Step phase-related excitability changes in spino-olivocerebellar paths to the c_1 and c_3 zones in cat cerebellum

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1. Chronically implanted microwires were used to record extracellular field potentials generated in the c_1 and c_3 zones in the cortex of lobules V and VI of the cerebellum by non-noxious stimuli delivered to the superficial radial nerve in the ipsilateral forelimb. Responses due to input via climbing fibre afferents were studied; their latency and other characteristics identified them as mediated mainly via the dorsal funiculus spino-olivocerebellar path (DF-SOCP).

2. Responses at individual sites were studied repeatedly with a range of stimulus intensities and during two different behaviours: quiet rest and steady walking on an exercise belt. For responses during walking, step histograms were constructed showing response mean size during different tenths of the step cycle in the ipsilateral forelimb, both in absolute terms and relative to mean size during rest.

3. Step histograms for the same site on different days or different stimulus intensities varied appreciably in form but in both cases the timing of the largest response was usually the same or shifted by only one step tenth.

4. In both zones the largest responses during walking occurred overwhelmingly during the E_1 step phase when the limb is extended forwards and down to establish footfall. Least responses were much less uniform in timing but were mostly during stance, particularly its early (E_2) part.

5. In many histograms the smallest responses were smaller in mean size than the responses during rest while the largest were larger. These changes were not paralleled by changes in nerve volley size, so presumably reflect step-related central changes in pathway excitability. Facilitations and depressions were differently affected by stimulus intensity and sometimes occurred independently, suggesting generation by separate mechanisms.

6. In both zones there were differences between recording sites which suggests that different DF-SOCP subcomponents innervate different parts of the zones. However, no systematic differences could be firmly established between the medial and lateral subzones of the c_1 zone.

7. The results are discussed in relation to the hypothesis that the DF-SOCP constitutes the afferent limb of a transcerebellar mechanism involved in adapting the evolving step.

The paravermal cortex of the anterior lobe of the cat cerebellum is divisible into several longitudinal zones based on distinct anatomically and electrophysiologically defined innervation patterns. Each zone is typically *ca* 1 mm in width but may extend across several lobules and folia (see for example, Voogd & Bigaré, 1980; Oscarsson, 1980). Proceeding laterally from the junction with the vermis these zones are the c_1, c_2, c_3, d_1 and d_2 zones of which c_1 and c_3 each comprise a medial and a lateral subzone. Each zone is innervated by climbing fibres originating from a restricted region of the contralateral inferior olivary nucleus and each zone is the terminus for a characteristic combination of spino-olivocerebellar paths (SOCPs; for a review see Oscarsson, 1980).

The c_1 and c_3 zones show certain similarities. Both receive tactile (and other) information from the ipsilateral forelimb mediated via SOCPs that travel in the dorsal and dorsolateral funiculi of the spinal white matter (DF- and DLF-SOCP, respectively). Of these two paths the DF-SOCP conducts the most rapidly. The medial c_1 and medial c_3 subzones are also anatomically linked (Ekerot & Larson, 1982) with significant numbers of their climbing fibres

being branches of the axons of the same olivary neurones (presumably located in the rostro-medial part of the dorsal accessory olive; see Trott & Apps, 1991).

In a previous paper (Lidierth & Apps, 1990) the excitability of the SOCPs to the c_1 zone during walking was studied by stimulating a cutaneous nerve (superficial radial nerve) in the ipsilateral forelimb with single non-noxious electrical pulses delivered at different times during the step cycle. The characteristic extracellular climbing fibre field potentials generated within the layers of the cerebellar cortex by the action of the impulse volley were recorded at six sites. When response sizes at different times during the step cycle were averaged across a number of trials, it was clear that pathway excitability varied during the cycle, being greatest in mid- to late swing and least (in 5 cases) during the first half of stance. Because the amplitude of the peripheral nerve volley varied little during the step cycle it was concluded that the response variations reflected the operation of some central modulatory or gating mechanism and evidence was presented (cf. also Apps, Lidierth & Armstrong, 1990) that it acted at a precerebellar level (i.e. at the level of the spinal cord, the cuneate nucleus or the inferior olive).

The cerebellar responses were recorded using glass-coated tungsten microelectrodes advanced through the dura and into the cerebellar cortex via a micromanipulator. Stable recordings could be obtained infrequently and only briefly, presumably because of drift of the microelectrode tip relative to the layers of the cerebellar cortex. The present paper describes a new investigation in which much more stable recordings were obtained via fine flexible microwire electrodes chronically implanted into both the c_1 and c_3 zones. Recordings could be made intermittently for up to 1 month following implantation both during walking and while the animal rested quietly without overt movement. The following questions could therefore be addressed. (1) Are patterns of step-related modulation in response size at individual sites maintained over time? (2) Is the modulation pattern at each site independent of stimulus intensity? (3) Are responses evoked during walking smaller than during rest (as previously demonstrated for a few sites in the c_2 zone by Apps *et al.* 1990)? (4) Are any differences detectable between responses recorded from the c_1 medial and lateral subzones (which receive their climbing fibres respectively from the dorsal accessory olive and middle levels of the medial accessory olive)? (5) To what extent do the findings for the c_3 zone, not previously studied, resemble or differ from those for the c_1 zone?

METHODS

General

In each of three purpose-bred adult cats an array of chronically implanted fine flexible microwires was used to record extracellular field potentials generated in the cerebellar cortex by non-noxious electrical stimulation of the superficial radial (SR) nerves via chronically implanted bipolar electrodes. Potentials were recorded while the animals sat or lay quietly at rest and while they walked at comfortable speed (*ca* 0·5 m s^{-1}) on an exercise belt. During walking, locomotor electromyograms were recorded from the lateral head of the triceps brachii muscle (an elbow extensor) in the ipsilateral forelimb. These signals were used to determine the timing of the nerve stimuli relative to the step cycle (see below).

All implantations were carried out at an initial aseptic operation with a surgical level of general anaesthesia (40 mg kg^{-1}, I.P. sodium pentobarbitone, Sagatal, Rhône Mérieux, Harlow, UK; maintenance doses I.V. as required to abolish corneal and flexion reflexes). Postoperative analgesia was maintained for 24 h with buprenorphine (Temgesic; 10 μg kg^{-1}, I.M.; Reckitt and Colman, Hull, UK). Recovery from the operation was rapid and uneventful and recordings were initiated usually 2 or 3 days later. The techniques employed have been fully described in previous papers (see Apps *et al.* 1990; Lidierth & Apps, 1990) except for the use of microwire electrodes.

Microwire electrodes

The cerebellar recording electrodes were platinum–iridium microwires, Teflon insulated except at the tip, and 25 μm in total diameter (Clarke Electromedical, Reading, UK). They were prepared and inserted as described by Armstrong & Drew (1984) who employed them in the cerebral cortex. In the present study wires were inserted (through the pia mater) to a depth of 1–2 mm, into the tips of the folia making up the paravermal part of lobule V of the anterior lobe (two were inserted into lobule VI just behind the fissura prima) and sealed in position by closing the skull defect with dental acrylic cement. Prior to insertion a scale drawing of the folia was prepared and the boundaries of the c_1, c_2 and c_3 cortical zones were determined electrophysiologically, as described by Trott & Apps (1991); the point of insertion of each wire was carefully charted on the drawing of the cerebellar surface.

The cerebellar responses

Study was confined to extracellular field potentials which were characteristic of the c_1 and c_3 zones (see Ekerot & Larson, 1979*a*; Trott & Apps, 1991). Of the fifteen microwires that yielded c_1 zone responses, nine were inserted directly into the zone; five of these yielded only c_1-type responses but at four loci such responses were followed by longer latency, bilateral responses that are characteristic of the c_2 zone (cf. Apps *et al.* 1990). Five further electrodes were inserted close to the c_1–c_2 boundary line and each gave responses characteristic of both zones. The final electrode was inserted into the medial part of the c_2 zone but yielded only c_1 zone responses. Of the seven wires classed as recording from the c_3 zone, four were inserted directly into that zone and yielded only c_3-type responses; the three others were inserted into the lateral part of the c_2 zone and two of these gave responses characteristic of both zones while the third gave only c_3-type responses.

