LOCOMOTION IN THE CAT
A BEHAVIOURAL AND NEUROPHYSIOLOGICAL STUDY OF INTERLIMB COORDINATION

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voor Corinne

CONTENTS

PREFACE

This thesis is based largely on the following articles:

1) Miller, S. and Van Der Meché, F.G.A., Movements of the forelimbs of the cat during stepping on a treadmill, Brain Res., 91 (1975) 255-269.

2) Miller, S., Van Der Burg, J. and Van Der Meché, F.G.A., Co-oordination of movements of the hindlimb and forelimb in different forms of locomotion in normal and decerebrate cats, Brain Res., 91 (1975) 217-237.

3) Miller, S., Van Der Burg, J. and Van Der Meché, F.G.A., Locomotion in the cat: basic programmes of movement, Brain Res., 91 (1975) 239-253.

4) Halbertsma, J.M., Miller, S. and Van Der Meché, F.G.A., Basic "programmes" for the phasing of flexion and extension movements of the limbs during locomotion in the cat, In: R. Herman, S. Grillner, P.G. Stein and D.G. Stuart (Eds.), Neural control of locomotion, Plenum Press, New York. In Press.

5) Miller, S., Reitsma, D.J. and Van Der Meché, F.G.A., Functional organization of long ascending propriospinal pathways linking lumbo-sacral and cervical segments in the cat, Brain Res., 62 (1973) 169-188.

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ASP Biological and Medical Press, Elsevier Division, Amsterdam.
Article 1, Figs. 1-5.
Article 2, Figs. 1-6 and 8.
Article 3, Figs. 2 and 4-7.
Article 5, Figs. 3 and 6-7.
Plenum Publishing Corporation, New York.
Article 4, Figs. 1-11 and 13.

CHAPTER 1.

GENERAL INTRODUCTION.

The alternating periods of flexion and extension movements at the different joints form the elements of the locomotor cycle, which may be adapted in force and timing to satisfy the requirements for support of the body, balance and direction of progression.

These basic elements of movement are produced by the activities of interneurones and motoneurones lying in the respective spinal segments innervating each limb. In his study of narcosis progression in the cat Brown (20) suggested that the flexion and extension movements were generated by groups of neurones driving the respective motoneurons. These groups were organized into functional half centres producing the signals necessary for the flexion and extension phases of stepping by virtue of mutual inhibition. The existence of half centres received some confirmation by Lundberg and his collaborators in studies on the effects of L-DOPA on spinal cord reflexes (82). The actual mechanisms by which the groups of interneurones produce phases of flexor and extensor activity have not yet been defined, although Grillner (62) and Pearson (115) have suggested some possible models.

How far each limb has its own independent neuronal centre for generating locomotor movements (the so-called stepping generator) is not entirely clear. In the hindlimbs, at least, even quite complex locomotor activity can be produced by lumbosacral segments disconnected from the rest of the nervous system (62,64). Brown (19) reported that rhythmic movements at the ankle remained in one limb when the spinal cord was divided in the upper lumbar region and the great part of the opposite lateral half of the lumbar spinal cord was removed. Good evidence therefore exists for somewhat independent stepping generators for each hindlimb. However, it is not known at present if locomotor movements of the forelimbs in the cat can be produced similarly by cervicothoracic spinal segments, or if, with the phylogenetic process of encephalization of motor control, forelimb movements are in some way dependent on structures in the brain stem. It should also not be overlooked that in different types of locomotion movements of the head, rib cage and entire vertebral column can occur which are linked in phase with the locomotor patterns of the limbs (72,140). In searching for the basic neural strategies underlying locomotion it is necessary to consider if the concept of four interconnected spinal centres each controlling one of the limbs (62,108), is sufficient or how far it needs to be enlarged to include movements of the trunk and head.

In the present investigation of interlimb coordination (chapter

4) the flexion and extension movements of the limbs were selected for analysis rather than measures of foot contact with the ground (50,74,77,111,120,140,145). The choice was influenced by the neurophysiological studies cited above which demonstrated that alternating periods of flexion and extension are the common elements of locomotor movements. Moreover, it carried the advantage that the investigation could be extended to include situations such as swimming and stepping while supported in the air, where the influence of gravity is negligible and foot contact with the ground does not occur. The investigation finally led to the conclusion of two fundamental patterns of locomotor movements: alternate and in-phase gaits (104,105). These forms of locomotion may be compared generally with the symmetric and asymmetric gaits derived from foot contact patterns. In addition, the classification carried the suggestion that the same subsets of neural activity could be used with relatively little modification in widely different forms of locomotion, for example, stepping, swimming and jumping.

In considering the problem of the neural control of locomotion, and in particular that of interlimb coordination, it became clear that little information was available of the movements of the forelimbs of the cat. For example, movements of the hindlimbs have been studied extensively (40,49,60,117) but there are only fragments of information about movements of the forelimbs. At best the movements are indicated generally as flexion and extension, or protaction and retraction (129). A systematic analysis of forelimb movements became necessary not only for the investigation of interlimb coordination in locomotion (9,107,108,140) but also for the interpretation of neurophysiological studies of brachial segments of the spinal cord (13,39,105,126,146, see chapter 3).

The present investigation of the neural control of locomotion began with a neurophysiological study of the long pathways linking the spinal centres controlling hindlimbs and forelimbs (chapter 5). At that time it was not known if the long propriospinal pathways were actually involved in the coordination of hindlimbs and forelimbs. However, the observation that coordinated stepping of the four limbs can occur in the high spinal cat (chapter 4) considerably advanced the interpretation of the function of these pathways. The hypothesis that long spinal pathways represent part of an intrinsic spinal system coordinating the locomotor activities of the forelimbs and hindlimbs has now received further support.

