Descending signals from the pontomedullary reticular formation are bilateral, asymmetric, and gated during reaching movements in the cat

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ABSTRACT

We examined the contribution of neurones within the pontomedullary reticular formation (PMRF) to the control of reaching movements in the cat. We recorded the activity of 127 reticular neurones, including 56 reticulospinal neurones, during movements of each forelimb; 67/127 of these neurones discharged prior to the onset of activity in the prime flexor muscles during the reach of the ipsilateral limb and form the focus of this report. Most neurones (63/67) showed similar patterns and levels of discharge activity during reaches of either limb, although activity was slightly greater during reach of the ipsilateral limb. In 26/67 cells, the initial change in discharge activity was time-locked to the Go signal during reaches of either limb; we have argued (Schepens and Drew 2004) that this early discharge contributes to the anticipatory postural adjustments that precede movement. In 11/26 cells, the initial change in activity was reciprocal for reaches with the left and right limbs, although activity during the movement was non-reciprocal. Spike triggered averaging produced post spike facilitation or depression (PSD) in 12/50 cells during reaches of the limb ipsilateral to the recording site and in 17/49 cells during reach of the contralateral limb. Some cells produced PSD in ipsilateral extensor muscles before the start of the reach and during reaches made with the contralateral, but not the ipsilateral limb; this suggests the signal must be differentially gated. Overall, the results suggest a strong bilateral, albeit asymmetric, contribution from the PMRF to the control of posture and movement during voluntary movement.
Introduction

The axons of neurones in the pontomedullary reticular formation (PMRF) have been shown to have diffuse projection patterns. Many reticular neurones innervate both cervical and lumbar levels of the spinal cord (Peterson et al. 1975) and some neurones have axons that cross the midline at the cervical or lumbar levels and innervate the gray matter of both sides (Matsuyama et al. 1988, 1997, 1999). In addition, reticulospinal axons also terminate on commissural interneurones so that an action on contralateral activity may also be mediated by this pathway (Jankowska et al. 2003; Matsuyama et al. 2004). As such, there is a firm anatomical substrate demonstrating that reticulospinal neurones can produce widespread effects throughout the neuraxis, including both ipsilateral and contralateral to the cell body.

Functional studies provide evidence that this anatomical substrate is used to facilitate the coordination of interlimb activity and to produce the complex patterns of muscular activity that are used to provide postural support in response to voluntary movements or unpredictable perturbations. In some of the earliest studies of the PMRF, Sprague and Chambers (1954) expanded on Magoun’s original thesis of a structure producing global excitation or inhibition (Magoun 1944; Magoun and Rhines 1946) to demonstrate that lower intensity stimulation of the PMRF in the decerebrate cat produced coordinated patterns of flexion and extension in the four limbs with flexion predominating in ipsilateral limbs and extension in contralateral limbs. More recent studies in awake animals have further amplified our understanding of the complex nature of the reticulospinal pathways. Microstimulation studies in awake cats (Drew and Rossignol 1990a) confirmed Sprague and Chamber’s (1954) original findings of a predominant ipsilateral flexion and contralateral extension bias (together with ipsilateral head turning), although recordings of electromyographic (EMG) activity also showed that the stimulation was equally effective in activating ipsilateral extensors and contralateral flexors (Drew and Rossignol 1990b). Moreover, a recent study has shown strong
bilateral projections to shoulder muscles in the primate (Davidson and Buford 2004). Together, these studies confirm that the PMRF is capable of influencing muscle activity at all levels of the neuraxis, both ipsilateral and contralateral to the stimulation site.

While stimulation to the PMRF produced a single characteristic pattern of activity when the cat was at rest, stimulation during walking transformed this pattern of activity into a more functional one that produced appropriate phase-dependent activation of muscles (Drew 1991; Drew and Rossignol 1984; Orlovsky 1972; Perreault et al. 1994). In the intact cat (Drew 1991), stimulation during the swing phase of the ipsilateral forelimb increased responses in ipsilateral flexors and, simultaneously, in contralateral extensors. Stimulation during contralateral swing facilitated activity in the contralateral flexors and produced facilitation or suppression of ipsilateral extensors. Responses were also observed in hindlimb flexor and extensor muscles and were, likewise, phase dependent. We have argued that this pattern of activity provides a flexible substrate that would appropriately facilitate the integration of postural responses into the locomotor pattern.

In support of this proposition, a recent study (Drew et al. 2004; Prentice and Drew 2001) showed that a large proportion of cells, including identified reticulospinal neurones (RSNs), exhibited multiple increases in activity as each limb in turn stepped over the obstacle. We suggested that the discharge activity of these cells provided information concerning the time and magnitude of the postural activity that occurred in the supporting limbs as any one limb stepped over the obstacle. However, we suggested that they could not specify the details of the postural pattern which would depend on the excitability of the spinal circuits and would be contingent on activity in other descending pathways. In this hypothesis, a substantial aspect of the final determination of the postural pattern is thus dependent on the rhythmical changes in the excitability of spinal interneurones onto which these fibres impinge. Discharge activity occurring during ipsilateral swing would facilitate ipsilateral flexor muscles and contralateral extensor muscles while activity occurring during ipsilateral stance would facilitate ipsilateral extensors and contralateral flexors (see Fig. 3 in
We have previously described the discharge activity of neurones in the PMRF when cats make reaching movements with the left limb, ipsilateral to the recording chamber (Schepens and Drew 2004). The question we now address is how the discharge activity of these cells is modified when the cat makes a reach with the right limb, contralateral to the recording site. In this situation, in which there is no base rhythmical activity in the spinal networks (as during locomotion), does the reticulospinal system continue to produce a similar pattern of activity during reaches of both the ipsilateral and contralateral limbs, or does it, instead, produce a pattern of activity specific to the requirements of each reach? For example, reaches of the left limb require increased activity in the extensors of the right forelimb and the left hindlimb while movements of the right limb require increased extensor activity in the left forelimb and the right hindlimb, i.e. reciprocal patterns of activity (see Figs. 2 and 3). The results favour a contribution to postural control similar to that observed during locomotion.

Preliminary results from these experiments have been published in Abstract form (Schepens and Drew 2000, 2001, 2003b)
Methods

Surgical Preparation and Protocol

These experiments were performed on the same two cats (RS22 and RS23) used in our previous publications (Schepens and Drew 2003a, 2004). All surgical and experimental procedures are described in detail in those two papers.

In brief, cats were trained to stand quietly on four force platforms and to reach to a tube to obtain a food reward (Fig. 1). A shutter over the end of the tube, and controlled by computer, denied access outside the confines of the task. Cats were trained to reach with both the left and right forelimbs. Following training, the cats were prepared for surgery under general anaesthesia (2-3% isoflurane with oxygen) and in sterile conditions. A rectangular base-plate (internal measurements 10 * 8 mm) was implanted over the left cerebellum to provide access to the brainstem reticular formation and pairs of Teflon-insulated, stainless-steel wires were sewn, bilaterally, into the muscle bellies of selected fore- and hindlimb muscles as well as some axial muscles. The muscles used in these studies and details of their activation patterns can be found in Schepens and Drew (2004).

Three microwires (50 μm diameter) were inserted into the spinal cord at L₂ to provide a means of antidromically identifying reticulospinal cells projecting to the ipsilateral, lumbar spinal cord. Following surgery the cats were administered analgesics during a period of 48 hrs (Buprenorphine 5 μg/kg) and antibiotics during a period of at least 10 days (Penicillin G 40,000 IU). All surgical procedures were approved by the institutional ethics committee and followed National guidelines.

Following recovery from the surgery, an electrode was introduced into the PMRF and the discharge activity of single neurones was recorded. All isolated single neurones were recorded, regardless of whether they could be antidromically identified from the microwire electrodes inserted at L₂ (reticulospinal neurones: RSNs) or not (Unidentified Neurones). Following isolation of a single neurone, cell discharge activity was recorded during a period of treadmill locomotion and the cat was
then transferred to the reaching apparatus. All isolated cells were recorded during both tasks, when possible, regardless of the pattern of discharge activity on the treadmill. Discharge activity was recorded during a minimum of 5 reaches from each forelimb (generally, 5 reaches with the left forelimb, 10 reaches with the right forelimb and then 5 more with the left forelimb). Supplementary reaches, if present, were made in blocks of 5 with each limb. The cat was then transferred back to the treadmill and another cell isolated.

Data Analysis

All data were recorded on-line. Forces exerted against the platforms (vertical, $v$; mediolateral, $ML$; and anteroposterior, $AP$) and electromyographic (EMG) data were recorded at 1 KHz while the untreated unit trace was digitized at 100 KHz for off-line discrimination using custom routines.

