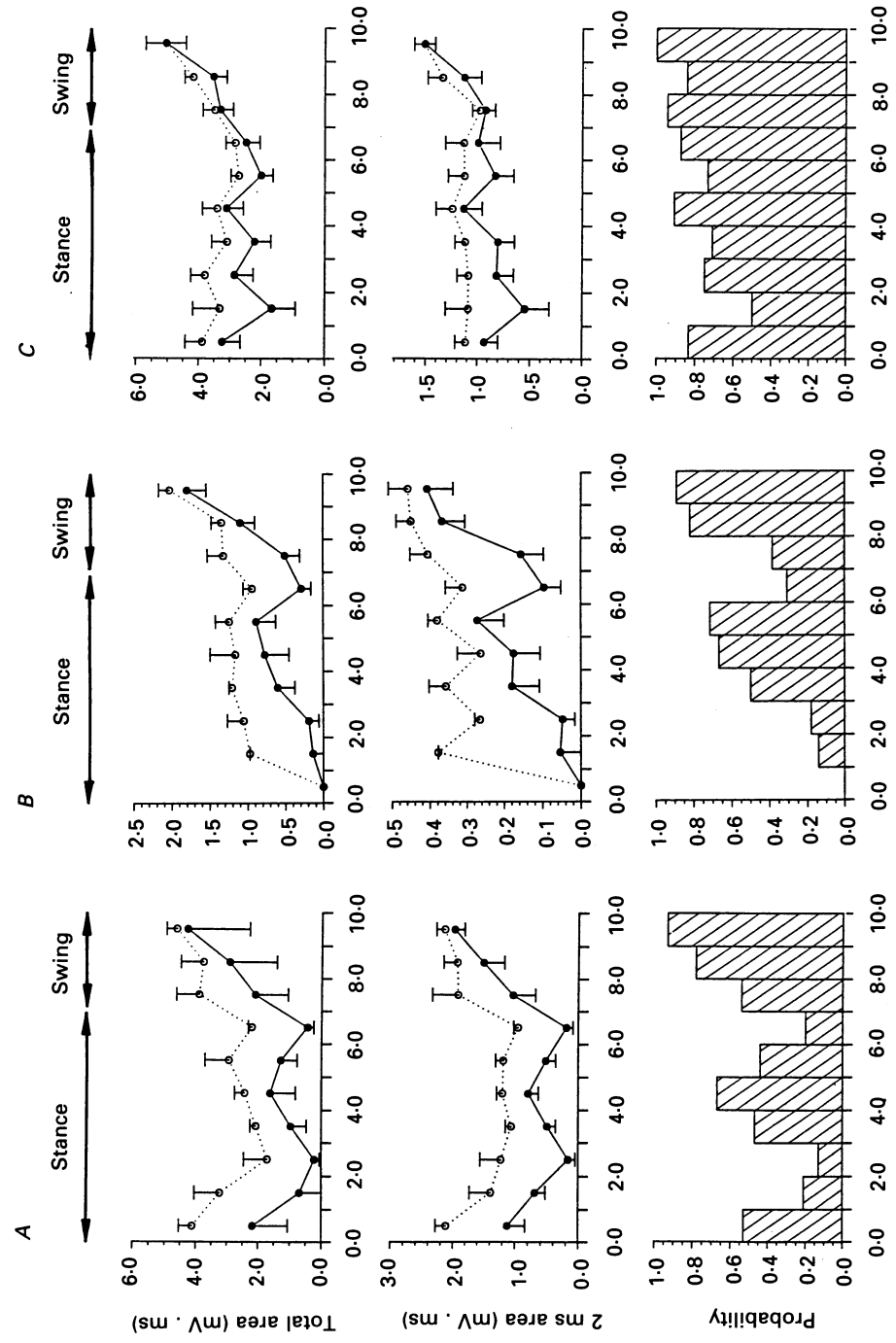

Fig. 3. *A–C* show a quantitative analysis of the step-related variation in the size of the climbing fibre-evoked potentials recorded at one site from each of the cats. The uppermost row of graphs shows the mean area (± S.E.M.) beneath the evoked potentials both with (●——●) and without (○ · · · ○) the inclusion in the calculations of those stimuli which failed to evoke responses (see text). The middle row shows the area beneath the first 2 ms of the responses. The lowest row shows the probability of evoking a detectable potential. The stimulus strengths were 1·7, 1·2 and 4·0 × *T* in *A*, *B* and *C* respectively.

observed variation in mean response amplitude; step-related variation of the size of the responses evoked by the successful stimuli also contributes.