At most recording sites responses attributable to climbing fibre input were positive–negative diphasic waves indicative of recordings obtained from the granular layer, however at some sites they were negative–positive waves, indicative of recording from the molecular layer. In the large majority of cases, response polarity was maintained between recording sessions on several

different days but occasionally a polarity reversal occurred, probably because between sessions the electrode tip had moved relative to the cortical layers. Response amplitudes to the same stimulus usually changed between recording sessions and such changes were usually progressive decreases with time after operation, though increases sometimes occurred. Such changes presumably reflect slow shifts in electrode tip position and/or changes in the recording characteristics of the microwires; electrode impedance has been shown to decline progressively over periods of implantation similar to those involved in the present study (Palmer, 1978).

Response size was measured by integration (mV ms; see Apps *et al.* 1990) of the whole of the initial phase of the response, whether positive or negative (see above). For most loci, most of the response (onset, 11–14 ms; duration, typically *ca* 5 ms) must have been mediated via DF-SOCP which is the fastest conducting pathway. However, some contribution to the measured area from activity mediated via DLF-SOCP cannot be excluded in some cases because such activity has onset latency 15–20 ms (Larson, Miller & Oscarsson, 1969). Threshold for a just-detectable cerebellar response was typically *circa* $1{\cdot}1T$ where T is the threshold for the most excitable fibres in the nerve. The present report is based on responses evoked by stimulation at intensities $1{\cdot}5$–$4T$. In most cases a single 0·05 ms pulse was delivered to the nerve but occasionally a pair of pulses 1 ms apart was used to facilitate response size. These stimulus parameters are inadequate to excite nociceptive afferents and the animals completely ignored the stimuli which were delivered at a frequency of 0·7 Hz. In some recording sessions it was possible to record simultaneously from two cerebellar sites (7 instances; see Results).

Recordings from superficial radial nerve

Throughout all recording sessions, the afferent volley in the SR nerve was monitored. The peak-to-peak amplitude of the nerve compound action potential was measured, and mean values during walking were expressed as a percentage of the means for similar stimuli delivered during rest (in the same recording session). In 16/56 comparisons there was no statistically significant difference between the average size of volley during locomotion and that at rest (Student's two-tailed t test, $P > 0{\cdot}05$). Of the remainder, there were twenty-eight cases in which the nerve volley during locomotion was significantly smaller (by 5·1–25·9%; two-tailed t test, $P < 0{\cdot}05$), and twelve cases in which the nerve volley was significantly larger (by 5·6–30·8%; two-tailed t test, $P < 0{\cdot}05$). Reductions were therefore more common than increases. An apparent change in volley size may as easily reflect an efficacy change (due, for example, to a mechanical instability) at the recording cuff, as at the stimulating electrodes, so the importance of any difference is difficult to assess (but see Discussion for possible implications). In all cases any variation in the mean size of the compound action potential during walking did not correlate with the fluctuations in size of the cerebellar response.

Data manipulation

The techniques used to store and analyse the cerebellar responses, the electromyograms and the SR nerve compound action potentials have been detailed in previous papers (Apps *et al.* 1990; Lidierth & Apps, 1990). In brief, for data obtained during walking, the step cycle was divided into ten equal epochs (a computer-based method was used in most cases to calculate the tenth in which the stimulus occurred; Marple-Horvat & Gilbey, 1992). In addition, the mean size of the cerebellar response in each epoch was calculated and used to construct a step histogram (see Figs 1 and 6). Though in the histograms presented in Results response size is given in absolute terms, histograms were also plotted in which bin height was expressed as a percentage of mean response size in the resting animal. Onset of the first epoch coincided with the onset of the locomotor electromyographic activity in triceps brachii muscle as determined from the EMG recordings (i.e. coincided approximately with onset of stance).

Each step histogram was normally based on responses evoked by more than 100 successive individual stimuli (i.e. 10 or more were usually averaged per bin) while response size during rest was estimated usually by averaging thirty to forty responses. As is usual for SOCP responses (cf. Apps *et al.* 1990; Lidierth & Apps, 1990) successive responses frequently fluctuated considerably in amplitude and even when stimulus intensity was well suprathreshold, a proportion of the stimuli often failed to evoke a measurable response. For this reason, standard errors of the mean are shown rather than standard deviations in the histograms of Figs 1 and 6.

Pairs of step histograms were compared by comparing the timing of their highest and their lowest bins and also via a statistical comparison of bin heights across the whole step cycle. The non-parametric Spearman rank-order correlation coefficient was calculated for the two sets of histogram bins and P values (one tailed) were determined and used to judge whether or not a significant positive correlation existed between the two histograms.

For some purposes (see Results) the extent of response size modulation during the step was represented via calculation of a modulation index given by the formula: 1 − (response size in the smallest bin/response size in the highest bin). This index takes a value of zero when modulation is absent and a value of 1 when there is a part of the step when no response is evoked.

RESULTS

The extracellular field potentials evoked in the cerebellar cortex by stimulation of the SR nerve and recorded with chronically implanted microwire electrodes were similar in shape, size and latency to those previously recorded in the c_1 zone when tungsten-in-glass microelectrodes were used (see Apps *et al.* 1990). Responses were recorded at fifteen c_1 and seven c_3 sites.

At almost all sites it was possible to compare step phase-related modulations in response size with response average size in the absence of movement (see Methods for further details). Results were routinely presented in the form of step histograms of the kind shown in Figs 1 and 6. An overall impression of the extent to which response size was modulated during the step cycle may be gained from the finding that among the fifty-eight step histograms available for the c_1 zone, the modulation index (see Methods) varied from 0·27 to 1. The range for the c_3 zone was 0·23–0·96 (17 histograms). If only the largest values for each site are considered then the range among c_1 sites was 0·53–1 (mean ± S.D., 0·71 ± 0·15) and that for c_3 sites was 0·39–0·96 (mean ± S.D., 0·66 ± 0·17).

The c_1 zone

Stability of response modulation patterns over time

The response to the same SR stimulus (i.e. the same multiple of T) was recorded on more than 1 day at each of five sites (for details see Table 1). Figure 1 presents example step histograms for two sites at which recordings were made 4 (Fig. 1*A* and *B*) and 27 (Fig. 1*C* and *D*) days apart .

On each occasion when two step histograms were compared, two aspects were taken into consideration: (1) the degree of overall similarity in the pattern of step phase response modulation was assessed via calculation of a Spearman rank-order correlation coefficient (see Methods); and (2) the epochs in which the average response sizes were smallest and largest were compared.

The results of the first procedure are presented in Table 1 which shows for each site the stimulus intensities used, the time separation between the recordings under comparison, the Spearman rank-order correlation coefficient (r_s), the associated P value (one-tailed test) and the presence (s.) or absence (n.s.) of a statistically significant correlation between each pair of histograms.

Among the twenty comparisons included there were eleven instances in which the two displays in the pair showed a statistically significant positive correlation. These instances involved each of the three recording sites most fully studied (1, 2 and 3 in Table 1) but for each of these there was at least one comparison which yielded no significant correlation. For the two sites at which only one comparison could be made there was in each case no significant correlation. Note that at site 2 there was,