Analysis routines were identical to those used in a previous publication (Schepens and Drew 2004). In brief, cells were classified as showing significant increases or decreases in discharge if they exceeded $\pm 2$ standard deviations (SD) of the average control activity, calculated from a 500 ms period preceding the onset of the Cue signal (Fig. 1). Cells showing increased activity were further classified as Phasic, Phasic/Tonic or Tonic, based on a comparison of the discharge activity in the control period, during the dynamic part of the reach (from the onset of cleidobrachialis [ClB] activity to entry of the paw in the tube), and during the static period (between 1000 and 1500 ms after ClB onset). Phasic cells were defined as those cells showing a significant increase during the dynamic period but in which discharge activity during the subsequent static period was $< 150\%$ of that during the control period. Cells with a tonic component had a discharge rate during the static period that was $> 150\%$ of the control period. Cells with a phasic/tonic discharge additionally had a discharge during the dynamic period that was $> 125\%$ of that during the static period (see Schepens and Drew 2004). When classifying cell activity during the period before the onset of the Go signal (the pre-trigger period) cell discharge was likewise considered to be significantly modified if it exceeded $\pm$
The onset of activity in the cell discharge and in selected muscles and force traces was measured from the computer traces during individual trials and was used to determine the temporal relationships of cell activity to different behavioural events. Linear regressions between either the latency of the onset of cell discharge or the lead time (latency of ClB onset - latency of cell onset) as a function of the time of onset of the ClB were used to determine if cell discharge was better related to movement onset or to the Go signal. Cells better related to the movement show a slope of 1.0 when cell discharge is plotted as a function of ClB onset; cells better related to the Go signal show a slope of 1.0 when the lead time is plotted against the ClB onset (Chapman et al. 1986; Schepens and Drew 2003a, 2004; Vicario et al. 1983). Linear regressions were also calculated between different epochs of the cell discharge and the onset and offset of activity in different muscles and force traces.

Quantitative analysis of the relationship between cell discharge activity and the magnitude of the EMG or force activity was calculated from temporal slices. For each individual trial both the instantaneous frequency of the cell activity and the amplitude of the EMG and force traces were integrated over consecutive 50 ms bins. A trial of 8 s duration would, therefore, yield 160 values for the cell discharge and for each of the 64 traces of analog activity. These temporal slices were repeated for each trial included in the analysis and the linear regression analysis was performed between the cell trace and each of the analog channels. Linear regression analysis was also performed using only the changes in cell and analog activity during the period from the Go signal until the time that the paw entered the tube. As this period includes both the initial, preparatory, anticipatory postural adjustments (pAPA) and the dynamic period from the onset of the ClB until the time that the paw enters the tube, we refer to this as the pAPA + dynamic period. In this case
temporal slices of 20 ms were used. Multiple regressions were compiled from the same data using the manual stepwise function in Systat (v9.0). In this case, traces were added one at a time in an order specified by the user (see Results).

For all of the recorded cells, we performed spike triggered averaging (STA) (Fetz and Cheney 1979, 1980) using the computer-rectified traces from all recorded EMGs. Averages were computed using: i) all action potentials in the entire trial (whole trial); ii) action potentials occurring from the period following the Go signal until the end of the trial (post-trigger), and iii) those occurring in the period prior to the Go signal (control). Averages were only retained if more than 1000 action potentials were available for any one period. Responses were considered to be significant if they exceeded ± 2SD of the control activity (50 ms before the trigger action potential) for a minimum of 3 ms. The latency of the responses was determined at the point where the averaged trace crossed the 2SD line used to determine significance.

To avoid confusion we always refer to muscles in the Results section with respect to the side of the body on which they were recorded, either left or right. In the Discussion, we use ipsilateral with respect to the site of the recording site, in the left PMRF, and not with respect to the limb performing the reaching task.
Results

Database

One hundred and twenty seven cells (including 56 RSNs) were recorded during a minimum of 5 reaches with both the left (ipsilateral to the recording site) and the right limb. These cells form a subset of the dataset (142 cells) used in a previous publication (Schepens and Drew 2004). The location of this subset (primarily within the nucleus reticularis gigantocellularis; see Fig. 3 Schepens and Drew 2004) and the conduction velocity of the axons of these cells (mean ± SD = 97.7 ± 17.0 m.s⁻¹, N=54 [the latency of 2 neurones was not measured]) was almost identical to that of the full dataset (98.1 ± 16.7 m.s⁻¹). Because our previous analysis (Schepens and Drew 2004) showed no major differences in the discharge characteristics of the RSNs and the unidentified cells, they are treated together in this manuscript. Sixty seven (67/127) neurones (including 36 RSNs) showed increased activity prior to the onset of the ipsilateral cleidobrachialis (iClB) muscle during the left reach; these cells discharging in advance of the prime flexor muscles responsible for the reach will form the major focus of this manuscript.

General Task Characteristics

Reaching movements of the forelimb are characterised by stereotypical changes in ground reaction forces (GRF) and EMG activity in all four limbs (Schepens and Drew 2003a). Fig. 2 illustrates some of the more prominent and pertinent changes. The initial changes during reach of the left forelimb (ipsilateral to the recording site), are observed as an increase in activity in the left lateral head of triceps (lTriL) and in Fv under the left limb (lFLv) together with a decrease in activity in the right TriL and in Fv under the right limb (Fig. 2, left; see also Fig. 3). These anticipatory postural adjustments preceding the movement itself (pAPAs) are thought to serve to displace the centre of mass into the triangle created by the three supporting limbs (Ioffé et al. 1982; Schepens and Drew 2003a). These pAPAs are followed by a large increase in the level of activity of shoulder
protractors (e.g. ClB) and elbow flexor muscles that begin shortly before the limb is lifted from the ground and continue throughout the reach, together with a large increase in $F_V$ under the right supporting forelimb and a decrease in $F_V$ in the reaching limb. There is also increased activity in the left vastus lateralis (VL) and in $F_V$ under the left hindlimb and decreases in activity in the right VL and in $F_V$ under the right hindlimb. These postural adjustments accompanying the movement (aAPAs) are also anticipatory in nature, in that the latency of activation is coincident with the onset of the activity in the prime movers, such as the ClB (Alstermark and Wessberg 1985; Schepens and Drew 2003a). During movements of the right forelimb, the changes in GRF are the exact reciprocal of those observed during movement of the left limb (Fig. 2: right).

The activity patterns in the major extensor muscles of the forelimbs were also reciprocal during left and right reaches. This is illustrated in Fig 2 but is clearer in Fig. 3A. During left reach (thicker line) the /TriL showed an initial, phasic, increase in activity that occurred just prior to the pAPA, and which was time-locked to the Go signal, and a second, brief, burst of activity that was time-locked to the onset of movement (see Schepens and Drew 2003a for a detailed examination of the temporal relationships of different muscles to the major events occurring during the reach). This second period of activity terminated at approximately the time that the limb reached the target and the paw was inserted into the tube. In contrast, during a right reach (thinner lines), this muscle showed an initial decrease in activity followed by a sustained increase as the weight of the animal was transferred to the left side. This pattern of activity was observed in the other extensors of the forelimbs that we recorded, namely the palmaris longus (PaL) and the supraspinatus (SSp) (not illustrated). The forelimb flexor muscles became strongly active subsequent to the pAPA and just before the limb was lifted from the platform. In the brachialis (Br) muscle, which is a pure flexor of the elbow, there was a sharp peak of activity that was followed by a lower level of sustained activity throughout the reach (Fig. 3B). During movements of the right limb there was a very low level of
activity that was sustained throughout the movement. A similar pattern of activity was observed in the shoulder retractor, the teres major (TrM) as well as in the wrist dorsiflexor, the extensor digitorum communis (EDC). The shoulder protractors, the cleidobrachialis and the cleidotrapezius (CIT), also exhibited a similar pattern of activity, with the exception that in these muscles there was one large burst that was maintained throughout the movement (see e.g. Fig. 2). The onset of activity in all of these flexor muscles was tightly linked to the onset of the movement (Schepens and Drew 2003a). The activity patterns in the shoulder muscles were more heterogeneous but all of them showed reciprocal changes in activity during the pAPA. As for the triceps muscle, the acromiotrapezius (AcT) (Fig. 3C) and the spinodeltoideus (SpD) (Fig. 3D) muscles showed an increase in activity during the pAPA during the left reach and a reciprocal decrease in activity during the right reach. During the reaching movement, the AcT also showed a similar pattern to the TriL although the level of activity during the left reach was maintained at a relatively higher level. This was even more the case in the SpD in which there was as high, or higher, a level of activity during the right reach as during the left reach. In other words, while this muscle showed a reciprocal pattern of activity during the pAPA, it showed a similar pattern during the latter part of the reach. A similar pattern of activity was also seen in the acromiodeltoideus.

As for the forelimb extensor muscles, the major hindlimb extensor muscles, such as the gastrocnemius (GL) (Fig 3E), also showed clear reciprocal patterns of activity. During the left reach, the level of EMG activity increased and during the right reach it decreased. A similar pattern was seen in the VL (see Fig. 2) and in the gluteus medius (GlM). This pattern of activity reflects the diagonal pattern of support that is observed as the weight of the cat is transferred onto the contralateral forelimb and the hindlimb diagonal to the supporting forelimb. Activity patterns in the hindlimb flexor muscles were more variable although they were generally reciprocal to the activity patterns observed in the hindlimb extensors. As illustrated in Fig. 3F, the semitendinosus (St) on the left side was generally inactive during the left reach but increased during a right reach when the left
hindlimb was unloaded. The sartorius (Srt) showed a similar pattern of activity, although during the left reach, the tonic activity present in this muscle during standing was frequently inhibited.

Lastly, in the axial muscles, the averaged pattern of activity was frequently similar throughout the reach for both left and right reaches. In the biventer cervicus (BvC), there was an initial short-latency decrease in activity and then a prolonged increase in activity. Both of these periods of activity were temporally-related to the Go signal. Similar patterns of activity were observed in the splenius (Spl) and the complexus (Com). The longissimus dorsi (LoD) muscle generally showed greater activity during the right, contralateral, reach. It was also quite noticeable that the activity patterns of these axial muscles were very variable on a trial by trial basis (and even from one average to another) and in many trials lacked any evidence of phasic activity at all. Such was not the case for the limb and shoulder muscles which showed a much more consistent pattern of activity.