Contribution of the dorsal funiculus spino-olivocerebellar pathway

It has been suggested elsewhere (Apps *et al.* 1990) that the area beneath the initial 2 ms of the climbing fibre-evoked potentials may be a better index of the number of Purkinje cells initially recruited by each stimulus than the area of the entire potential. However, for the responses evoked in the c_2 zone, the area beneath the entire field and that beneath the initial 2 ms were found to be proportional to one another (see Fig. 6 of Apps *et al.* 1990). For responses evoked in the c_1 zone, the area beneath the initial 2 ms may still be a useful additional measurement as it should reflect only the recruitment of Purkinje cells by the short-latency DF-SOCP and should therefore reflect the excitability of a single functionally discrete SOCP rather than the net excitability of several, potentially heterogenous SOCPs terminating in the zone. Note, however, that the DF-SOCP responses at recording sites in the medial and lateral parts of the c_1 zone will be evoked through climbing fibres arising from the rostral dorsal accessory olive and middle part of the medial accessory olive respectively (Campbell & Armstrong, 1985).

The middle row of graphs in Fig. 3 show the mean areas (±S.E.M.) underlying the initial 2 ms of the climbing fibre-evoked potentials. As with the total areas of the potentials, the means (and S.E.M.s) are shown both with (●——●) and without (○···○) those stimuli which failed to evoke a response included in the calculations. It is clear that the area underlying the initial 2 ms of the responses varies during the step in a pattern essentially similar to that seen when the area underlying the whole response is examined.

For the trials illustrated in Fig. 3*A* and *C* the latency to onset of the climbing fibre-evoked responses remained relatively constant at 12·4±0·5 ms (mean±S.D., $n = 81$ stimuli successful in evoking a response) and 12·9±0·8 ms ($n = 106$ successful stimuli) respectively. The initial component of these responses was therefore due to activation of the Purkinje cells by the short-latency DF-SOCP and the area beneath the initial 2 ms of the responses will have reflected the recruitment of Purkinje cells via that pathway. For the trial illustrated in Fig. 3*B* the latency to onset of the field was 13·2±1·12 ms ($n = 42$ successful stimuli), but the increased variance was largely due to a single response evoked at a latency of 19·1 ms by a stimulus delivered during the second tenth of the step. In view of its long latency, it is unlikely that this field was evoked through the DF-SOCP and as it was the *only* response evoked by any of seven stimuli delivered in the second tenth of the step the excitability of the DF-SOCP may have been close to zero during this period as it was in the first tenth (Fig. 3*B*).

Effects of increased stimulus strength

The effects of increasing the strength of the superficial radial nerve stimulus were assessed in one cat for which clear responses were evoked by particularly low stimulus intensities. The resulting data are illustrated in Fig. 4 which shows the mean total area beneath the climbing fibre-evoked potentials recorded from three different recording sites in response to stimulation of the ipsilateral superficial radial nerve at

$2 \times T$ during locomotion. The data are from the same cat as those shown in Figs 2 and $3B$ where the stimulus strength was $1{\cdot}2 \times T$ and one of the curves in Fig. 4 (■——■) is based on data collected from the same site as in those figures.

The dependency of the size of the climbing fibre-evoked potential on stimulus timing relative to the step cycle was much reduced with stimuli of $2{\cdot}0 \times T$ (Fig. 4) as