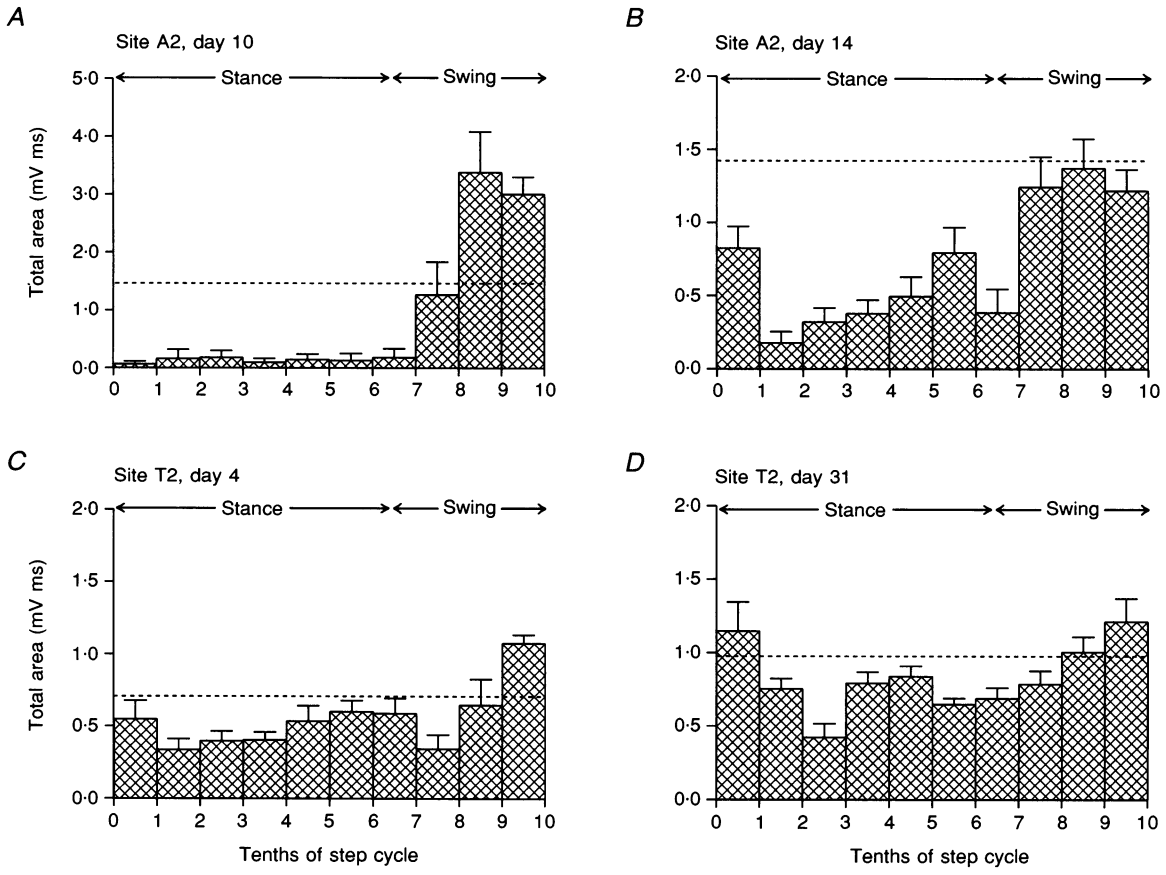

Figure 1. Step histograms for two c_1 recording sites

In each of *A*–*D* the step cycle has been divided into ten equal time bins, onset of bin 1 coinciding with the onset of locomotor EMG in the ipsilateral triceps brachii muscle. Height of each bin represents the mean size of the cerebellar response evoked during walking by stimulation of the ipsilateral superficial radial (SR) nerve in that tenth of the step (see Methods). The horizontal dashed lines indicate mean size of the response evoked by similar stimuli delivered in the resting animal. *A* and *B* were obtained for the same (medial) recording site studied in two recording sessions 4 days apart; stimulus intensity, 2*T*. *C* and *D* are for a second (lateral) site studied in two sessions 27 days apart; stimulus intensity, 3*T*. The periods of stance and swing are approximate timings for trajectory of the ipsilateral forelimb in this and subsequent figures.

exceptionally, a significant *negative* correlation between the two histograms for stimulation at $3T$ (see asterisk in Table 1).

When times of smallest response were compared the findings were again mixed, as may be seen from Fig. 2*A*, which shows for each of the five sites in Table 1 the extent (in terms of tenths of a step) to which the time of least response shifted between recording sessions.

Note that sites 1, 2 and 3 of Table 1 are each represented more than once because at these sites comparisons were made for more than one stimulus intensity, and for some intensities more than one comparison could be made. Comparisons for these sites are indicated respectively by open, diagonal and filled bars and inspection shows that at each site some comparisons revealed similar and some different degrees of shift. Given that a five-tenths shift (i.e. half a cycle) is the maximum possible it is clear that shifts were frequently substantial. Size of shift showed no tendency to be larger for longer time intervals between recording sessions and shifts occurred in both directions relative to the start of the step cycle with only a slight predominance of shifts to an earlier time of least response (not illustrated).

When times of *largest* response were considered, it is clear from the frequency histogram of Fig. 2*B* that these were markedly more stable. Among the five sites there were three at which in all the possible comparisons the time of largest response was the same. At the remaining two sites there were shifts in time of the largest response in a proportion of the available histograms (see Fig. 2*B*, filled and hatched bars).

The relatively low number of statistically significant positive correlations and the instability in the time of least response may of course reflect systematic variations over time in the patterns of response size modulation during the step cycle. However, an alternative

Table 1. Statistical comparison of step histograms produced at individual c_1 recording sites

Recording site	Stimulus intensity (T)	Time separation (days)	r_s	P (one tail)	Correlation
1	2·0	1	0·21	0·28	n.s.
		10	0·56	<0·05	s.
		9	0·37	0·15	n.s.
	2·5	1	0·68	0·01	s.
	3·0	1	0·55	<0·05	s.
		10	0·15	0·33	n.s.
		9	0·61	0·03	s.
2	1·5	1	0·65	0·02	s.
	2·0	1	0·28	0·20	n.s.
		13	0·55	<0·05	s.
		14	−0·15	0·34	n.s.
	3·0	14	−0·73	<0·01	s.*
3	2·0	4	0·41	0·12	n.s.
	3·0	6	0·88	<0·001	s.
	4·0	1	0·68	0·01	s.
		6	0·79	0·003	s.
		7	0·76	0·006	s.
	4·0 (pair)	2	0·81	0·002	s.
4	3·0 (pair)	15	0·45	0·09	n.s.
5	3·0	27	0·44	0·10	n.s.

Comparison made between sites recorded in different recording sessions by stimulation of SR nerve at the same intensity. Each horizontal row was generated by comparing two histograms. Note that where the same stimulus intensity is accompanied by three rows, this arises because three histograms were available for comparison in pairs. r_s, Spearman rank-order correlation coefficient; s., statistically significant correlation existed between the two histograms; n.s., no significant correlation; pair, use of paired stimuli to increase response size (see Methods); * significant negative correlation.

explanation might reside in the well-known tendency for SOCP responses to fluctuate considerably between trials and in the fact that the height of each histogram bin was necessarily calculated from a relatively small number of individual responses. Inspection of the histograms indicated that whereas the highest bin was frequently appreciably larger than all others, the smallest was often little different in height from one or more of the others (see, for example, Fig. 1*A*). It is therefore possible that chance fluctuations in response size may have contributed both to the greater apparent instability in timing for the least, compared with the greatest, response and to the production of non-significant Spearman correlation coefficients.

If this were the case then it might be predicted that the likelihoods of a significant correlation and of stability in the time of least response would both be greatest when the pattern of response modulation was particularly pronounced. This proposition was tested by calculating for each histogram a modulation index which increased (from 0 to 1) as the depth of modulation increased (see Methods). When the Spearman coefficient for each comparison ($n = 20$) was plotted against the sum of the modulation indices for the two histograms involved (not shown), linear regression analysis revealed a small but significant positive correlation ($r = 0{\cdot}45$; $P = 0{\cdot}02$, one tailed) in accordance with the proposition above. When size of shift in the time of least response was treated similarly (not shown), a small but significant negative correlation emerged ($r = -0{\cdot}46$; $P = 0{\cdot}03$, one tailed) again in accordance with the proposition above.

Stimulus intensity dependence of the responses at c_1 sites

The use of microwires also allowed investigation of the effect of different stimulus intensities to the SR nerve on the absolute amplitude of the responses at individual recording sites and on their step phase modulation patterns. To minimize any effect on response size of 'drift' in electrode tip position, or possible changes in the effectiveness of the nerve stimulation, study was confined to comparisons of data gathered in the course of a single recording session.

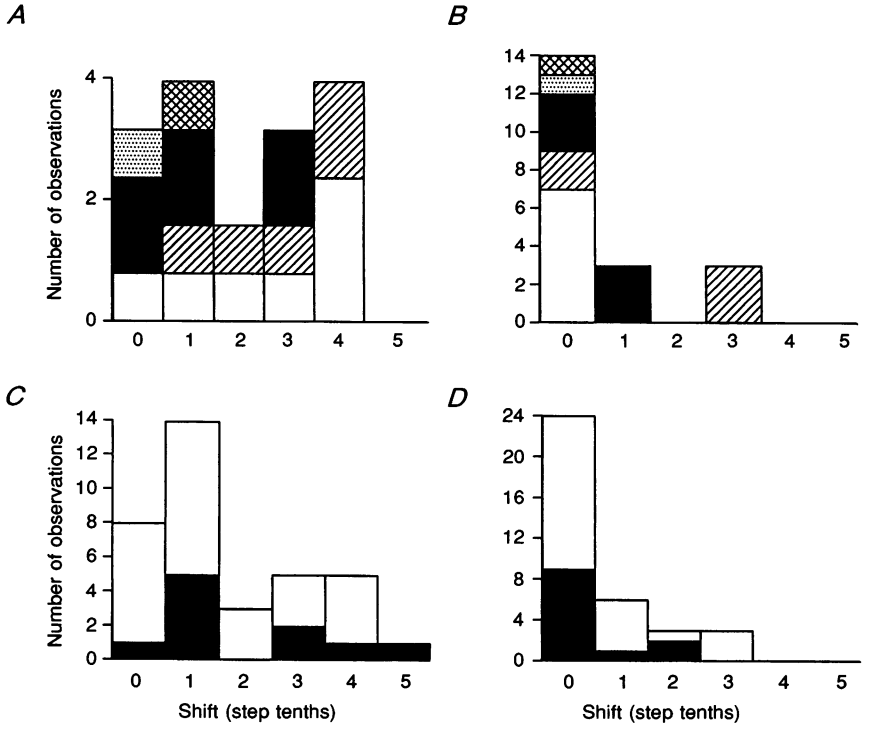

Figure 2. Shifts in step timing for the smallest and the largest cerebellar responses evoked during walking at c_1 sites