*General Cell Characteristics*

Despite the clear reciprocal nature of the vertical forces and the EMG activity of many of the major extensor and flexor muscles, most of the reticular neurones that we recorded showed broadly similar patterns of activity during reaches of both the left (ipsilateral to the recording site) and the right (contralateral) forelimb. Indeed, all except 4/67 neurones showed increases in activity during both the left and right reaches. Figure 2 shows 1 example of a tonically discharging neurone and Fig. 4 shows 4 other examples, one of which discharged in a tonic pattern (R22T32A), one in a phasic/tonic pattern (R22T30C) and two phasically. In each of these examples, the cells discharged with the same pattern of activity during the right reach and either with similar or elevated discharge frequencies.

Of the 20 cells that discharged phasically (see Methods and Schepens and Drew 2004) during the reach of the left, ipsilateral, forelimb, 15/20 also discharged phasically during the reach of the right, contralateral forelimb (see examples in Fig. 4), 3 further cells showed slightly elevated
increases of activity in the static phase of the movement causing their classification to change to phasic/tonic and only 2 cells showed a reciprocal decrease during the contralateral forelimb reach (Table I). Among those cells classified as discharging in a phasic/tonic manner during the left reach there was slightly more change. Eighteen (18/37) discharged in a similar manner during the left and right reach while a further 10 showed a reduction in the ratio between the phasic and tonic components that resulted in a reclassification as tonic cells. Five other cells showed a reduction in the tonic component so that they were now classified as discharging in a purely phasic manner during the right reach. Among the cells classified as discharging in a tonic manner during the left reach, 4/10 showed an identical pattern of discharge during the right reach and 6/10 were reclassified as discharging in a phasic/tonic manner. Despite these changes, it should be emphasized that, overall, 38/47 (81%) of those cells discharging with a tonic component (phasic/tonic and tonic cells) during the left reach continued to discharge with a tonic component during the right reach. The changes in classification during the left and right reach support our previous statement (Schepens and Drew 2004) that the cell discharge patterns form a continuum, from those cells discharging in a purely phasic fashion to those discharging in a purely tonic pattern, but with the majority of cells showing both a phasic and a tonic component.

Peak discharge rates during left and right reaches were also similar. Fig. 5A illustrates the relative magnitude of the peak discharge during the dynamic phase of the movement for all those cells that showed increased activity before ICIB onset during the left reach. Inspection of this figure shows that the discharge rate for most cells was generally similar and clustered around the diagonal line of equal magnitude, although there were some neurones showing clear increases of activity during the right reach (see e.g. Fig. 4) and others that discharged less. A linear regression analysis showed a slope for this relationship of 0.71 ($R^2 = 0.53$) indicating that, as a population, the discharge rate was slightly less for the right reaches than for the left ones. Discharge rates during the static
period (Fig. 5B) showed a similar relationship in that most cells showed appreciable activity during reaches of each limb. For this population, however, there was a clearer indication that discharge was less for the right reaches than for the left ones (slope: m = 0.43, R² = 0.30).

**Temporal relationships of discharge activity during reach**

As we previously emphasized (Schepens and Drew 2004), during a reach with the left limb, the onset of the discharge activity of neurones in the PMRF may be time-locked either to the Go signal or to the onset of the prime flexor muscles, the Br and the ClB. We have proposed that cells whose discharge is time-locked to the Go signal contribute to the initiation of the pAPA. Cells whose discharge activity is time-locked to the onset of the flexor muscles are suggested to contribute to the initiation of the movement and the accompanying postural adjustments (aAPAs). In many cells, we saw evidence of both relationships and most cells also continued to discharge throughout the dynamic phase of the movement with many continuing to discharge throughout the entire movement, until the reaching limb was replaced on the support surface.

Some of these characteristics changed during reaching with the right (contralateral) limb while others remained the same. In the following sections we, therefore, address separately the temporal relationships of the different features of the cell discharge, both to the onset of the movement, as well as to later aspects, such as the termination of the dynamic phase of the reach. Moreover, because our initial analyses showed that most of the important features of the discharge activity during right as compared to left reaches were observed in cells of all 3 types, phasic, phasic/tonic and tonic, we will present results from these cells together, emphasizing differences where apparent.

**Discharge activity related to the Go signal**

Initial changes in discharge activity that were time-locked to the Go signal could occur as...
either a decrease in activity (observed only in cells with a tonic discharge prior to the Go signal) or as an increase in activity. Eleven neurones exhibited a decrease in activity during the left reach that was time-locked to the Go signal. During the right reach, all 11 of these cells showed a reciprocal pattern of activity, in this initial period of activity, in that they now exhibited an increased period of activity, equally time-locked to the Go signal.

An example of one such cell is illustrated in Fig. 6A. During the left reach, the neurone showed a clear decrease in the level of activity that occurred at a fixed time following the Go signal. This decrease in activity was clearly time-locked to the Go signal as illustrated by the graph of Fig 6B (left) which illustrates the linear relationship between lead time and the onset of activity in the lClB (filled circles). During the reach of the right limb, contralateral to the recording site, the initial change in the discharge of the cell was a short-latency increase in the activity (Fig. 6A, right). As illustrated in the graph of Fig. 6B (right), there was a significant, linear relationship between the lead time of the cell discharge and the onset of activity in the rClB. Two other examples of neurones showing similar reciprocal changes in the early period of the discharge activity are illustrated in Fig. 6C.

The relationship between lead time and the onset of activity in the ClB for all trials from the 9 cells in which the early discharge could be accurately measured during both left and right reaches is plotted in Fig. 6D. As for the example of Figs. 6A,B, the population data show a clear relationship to the Go signal for both the left and right reach. The value of the intercepts for the population data was 57 ms for the left limb and 50 ms for the right limb.

During left reaches, we previously reported (Schepens and Drew 2004) that, following the initial decrease in activity, some of these cells (8/11) showed subsequent increases in activity that were also time-locked to the Go signal. Such is the case, for example, for the increase in activity following the initial decrease in activity during the left reach for the cell illustrated in Fig. 6A. We referred to these as secondary increases. This distinction is not pertinent during the reach with the
right limb because the initial change was a short-latency increase in activity. Any secondary increase, if present, is, therefore, not easily detectable in the individual trials. This is the case for the cell in Fig. 6A, although the averaged activity in the PEH suggests that such a secondary increase might occur.

In contrast to the cell illustrated in Fig. 6, the example neuron illustrated in Fig. 7 showed a non-reciprocal pattern of activation during the earliest part of the discharge. During the left reach, Fig. 7A, B left, there was a short latency increase in cell discharge activity that was time-locked to the Go signal. During reaches made with the right, contralateral, limb, this cell discharged in an identical manner (Fig. 7A,B right). This relationship was similar in all 10 cells for which latencies could be measured during both left and right reaches (Figs. 7C, D).

A similar pattern of non-reciprocal activity was also observed in many of the neurones discharging phasically. Figure 8A, B illustrates one example in which the discharge was time-locked to the Go signal during the left and right reach in the same manner as for the more tonically discharging cells illustrated in Fig. 7. In the illustrated example, as in many of the other phasically discharging cells, the neurone showed a short latency increase in discharge that preceded, and which was maximal during, the pAPA (gray bar). Increases in activity that were significantly related to the Go signal during both left and right reach could be measured in 4 other cells (see e.g. Fig. 8C) and the relationship of this small population to the Go signal was homogenous (Fig. 8D) and similar to that observed for the single cell illustrated in Fig. 8B.

**Discharge activity related to the movement onset**

During the left reach, the initial *increase* in activity in 16 neurones with a phasic/tonic or tonic discharge, and in 3 neurones with a phasic discharge, was significantly related to the onset of the *ClB* onset, and therefore the movement (Schepens and Drew 2003a). During the right reach,
only 1/19 of these cells showed a similar, significant, relationship between the initial increase in activity and /ClB. Indeed, in 11/19 cells, the initial increase in activity during the right reach was significantly related to the Go signal. While this change in temporal linkage might suggest a change in function, it should be emphasized that the comparison is complicated by the reciprocal nature of the initial change in cell discharge of the type illustrated in Fig. 6. While a movement-related increase can be readily determined in a cell that shows an initial decrease in cell activity (the situation during the left reach), it can only with great difficulty be detected following an initial Go-related increase (the situation during the right reach). In other words, the time of onset of the movement-related activity during the right reach could be masked by the preceding Go-related activity.

Discharge activity related to other events during the movement

Many of the phasic/tonic cells showed a pronounced phasic phase of activity during the right reach that, as illustrated in Fig. 9B was frequently followed by a clear depression of the discharge. This decrease in the discharge was clearly better related to the movement as it was only evident when the cell discharge was synchronised to the onset of the rClB (compare Fig. 6A, right, with Fig. 9B). Synchronizing the discharge on the /ClB also revealed a similar, but smaller depression, during the reach made with the left limb (Fig. 9A). Linear regression analysis confirmed the relationship between the end of the period of cell discharge and several different movement-related events. For example, during both the left (Fig. 9C) and right (Fig. 9D) reach, the end of the phasic period of activity was significantly related to the end of the period of activity in the major muscles active during the reach, e.g. the Br (not illustrated) and the TrM. This decrease in activity also correlated with the transient decrease in force seen in the supporting limb (Fv, unloading) at this same time. In addition, there was also a significant relationship with the second period of phasic activity in the AcT, the end of the phasic period of activity in the back muscle, LoD, as well as with the period of
activity of several other muscles (not illustrated). This underlines the close relationship in the postural changes in different groups of muscles with quite different anatomical functions.