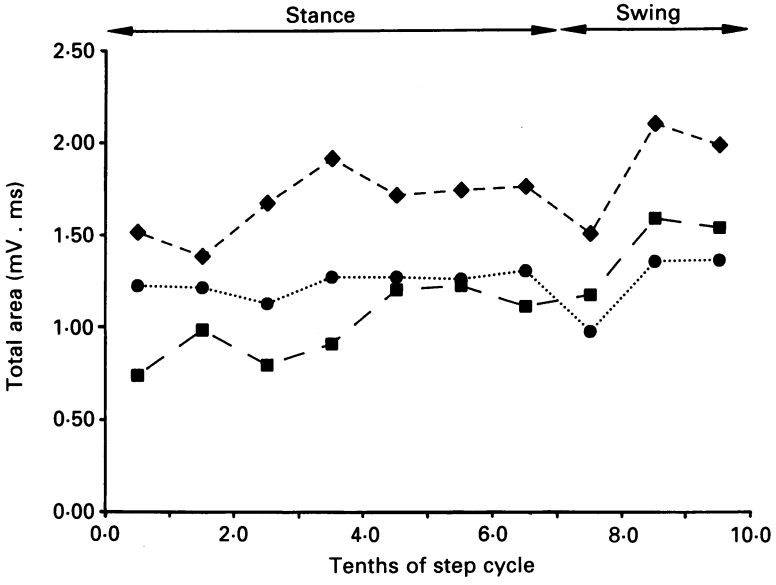

Fig. 4. The mean area beneath the climbing fibre-evoked potentials with stimulus strengths of $2{\cdot}0 \times T$ for three recording sites in the same cat for which data are shown in Fig. $3B$. One of the traces (■——■) is from the same recording site as in Fig. $3B$.

compared with stimuli of $1{\cdot}2 \times T$ (Fig. $3B$). None the less, for two of the curves in Fig. 4 (◆– – –◆ and ■——■) a reduction in the area of the response is seen during the early part of the swing phase in the ipsilateral forelimb and for all of the curves, the responses were largest during late swing. Mean response amplitude was least during early stance for two of the sites at $2{\cdot}0 \times T$ although it is clear from Fig. 4 that there was only modest variation in the amplitude of the evoked responses during the stance phase.

Consistency of the locomotion-related variation

The consistency of the pattern of variation in the size of the climbing fibre-evoked responses is illustrated in Fig. 5 which shows the distribution of the minimum (▨) and maximum (■) mean response areas during the step cycle for one sample from each recording site ($n = 3$, 2 and 1 from the three cats). With only one exception, the minimum response size occurred during the first half of the stance phase in the ipsilateral forelimb (Fig. 5). The single exception was one of the cases illustrated in Fig. 4 (●···●) where the minimum occurred during the period of transition

between the stance and swing phases. By contrast, in every case the maximum mean response was seen during the final fifth of the step, i.e. during mid- to late swing, and most frequently during the final tenth (Fig. 5).

DISCUSSION

The size of the potentials evoked by climbing fibres in the cerebellar cortical c_1 zone in response to electrical stimulation of cutaneous afferents in the superficial

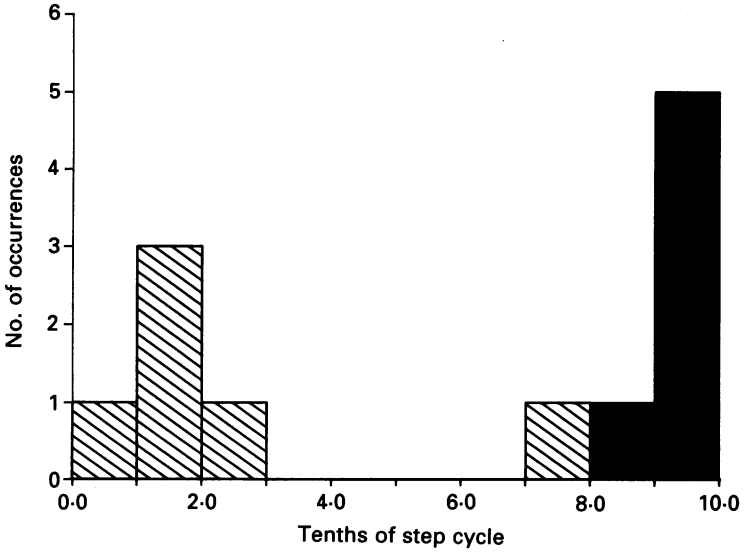

Fig. 5. The distribution across the step cycle of peak (■) and minimum (▨) mean response sizes for each recording site in each cat ($n = 6$).

radial nerve has been shown to be dependent on the phase of the step cycle in which the stimulus is delivered. As the compound action potential in the stimulated nerve was monitored and found to show no locomotion-related variation in amplitude, it may be concluded that the variable amplitude of the climbing fibre-evoked potentials reflects a central, step-related modulation of the excitability of the SOCPs. Such modulation of the SOCPs innervating the cerebellar cortical c_2 zone has been reported elsewhere (Apps *et al.* 1990).