One of the puzzling features of the neurophysiological experiments was the varying mixture of excitatory and inhibitory influences to motoneurones evoked over long propriospinal pathways. The question was raised whether the mutually antagonist effects belong to different functional mechanisms or to different phases of a normally cyclical process. The latter hypothesis was tested further in decerebrate cats stepping on the treadmill, by investigating the influence of electrical stimulation of the paw of one limb girdle on the EMGs of flexor and extensor muscles of limbs in the other girdle (chapter 6). The results indicate that the reflex effects of cutaneous stimulation of a limb conducted over long propriospinal pathways are gated in a predictable manner to flexor or extensor motoneurons depending on the phase of the step cycle. The significance of these effects is discussed in relation to the mechanisms of interlimb coordination.

CHAPTER 2.

METHODS OF BEHAVIOURAL EXPERIMENTS.

The behavioural observations were made on 3 normal cats (F5,F6 and F8) stepping freely on the ground at velocities between 0.5 and 5.5 m/sec; 12 normal cats (F2-13) trained to step on a motor-driven treadmill at velocities between 0.3 and 6.0 m/sec; 8 decerebrate cats (DC1-6, HJ1 and HJ2) and 4 spinal cats (SP1-4) stepping on the treadmill, and 9 normal cats swimming (F5,6,8 and 13 and Z1-5). With the exception of F12 (9 months old, 1.5 kg) the cats were adult and weighed 2.5 to 4.5 kg.

Freely moving cats

Under freely moving conditions the cats followed a piece of food held by an experimenter around a 9 m arc of 8 m radius. The camera stood at the centre of the arc and swivelled to follow the cat as it stepped around the arc. Between 3 and 7 consecutive steps could be recorded in each traverse. Two cats (F6, 4.0 kg and F8, 4.0 kg) were analysed systematically over a range of velocities. Sample measurements were made on the third cat.

Normal cats stepping on the treadmill

These cats were trained in daily sessions of 10-15 min over 2-3 weeks. Various positive and negative conditioning procedures were used, e.g. food rewards and compressed air jet directed at the hind-quarters. The best results were achieved with food rewards and frequent handling of the cat by the experimenters. Care was taken that the cats were 'at ease' - evidenced by an upright (and not crouching) gait, ears pointing forwards and tail held high. The treadmill was 1.5 m long, 30 cm wide and with walls 60 cm deep. In these experiments the belt was set in a horizontal position. The long front wall was of transparent Perspex. The short wall in front of the cat's head contained a wire mesh window through which the cat could see the experimenter, and a blind drawer through which food rewards were passed. During a training session the treadmill velocity was kept constant for periods of 30 sec to 2 min. At the onset of a session a slow pace was chosen, but after [illegible] the velocities followed no set order. Galloping was restricted to 30 sec and not more than 2 periods per session, since the cats tired quickly and even became deconditioned. Measurements were made when the cat learned to follow the velocity of the treadmill remaining in approximately the middle of the treadmill and touching neither the rear nor the front wall. Under these conditions, as Arshavsky et al. (9) have demonstrated for the dog, the parameters of stepping are generally very reproducible. Up to 30 successive steps (usually 10-20) were analysed for each velocity of the treadmill. The stepping patterns of 3 cats (F6, 4.0 kg; F8, 4.0 kg and F13, 2.5 kg) were systematically analysed over a range of velocities. The remaining 9 cats were analysed at a few chosen velocities and the results corresponded to those of the 3 cats analysed in detail.

Normal cats swimming

These cats were plunged into a Plexiglas bath 2 m long, 25 cm wide and filled with water at 30-33° C to a depth of 45 cm. At one end there was a ramp by which the cats could climb out of the water. Cats which 'protested' on the first trial were not retried. The number of swimming locomotor cycles was usually increased by holding the tail when the cat reached halfway across the bath: this manoeuvre did not affect the coordination pattern of swimming.

Decerebrate cats

Locomotion in these cats was obtained by stimulating in the mesencephalon (132). The electrodes were bilateral and concentric and had an outside diameter of 200 µm. Usually only one electrode was used, although locomotion sometimes appeared more symmetrical with bilaterally placed electrodes. Rectangular current pulses of 1 msec and at 30-100 Hz were used over a range of 50-300 µA to elicit locomotion. The cats were investigated (1) suspended in the air by strings attached to the lumbar fascia and the spine of C7, and by a headholder, (2) suspended with part of their body weight supported by their limbs on the treadmill belt (stepping), or (3) suspended immersed in a watertank.

Spinal cats

The spinal section was performed at C_1 (see also chapter 5). The following drugs were used to obtain stepping movements: L-DOPA (L-dihydroxyphenylalanine), 50-100 mg/kg; the monoamine oxidase inhibitor Nialamid, 40 mg/kg; and the peripheral DOPA decarboxylase inhibitor Ro 4-4602/1 from Roche, 25-50 mg/kg. All drugs were given intravenously in a saline solution.