Similar relationships between the end of the period of phasic cell discharge and the termination of the phasic period of activity in different muscle groups were found in many cells. These relationships are shown in Fig. 9E, F for all of those cells with a tonic component (solid lines) in which the relationship between the end of the phasic discharge and the end of the period of activity in the Br (or the TrM; see legend) was significant ($p < 0.05$). The slope of most of these regressions approached 1.0 and most had an intercept that was close to 0; this was more evident for the relationships during right reach than during the left reach. Similar relationships were found for 5/6 of the cells discharging with a phasic pattern of activity during the left and right reach and for which the offset of cell discharge could be measured in individual trials (dotted lines). The homogeneity of these responses is illustrated by the scatterplots in Fig. 9E, F which show the data from individual trials in 23 cells.

**Pre-trigger Activity**

Cell discharge frequency in some cells increased prior to the onset of the Go signal (Schepens and Drew 2004). This pre-trigger activity was related to the changes in the level of the EMG activity that occurred following the appearance of the cue. The traces of weight distribution during the reach show that, during both left and right reaches, there was a shift of the weight forward over the forelimbs (see Figs. 10 A, B) and that this shift in weight generally started following the cue tone (open circles) but prior to the Go Signal. The mediolateral traces on the other hand showed a reciprocal change in activity with the weight being shifted over the right limbs during the left reach and over the left limb during the right reach. Again, there was sometimes a similar change in weight distribution following the cue onset in the pre-trigger period as seen in Figs. 10A and B.

In the example illustrated in Figs. 10A, B, the cell showed a qualitatively similar and
significant (see Methods) increase in activity before the Go signal during both the left and right reach. Concomitantly, there was an increase in the activity of the lAcT during both reaches and a forward shift of the weight distribution in both cases. There was also symmetrical increases in activity in several other muscles, such as the rAcT, the lTrM and the rTrM (not illustrated). As indicated in the preceding paragraph, the changes in the mediolateral weight distribution were reciprocal. Linear regression analyses between cell activity and each of the 64 EMG and force traces that were measured showed the highest coefficient of determination for the lAcT muscle during both the left and right reaches (Figs. 10C and D). These relationships were substantially higher than those made using the change in the AP weight distribution of the cat.

Altogether, 11/67 cells showed significant increases in activity prior to the Go signal during both the left and the right reaches. In 8/11 cells, the best correlations with the cell discharge frequency during the pre-trigger period were found with one of the muscles acting around the shoulder, either the AcT or the TrM. In addition, there were also slightly less high correlations with the activity in the Srt in 5/11 cells. Those cells showing strong linear relationships were also those that showed the largest changes in activity during the pre-trigger period as a percentage of the control activity. In some cases, increases in activity in the shoulder muscles in the pre-trigger period were as clear as those illustrated in Fig. 10. In 9/11 of these cells the initial change in discharge activity following the Go signal was a short-latency increase in discharge activity during both the left and right reach. As such most of these cells would be classified as discharging in a non-reciprocal fashion, similar to those in Fig. 7, although in only 2 of these cells was it possible to measure the latency of the cell discharge.

Another 10/67 cells showed increased activity in the pre-trigger period during the left reach but no significant change during the right reach. In 6/10 of these cells, there was no indication of any change in the weight distribution in the AP direction during the right reach. As such, the lack of any change during the right reach may simply reflect the fact that the cat made adjustments to its posture
in the pre-trigger period only during the left reach. In the other 4/10 cells, there were clear changes in posture during the pre-trigger period during the right reach. All 4 of these cells showed an initial reciprocal pattern of discharge activity following the Go signal, similar to the example in Fig. 6.

A further 4/67 cells showed decreased activity during the pre-trigger period during both the left and right reach. No consistent relationships were observed between cells discharge activity and EMG or force activity in these cells, although there was a tendency for decreased muscle tone in the BvC during the pre-trigger period.

Quantitative Relationships

We determined detailed relationships between cell discharge frequency and the magnitude of the EMG activity for that subset of neurones with a tonic component for which we were able to measure temporal relationships (27/47), as well as for 12/15 neurones that discharged phasically during both the left and right reach.

Because of the close relationships between changes in activity in different muscles, high coefficients of determination ($R^2$) were found for multiple muscles during the left reach, although the correlation with the change in the $r$TriL was consistently high for muscles with a static component in their discharge (see Fig. 13 in Schepens and Drew 2004). During the right reach, this relationship was lost and the correlations were much reduced. This is illustrated in Fig. 11A (2<sup>nd</sup> from left) by plotting $R^2$ for the population of cells showing a tonic component during the left and right reach. All of the lines joining the coefficients of determination for the left and right reach are negative illustrating the greater, positive, relationship during the left reach. The opposite pattern was seen for the $l$TriL, i.e., correlations were negative during the left reach and positive during the right reach (Fig. 11A, left). Similar relationships during left and right reach were observed for the AcT and the SSp (not illustrated) and a reciprocal relationship was observed in the VL (i.e., positive responses in the $l$VL during left reach and in the $r$VL during the right reach, not illustrated).
Relationships in the forelimb and hindlimb flexors, as well as in axial muscles were weaker and more variable. From the point of view of the change on overall body posture, there was a positive relationship between cell discharge and the shift of the weight to one or the other side during the left and right reaches, respectively; in contrast, there was only a weak relationship to the forward shift of the body during the reach (Fig. 11A).

Figure 11B shows that these relationships were maintained when considering only the level of activity during the time from the Go signal until the time that the paw entered the tube (pAPA + dynamic), although the relationships were frequently weaker. In addition, the non-reciprocal cells (blue lines) showed a poor relationship with the rTriL during the left reach. This is primarily explained by the fact that the rTriL shows an initial decrease in activity, followed by an increase, while the cell shows only an increase (Fig. 7). The population of cells with a purely phasic pattern of discharge during the left and right movements (Fig. 11C) showed some major differences in comparison with the population with a tonic component. In particular, the relationship between cell discharge frequency and the level of activity in the rTriL, and that with the lateral shift in body weight, was the reverse of that observed in the phasic/tonic and tonic cells.

Not only did cells show high correlation coefficients with multiple muscles but there was a relationship between the strength of the relationship with different muscles. This is illustrated in Fig. 11D for 3 pairs of muscles as well as for the measures of the centre of vertical pressure. When a cell showed a strong positive relationship with the rTriL it normally showed a strong negative relationship with the lTriL (Fig. 11D, left). Similarly a strong positive relationship with the rTriL was associated with a strong positive relationship in the diagonally located lVL and there was also a positive relationship between the left and right ClB. There was no relationship between the strength of the correlation with the forward and lateral shift of weight suggesting independent control of these two behavioural events. Good relationships were also observed between lBvC and rBvC but not
between the lBvC and the rTriL (not illustrated).

Because of the widespread anatomical branching of many reticulospinal axons (see Introduction) we considered the possibility that better relationships between cell discharge and EMG activity might be obtained by examining multiple muscles. To test this, we performed a multiple regression in which we added muscles in a stepwise fashion based on the results from the linear regression analyses and on considerations of the goal of the behaviour. During the left reach, the rTriL was the first muscle entered as it was most frequently among the muscles showing the best relationship to cell activity in the linear regression analysis (Fig. 11A). The lClB in the left limb (the one performing the reach) was added subsequently, followed by the rAcT because it was active during both the dynamic and static phases and also produced high correlation coefficients in the linear regression analysis for many cells (not illustrated). Subsequently, we added the complementary muscles in the left forelimb, the Srt and the VL, as representative muscles for the hindlimbs, and finally we added representative axial muscles. For the right reach, the muscles were added in the reverse order.

Fig. 12A shows the results of this analysis for all of those cells showing a reciprocal pattern of activity (red lines) in the period immediately following the Go signal (see e.g. Fig. 6) as well as for those showing a non-reciprocal pattern of activity (blue lines) similar to that illustrated in Fig. 7. In general, during the left reach, the reciprocal cells showed an increase in the value of $R^2$ when the lClB and the rAcT were added to the regression. Subsequently, however, the addition of further muscles produced very little further change in the value of $R^2$. During the right reach (Fig. 12D), two differences were observed. First, the overall value of the regression was lower during the reach of the contralateral limb than during the left reach, that is the regression explained less of the variance in this condition. Second, although there was an increase in the value of $R^2$ as the other forelimb muscles were added, as for the left reach, there was an additional increase in several cells as the left
(contralateral) Srt was added to the equation.

The overall change in the value of $R^2$ is summarized for the reciprocal cells in the population averages of Fig. 12B. The black triangles indicate the cumulative value of $R^2$ as each muscle in turn was added to the equation showing that, on average, ~60% of the variance in the behaviour during the left reach could be explained by combining the activity in the first 4 muscles. During the right reach, the same population of cells explained < 40% of the variance for the equivalent 4 muscles and only attained 40% after adding representative muscles from all 4 limbs as well as axial muscles. The gray circles in the plots of Fig. 12B indicate the correlations obtained when using only the data from the dynamic period of the reach while the green squares indicate the correlations obtained during the static period of the reach. These data show that the cells with a reciprocal pattern of activity are much better correlated during the dynamic part of the reach than during the static portion when activity in the muscles is primarily confined to the extensors of the supporting limbs.