Origin of the variation in spino-olivocerebellar pathway excitability

It was argued previously that the variation in response amplitude is most likely to have arisen at a pre-cerebellar level in the SOCPs (Apps *et al.* 1990). This was because the synaptic action of climbing fibres on Purkinje cells is exceptionally strong. Thus, Purkinje cells discharge complex spikes in response to climbing fibre inputs even when they are powerfully inhibited following activation of inhibitory intracortical interneurones by local surface ('LOC') stimulation of the cerebellar cortex (Eccles, Llinás, Sasaki & Voorhoeve, 1966*b*). For this reason, it was suggested that the

changes in the *probability* of evoking climbing fibre-generated field potentials in the c_2 zone during stepping could not have arisen from inhibition of Purkinje cells (Apps *et al.* 1990) and this argument applies equally well to the present data where changes in probability were also observed (Fig. 3).

However, it remains the case that variation in the *size* of the potentials may be influenced by Purkinje cell excitability. The size of the climbing fibre-evoked EPSP in individual Purkinje cells is dependent on the membrane potential, as with other chemical synapses, and varies linearly with small intracellularly injected currents (Eccles *et al.* 1966*a*; Llinás & Sugimori, 1980). When Purkinje soma are synaptically inhibited by the action of basket and stellate cells the somatically recorded climbing fibre-evoked EPSPs are reduced during the rising phase of the IPSP, i.e. when the somatic conductance is greatest, but are potentiated and prolonged by the hyperpolarization during the period following the peak of the IPSP (Eccles *et al.* 1966*b*). With extracellular recordings, such as those presented here, and in the presence of synaptic inhibition of the Purkinje cells, the negative-going climbing fibre-evoked potentials recorded at the level of the climbing fibre synapses in the molecular layer are increased and prolonged (Jansen & Fangel, 1961; Eccles *et al.* 1966*b*), while the positive-going extracellular fields recorded at or closer to somatic level are reduced (Eccles *et al.* 1966*b*). The data presented in Fig. 3*B* and *C* are based on measurements of positive-going (somatic) potentials while those in Fig. 3*A* are principally of the negative (dendritic) component of negative–positive potentials. Therefore, if the pattern of step-related modulation in the amplitude of the climbing fibre-evoked potentials was due to variation in the excitability of Purkinje cells the direction of the modulation in Fig. 3*A* would be the opposite of that in Fig. 3*B* and *C*. This is not the case which suggests that the variation originates at a pre-cerebellar level in the SOCPs and that the variations observed at the cerebellar cortical level are due to variation in the numbers of olive cells and thus of Purkinje cells recruited by the stimuli.

Nature of the spino-olivocerebellar pathway modulation

Only single complex spikes are generally fired by individual Purkinje cells in response to peripheral nerve stimuli (e.g. Oscarsson, 1969), and their discharge therefore represents an all-or-none response in each cell. As the probability of evoking a climbing fibre-mediated multiunit field potential varied during stepping it is appropriate to ask if the modulation of the SOCPs was similarly of an all-or-none character whereby transmission in the SOCPs was switched on or off, or whether there was a continuously variable gating of the SOCP excitability. Figure 3 shows that a systematic step-related variation was present in the mean amplitude of the climbing fibre-evoked potentials even when the stimuli that were unsuccessful in evoking responses were excluded from the calculations. This implies that a continuous modulation of the response amplitude was occurring. The variation in response probability might then be explained if SOCP excitability was sometimes carried sufficiently far from threshold for transmission failure to occur.

Although single olivary neurones do not exhibit movement-related discharges, multiunit spike trains recorded from small groups of neighbouring olivary neurones are movement related (Boylls, 1980; Gellman *et al.* 1985). If several small groups of

this type were to contribute to producing the field potentials recorded in this study a gating mechanism of the on–off type, if operating independently in each of the groups, could give rise to results similar to those in Fig. 3. In this case, provided the number of contributing groups was small, the discrete contributions of each of the groups to the evoked potentials might give rise to a frequency distribution histogram of response amplitude that was multimodal. This was not in fact the case (not shown, but note the overlap of standard errors of the mean areas in Fig. 3).

Thus, the data suggest that step-related variation in the size of the climbing fibre-evoked potentials is due mainly to a continuously variable regulation of the SOCP excitability though the presence of an on–off type gating mechanism acting in parallel cannot be entirely excluded.