Measurements of joint angles

Movements of the limbs have been measured at the scapula and at the shoulder, elbow, wrist, hip, knee and ankle joints from 16 mm film at approximately 67 frames/sec, and by automatic analysis using a television system at a sampling rate of 50 or 60 Hz (45,69). The joint angles have been estimated from the positions of the bony landmarks indicated in Fig. 2.1, either by inspection of the bony landmarks as they can be recognised through the skin or by the positions of paper discs glued to the skin over the respective bony landmarks while the cat was standing upright. By convention, flexion occurs when the angle becomes smaller, and extension when it increases. There are qualifications to this convention for the wrist

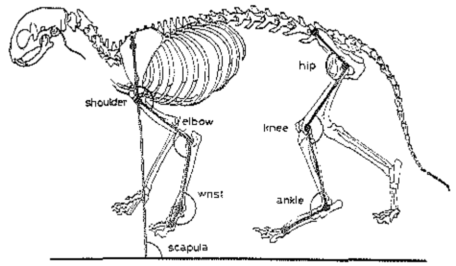

Fig. 2.1. Skeleton of cat to indicate angles measured for joint movements. Filled circles overlie bony landmarks used as reference points for the estimation of the angles.

digits and toes (see chapter 3). The cats were closely shaved on the side of the body facing the camera. For ease of recognition the bony landmarks around each joint were identified with discs of paper of 3-5.5 mm diameter glued to the skin (Fig. 2.1). The correspondence of these discs with the bony landmarks was checked in 16 mm films of 2 normal cats stepping on the treadmill in which the bony landmarks could be clearly observed through the skin. It was also checked in one normal cat stepping on the treadmill by X-ray photography on 35 mm film at 80 frames/sec. In this case the dots were replaced by lead discs. For the hindlimb the skin remained closely related to the bony landmarks in all the places indicated in Fig. 2.1 except at the knee. Here considerable slippage of the skin occurred in all forms of stepping and this point could not be used as a reference for determining the absolute excursions of these joints (Fig. 2.2C). The changeover points of flexion and extension, however, occurred at the same time whether the joint angle was measured strictly from inspection of bony landmarks or from the positions of discs on the skin. In the forelimb the skin only remains closely related to the bones of the wrist. At the elbow the same argument applies as at the knee: the changeover points of the skin movement coincide with the changeover points of the joint movements (Fig. 2.2B). The skin over the shoulder, however, shifts in a more complicated fashion (Fig. 2.2A), but it does not distort the timing at the elbow of the changeover points of flexion and extension. The onset of flexion and extension movements at the shoulder cannot be reliably estimated from the positions of discs on the skin. It was concluded from these

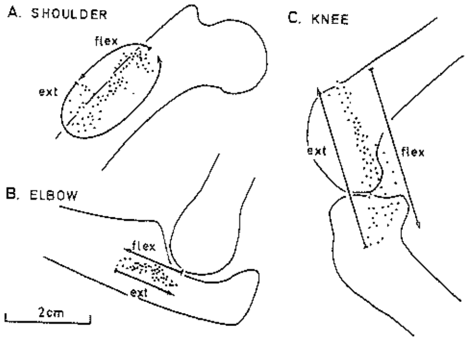

Fig. 2.2. Slippage of skin over bony landmarks at shoulder, elbow and knee joints during stepping at 1 m/sec on treadmill. The data were obtained from measurements of an X-ray film taken at 80 frames/sec. The dots indicate positions of lead discs (4 mm diameter) glued to the skin. The arrows show the direction of slippage of the skin with respect to flexion (flex) and extension (ext).

controls that measurements taken from elbow, hip and knee joints by means of discs over the bony landmarks give reliable results for the time relations of the onsets of flexion and extension; for absolute joint angle excursions, they need to be corrected. The turning points of flexion and extension were determined by the film records and the television technique (45) from the frame or sweep in which the particular joint angle became smaller or larger, respectively. The error measurement from film could be ± 1 frame (± 15 msec), and with the television technique ± 10 msec. The errors in the estimation of joint angles are difficult to determine. At the hip, knee, ankle and elbow joints the maximum error is ± 5°. At the scapula, shoulder and wrist the error might be greater in some circumstances. In the scapula the angle of the spine is measured with respect to the horizontal plane (Fig. 2.1). This gives a reasonable estimate of the movements of the scapula over the rib cage, but does not take account of the small changes in the curvature of the thoracic vertebral column which occur during locomotion. In most cats it was possible to estimate the angles at these joints in the limbs of the side of the body opposite to the camera. Movements at the knee and elbow joints show consistent linkage with movements at other joints in each limb in both the dog (9,132) and the cat (41,49,109) and may thus be considered indices of flexion and extension movements (see also chapter 3).

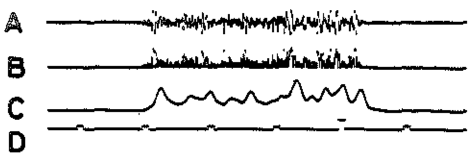

Fig. 2.3. Processing of EMG signals. A. raw EMG with the high pass filter at 30 Hz (-3dB); B. after full wave rectification; C. after low pass filtering at 100 Hz (>-40 dB); D. time scale 100 msec between pulses.

Electromyograms

In 4 normal cats stepping on the treadmill (F2,3,5 and 6) electromyograms (EMGs) were recorded from the hindlimb and forelimb muscles by the method of Engberg and Lundberg (41). The muscles included biceps femoris posterior and anterior, sartorius, quadriceps femoris, latissimus dorsi, pectoralis major and minor, triceps brachii and biceps brachii. The bipolar electrodes used were made of enamelled copper transformer wire of 150 µm diameter. The wires were introduced percutaneously during short Fluothane anaesthesia. A reliable index of correct electrode placement was obtained if palpable contraction of the respective muscle occurred on stimulation of each electrode with pulses of 1 msec duration, at 5 Hz and at currents below 500 µA. The EMGs were recorded on magnetic tape and were synchronised with the 16 mm film camera.