The pattern of correlations obtained from the non-reciprocal cells (blue lines) was somewhat different from that observed in the neurones showing a reciprocal pattern of activity. In particular, these cells showed a much more variable pattern of correlation than did the reciprocal neurones for both the left and right reaches suggesting that they form a less homogenous population. As a result, the cumulative values of $R^2$ observed in the population average of the activity during the left reach (Fig. 12C) are substantially lower from those observed for the reciprocal population. Moreover, both Figs. 12A and 12C show that the strength of the correlations is relatively similar for both the left and the right reaches. Interestingly, for the left reach, the strength of the correlations during the static period of the behaviour is almost equal to that observed during the dynamic period and the overall behaviour. This is in part because of an increased strength of correlation during the static period and in part to a decreased correlation during the dynamic period.

Other cells with a tonic discharge showed results similar to those for the reciprocal group with higher values of $R^2$ for left reaches than for right reaches (not illustrated).
Causal Relationships

Spike triggered averaging (STA) was used to examine causality in all 67 cells forming the major database. For this analysis, we used all action potential from all trials from the whole trial. Only cells for which we recorded > 1000 spikes were included in the final analysis. Overall, this yielded results for a total of 50 cells during the left, ipsilateral, reach and for 49 cells during the right, contralateral, reach. In both cats, EMG electrodes were implanted into 24 muscles, although some electrodes were lost over time.

Post-spike facilitation (PSF) or depression (PSD) was observed in a total of 16 muscles from 21/50 cells during the left reach and in 44 muscles from 17/49 cells during the right reach. In most muscles, 49/60 (82%), PSD was observed. An example of the most typical responses that were observed is illustrated in Fig. 13 for the cell illustrated in Figs. 6A and 9. In this cell, STA using a total of 11,537 action potentials recorded during the left reach showed no signs of PSF or PSD in any of the 24 muscles recorded during this experiment. In contrast, STA during the right reach, using 8,924 action potentials showed significant PSD in 4 proximal muscles, the lAcT, lSSp, lTrM and the lTriL (Fig. 13B); there was additionally PSD in the lPaL (not illustrated). In other words, these responses were observed in the extensors of the supporting limb, ipsilateral to the recording site but contralateral to the reaching limb. These responses were equally seen from averages made using action potentials only occurring prior to the onset of the Go signal (control, Fig. 13C) and from those occurring only following the Go signal (Fig. 13D). Similar responses were, of course, observed in the control period preceding the movements of the left limb. The validity of the responses is shown by Fig. 13E which shows the similarity in the PSDs obtained from compiling STAs from successive groups of 8 trials during the right, contralateral, reach. The fact that STA was observed in the control period, prior to the Go signal, but was observed only during movements with the right, contralateral, limb suggests that there must be some modulation, or gating, of the synaptic efficacy during the left reach.
Almost identical responses were obtained from 7 other cells; 2 examples are shown in Fig. 14A. In both of these cells, STA using action potentials from the complete trial showed a clear post-spike depression of activity in the \textit{lAcT} and the \textit{lSSp} during the right reach but no significant effects during the left reach. There was also depression of the activity in the \textit{lTrM}, \textit{lTriL}, \textit{lPaL} and \textit{lGlM} in the cell illustrated in Fig. 14A and of the \textit{lTrM} of the cell illustrated in Fig. 14B (not illustrated). As for the cell illustrated in Fig. 13, there was clear evidence of post spike depression in the control period, before the Go signal, for both the left and the right reach, despite the small number of action potentials available to construct the average. Similar modulation of the responses were seen in the other 5/7 cells showing this pattern of response. All of the cells displaying strong PSD in the left forelimb muscles during the right reach showed a phasic/tonic discharge during both the left and the right reach. Moreover 6/8 were also identified antidromically from the electrodes in the lumbar spinal cord showing that these were neurones capable of influencing both the fore-and the hindlimbs.

The other common pattern of responses, observed in 6 cells (including 5 identified as RSNS by the electrodes in the lumbar spinal cord) during left reach, was a clear depression of activity in the hindlimb extensors (\textit{GL}, \textit{VL}, \textit{GlM}) of the left limb and a small, but significant, facilitation of the activity in the \textit{lSrt}. In 3/6 cells (all identified by stimulation of the lumbar spinal cord), there was facilitation of the \textit{lSrt} and depression of the \textit{lGL} and \textit{lGlM} during both the left and right reach. One such example is illustrated in Fig. 14C. Note that the PSD in the \textit{lGlM} is also visible in the control condition, at least for those trials in which the cat is instructed to make a right reach. In 4 cells there was a depression of activity in the \textit{lTriL} during left reach and in 3 cells a facilitation of the activity in the \textit{rTriL} during the right reach. Changes in activity in the BvC were seen in 3 cells and changes in LoD were seen in 3 different cells.

For the forelimb muscles, the average latency was $8.8 \pm 2.4 \text{ ms} \ (N = 43)$ and for the hindlimb muscles it was $10.7 \pm 3.2 \text{ ms} \ (N = 17)$. We saw no evidence that cells producing post-
spike responses were preferentially localised in any one region of the PMRF.

Other Cell Types

In addition to those 67 cells that increased their discharge activity prior to the onset of the iClB activity, we also recorded 60 other reticular neurones during both the left and right reach. During the left reach 14 cells showed decreased activity following the Go signal, 13 cells an increase in activity subsequent to the onset of the iClB, and 10 showed a mix of these 2 characteristics; a further 11 neurones showed no significant change in activity or were silent (Schepens and Drew 2004). During the right reach, 38/48 (79%) showed very similar patterns of activity to those observed during the left reach. For another 8/10 neurones, the major difference was the appearance of a significant increase in discharge following the Go signal (Fig. 15), similar to that illustrated in Fig. 6.
Discussion

The results from this study support the view (Schepens and Drew 2004) that the reticular formation contributes to the coordinated activity of posture and movement during voluntary movement. Consideration of the discharge activity of reticular neurones during reaches of both the left and right limbs provides strong support for a contribution of this structure to both the pAPAs, preceding movement, as well as to the complex patterns of muscle activity responsible for the movement and the coordinated patterns of postural support that accompany it. The present study extends our information concerning the contribution of the PMRF to the control of movement and posture by demonstrating that reticular neurones are active during reaches made with either forelimb, although discharge frequency was generally greater with reaches made with the left limb, ipsilateral to the recording site. In addition, there were some consistent differences between the patterns of discharge activity during the left and right reach, particularly with respect to the earliest discharge that was time-locked to the Go signal. Moreover, consideration of the results obtained from the regression analyses and from the STA suggests that the bilateral signal is asymmetric in nature and that the final expression of the descending signal is modified (gated) according to the limb moved.

General Characteristics

One of the most striking findings in this study was the overall similarity in the pattern and the frequency of the discharge of these cells despite the reciprocal nature of the overall behavioural strategy. As illustrated in Figs. 2 and 3, the reaching movements with the left and right forelimbs were characterized by reciprocal changes in activity in F_v as well as in the major extensor muscles of each of the four limbs. Moreover, the major flexor muscles in the reaching limb were clearly phasically active only during the movements of the respective limb, left or right. Further, the movement of the centre of vertical pressure is directed to the right side during movements of the left
forelimb and to the left side during movements of the right limb (Schepens and Drew 2003a) and the centre of mass is likely to show a parallel displacement (Ioffê et al. 1982). It is, therefore, unlikely that the discharge activity of these cells is contributing to the control of any overall, global, variable of the movement or the postural responses that control them, at least in any simple manner.

As such, we suggest two primary, non-exclusive, explanations for the similarity in the discharge pattern of the cells. The first is that the activity of these cells is related to groups of muscles that show similar activity patterns during left and right reach. For example, Fig. 3 illustrates that some shoulder muscles (e.g. AcT) show broadly similar activity patterns during the reach of each limb, as do the axial muscles. The second possibility is that the cell discharge contributes to the production of activity patterns in different muscle groups during the left and right reaches and that there is, therefore, a gating mechanism that regulates the synaptic efficacy of the discharge at the level of the spinal cord. Such a mechanism would be compatible with the results from studies during locomotion (see below) as well as the differential effects obtained from the STA analysis.

Relationship to a single group of muscles

The simplest explanation of the general similarity of the pattern of discharge activity is that a given cell contributes to the activity of a given muscle, or group of temporally-coincident synergistic muscles, during both the left and the right reach.

Figure 6, for example, suggests that such an explanation might be compatible with the overall pattern of discharge of those cells classified as exhibiting a reciprocal pattern of activity. These cells show a brief decrease in activity time-locked to the Go signal during the left reach and an increase in activity, equally time-locked to the Go signal, during the right reach. It is likely that this initial activity is related to the pAPA that precedes movement (Schepens and Drew 2004). Subsequently, these cells show a sustained increase during the left reach and a more phasic/tonic
discharge during the right reach. These characteristics are similar to those exhibited by the rTriL and the rAcT during the left and right reach (Figs 3 and 6). However, linear regression analyses rarely showed a strong relationship between cell discharge and either of these muscles during both the left and the right reach. As illustrated in Fig. 11, there was frequently a strong relationship between these reciprocal cells and the activity in the rTriL during the left reach, but not during the right reach; a similar pattern was seen for the rAcT (not illustrated). Although the correlations with some other muscles, such as the lClB, were more equal during the left and right reach (not illustrated), it must be emphasized that the levels of activity in these muscles during the right reach were very low (Fig. 2). Taken together, the data suggest that there is little evidence that these reticular neurones contribute in any simple manner to the activation of any given muscle, or group of functionally synergistic muscles, during both the left and right reach.