Functional significance of the modulation

In passive but awake cats the SOCPs are extremely sensitive to cutaneous stimulation, especially in those pathways relaying forelimb inputs to the paravermal cortex of lobule V (Gellman *et al.* 1985; Armstrong *et al.* 1988). Despite this, individual Purkinje cells do not discharge complex spikes in response to paw contact or lift during stepping (Armstrong *et al.* 1988) even though the force applied to the paw during the support phase of the step cycle is an order of magnitude greater than that required to maximally activate the DF-SOCP in decerebrate cats (Rushmer, Roberts & Augter, 1976). Instead, it appears that a gating mechanism operates which prevents such self-generated stimuli evoking complex spikes although unexpected peripheral inputs may still do so (Gellman *et al.* 1985; Andersson & Armstrong, 1987). The modulation of the amplitude of the climbing fibre-evoked potentials reported here may reflect the operation of this gating mechanism. Thus, the excitability to superficial radial nerve stimuli of the SOCPs innervating the c_1 zone was reduced during early stance, when foot contact occurs and the limb becomes supporting, and at the transition from stance to swing, when paw lift occurs, in the ipsilateral forelimb. The excitability of the pathways was thus reduced at those times of the step when the largest self-generated input from the paw will occur which may explain the absence of complex spikes at these times.

In light of the demonstration that unexpected input may evoke olivary (Gellman *et al.* 1985) or complex spike discharges (Andersson & Armstrong, 1987), it is noteworthy that the peak of excitability to superficial radial nerve stimuli in the c_1 zone SOCPs invariably occurred during the second half of swing in the ipsilateral forelimb (Fig. 5). It is during this period of the step that the limb is extended forward (the E_1 phase of the step) and is most likely to encounter an unexpected obstacle which will contact the paw dorsum, i.e. the skin supplied by the superficial radial nerve. Of four c_1 zone Purkinje cells examined by Andersson & Armstrong (1987), none responded to the locomotor perturbation caused by paw placement on a rung of a horizontal ladder which gave way under the weight of the animal. By contrast, 65% of Purkinje cells in the lateral vermis (b zone) responded to such a perturbation. The failure of c_1 zone Purkinje cells to respond to such perturbations during early stance may be due to the depression of transmission in the c_1 zone SOCPs shown here. Thus the c_1 zone SOCPs may monitor and respond to perturbations during swing while the b zone SOCPs may do so during stance. However, in the present study,

when stimulus strength was increased the extent of the modulation in SOCP excitability was much reduced and the depression during stance was less clear (Fig. 4). This implies that larger stimuli, and therefore perhaps grosser perturbations, may effectively activate the SOCPs irrespective of the phase of the step cycle in which they occur.

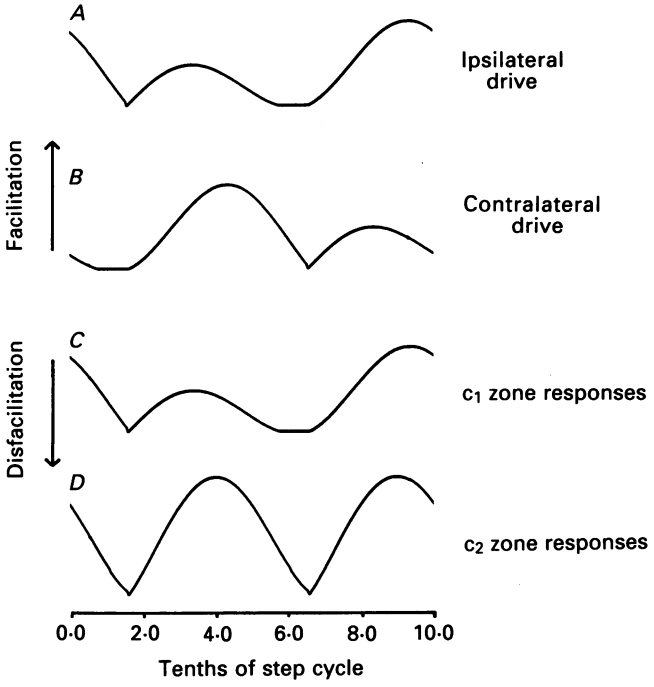

Fig. 6. A schematic plan to show how the variation in size of the climbing fibre-evoked responses in the c_1 and c_2 zones might arise from two modulatory drives each related to the movement cycle in one forelimb. In the c_1 zone only the ipsilateral drive is effective in modulating the evoked responses. For the c_2 zone, however, the ipsilateral and contralateral drives summate to produce two peaks during each step (see text).