A, pairs of step histograms generated at the same site by similar stimuli delivered during two different recording sessions were compared as to the extent of any shift in the position of the bin in which response size was least ($n = 20$). Same 5 sites as in Table 1; different patterns relate to different sites studied at one or more stimulus intensities (see text). Note that 5 step tenths is the maximum shift possible. *B*, similar to *A* except the shifts relate to the bin in which mean response size was largest ($n = 20$). Same 5 sites as in *A* and Table 1. *C* and *D*, effect of intensity of nerve stimulation on step timing for the smallest and largest cerebellar responses evoked during walking. *C*, frequency distribution for shifts in time of least response occurring when two different intensities were employed at the same c_1 site on the same day. ■, 12 step histogram comparisons for 2 and 3*T*. □, a further 24 comparisons at the same or other sites (see text). *D*, as *C* but for shifts in time of largest responses.

Table 2. Effect of stimulus intensity difference on correlation between pairs of c_1 zone step histograms

$\Delta I(T)$	s.	n.s.
0·5	8	4
1·0	8	12
⩾1·5	0	4

Frequency of presence and absence of a statistically significant positive correlation between pairs of step histograms when the comparisons involved different sizes of differences in stimulus intensity. $I(T)$, intensity difference in multiples of T; s. and n.s., significant correlation and no significant correlation, respectively. Total of 36 comparisons (see text).

Figure 3 shows the effect of intensity on response mean amplitude as determined in the resting animal at each of nine sites, at all of which both 2 and $3T$ were used (and at 7 of which an additional intensity was also employed). These sites differed markedly: at some an increase in intensity from 2 to $3T$ had little effect on response size whilst at others it was increased substantially.

Two plots in Fig. 3 are distinguished by filled circles and two by filled squares to indicate that the responses at the two loci concerned were recorded simultaneously. Note that in one case (filled squares) the intensity dependence of response size differed markedly between the two loci, despite the fact that the relevant responses were generated by the same stimuli to the nerve (see Discussion).

With regard to possible effects of stimulus intensity on the pattern of step phase dependence of responses evoked during walking, data were available for all nine sites considered above, plus a further three sites studied at 3 and $4T$ (two with paired stimuli; see Methods). The analysis procedure followed was similar to that used to compare results obtained by delivery of the same stimulus on different dates, except that the histograms compared in pairs were obtained in the same recording session and involved different stimulus intensities. The total number of available comparisons was thirty-six and among these the Spearman correlation coefficient was positive and statistically significant in sixteen cases, and non-significant in the remaining twenty. Table 2 shows that when comparisons were grouped according to the extent of the stimulus intensity difference between the histogram pairs, the likelihood of a statistically significant correlation decreased, as the intensity difference increased (see Discussion).

The effect of stimulus intensity on the time at which response size was smallest during the step cycle is documented by Fig. 2*C*, which shows the frequency with which different sized shifts were encountered. Comparisons between 2 and $3T$ are represented by the filled areas; the open areas show twenty-four other comparisons either at the same nine sites or at three sites where only 3 and $4T$ were employed. Only in 8/36 cases (22%) was there no shift in the time of least response. On no fewer than eleven occasions (31%) the change exceeded two tenths of a cycle.

By contrast, the time of largest response was markedly more stable, as is evident from the frequency histogram of Fig. 2*D*: in no fewer than 24/36 cases (67%) a difference in stimulus intensity was accompanied by no shift; the largest change was three tenths of a step cycle and such a change occurred on three occasions (8%) only. For both the largest and smallest responses, timing shifts that accompanied increases in stimulus intensity occurred with similar frequencies in both directions relative to the start of the step cycle.

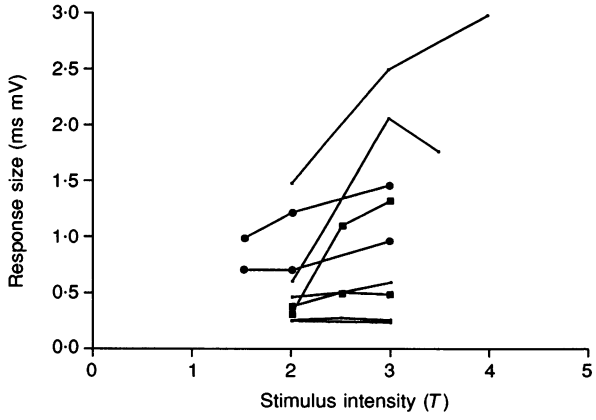

Figure 3. Relationship between intensity of stimulation of SR nerve and amplitude of field potentials at c_1 sites

The responses evoked in the resting animal at 9 recording sites in the c_1 cerebellar zone are shown. Stimulus intensity is in multiples of threshold (T) for the most excitable fibres in the nerve.

Step cycle timing of the largest and smallest responses at c_1 sites

The results both confirm and extend the findings of Lidierth & Apps (1990) who found for six c_1 recording sites studied with tungsten-in-glass microelectrodes that the largest responses occurred in step tenths 9 (1 site) or 10 (5 sites).

In the present study a total of fifty-eight histograms were available for fifteen c_1 recording sites and a frequency distribution for the time of largest response is shown in Fig. 4*A* where it is clear that the overwhelming majority (51/58; 88%) occurred in bins 9 and 10, which correspond to the second half of the swing phase of the step. A further three cases fell into bin 1 so that overall, in no fewer than 54/58 cases (93%), the largest responses occurred in the period of the E_1 step phase from the start of forelimb extension (midway through swing) to around footfall.

With regard to the step timing of the *smallest* responses, Lidierth & Apps (1990) reported that this varied more between sites. The frequency distribution of different timings in the present study is presented in Fig. 4*B*, which confirms and extends this finding. Note, however, that response mean size was least during stance (tenths 2–6 inclusive) in no fewer than 50/58 histograms (86%).

Figure 4*B* includes timings obtained with a range of intensities and also different numbers of timings for the different individual sites. The possible influence of these factors on the frequency distribution was therefore assessed by limiting consideration to