Simultaneous recordings of movements and EMGs in different types of stepping were made in one decerebrate cat with the automatic television recording technique (45). In this technique the positions of small white paper discs glued to the skin above the bony landmarks about the different joints are digitized at a sampling rate of 60 Hz. The skin overlying the scapula was tightly stitched to the spine of the scapula, so that the paper discs could give an accurate estimate of the scapula's movement with respect to the horizontal plane. At the same time 4 channels of EMG activity are digitized at 240 Hz. Before digitization the raw EMG (Fig. 2.3A) is high pass filtered at 30 Hz (-3 dB) and treated to full-wave rectification (Fig. 2.3B). The signal is then passed through a low pass filter (Fig. 2.3C) in which frequencies above 100 Hz are suppressed by 40 dB. During computation, the EMG signals are subjected to further software filtering as described by Halbertsma (69).

The following conventions are used: homolateral limbs refer to the hindlimb and forelimb of the same side of the body and homologous limbs refer to either the pair of hindlimbs or the pair of forelimbs.

CHAPTER 3.

MOVEMENTS OF THE FOUR LIMBS OF THE CAT DURING STEPPING ON A TREADMILL.

INTRODUCTION

The movements about the different forelimb joints and their time relations over a range of velocities of locomotion have been investigated in normal cats trained to walk on a treadmill. Particular attention has been given to movements at the shoulder joint and of the scapula over the rib cage, since the set of these joints largely defines the position of the arm. The positions of these joints might also be of significance for the initiation of stepping movements, as has been shown for the hip joint (60,61). The muscles acting at these joints are the proximal group of muscles within the classification of Kuypers (88). Anatomical studies have shown that there are direct long ascending propriospinal projections which terminate preferentially among the motoneuronal cell groups of the shoulder girdle muscles (48,138). Neurophysiological investigations of these pathways have further revealed that excitatory actions from lumbosacral segments are directed primarily to motoneuronal cell groups innervating proximal muscles and that some of the projections are monosynaptic (13,103,105). From evidence presented in this chapter it has been concluded that movements of the scapula have an important role in the generation of locomotion in the forelimbs.

Movements of the wrist and digits have proved difficult to define in terms of extension and flexion (126,137). Observations of the wrist and digits during locomotion have led to a classification which is compatible with anatomical and functional considerations.

METHODS

The material presented in this section has been obtained from the 12 normal adult cats (F2-13) trained to step on a motor-driven treadmill. The observations reported have been made on all cats: for the time relations of the movements between the various joints 3 cats (F6,10 and 13) were investigated in particular detail.

Observations have also been made on the 9 normal cats swimming (F5,6,8 and 13; Z1-5) and 8 decerebrate cats (DC1-6; HJ1 and HJ2).

By convention an increase of the joint angle indicates extension and a decrease flexion of the joint (Fig. 3.1A). There are qualifications to this rule for the wrist and digits and this is discussed in Results. The measurements at the scapula and shoulder joint have been made from cats where the respective bony landmarks could be recognized through the skin.

The gaits described as walk, trot and gallop have been defined according to the patterns of foot contact as described by Stuart et al. (140).

RESULTS

Movements at Individual Joints

Scapula

In contrast to the pelvis with its fixed attachment to the vertebral column, the scapula has a loose, sliding connection with the body of the cat. The movements of the principal joints of the forelimb during a step cycle are shown in Fig. 3.1C. The upper part of the dotted line indicates in each case the direction of the spine of the scapula and this is shown in further detail in Fig. 3.1B. The positions of the scapula in relation to the vertebral column were determined from a 35 mm film taken with X-ray photography at 80 frames/sec. The field viewed by the camera was not sufficiently large to include simultaneously all the forelimb joints and the figurines in Fig. 3.1C were traced from 16 mm film under normal lighting conditions, where the spine of the scapula could be easily recognized through the skin. For both situations the same cat was set to step at approximately 0.9 m/sec. The numbering of the figurines in Fig. 3.1C corresponds to the respective positions of the scapula in Fig. 1B.

The scapula makes large and complicated movements over the rib cage (see also refs. 36,73 and 85). To simplify description of these movements it is assumed that the movements of the scapula are confined to the parasagittal plane of the body. The rib cage which forms the articulating surface with the scapula is curved both in the rostrocaudal and in the dorsoventral directions. This means that as the scapula slides rostrally or ventrally the glenoid cavity tends to turn medially (see also ref. 85). During locomotion the movements of the scapula can be resolved into two main vectors: (a) rotation, where the spine turns about a point situated in the dorsal third of the plate of the scapula, and (b) dorsoventral and rostrocaudal shifts over the surface of the rib cage. The result of these vectors is the semilunar movement of the glenoid cavity shown in Fig. 3.1B.

The terms flexion and extension are applied to the scapula such that they correspond to the phases of flexion (protraction) and extention (retraction) at the more distal joints, as described below. Flexion of the scapula is characterized by a clockwise (observer facing the scapula, cat facing left) rotation and a rostral and dorsal shift. In extension the reverse takes place: an anticlockwise