Comparison of the c_1 and c_2 zone responses

The level within the SOCPs at which the variation in their excitability occurs cannot be determined from the present data. However, comparison of the data from the c_1 zone with that presented earlier from the c_2 zone (Apps *et al.* 1990) suggests that common influences may act on the SOCPs innervating the two zones.

Figure 6 shows schematically how variation in amplitude of the c_1 zone responses (Fig. 6*C*) might be generated by a modulatory drive which is related to the movement cycle of the ipsilateral forelimb (Fig. 6*A*). In the c_2 zone, which receives climbing fibre input related to both forelimbs, a similar but 180 deg phase-shifted drive (Fig. 6*B*) related to the movement cycle of the contralateral forelimb may also be effective and summate with the ipsilateral drive. This would produce a pattern of modulation in c_2 zone responses in which there are two peaks of activity in each step cycle as shown in Fig. 6*D*. Variation of the relative amplitudes or effectiveness of the

ipsilateral and contralateral drives may then alter the relative amplitudes of the two peaks of c_2 zone SOCP excitability. This pattern of step-related variation in amplitude of the c_2 zone responses (Fig. 6*D*) closely resembles the experimentally observed pattern where the temporal distribution of peak excitability in the c_2 zone SOCPs was bimodal with peaks in mid- to late stance at some recording sites and in late swing at others (Apps *et al.* 1990).

Origin of the modulatory drive

Cutaneous reflexes are gated during locomotion so they may be evoked only in specific phases of the step cycle, e.g. the stumbling corrective reaction is evoked during swing but not during stance when it would involve lifting the supporting limb from the ground and thus be counter-productive (Forssberg, Grillner & Rossignol, 1977). Such gating also occurs during fictitious locomotion where peripheral feedback due to the movements of stepping is absent (Andersson, Forssberg & Grillner & Lindquist, 1978). The gating must therefore arise in the central nervous system, perhaps from the central pattern generator for locomotion. The modulation of the SOCPs similarly may be generated by central mechanisms but peripheral feedback may also play a significant role. Thus, electrical stimulation of peripheral nerves may evoke potent inhibition of the response of the SOCPs to a subsequent nerve stimulus (Armstrong & Harvey, 1966; Newman & Paul, 1966; Andersson, 1984). In particular, inhibition of the responses evoked by forepaw nerve stimulation in the cerebellar cortical c_1 zone via the DF-SOCP may be inhibited at the level of the cuneate nucleus by preceding stimulation of another forepaw nerve (Lidierth, 1990). Naturally occurring inputs arising from paw mechanoreceptors during stance and at paw-lift might then evoke inhibitory actions that contribute to producing the variation in SOCP excitability reported here. In addition, Kolb & Rubia (1980) have reported that the climbing fibre-evoked response to a wrist dorsiflexion in Purkinje cells of the c_1 zone in decerebrate cats is dependent on the initial wrist joint angle. The excitability of the SOCPs may therefore be modulated by limb position which is continually changing during locomotion. It is relevant in this respect that joint afferents are known to be a potent source of excitation to the SOCPs supplying the paravermal cortex (Eccles, 1978).

Localization of function in the cerebellar cortex

Oscarsson (1980) has suggested that the sagittal zones of the cerebellar cortex are its basic functional units. However, when the step-related discharges of simple spikes were compared for the zones of the paravermal cortex they showed only small variations between zones (Armstrong & Edgley, 1984; Edgley & Lidierth, 1988). Averaging of the discharge patterns among many cells showed small changes in the phase of the step at which maximal discharge occurred in the c_1, c_2 and c_3 zones. However, the phase shift was equally large between the medial and lateral halves of the c_2 zone (Edgley & Lidierth, 1988) which implies that the phase shift occurs gradually across the cortex and not abruptly at the borders of the zones. The present data, together with those from the c_2 zone (Apps *et al.* 1990), demonstrate a much clearer difference between the c_1 and c_2 zones, by showing that the peak excitabilities of the SOCPs supplying the two zones occur 180 deg out of phase during the step

cycle (see above). Although electrical stimulation of nerves, as used here, may provide a highly artificial input to the SOCPs, the changes in response size nevertheless reflect a modulation of the SOCP excitability which arises naturally during stepping. There is therefore a substantial difference in the natural pattern of modulation of the c_1 and c_2 zone SOCPs which presumably reflects a distinct functional role for the two zones and thus provides clear evidence in support of Oscarrson's (1980) hypothesis.

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