**Reciprocal relationship to homologous muscles**

An alternative hypothesis is that the discharge activity of a given cell signals the EMG activity in one group of muscles during the left reach and the activity in a different group of muscles during the right reach. This is suggested, for example, by the data shown in Fig. 11A for the TriL. During the left reach, the discharge frequency of the cell is best related to the activity in the rTriL while during the right reach it is best related to the activity in the lTriL. In other words, when considering the entire behavioural period, discharge frequency correlates with the period of activity in the coTriL during both the left and the right reach. In addition, the activity in the lTriL is reciprocal, in that during the left reach activity in this muscle decreases as discharge frequency increases, while during the right reach it shows a parallel increase. The reciprocal nature between cell discharge and the behaviour of the animal is also indicated by the relationship with the lateral shift in body weight during the reach (Fig. 11A). During the left reach, cell discharge increases as the body shifts to the right; during the right reach, cell discharge increases as body weight is shifted...
to the left (giving the negative relationship in Fig. 11A). This relationship was equally observed in
the pre-trigger period in which cell activity before the Go signal increased irrespective of the
direction of the lateral shift of the body (Fig. 10).

The argument that cell discharge is related to activity in different groups of muscles
depending on the limb moved is also supported by the temporal relationships illustrated in Fig. 9.
During the left reach, there is clearly a relationship between the end of the phasic period of cell
discharge and the end of the period of phasic activity in the prime flexor muscles such as the /Br and
the /TrM during the dynamic period of the reach. During the right reach, however, there is clearly
a strong temporal relationship between the end of the phasic period of discharge and the end of the
period of activity in the /Br and the /TrM. The lack of a strong relationship between cell discharge
frequency and the magnitude of the activity in different muscles reflects the complex nature of the
discharge in these reticular cells and particularly the strong discharge that occurs during the pAPA.
For example, Fig. 8 clearly shows a strong period of activity in this cell prior to any activation of the
iBr. As such, linear regressions made from the onset of the Go signal to the end of the dynamic
period (pAPA+dynamic, Figs. 11B, C) are biased according to the relative strength of the discharge
during the pAPA and during the reach itself. Although a confound to the analysis, this also serve to
emphasise that there is no simple relationship between the discharge characteristics of reticular
neurones and any one group of muscles.

A similar organization of reticulospinal influence during reaching and locomotion

The results from the multiple regression, illustrated in Fig. 12, suggest that not only is the
discharge related to different groups of muscles during the left and right reach but that the cells might
encode the relationships between groups of muscles and in different limbs. Indeed, combining the
activity in the coTriL with that in the iClB, for both the left and right reach resulted in a substantial
increase in the value of the coefficient of determination, especially for those cells showing a
reciprocal pattern of activity. This type of organization is similar to that observed during locomotion and a schematic representation of this organization, similar to that proposed for locomotion (Drew et al. 2004), is shown in Fig 16. In this view, signals from the left and right motor cortex, responsible for the command to reach for the right and left limbs, respectively, impinge onto RSNs in the left PMRF. As stated in the Introduction, many of these neurons either branch to innervate both sides of the spinal cord (Matsuyama et al. 1988, 1997, 1999) or communicate with the contralateral side via commissural neurones (Jankowska et al. 2003; Matsuyama et al. 2004). They could, therefore, influence interneuronal networks on each side of the spinal cord. However, whereas during locomotion, the magnitude of the responses related to activity in the left and right limbs appears to be quite similar (Prentice and Drew 2001), the evidence from these experiments suggests a more asymmetric signal, especially for the reciprocal cells (see e.g. Fig. 12B).

We suggest that the interneuronal networks in the spinal cord that are activated by the descending signals from the reticular formation would include those that are normally activated during locomotion. Whereas, during locomotion, the gating of the signal is determined by both the rhythmical activation of the interneuronal networks and, possibly, a contingent signal from other descending pathways (Prentice and Drew 2001; Drew et al. 2004), we suggest that the gating during reaching is determined largely by the descending signal for movement, from the motor cortex and elsewhere. More specifically, we propose that the signal from the motor cortex, in addition to activating the interneuronal networks responsible for the reaching movement, would also gate the spinal interneuronal pathways onto which the reticulospinal axons impinge. Moreover, different pathways or different functional groups of cells might differentially modify these pathways at different times during the overall movement. In addition, it is possible that immediately following the initial pAPA, movement-related afferent input may also contribute to modify transmission in these interneuronal pathways.
The signal is gated.

The strongest support for the idea of a gated signal comes from the results of the STA analysis (Figs. 13 and 14). In most cases, particularly for the PSD, the onset of the post-spike responses identified by the STA was sharply demarcated and always began after the onset of the trigger spike. Moreover, the latency of these responses was compatible with the latencies of the responses evoked in forelimb and hindlimb muscles by trains of stimuli applied to the reticular formation (Drew and Rossignol 1990b). This suggests that these post-spike responses provide evidence of a causal relationship between the recorded neurone and the target muscle, as for cortico- and rubromotoneuronal cells (Cheney et al. 1991). None of the responses showing PSD included in our analysis began prior to, or just after the trigger spike, and none exhibited a broad peak, as would be expected if the post-spike effect was due to synchronous discharge in adjacent populations of cells (Cheney et al. 1991; Smith and Fetz 1989). Nonetheless, we cannot rule out that some of the post-spike facilitatory responses (e.g. Srt in Fig 14C) might be the result of synchronous inputs.

Although only a few cells provided positive evidence of a causal relationship, the most striking result was the depression in the activity of the extensor muscles of the left (ipsilateral to the recording site) limb during the right reach. During the left reach there was no sign of either facilitation or depression. One of the interesting points in this result is that in all cells showing this pattern of activity the depression was present in the control period before the Go signal. This means that during the left reach this inhibition was actively gated out. This provides clear evidence of a modulation of the descending signal during the reach, consistent with the hypothesis proposed with respect to Fig. 16. Moreover, it was equally striking that 5/8 of the cells in which this pattern of activity was observed discharged with a reciprocal pattern of activity, suggesting that this population of neurones might form a functionally homogenous subset of the whole population.

The depression of the activation of the ipsilateral extensor muscles is compatible with the results from locomotion studies in which microstimulation of the PMRF during locomotion in the
intact cat frequently produces a depression of the activity ipsilateral extensors when the stimulation is applied during left stance and, therefore, during right swing (Drew 1991); an analogous situation to the right reach. It is also similar to the results recently obtained by Davidson and Buford (2004) who have shown depression of activity in the ipsilateral extensors by single pulse microstimulation during a reaching movement. At the same time, the result is somewhat paradoxical, as activity in these cells depresses activity in the ipsilateral extensors at a period during which sustained activity is required for postural support (see Fig. 6). It is possible, therefore, that this signal should be seen as one providing inhibitory sculpting of the activity in the ipsilateral extensors. This would be compatible with one of the suggested functions for the cerebellum (Armstrong and Edgley 1984; Eccles et al. 1967) which, via the fastigial nucleus, provides strong monosynaptic input to RSNs in the PMRF (Eccles et al. 1975; Mori et al. 2000). It is possible that this functional subset corresponds to the population of RSNs described by Takakusaki et al. (1989, 2001, 2003) in the decerebrate cat as producing powerful inhibition of extensor muscle activity.

An asymmetrical signal

The fact that this response is only observed in the ipsilateral extensor muscles during reaches made with the limb contralateral to the recording site in the PMRF is a strong argument not only for gating of the descending signal but also provides more evidence of a strong asymmetry in the descending control to each limb. The data from the STA suggest that at least part of the inhibitory control for each limb comes only from the ipsilateral side. Microstimulation studies during locomotion (Drew 1991, Drew and Rossignol 1984) suggest that facilitation of the extensors on the ipsilateral side is likely to come at least in part from reticular neurones in the contralateral (right) PMRF. Examined from the other point of view, increased activity of the reticular neurones in the left PMRF is likely to contribute primarily to activity of the extensors of the right forelimb (as shown in Fig. 11). The fact that no sign of PSF was observed in the rTriL during the left reach suggests that
this pathway may be less direct than that to the ipsilateral extensors, even though the latter is also likely to be at least disynaptic (Peterson 1979). These connections are illustrated schematically in Fig. 17. This figure also shows putative facilitatory connections from reticular neurones to ipsilateral extensors as well as to ipsilateral and contralateral flexors. These connections are suggested on the basis of the linear regression analyses (Fig. 11) and by the temporal analysis of Fig. 9. This is compatible with the results from our microstimulation studies during locomotion (Drew 1991).

Separate Modulation of the APA and movement-related discharge

In addition to the gating of the signal according to the limb to be moved, it is probable that there is also differential control of the initial discharge that is time-locked to the Go signal and suggested to be related to the pAPA and the later movement-related signal. This suggestion is based in particular on consideration of those cells showing a reciprocal pattern of discharge time-locked to the Go-signal (e.g. Fig. 6) and of those cells showing decreased activity during the left reach and an increase time-locked to the Go-signal during the right reach (Fig. 15). In both of these cases, it seems clear that the activity related to the pAPA is modulated independently of the movement-related activity. This supports our previous suggestion (Fig. 16, Schepens and Drew 2004) that the neurones in the PMRF receive convergent input containing signals related either to the pAPA or to the movement and integrates these into a unified descending command signal to control posture and movement.