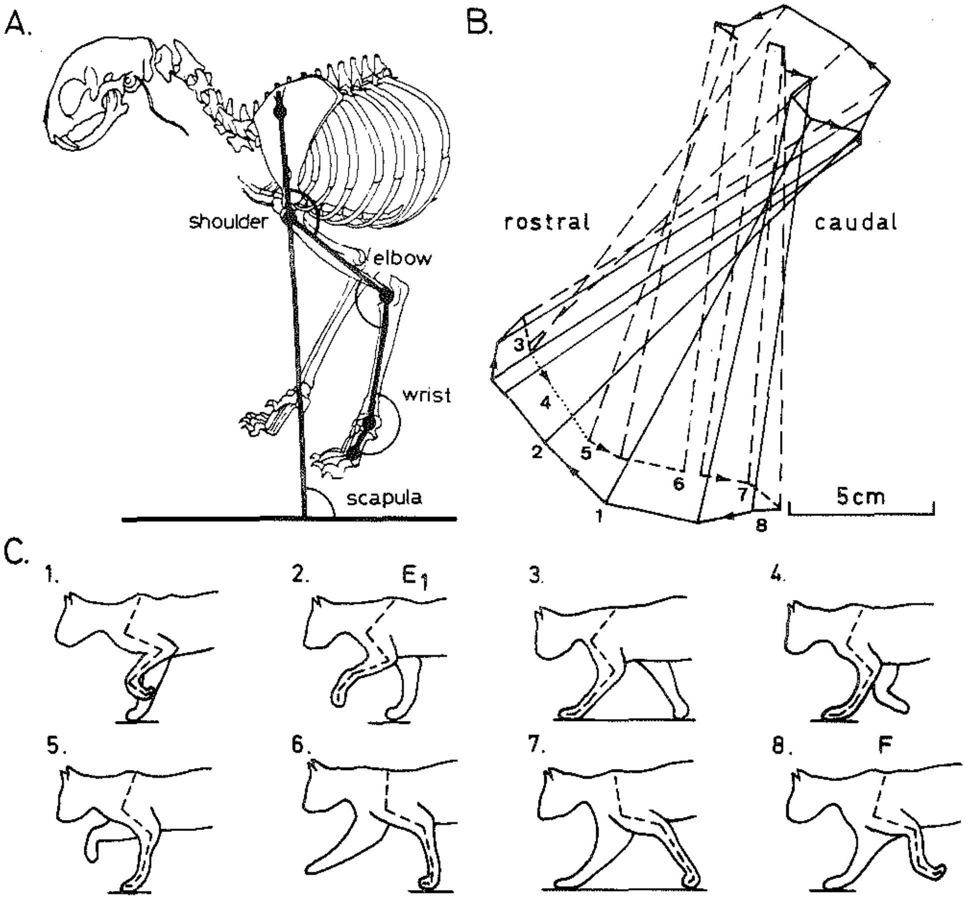

Fig. 3.1. Movements of the forelimb. A: skeleton of cat to show the angles measured at each joint. Filled circles indicate the bony landmarks from which the angles were calculated. The upper 4 circles represent the positions where the paper discs were glued to the skin for estimation of joint angle by the television sampling technique. B: movements of the spine of the scapula during locomotion at 0.9 m/sec. The movements are related to the position of the upper thoracic vertebrae and were obtained with X-ray photography. Continuous lines indicate the position of the scapula during flexion; broken lines movements during extension. The time separation between adjacent vertical lines is 3 frames (about 37.5 msec). The fine dotted line between positions 3 and 5 indicates some uncertainty in the measurements: at this point the left and right scapulae overlapped in the X-ray film and were difficult to distinguish. Arrows show the direction of movement. The numbers correspond to the positions of the forelimb shown in the figurines. C: figurines of the movements of the forelimb. Same cat and velocity as in B, but traced from a 16 mm film under normal lighting. The dotted lines indicate the direction of the bones of the limb, E_1 the onset of extension at the elbow, F the onset of flexion at the elbow. The numbers correspond to the numbered positions of the scapula in B.

rotation and a caudal and ventral shift. Rotatory movements are most prominent during the early parts of both flexion and extension. The rotation in the step illustrated in Fig.3.2.2B occurred over about 60° and this remains rather constant over different velocities (Fig. 3.2, open circles). The hysteresis between flexion and extension movements is caused by the sinking downwards of the rib cage when the forelimb makes contact with the ground. No yield, i.e. an interruption of the extension movement by a short period of flexion provoked by the weight of the body, has been observed. In this respect the scapula is comparable to the hip joint (40,117).

In alternate gaits, e.g. the trot (108), the movements of left and right forelimb are separated by half a step cycle and have the same form. In the gallop the movements of the forelimbs occur more closely in phase and differ in form. Because they are not moving completely in phase, one forelimb leads the other, the trailing one. Between the leading and trailing forelimb there are differences in the duration of the flexion and extension phases of the scapula. Two gallops have been selected to demonstrate this. Here it is sufficient to mention that in the right rotatory gallop the measured left forelimb is leading (Fig. 3.2E) and in the left rotatory gallop the same limb is trailing (Fig. 3.2D). In the leading limb, the flexion phase is longer and the extension phase shorter than the respective phases in the trailing limb (Fig. 3.5E and D, respectively).

At all velocities of locomotion the scapula starts its extension phase before the foot makes contact with the ground. Note in Fig. 3.2D and E that the period between the start of extension at the scapula and contact is prolonged for the trailing limb. This results partly from the different time course of the scapula movement (Fig. 3.2) and partly from the fact that the leading forelimb on making contact lifts the rib cage so that the trailing limb has to retract further caudalwards before making its contact with the ground.

Shoulder and elbow

At the shoulder and elbow joints comparable flexion and extension movements take place (Figs. 3.1C and 3.2). During flexion the angles (indicated in Fig. 3.1A) decrease. The extension period can be divided, as in the hindlimbs (117), into 3 parts. The first extension (E_1) is defined by the onset of opening of the joints. At this moment the scapula is still in flexion and the foot in the air. The second extension (E_2), by comparison with the hindlimb (117), starts at the time of contact with the ground and of the onset of the yield in the more distal joints (shoulder, elbow and wrist). The scapula enters extension about 15-75 msec before this moment, depending on the velocity (Fig. 3.2). In the third extension (E_3) all the joints extend together to increase the thrust of the body upwards and forwards (Figs. 3.1C and 3.2).