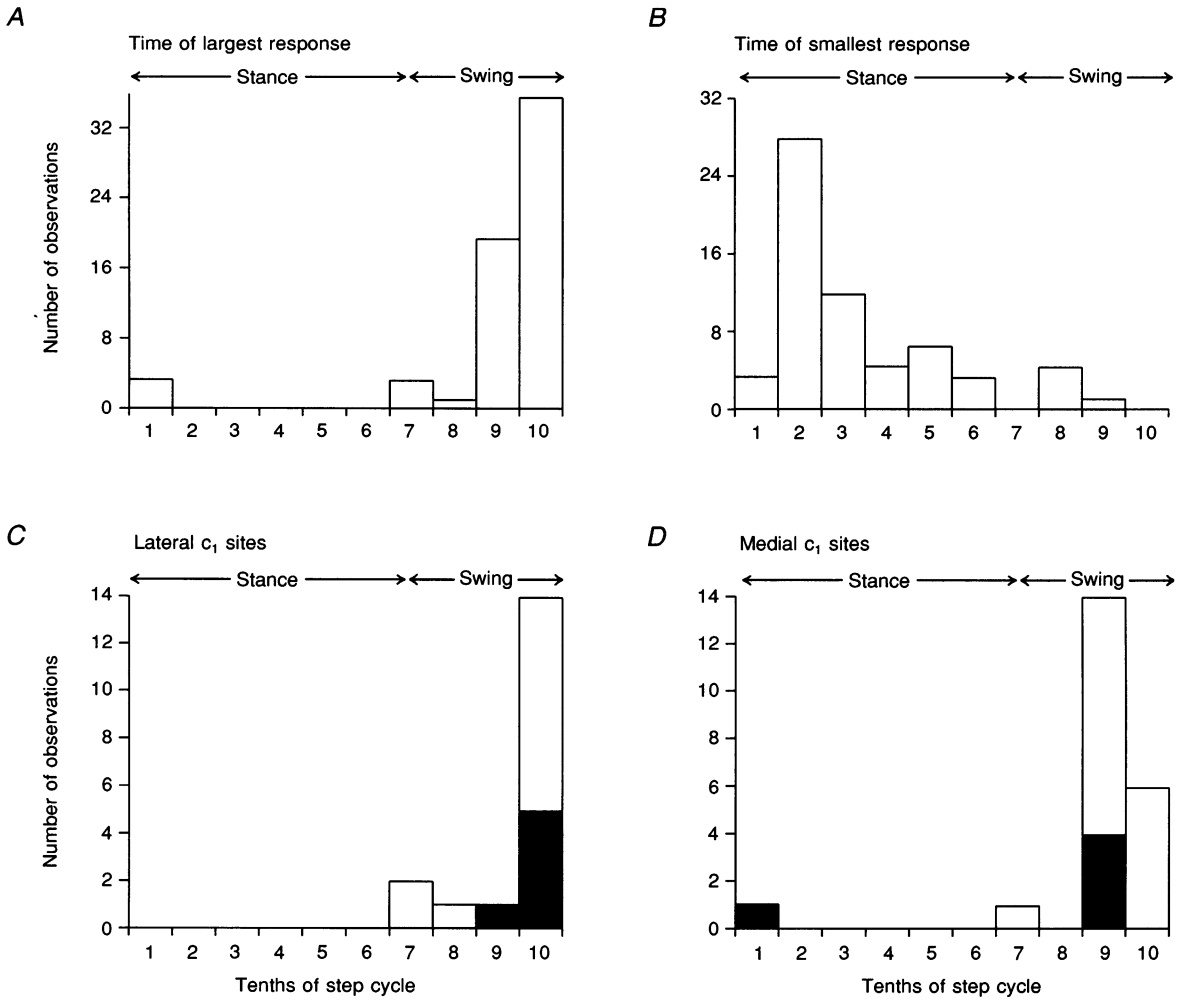

Figure 4. Frequency distributions for times of largest and least cerebellar response in c_1 zone step histograms

A shows number of histograms in which mean size of response to SR stimulation was largest in each tenth of the step cycle in the ipsilateral forelimb. Data are taken from 58 step histograms from 15 recording sites. *B*, as *A* but for times at which responses had smallest mean size. *C*, as *A* but for 18 histograms from the 6 most lateral wires. *D*, as *A* but for 22 histograms from the 5 most medial wires.

step histograms obtained at a single intensity ($2T$; $n = 16$; 11 sites) or to one chosen for each site (the one with the largest modulation index; $n = 15$). However the distribution of timings (not shown) was very similar to that in Fig. 4*B*.

Comparison of c_1 responses evoked during walking and during rest

Apps *et al.* (1990) reported that SOCP responses evoked from SR nerve stimulation at sites in the c_2 zone were considerably smaller during walking than when the animal rested quietly, but no such comparison was made for c_1 sites by Lidierth & Apps (1990). In the present experiments a systematic comparison was made for all fifteen sites studied.

The dashed lines in the step histograms of Fig. 1 indicate the mean size of the responses evoked during rest by the same stimulus in the same recording session. It is evident that in all of these cases responses during walking were substantially smaller over a considerable portion of the step cycle. However, in three cases (Fig. 1*A*, *C* and *D*) there was a briefer portion of the cycle during which the responses were larger than during rest.

Figure 5*A* is a frequency distribution in which response size in the highest bin of each of fifty-six step histograms has been expressed as a percentage of mean response size during rest and it is evident that a wide range of values was encountered. If a facilitation is taken to exist when the response in the highest bin is at least 125% of rest size then facilitations were present in 32/56 cases (57%).

The criterion of 125% is an arbitrary one but when, for a sample population of histograms, mean response at rest was compared with the mean response in the highest bin via a two-tailed t test, then for all those facilitations identified by its use the difference between the means emerged as statistically significant. The t test was not used routinely because the sizes of the individual responses were not normally distributed. Nevertheless, the result of this cross-check suggests that the 125% limit does constitute an acceptable indicator for the presence of a facilitation.

There were only two recording sites at which a facilitation was never evident; at one of these the largest responses in the three available histograms were 102, 99 and 96% of rest size while at the other the largest responses in the two available histograms were 92 and 73% of rest size.

Among the thirteen other sites in which facilitation was sometimes or always present its extent did not correlate with stimulus intensity either overall or at individual sites. The filled areas in Fig. 5*A* represent the largest responses (i.e. greatest bin heights) ever encountered at each of the fifteen recording sites; the values for facilitation ranged from 126 to 449% of response mean size in the resting animal.

Facilitations were fairly brief: although at a few sites there were some histograms where they encompassed at least three tenths of a step cycle, at most sites they were present in only one or two tenths. The timing of the largest responses relative to the cycle has already been discussed.

Figure 5*B* is a frequency distribution similar to that of Fig. 5*A* except that it shows response size in the smallest bin in each step histogram. If a response reduction is taken to exist when a response is 75% or less of rest size

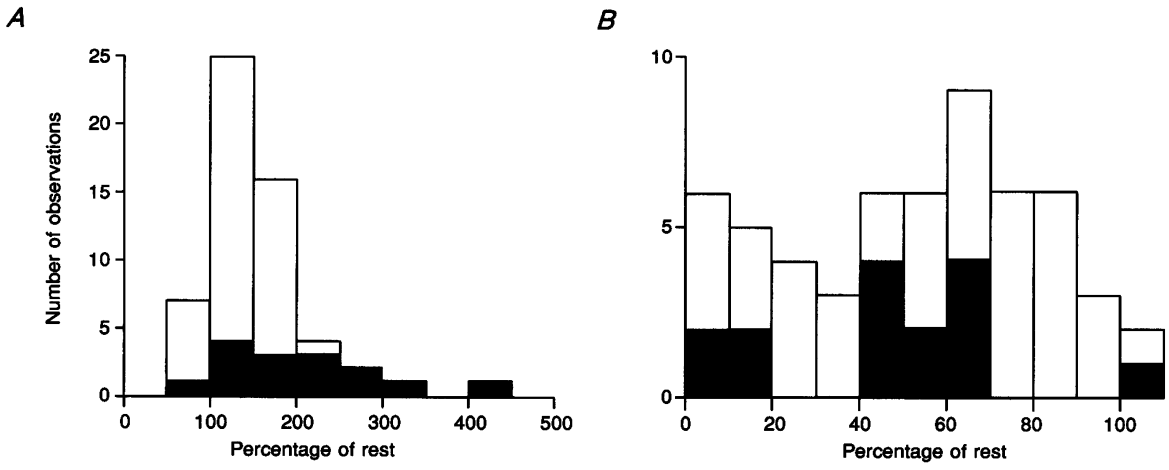

Figure 5. Frequency distributions of response size relative to rest for the largest and smallest responses in c_1 zone step histograms

Response sizes (i.e. bin heights) are expressed as a percentage of mean response size in the resting animal. Only 56 histograms out of 58 are included because in two cases responses during rest were not available for comparison. *A* shows the largest responses; filled areas show greatest bin height encountered at each of the 15 different recording sites. *B*, as *A* except that the smallest responses are represented; filled areas represent the least bin height ever encountered at each site.

then such reductions were present in 42/56 histograms (93%). Among the fifteen recording sites there was only one site at which a depression was never evident. Nevertheless, it is evident from Fig. 5*B* that histograms varied widely in regard to the size of the smallest responses. Wide variation also occurred between different sites as evident from the filled areas in Fig. 5*B* which indicate the smallest responses encountered in any histogram from each of the fifteen recording sites.

Further analysis showed that unlike the highest bin, which showed no consistent relationship between height and stimulus intensity, the smallest usually increased in size as intensity increased, i.e. the degree of response reduction progressively diminished (see Discussion). Such change was not confined to the smallest bin but was also evident when response reduction across the step cycle was estimated by summing all the 'reduced' bins in the histogram. In general, response reductions lasted longer than augmentations, frequently for around half the step cycle (see Fig. 1).

The medial and lateral c_1 subzones

The medial c_1 subzone receives its climbing fibres from the rostral dorsal accessory olive and the lateral c_1 subzone from middle–rostral levels of the medial accessory olive (Campbell & Armstrong, 1985; Apps, Trott & Dietrichs, 1991; Trott & Apps, 1991). Therefore, although both these olivary regions function as SOCP relay stations, an anatomical difference clearly exists between the two subzones that might be accompanied by functional differences.