A signal related to control of the Forelimbs and the Hindlimbs

In the above Discussion, we have addressed the functional significance of these discharge patterns primarily with respect to the changes in activity in the forelimbs, and this despite the fact that a number of these neurones were identified as projecting to the lumbar spinal cord (Schepens and Drew 2004). This is justified for several reasons. First, our previous analysis showed no
functional distinctions between RSNs and unidentified neurones (Schepens and Drew 2004). Second, a majority of RSNs that project as far as the lumbar spinal cord also innervate the cervical spinal cord (Peterson et al. 1975). Third, the instructed task was for a voluntary movement of the forelimbs. Nevertheless, we do not intend to imply that these neurones will contribute only to the patterns of activity in the forelimbs. Indeed, it is likely that many of these neurones will influence activity of muscles in both the forelimbs and hindlimbs, and probable that some may preferentially activate hindlimb muscles. In these experiments, it is difficult to differentiate between these possibilities (although see next section) because the movement of the forelimb induces a coordinated pattern of postural support that is distributed between the four limbs (Schepens and Drew 2003a). This is implicit in finding of strong linear relationships between the cell activity and the extensors of the forelimbs (Fig. 11A) and hindlimbs (not illustrated). It is also explicitly demonstrated by the finding that cells that show a strong positive relationship with the $r$TriL equally show a strong positive relationship with the $l$VL, an extensor in the diagonally located hindlimb (Fig. 11D). A similar relationship occurs between the $l$TriL and the $r$VL (not illustrated).

A contribution of reticular neurones to postural modification in fore- and hindlimbs would be compatible with the finding that many RSNs increase their discharge as both the forelimbs and the hindlimbs step over an obstacle during locomotion (Prentice and Drew 2001). Moreover, it is compatible with the finding that 6/8 of the neurones that produced PSD in the ipsilateral forelimb extensors were positively identified as RSNs with an axon projecting to the lumbar spinal cord. A causal contribution to the control of postural activity in the hindlimbs was demonstrated in some cells by the expression of PSF and PSD in flexors and extensors, respectively, of both the ipsilateral and contralateral hindlimbs during left and right reach. This might suggest a subpopulation of neurones that contribute preferentially to the coordinated change in hindlimb muscles during movements of the forelimbs. This would be compatible with our previous report that the postural changes in the fore- and hindlimbs might be independently controlled (Schepens and Drew 2003a).
Nonetheless, as for the population of neurones producing PSD in the ipsilateral extensor muscles, it is possible that these neurones also influence other muscles, including those in the forelimb either through pathways with weaker synaptic efficacy or through polysynaptic connections.

Finally, although the results from the multiple regressions show that up to 60% of the total variance in cell discharge can be explained by combining flexor and extensor muscles from different limbs in a linear, combinatorial fashion (Fig. 12), it is possible that these reticular neurones may better encode higher-level features of the postural responses. For example, recent studies by Ting and MacPherson (2005) have suggested that the compensatory postural responses that result from horizontal displacement of a support surface might be the result of the activation of a limited number of synergies that activate multiple muscles through a weighting matrix. It is possible that some of the activity patterns that we observe here would be more compatible with the activation of these more abstract, or high-level, signals.

**Several subpopulations of neurons**

The data presented in this manuscript suggest the existence of at least 3 different subpopulations of neurones, each of which probably contributes to activity both during the aAPA and during the movement. The broadest division is between those neurones that have a tonic component and those that do not. We have previously suggested, based on the level of discharge activity in different parts of the behaviour, that phasic and phasic/tonic neurones may fall on a continuum (Schepens and Drew 2004). However, the quantitative analyses in this study suggest that there may be real functional differences in these neurones that go beyond a simple comparison of the discharge pattern. This is particularly evident when inspecting the linear regressions compiled from the pAPA + dynamic period as illustrated in Figs.11B, C. Whereas cells with a phasic/tonic pattern of activity increase their discharge with the lateral movement of body weight over the supporting limbs (Fig. 11B), those with a purely phasic period of activity increase their discharge
in the inverse manner (Fig. 11C). As mentioned in preceding paragraphs, this difference is because of the relatively increased discharge activity of the phasic cells during the APA as the body weight is initially transferred over the reaching limb. As such, while contributing to the reach itself, as suggested by the later discharge activity, temporally related to the end of the period of activity in the flexor muscles (Fig. 9), these phasic cells may have a preferential role in contributing to the anticipatory postural adjustments preceding the movement. In contrast, although the phasic activity of the phasic/tonic cells undoubtedly contributes to the APA, the linear regressions suggest a preferential contribution to the flexor muscle activity during the reach and the postural activity that accompanies that movement.

Inspection of the activity patterns of those cells with a tonic component suggest at least two subpopulations, distinguished in particular by the initial changes in activity time-locked to the Go signal. One population shows a reciprocal period of activity during the pAPA (Fig. 6) and the other a non-reciprocal pattern (Fig. 7). How this change in the pattern of activity relates to the changes in muscle activity is not clear. That the differences between these populations is real, however, is suggested by several other findings. For example, while both populations of cells show strong relationships with the rTriL during the left reach when the entire behaviour is considered (Fig. 11A), the cells showing a non-reciprocal discharge show only a very weak contribution to this muscle when only the pAPA + the dynamic period is considered (Fig. 11B: blue lines). This might suggest the cells with a reciprocal discharge time-locked to the Go signal might have a more preferential relationship to the dynamic part of the movement than the non-reciprocal cells. This is also supported by the multiple regression analysis (Fig. 12) which shows that, as a population, the reciprocal cells are much better related to muscle activity during the pAPA + dynamic period than during the static period while the non-reciprocal cells show an almost equal relationship in the two phases.

Interestingly, the results from the STA showed that most of those cells showing PSF with the
ipsilateral forelimb extensors exhibited reciprocal patterns of activity while all 3 cells showing bilateral responses in the hindlimb muscles had a non-reciprocal pattern of activity. This might provide some further indication of the relative functions of these two populations. Cells with a reciprocal pattern of activity might preferentially contribute to forelimb activity and those with a non-reciprocal pattern of activity might preferentially contribute to hindlimb activity. This would be compatible with the fact that the hindlimb extensor muscles do not show the same reciprocal modification of activity during the APA as do the forelimb muscles (see Fig. 3) and with our previous statements concerning independent control of the fore- and the hindlimbs (Schepens and Drew 2003a).

Concluding Remarks

The results from these experiments provide further evidence that the PMRF contributes to the coordination of both movement and posture and that this activity is bilateral. This finding complements the results from locomotion studies that show discharge activity related to EMG activity in the left and right limbs both during unobstructed locomotion (Drew et al. 1986; Matsuyama and Drew 2000; Shimamura and Kogure 1983) and during voluntary modifications of gait (Prentice and Drew 2001). We have argued that the final expression of the descending signals from the reticular formation is gated by the rhythmical activity of the interneuronal networks on which these signals impinge (Drew 1991; Drew et al 2004; Prentice and Drew 2001; see also Orlovsky 1972). The results from this study extend these arguments in several ways. First, the fact that the reaching movements are made from a stable and static standing posture allows us to make precise temporal correlations between cell activity and different behavioural events. This clearly shows that reticular cells contribute to multiple parts of the behaviour including the postural responses preceding the movement. Second, the data clearly show that the descending signals during reach are asymmetric, discharging more strongly and showing better relationships with EMG activity.
during reaching movements made with the left (ipsilateral) limb than those with the right limb. 

Third, we have several lines of evidence suggesting that the signal is gated at the spinal level, including direct proof for a small subset of cells that produced PSD of the ipsilateral extensor muscles, but only during reaches with the contralateral limb. This evidence provides strong support for arguments previously made only on the basis of more indirect evidence.

As for the mechanism involved in producing the gating we suggest that the command for movement, originating in large part from the motor cortex, is responsible for modifying the transmission in interneuronal spinal pathways during the movement. A question remains, however, as to the signal responsible for the gating of the anticipatory postural responses that precede the movement and are time-locked to the Go signal. We suggest two possibilities. One is that descending signals from the motor cortex are equally responsible for modifying the spinal networks before the onset of the reaching movement as well as during it. Motor cortical cells related to the Go signal in a similar task have been reported by Perfiliev (2005) although the author suggests that these cells are more involved in movement initiation and selection than in postural control. The other possibility is that some of the reticular neurones themselves, in particular those showing an initial reciprocal pattern of activity, may produce the gating. If such is the case, then these neurones may receive an input signalling the initiation of the pAPA either from the motor cortex (Birjukova et al. 1989; Kably and Drew 1998a,b; Matsuyama and Drew 1997) or other premotor cortical areas (Matsuyama and Drew 1997; Viallet et al. 1992).
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### Table 1

Comparison of discharge pattern during ipsilateral and contralateral reach

<table>
<thead>
<tr>
<th>Ipsilateral Reach</th>
<th>Phasic</th>
<th>Phasic/Tonic</th>
<th>Tonic</th>
<th>Reciprocal</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phasic</td>
<td>(20)</td>
<td>15</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Phasic/Tonic</td>
<td>(37)</td>
<td>5</td>
<td>18</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Tonic</td>
<td>(10)</td>
<td>6</td>
<td>4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The Table indicates the number of cells discharging in a similar (Bold) or different manner during both ipsilateral and contralateral reaches.
Figure Legends

Fig. 1: A: Description of the task. A tone of 0.5 s indicated the onset of the trial. After a period of 1.5 s, a second tone, the cue (random duration of 0.5 - 1.5 s), instructed the cat to make a movement with the left limb (400 Hz tone) or the right limb (4KHz tone). At the end of this delay, a shutter opened (Go signal) giving the cat access to food in the tube for a period of 3 s.