As the velocity is increased (Fig. 3.2A-E), the movements at the shoulder and elbow are now elaborated faster, but the form of the movements remains the same, though with an increase in the absolute value of the yield. There are, however, striking differences again in the gallop between the leading and trailing limbs. If the limb is leading (Fig. 3.2E) the flexion phase is longer and the extension phase shorter than when the limb is trailing (Fig. 3.2D), and this is the same picture in fact as described above for the scapula. An important contrast to the scapula, however, is that the absolute value of the joint angle excursions in the two types of gallop is different. The scapula traverses the same absolute excursion in

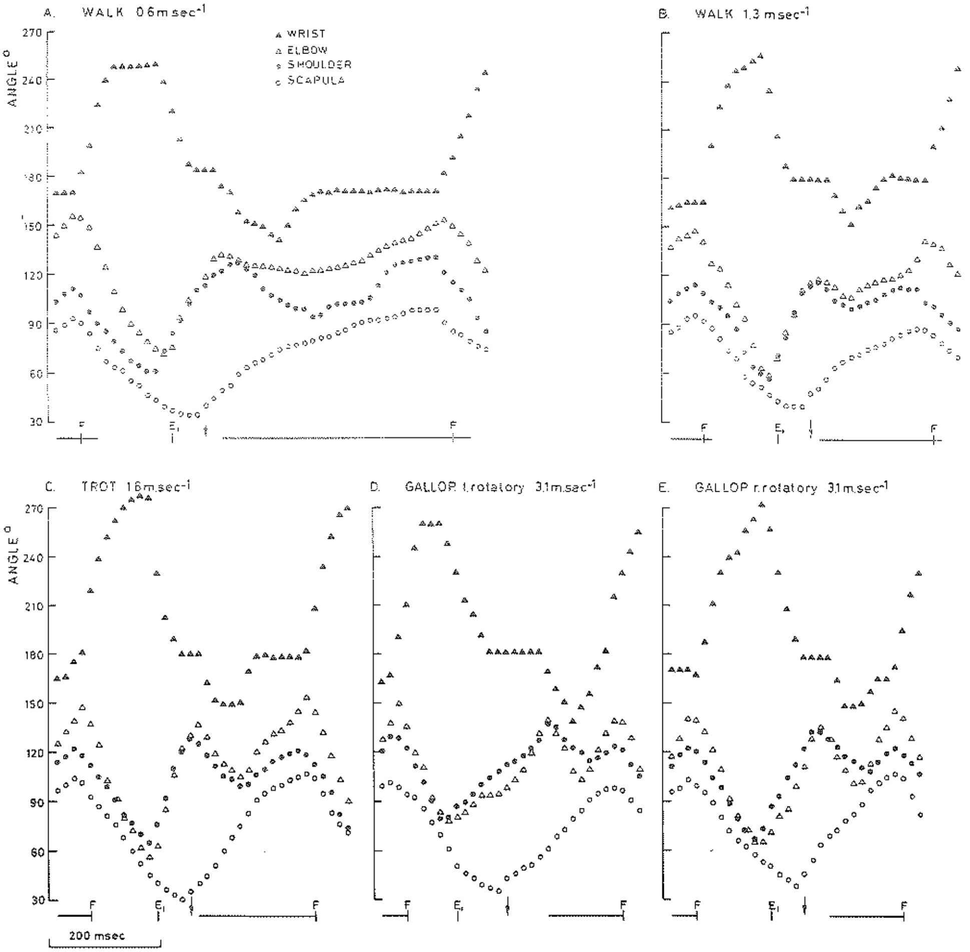

Fig. 3.2. Change of angle at the scapula and shoulder, elbow and wrist joints during step cycles at different velocities. All data are from 16 mm films of the same cat. The horizontal bar indicates the duration of foot contact with the treadmill; E$_1$ and F the onset of extension and flexion, respectively, at the elbow; the arrows give the onset of extension of the scapula.

different time settings, but in the shoulder and elbow joints of the trailing limb the absolute values of the angles reached at the end of flexion are not as small; in other words, the flexion movement is not as pronounced. The outcome of these differences in terms of coordination of the forelimb movements is to bring the onset of the E_1 periods of each limb more into phase (see chapter 4).

Wrists and digits

The wrist joint is capable of a range of movements about a transverse axis of at least 120°. The slight radial and ulnar deviations of the wrist, supination and pronation movements, and the spreading of the digits during the extension phase of the limb have not been treated in this analysis, since they could not be recorded with the present film and television techniques. Together with the articulations of the digits, the wrist joint provides a flexible base for the forelimb under varying conditions of terrain and also a flexible instrument for manipulation and other functions.

The backward or caudal aspect of the wrist joint was chosen for measurement of the joint angle since this angle decreases and increases during flexion and extension, respectively, of the other joints of the limb. This designation is also consistent with observations of the flexion reflex (see Discussion). The movements at the wrist and digits have been described in the present work in terms of palmar flexion and dorsiflexion, since these movements do