The characteristics of the responses recorded via the five electrodes inserted most medially were therefore compared with those for the six placed most laterally. When the two groups of responses were compared in regard to the stimulus intensity dependence of their response size, and the size of the largest and smallest responses relative to response size during rest, no systematic differences were encountered. Only for one parameter, the step timing of the largest response, did the data perhaps hint at a medial–lateral difference. Frequency distributions for this parameter within the lateral and the medial groups of sites are shown in Fig. 4*C* and *D*, respectively. For lateral sites eighteen histograms were available and in the large majority the largest response occurred in step tenth 10; for medial sites there were twenty-two histograms and the largest response occurred most frequently in step tenth 9 (cf. Fig. 1*A* and *C*, which show examples of step histograms from a medial and a lateral site, respectively). Because different sites are

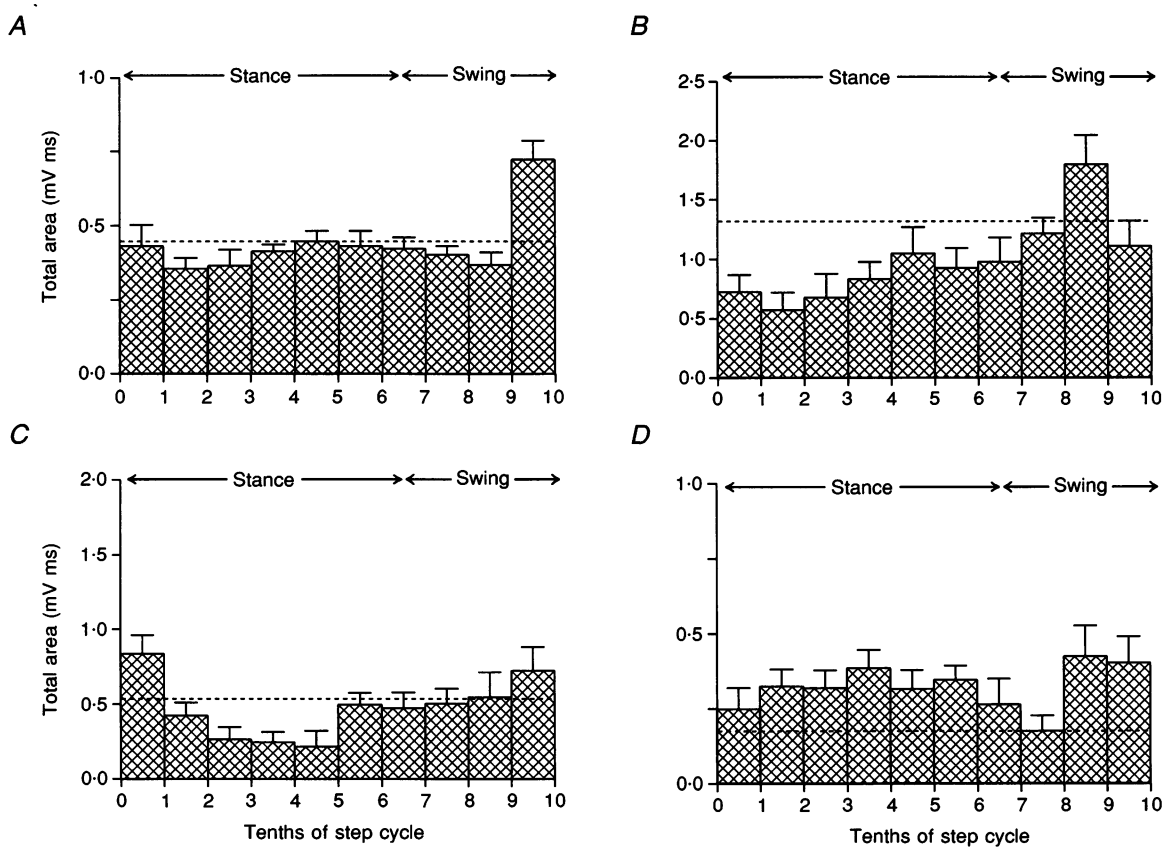

Figure 6. Step histograms for four c_3 recording sites

In each case the ipsilateral SR nerve is stimulated at 2*T*. Each histogram was constructed according to the conventions in Fig. 1.

represented in Fig. 4*C* and *D* by different numbers of histograms the filled areas show, for each of the six lateral and five medial sites, the timing of the largest response in the histogram in which response facilitation (relative to the resting condition) was most evident. It should be noted that among both groups of sites the difference in mean response size between the highest and the next highest (and usually adjacent) bin was most often not statistically significant (one-tailed *t* test). It would therefore be unsafe to regard Fig. 4*C* and *D* as establishing a difference between the two subzones and it is best regarded as an encouragement to further study (see Discussion).

If time of largest response was found to differ when responses recorded simultaneously from a medial and a lateral site were compared, the case for a difference between the subzones would be strengthened because the same nerve stimulus would be involved. Unfortunately such comparison was possible for only one pair of sites: time of largest response was the same in two histogram comparisons and differed by two tenths of a cycle in a third so no clear conclusion seems warranted.

The c_3 zone

Because the c_3 zone is located further from the cerebellar mid-line it was more difficult to access than the c_1 zone and fewer microwires could therefore be implanted within it. In addition, a smaller proportion of wires yielded measurable responses, so useful recordings were obtained from only seven recording sites (4 in one animal, 2 in another and 1 in a third). Like in the c_1 zone, response latency at all seven sites was consistent with production mainly via DF-SOCP, and the responses could be evoked only from the ipsilateral and not the contralateral SR nerve. Example step histograms for four sites are shown in Fig. 6.

Response modulation patterns over time at c_3 sites

Only at one site were responses to the same stimulus intensity studied on more than one occasion; intensities of 1·5 and 2*T* were each employed twice in recording sessions 6 days apart. At both intensities the time of least response differed between the two recording sessions. In contrast, the largest responses occurred in the same tenth in both sessions at each of the two intensities. In regard to the Spearman rank correlation coefficients, neither comparison revealed a statistically significant correlation. In general, therefore, and so far as conclusions may be drawn from a single site, the findings in regard to temporal stability of response modulation pattern were similar to those for the c_1 zone.

Stimulus intensity dependence of responses at c_3 sites

There were four recording sites at which two or more stimulus intensities were employed in the resting animal in the same recording session. As at most c_1 sites the intensities used were in the range 1·5–3*T* and at none of the sites did increases in intensity lead to large increases in mean response size. The largest change was an increase of 43% for a stimulus increase from 1·5 to 2·5*T*. Confining comparison to responses evoked by 2 and 3*T* (cf. the c_1 zone above), information was available for three sites; at one of these sites response size increased slightly (by 14%) whilst at the other two, it showed a slight decrease (by 14 and 15%).

In summary, the c_3 sites appeared to resemble those c_1 sites at which response size did not show marked intensity dependence but it cannot be excluded that study of additional sites might reveal some resembling those c_1 sites with marked intensity dependence.

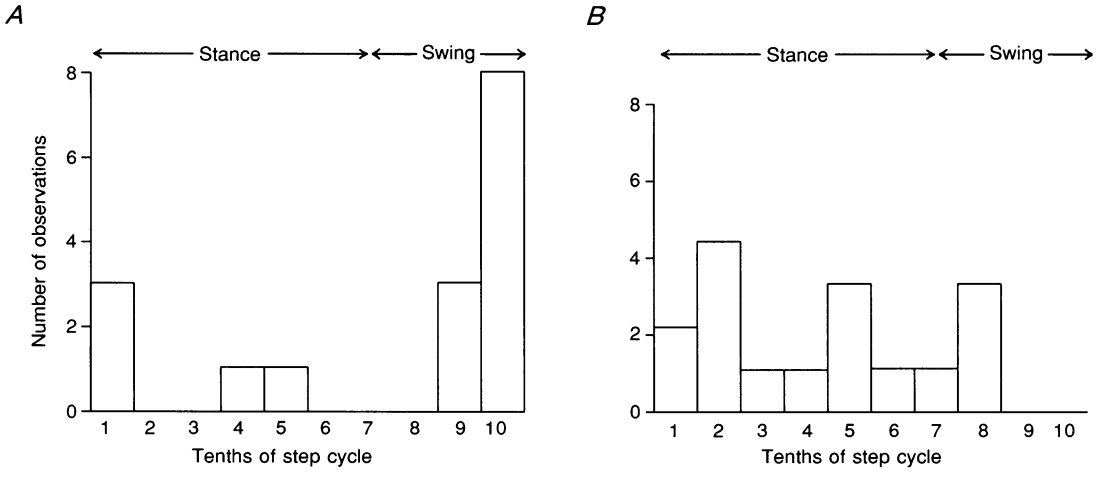

Figure 7. Frequency distributions for times of largest and least cerebellar response in c_3 zone step histograms

A and *B* show the times of occurrence during the step cycle of the largest and smallest responses, respectively, in 16 histograms from 7 different recording sites.