Fig. 2: Example of cell discharge, vertical ground reaction force (Fv) and electromyographic (EMG) activity in selected muscles during a left and right reach. Each trace is scaled identically for the left and right reach allowing comparison of the relative magnitude of the activity. Data are synchronized to the onset of the Go signal. Ipsilateral and contralateral are used with respect to the location of the recording chamber which, in both cats, was placed over the left pontomedullary reticular formation (PMRF). The gray bar in this figure, as well as in Figs. 3 and Figs. 6-8, identifies the activity during the preparatory anticipatory postural adjustment (pAPA). As in our previous paper (Schepens and Drew 2003a) we define the pAPA as the period from the initial change in force under the reaching limb until the onset of the period of activity in the prime flexor muscles, such as cleidobrachialis (ClB). Abbreviations: FL, forelimb; HL, hindlimb; l, left; r, right; TriL, lateral head of triceps brachii; VL, vastus lateralis.

Fig. 3: Examples of EMG activity recorded from the left limb during reaches with the left (thick traces) and right (thinner traces) limb. Activity in each muscle is scaled identically during the left and right reaches. Data are synchronized to the onset of the Go signal. Note that most data are taken from a single experiment in cat RS23, only the activity patterns in the hindlimb extensor muscle are taken from a different experiment (cat RS22). Abbreviations: AcT, acromiotrapezius; Br, brachialis;
BvC, biventer cervicus; GL, gastrocnemius, lateral head; LoD, longissimus dorsi (level of L); SpD, spinodeltoideus; Srt, sartorius, anterior head.

Fig. 4: Four different examples of cell discharge activity during a left and right reach together with the activity of selected force and EMG activity. Data are synchronised to the Go signal.

Fig. 5: Comparison of the magnitude of peak discharge during reaches of each limb. A: discharge rate during the dynamic phase of the movement; B: activity during the static phase of the movement: (●), phasic cells; (○), tonic cells; (△), phasic/tonic cells. Cells illustrated in Fig. 4 are identified. Solid line indicates equi-magnitude line; dotted line shows linear regression. m, slope; I, intercept; N, number of cells; R², coefficient of determination. Note that as in all other figures, left and right are equivalent to ipsilateral and contralateral to the recording site,

Fig 6: A: Post-event histograms (PEHs), raster displays and averaged EMG activity of a cell that showed reciprocal, short-latency, changes in activity during left and right reaches. Activity is triggered on the Go signal. B: scatterplots showing the relationship between both the latency of the cell discharge (○) and the lead time (●) (see Methods) with the latency of the onset of activity in the ClB. C: two other examples of neurones showing reciprocal changes in the earliest period of discharge. Left reach is represented by the thicker of the two lines, right reach by the thinner line. D: scatterplots of latency (○) and lead time (●) as a function of the latency of ClB onset for all trials measured from 9 cells for which the initial change could be measured during both left and right reach.

Fig. 7: Examples of cells that showed identical short-latency increases in activity during left and
right reaches. Figure organised in the same manner as Fig. 6. Data in D are from 10 cells in which
the onset of activity could be determined during both left and right reach.

Fig. 8: Example of a phasic cell during left and right reaches, organized as for Figs 6 and 7. The data
in D are from 5 cells in which the onset of activity could be determined during both left and right
reach. Note that statistics are provided only for the regression of lead Time as a function of ClB
onset.

Fig. 9: Relationship between the end of the phasic period of activity and the end of the dynamic
period during left (A) and right (B) reach. A and B organized as in Fig. 6 except with the data
triggered on the onset of activity in the iClB (first dashed vertical line). The second dashed vertical
line is aligned with the end of the phasic period of activity in the TrM. C and D: scatterplots showing
the relationship between the onset of the decrease in cell activity (‘Off’ in the histograms of A and
B) and the time of selected periods of activity during left (C) and right (D) reach. Arrows in A and
B indicate the events used in the scatterplots of C and D. E, F: regression coefficients and
scatterplots for those cells showing a significant relationship between the onset of the decrease of
cell activity and the end of the period of activity in Br for left (E) and right (F) reaches. Cells with
a purely phasic discharge are represented by dotted lines. Note that for some cells, Br was not
available and we, therefore, used the TrM which has a similar profile of activity (Schepens and Drew
2003a).

Fig. 10: A, B: PEHs and raster displays showing qualitatively similar increases in pre-trigger activity
during left (A) and right (B) reaches. Open circles on the rasters indicate when the tone cue was
initiated. Also displayed are selected EMG traces and an indication of the weight distribution of the
cat in the anteroposterior and mediolateral planes. Cue onset indicates the average time of the cue onset during the left and right reach. In the anteroposterior plane the weight distribution of the cat is calculated as the deviation of the weight, in Newtons, from an idealised situation in which 60% of the weight is over the forelimbs (Schepens and Drew 2003a). Similarly in the mediolateral plane, the graph illustrates the deviation of the weight, in Newtons, to one side of the other with respect to the ideal situation in which 50% of the weight is over each side. C, D: scatterplots illustrating the relationship between cell discharge frequency during the pre-trigger period and the activity in the lAcT and the deviation in AP weight distribution. See Methods for details on how these data were calculated.

Fig. 11: A: The coefficients of determination for the regressions of cell discharge for the TriL and for the shift in weight, determined from the entire trial, are plotted for left and right reach. Red lines indicate cells that have a reciprocal pattern of activity during the reach. Data are plotted only for cells having a tonic component. B: Coefficients of determination calculated from the time of the Go signal until the time that the paw enters the tube (pAPA + dynamic) for cells with a tonic component. Blue lines indicate cells discharging with a non-reciprocal pattern of activity. C A similar display for cells with a phasic discharge pattern. Note that relationships that had negative slopes were represented as having negative values for the coefficient of determination. D: The coefficients of determination calculated from linear regressions with one muscle are plotted as a function of the coefficient of determination calculated from a different muscle. Data are taken from linear regressions performed on data from the entire trial.

Fig. 12: A: Multiple regressions for cells identified as discharging with an early reciprocal pattern of activity (red) or with an early non-reciprocal pattern of activity (blue). Each graph plots the
cumulative coefficient of determination as additional muscles are added, in a stepwise manner, to the regression. B, C: Average values of $R^2$ for all reciprocal (B) and non-reciprocal (C) cells. Black triangles, data from the entire trial; gray squares, data from the dynamic period; Green squares, data from the static period.

Fig. 13: Spike triggered averages (STA) compiled using all action potentials (N) from the entire behavioural trial during left (A) and right (B) reaches. C: STA compiled from the action potentials during the period before the Go signal during the right reach. D: STA compiled from the entire period following the Go signal during the right reach. E: STA compiled from the entire behavioural period from 4 different parts of the database, each consisting of 8 consecutive trials. Each of the traces is scaled to its own minimum and maximum. Horizontal lines during the pre-spike period in each EMG trace indicate $\pm 2$ standard deviations. Abbreviations: SSp, supraspinatus.

Fig. 14: Further examples of results from STA. A and B: examples of 2 cells showing similar results to those illustrated in Fig. 13. C: example of a cell producing similar post-spike responses in hindlimb flexor and extensor muscles during left and right reach. Control data were compiled only from action potentials occurring prior to the Go signal.

Fig. 15: Example of a cell showing a decrease in activity during the left reach and an increase in discharge, time-locked to the Go signal, during the right reach.

Fig. 16: Schematic illustration of one way in which the reticulospinal system may contribute to the bilateral control of movement and posture during reaching. Reticulospinal cells in the PMRF receive bilateral input from cells in the motor cortex so that they are activated during left (orange) and right
blue) reaches. Each reticulospinal cell projects to interneurones that form part of and/or are influenced by the CPG during locomotion (shaded region inside oval). We suggest that the intrinsic spinal connections that facilitate coordinated and bilateral activity between flexors and extensors during locomotion also facilitate the same patterns of activity during reaching movements made from a standing position. However, in the case of reaching movements made from a static position, it is the descending command that initiates the reach that is also responsible for producing the gating signals that ensure that the descending signal from the reticulospinal system influences the appropriate groups of muscles.

Fig. 17: Schematic illustration to emphasize the bilateral and asymmetric nature of the descending signal from the reticular formation. The results emphasize that one group of reticular neurones has a strong inhibitory effect on ipsilateral neurones (but only during reaches of the contralateral limb). Thus neurones in the left PMRF (2) inhibit neurones on the left side and neurones in the right PMRF (3) inhibit neurones on the right side. Such neurones may also facilitate activity in the extensors of the other side. The results from this study, as well as those from previous locomotion studies (see text) also suggest the presence of neurones (1) that have facilitatory inputs to flexor and extensors on each side of the body. The expression of the coordinated postural responses will depend on gating signals from descending pathways (see Fig. 16 and associated text and legend). Note that the crossed responses may be mediated either by axons that innervate each side or via commissural neurones (see text).
**Fig. 1**

- **Tone 1** = Left Reach
- **Tone 2** = Right Reach
- **Pre-Trigger Period**
- **Cue Signal**
- **Go signal**
- **Shutter open**
- **Left Reach**
- **Right Reach**
Fig. 2
Fig. 3
Fig. 4
**A** Phasic discharge

- $N = 41$
- $R^2 = 0.53$
- $m = 0.71$
- $i = 23.4$

**B** Tonic discharge

- $N = 38$
- $R^2 = 0.30$
- $m = 0.43$
- $i = 25.7$

**Fig. 5**
Fig. 6
Fig. 8
Fig. 9
Fig. 10

A Left (ipsilateral) Reach

B Right (contralateral) Reach

C

D

Spikes/s

Time (ms)

Spikes/s

Time (ms)

Fig. 10
Fig. 11
Fig. 12
Fig. 14
Fig. 16