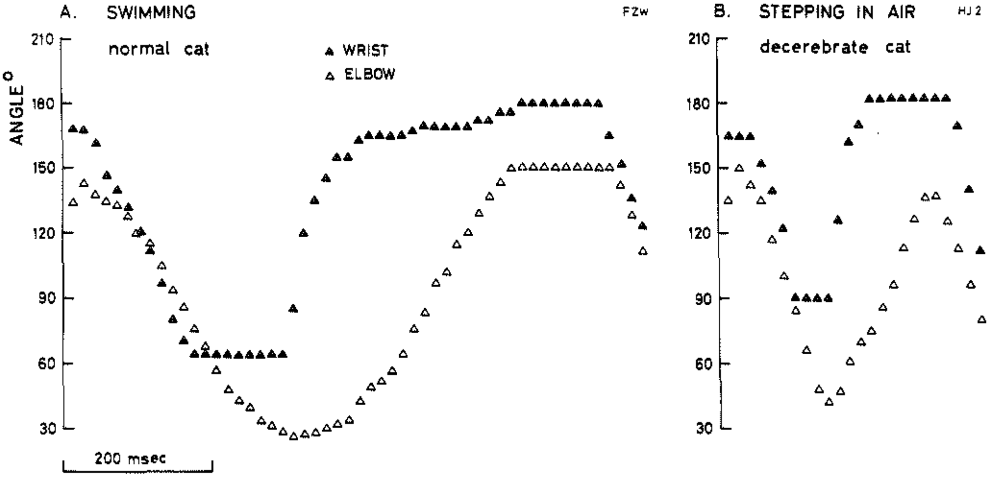

Fig. 3.3 Changes of the joint angle at the elbow and wrist during (A) swimming (normal cat), and (B) stepping while suspended in the air (decerebrate cat). Note that the angle at the wrist joint does not exceed 180°; compare with Fig. 3.2.

not always bear a constant association with flexion and extension of the more proximal joints depending on the type of locomotion, i.e. stepping on a surface and supporting the weight of the body, or swimming or, in the decerebrate cat, stepping in the air.

In the situation where body weight is not supported by the limbs (swimming or stepping in the air) the following sequence of movements occurs. At the moment at which the elbow and shoulder start to flex the wrist and digits perform a rapid palmar flexion and the angle of the wrist joint decreases. This movement proceeds to a point of extreme palmar flexion where the paw may be curled almost into a ball. Dorsiflexion begins approximately at the moment at which the elbow and shoulder begin their extension (Fig. 3.3). Once again the movement of dorsiflexion is rapid. The wrist and digits uncurl to become straight (approx. 180°) shortly before the time at which the limb begins to move caudalwards under the influence of extension of the scapula. The wrist and digits maintain this setting throughout the remainder of the extension phase. In these movements, then, plantar flexion of the wrist and digits occurs with flexion, and dorsiflexion with extension of the more proximal joints.

During the stepping on the ground, where the body weight is supported, contact occurs at the end of the E_1 phase of the more proximal joints. The wrist yields by undergoing dorsiflexion and then palmar flexion (Fig. 3.2). The movement is probably accompanied by active contraction of the muscles producing palmar flexion, since the wrist can be passively dorsiflexed at least 45° below the straight straight position (180°). In cats stepping in the air palmar flexion can be triggered during the extension phase of the proximal joints by tactile pressure on the footpads, and this is presumably the forelimb equivalent of the extensor thrust reflex described for the toes

Thus, *contact of the foot with the ground contributes to an active palmar flexion to support the body*.

The same mechanism can be observed in the toes of the hindlimb. During swimming or stepping in the air, there is a rapid plantar flexion at the onset of the flexion phase at the proximal joints, and a rapid dorsiflexion of the toes coincident with the first extension at the knee and ankle. Pressure on the footpad (40) during extension causes the toes to give a powerful plantar flexion or extensor thrust In 3 decerebrate cats in which the hindlimbs were deafferented (107), hardly any plantar flexion or dorsiflexion occurred at the toes and there was no extensor thrust on contact of the footpads.

At different velocities the movements of the wrist are remarkably stable (Fig. 3.2A-E). Note that the angular acceleration does not change much, but that it is the period where the wrist is held at approximately 180° which is varied in duration. For the two gallops the same changes apply to the wrist as to the other joints: for the trailing limb the flexion phase is shorter and the extension phase longer (compare Fig. 3.2D and E).

Time relations between movements of the different joints of the forelimb

The onsets of flexion and extension have been measured at the scapula, shoulder, elbow and wrist for 3 cats over several velocities (Fig. 3.4). At the wrist flexion and extension imply palmar flexion and dorsiflexion, respectively. The onsets have all been related to the onset of the respective movement at the elbow joint, because this joint has been used for estimating coordination of hindlimb and forelimbs (chapter 4).

The striking feature of these histograms is that the onset of extension of the scapula occurs significantly later than that of the other more distal joints ($P < 0.01$; *t*-test). In the gallop this delay is significantly greater ($P < 0.01$; *t*-test) if the forelimb is trailing (Fig. 3.4D). If the cat changes its gallop by altering the lead order of the forelimbs, the delay of the extension of the scapula is adjusted in one or two steps between the values shown in Fig. 3.4D and E.