With regard to the effect of stimulus intensity on response size modulation during the step cycle, data were available for five sites (4 with two intensities, 1 with three). Among these sites the largest change in the step timing for least response size amounted to five tenths of a step at one site and four tenths at another. At the three remaining sites the timing was the same at each of the (two) stimulus intensities employed.

With regard to the timing of the largest responses, changes in stimulus intensity were accompanied by only modest shifts. At one site the timing was the same for both intensities used, and at another three the largest shift was one-tenth of a cycle. The only site with a larger shift (of three tenths) was one at which two intensities were used and in one of the histograms involved mean response size in the highest bin was calculated on the basis of only three individual responses. In general, therefore, the findings closely resembled those for c_1 sites in showing that time of largest response showed little dependence on stimulus intensity.

Step cycle timing of the largest and smallest responses at c_3 sites

A total of seventeen histograms were available for the seven c_3 recording sites but in one of these the time of greatest response could not be regarded as securely determined (because the relevant bin comprised only 3 individual responses; cf. above). A frequency distribution for the timing of the largest responses in the remaining sixteen cases is shown in Fig. 7*A*; in no fewer than fourteen (88%), the largest responses occurred in the period from mid-swing to around the time of footfall (tenths 9, 10 and 1). Among c_1 sites the corresponding proportion was 93%. In the two remaining c_3 histograms (both from the same recording site) the largest responses were in tenths 4 and 5. There were no c_1 sites at which the largest responses occurred in these tenths, which correspond to the period of mid-stance (cf. Fig. 4*A*). The distribution of times of least response ($n = 16$) is shown in Fig. 7*B*. Only tenths 9 and 10 were excluded; 10/16 cases (63%) involved tenths 2–6 inclusive (a period that spans most of stance).

Comparison of c_3 responses evoked during walking and rest

Inspection of the step histograms in Fig. 6 shows that in three cases (Fig. 6*A*, *B* and *C*) the responses during a substantial portion of the step cycle were depressed relative to the mean amplitude during rest, this phenomenon being more marked in Fig. 6*B* and *C* than in Fig. 6*A*. Nevertheless, in all three cases there was a briefer portion of the cycle in which the responses were larger than during rest. In the fourth case (Fig. 6*D*) the responses were always larger than resting size and in part of the cycle, markedly larger.

Across the histograms available for the c_3 sites and employing the same definition as for c_1 sites, facilitation was present in 53% of cases (cf. 59% for the c_1 zone) and there were only two sites at which facilitation was never evident (2 histograms available at both these sites). There were three sites where it was present in the only available histogram, one site where facilitation was present in all three histograms and at the remaining site two of the six histograms showed facilitation while the remainder did not. For the five sites which sometimes or always showed facilitation the largest responses ever seen ranged quite widely, from 137 to 255% of rest size.

Response reductions were present in 63% of histograms (cf. 93% for c_1 zone) and all seven sites showed reductions except one for which a single histogram was available. Degree of reduction varied considerably and this variation occurred both between different histograms for the same site and between different sites. This recalls the findings for the c_1 zone but whilst in 20% of c_1 histograms the smallest responses were less than 20% of rest size, there were no reductions of this size in the c_3 zone. At all four c_3 sites where two or more stimulus intensities were used, an increase in intensity led to a slight reduction in the extent of response depression (cf. the c_1 zone).

Because of the limited number of c_3 sites, no attempt was made to seek functional differences between c_3 medial and lateral subzones (see Introduction and Discussion).

DISCUSSION

This is the first study in which chronically implanted microwire electrodes have been used to record extracellular field potentials generated in mammalian cerebellar cortex by activity generated in spino-olivocerebellar pathways as a result of impulse volleys in a peripheral nerve. Study was confined to the tips of lobules V and VI and to responses with the characteristics expected for those mediated to the c_1 and c_3 paravermal zones mainly via the DF-SOCP; these responses were indistinguishable from those in an earlier study with glass-coated tungsten microelectrodes (Lidierth & Apps, 1990). The use of microwires has proved, however, to have the important advantage of much greater recording stability so that individual sites can be investigated repeatedly, with a range of stimulus parameters and during different behaviours (in this case steady walking and quiet rest). However, after implantation the location of the electrode tip cannot be controlled and the proportion of electrodes yielding measurable responses is fairly low (less than half), presumably because the tips are often unfavourably located with respect to the neural elements (the Purkinje cells), the activity of which gives rise to the field potentials. The choice of recording technique in future studies will therefore depend on the particular experimental aims.

Responses in the c_1 zone

The present study has amply confirmed the findings of Lidierth & Apps (1990) in that the c_1 SOCPs (mainly DF-SOCP; see Methods) are subject to substantial step phase-dependent modulation in excitability as judged from their ability to transmit volleys initiated by low intensity stimulation of SR nerve. In addition, the time at which excitability is greatest during the step cycle was found to be rather stable between recording sessions days apart. Moreover, although other aspects of the modulation pattern were more variable over time (e.g. time of least excitability), some evidence was found (see Results) to suggest that chance may have generated at least part of the apparent instability. In future studies with different behavioural tasks it may be possible to accumulate larger numbers of responses for measurement and to assess the effect of chance variations in response amplitude by studying the extent to which 'instabilities' diminish as sample size is increased. In the present study, however, sample size was restricted by the need to avoid the animals becoming restless or tired.

Similarly, the time of greatest pathway excitability was usually uninfluenced by the intensity of the nerve stimulus and chance fluctuations in bin height are likely to have contributed to the relative instability found for other parts of the modulation pattern. However, in this case chance is unlikely to provide the whole explanation, because the likelihood of a statistically significant correlation between pairs of histograms decreased with increasing difference between the two stimulus intensities used to evoke the two sets of responses. This argues for some real effect of intensity on the step-related pattern of response size modulation, though visual comparison of the histograms indicated that any such effect was modest as obvious changes in shape were unusual.

In regard to the absolute timing of the largest response, overwhelmingly it occurred in bins 9, 10 or 1. This period corresponds approximately to the E_1 step phase when the ipsilateral forelimb ceases to flex (midway through swing) and is extended forwards and downwards until footfall (approximately midway through bin 1). Our findings here are in excellent agreement with the more limited results of Lidierth & Apps (1990) but the present study has also revealed that at no fewer than 13/15 c_1 sites, responses in part or all of this period were usually (at some sites always) larger than those evoked by the same stimulus when the animal rested quietly.

Because nerve volley size sometimes (but by no means always) appeared to differ somewhat between walking and rest (see Methods), the possible influence of such a difference must be considered. However, response facilitations were not confined to cases when the volley appeared larger during walking but were as common when it appeared smaller and when no difference existed between the two behavioural conditions. Moreover, when the extent of facilitation was plotted against volley size, expressed as a percentage of size during rest (not shown), no significant relationship existed either at individual sites or across all cases ($n = 56$). Therefore it can be presumed safely that when facilitations are present they reflect an increase in SOCP excitability brought about by some central mechanism.

Lidierth & Apps (1990) suggested that responses were largest during the E_1 phase because it is then that under natural conditions, e.g. during walking through undergrowth, the skin supplied by SR nerve is most likely to make unexpected contact with obstacles to progression (particularly, perhaps, during darkness). By showing that the responses are actually facilitated, the present findings add force to this suggestion.

As to the possible behavioural consequences of increased SOCP excitability at this time, it should be noted that the Purkinje cells of the c_1 (and c_3) zone project to and inhibit the neurones of nucleus interpositus anterior (e.g. Trott & Armstrong, 1987; Garwicz & Ekerot, 1994), which in turn provide a powerful excitatory projection to the red nucleus (and to the ventrolateral thalamus which projects to the motor cortex). Damage to nucleus interpositus results in otherwise intact cats in hypoflexions of the ipsilateral limbs during walking (Chambers & Sprague, 1955*b*) while damage to, or temporary cooling of, the paravermal cortex results in hyperflexions (Chambers & Sprague, 1955*a*, *b*; Udo, Matsukawa, Kamei & Oda, 1980). Transmission in SOCPs resulting from a stimulus such as a skin tap will lead to the near-synchronous occurrence of climbing fibre input to substantial numbers of c_1 (and c_3) zone Purkinje cells and because such input generates a complex spike (often followed by a pause in simple spike discharge) in each cell (Eccles, Llinás & Sasaki, 1966) there will be a substantial change in the pattern of synaptic input to the interpositus neurones beginning with a latency of approximately 12 ms.

Given that the interposito-rubral conduction time is only *ca* 1 ms (Tsukahara, Toyama & Kosaka, 1967) and that rubrospinal volleys can evoke EMG changes in muscles of the forelimb with latencies as short as 5–6 ms (Shapovalov, 1975) it is clear that a tap delivered in the innervation territory of SR nerve might initiate EMG changes in the forelimb within *ca* 20 ms. Swing lasts *ca* 200 ms under the conditions of the present experiments so the response facilitations we have observed may reflect the existence of a temporally tuned transcerebellar mechanism, designed to intervene in the execution of the current step when an obstacle is contacted as the limb is manoeuvred towards footfall. It is perhaps worthwhile to add that the patterns of simple spike discharge among c_1 and c_3 zone Purkinje cells have previously been studied in cats walking under the same conditions as employed here and in both zones the overall mean rate of discharge was at peak (*ca* 60 impulses s^{-1}) during swing (Armstrong & Edgley, 1984; Edgley & Lidierth, 1988).

The time during the step at which c_1 responses were *smallest* was much more variable, nevertheless, in 86% of available histograms it occurred during the stance phase and in most cases in the first half of that phase, as also found by Lidierth & Apps (1990). This is a time when loading of the foot and its consequent mechanical deformation might be expected to generate activity in the SOCPs and Lidierth & Apps argued that the small size of the responses to nerve stimulation might therefore reflect the operation of a pathway-gating mechanism designed to reduce transmission of predictable peripheral inputs resulting from the animal's own volitional movements. That such a mechanism can operate is indicated by the work of Gellman, Gibson & Houk (1985) who showed that cells in the rostral dorsal accessory olive do not discharge when cats make forepaw contact with a visible target surface actively reached for, but do discharge when, part way through such a movement, unexpected contact is made with a similar surface out of their line of sight. The present finding that in 75% of histograms (including some or all of those for 14 of the 15 recording sites) the smallest responses were smaller in mean size than in the resting animal (and often considerably smaller) suggests indeed that an active suppressive mechanism is in operation and therefore reinforces the suggestion of Lidierth & Apps (1990).

The possibility must be considered that the response reductions arose in part because nerve volley size quite frequently appeared smaller during walking than during rest (see Methods). However, reductions were also observed when the volley appeared unchanged or larger. Moreover, when the size of the reduction in the cerebellar response was plotted against volley size expressed as a percentage of its rest size, no significant relationship existed (not shown). Therefore, as for facilitations, it seems safe to conclude that the reductions reflected the operation of a central mechanism that reduced SOCP excitability.

It is interesting that the extent to which the smallest responses were reduced relative to rest size usually decreased when stimulus intensity increased, while no relationship was found between stimulus intensity and the extent to which the largest responses were facilitated. Moreover, facilitation was sometimes found unaccompanied by depression and *vice versa* (in 14 and 32% of histograms, respectively). Such dissociations may suggest that, rather than the two phenomena arising from the waxing and waning during the step of some single central modulatory influence, two separate influences might have been operating, one to increase and the other to decrease pathway excitability. Whether these influences operate at the pre-olivary or the olivary level (or both) remains to be determined.

The largest *individual* response evoked during walking at the time of *least* excitability in the pathway(s) was never, at any site, larger than the largest response evoked at the time of greatest excitability, but was sometimes larger than the *smallest* such response. Moreover, in 45% of histograms there was at least one stimulus delivered at the time of greatest excitability which failed to evoke any cerebellar response. It is difficult to gauge the functional implications of such fluctuations in responsiveness between trials though it presumably reflects variation in some central influence on pathway excitability that is additional to the step phase-dependent influence revealed by the step histograms. The existence of such an influence appears at first sight to limit the reliability of DF-SOCP as a step phase-dependent channel conveying peripheral input to the cerebellum. However, it is widely thought that the SOCPs do not simply report peripheral events, but rather mismatches between intended and achieved movement. Given that our stimuli were delivered to awake behaving animals, what was 'intended' by the animal may have differed from trial to trial in ways we could not detect or control.

An additional possibility is that at any one moment the step-unrelated fluctuations in responsiveness may occur differentially in the parts of the path terminating in different parts of the c_1 zone and any corresponding fluctuations in the response of the deep nuclear cells might then be smoothed out by the extensive convergence existing in the cortico-nuclear projection. In this way, the transcerebellar path might function more 'reliably' than suggested by recordings from one cortical site. On the other hand, it is equally possible that the fluctuations occur synchronously across wide areas of the zone, in which case it would be important to discover their origin. Fortunately, the extent to which fluctuations occur in parallel at different sites in a zone can be investigated by recording from them simultaneously; a study of this kind is in progress.

Finally, it should be noted that different sites in the c_1 zone have been shown to vary considerably in respect of the effect of stimulus strength on response size during rest and the maximum extent to which their responses are facilitated and depressed during the step cycle. This suggests significant functional heterogeneity between the DF-SOCP components terminating in different parts of the zone. The relationship remains to be determined between this heterogeneity and the existence within the zone of numerous 'climbing fibre microzones' (Ekerot & Larson, 1979*b*; Ekerot, Garwicz & Schouenborg, 1991), each differing in regard to the somatic afferent receptive field characteristics of the olive cells providing the climbing fibres. At a coarser level of spatial resolution it also remains to be discovered whether there are any important functional differences in the locomotor context between the medial and the lateral c_1 subzones which receive their climbing fibres from different groups of olive cells (located indeed in different olivary subnuclei; see Results).

In this connection further investigations are required in which larger numbers of responses are recorded, preferably with simultaneous monitoring of pairs of sites. Moreover, conventional microelectrodes should probably be used to enable systematic tracking across the width of the c_1 zone and verification of tip positions via placement of microlesions or dye marks.

Responses in the c_3 zone

The SOCPs to the c_3 zone have not previously been studied in the awake animal, so although fewer sites were investigated, the findings are of considerable interest.

In fact, the only differences from the c_1 zone were the occurrence of one c_3 site at which the largest response occurred in mid-stance, the presence in step histograms from four c_1 sites of depressions greater than at any of the c_3 sites, and the absence among four c_3 sites studied of any at which an increase in stimulus intensity from 2 to $3T$ led to any marked increase in response size in the resting animal (about half of c_1 sites showed such an increase).

The presence of substantial similarities between the two zones is not wholly surprising because some olive cells in the rostral part of the dorsal accessory olive which project to the tips of the folia in lobule V have axons that branch to provide climbing fibres to Purkinje cells in both the medial c_1 subzone and the medial part of the c_3 zone (Ekerot & Larson, 1982). Furthermore, a WGA-HRP retrograde tracing study by Trott & Apps (1991) has shown a large degree of overlap between the distribution of cells within the rostral part of the dorsal accessory olive projecting to medial c_1 as compared with medial c_3. Of course, such congruence does not of itself provide evidence for axonal branching between the two zones and it is highly probable that many olive cells project to only one of these two areas (cf. Apps *et al.* 1991), so the similarities were by no means entirely predictable.

Some olive cells (at middle rostro-caudal levels in the medial accessory olive) provide climbing fibres to both the lateral c_1 subzone (or cx zone; see Campbell & Armstrong, 1985; Apps *et al.* 1991) and to the x zone in the vermis, while others (in rostral dorsal accessory olive) innervate both the lateral part of the c_3 zone and the laterally located d_2 zone. Since all these zones receive similar SOCPs, it is likely that if the complete medio-lateral extent of lobule V (i.e. zones a, x and b in the vermis and paravermal zones c_1, c_2, c_3, d_1 and d_2) was surveyed, then similar patterns of step-related response modulation would be found in the x, c_1, c_3 and d_2 zones. Studies of x and d_2 are technically feasible so this prediction is open to experimental test. If it is verified the problem will nevertheless remain of understanding why it is that so many zones are innervated by SOCPs that appear organized to have their greatest excitability in the E_1 phase of the step cycle.

Of the remaining zones, which alternate in sequence with those above, only c_2 has been investigated and its responses showed quite different patterns of step-related modulation in size; studies of the remaining zones are therefore clearly required.

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