F6

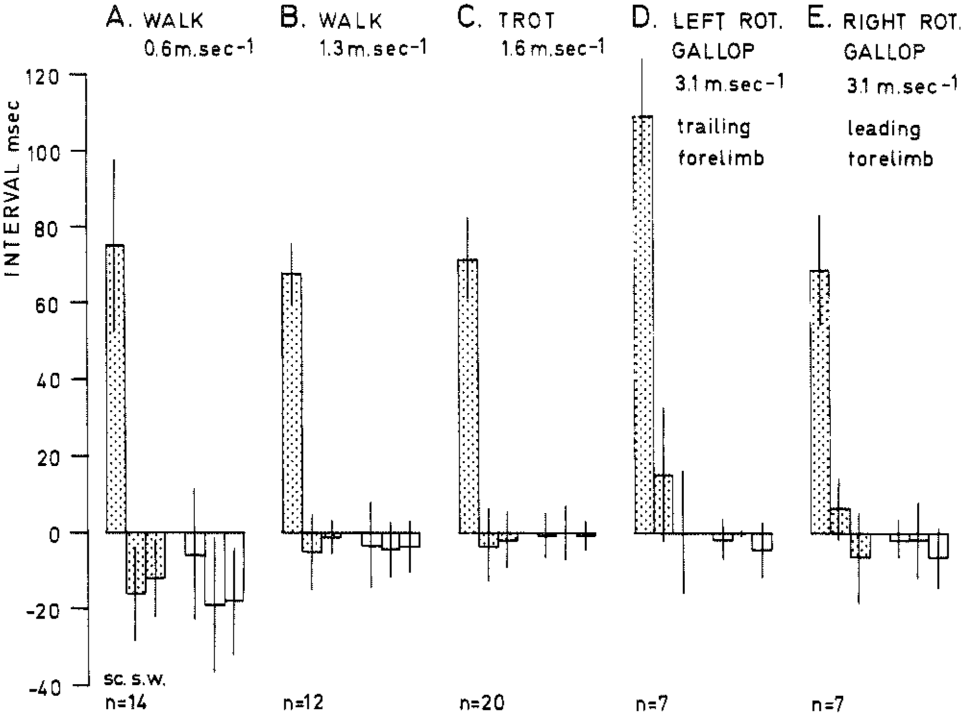

Fig. 3.4. Onsets of extension and flexion phases of locomotion at the scapula (sc) shoulder (s) and wrist (w) with respect to those at the elbow. The ordinate indicates the time interval between the onset of the movement at the particular joint shown and that of the elbow. Each block indicates the average interval at each joint for n successive steps. Stippled blocks indicate extension, open blocks flexion. The vertical bars show the standard deviation.

Above about 1 m/sec the flexion and extension movements of the wrist and shoulder are closely related to those of the elbow. The values illustrated for the cat in Fig. 3.4 did not differ significantly from the elbow ($P > 0.05$; *t*-test), and similar observations were made in the other two cats. Below 1 m/sec the stepping of all cats is more variable. At 0.6 m/sec (Fig. 3.4A) the onsets of flexion and extension at the shoulder and wrist differed significantly from the elbow (all cases, $P < 0.01$; *t*-test). Emphasis should not be given to these differences since they were not repeated in the other two cats. In fact, it is clear that the onsets of flexion and extension in the joints of the forelimb form a pattern which is consistent at all velocities of stepping.

Comparison of flexion and extension periods at different joints

Mean flexion and extension periods have been calculated for the scapula, shoulder, elbow and wrist to test if there were differences (Fig. 3.5). At the wrist flexion implies the rapid palmar flexion during the flexion phase (Fig. 3.2); extension implies the remainder of the step cycle including the dorsiflexion and yield movements (Fig. 3.2).

Once again the scapula behaves differently to the distal joints. At all velocities the extension period of the scapula is shorter than that at the more distal joints, since the onset is delayed (Fig. 3.3); the flexion period is consequently longer. At velocities above 1 m/sec this tends to make the flexion and extension periods roughly equal. For the shoulder, elbow and wrist the periods of flexion and extension are similar, emphasizing further the unitary pattern of movement at the joints. Finally, the asymmetry of action of the

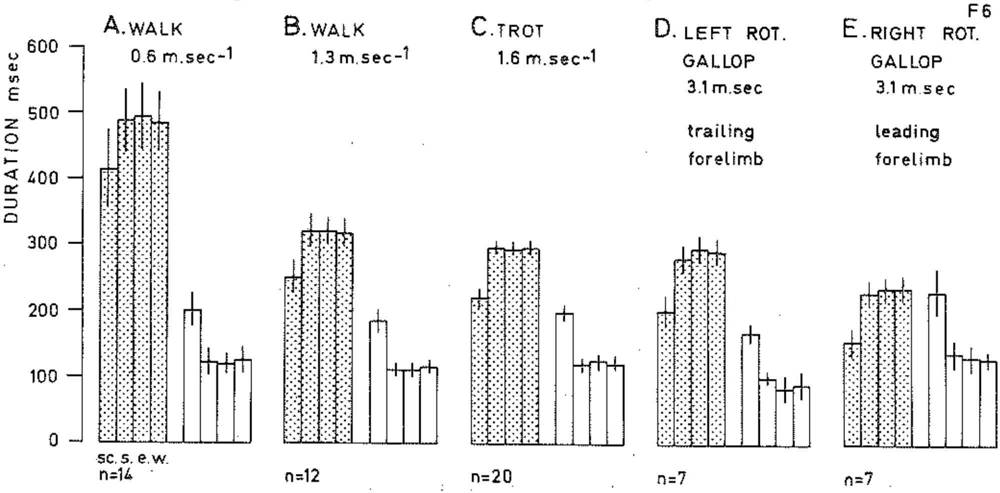

Fig. 3.5. Durations of the phases of flexion (open blocks) and extension (stippled blocks) at the scapula (sc), shoulder (s), elbow (e) and wrist (w) at different velocities. Same cat as in Fig. 5.4. Each block is the average of n successive steps. The vertical bars indicate standard deviation.

leading and trailing forelimb in the two types of gallop (Figs. 3.2 and 3.4) is observed, as might be expected, in the durations of flexion and extension. In the trailing forelimb the extension is longer and the flexion shorter. The reverse occurs for the leading forelimb, where the flexion period of the scapula is actually longer than that of extension (see also chapter 4).

DISCUSSION

In normal cats stepping on a treadmill an analysis has been made of movements of the scapula and of the shoulder, elbow and wrist joints and digits.

Movements of the scapula

The scapula is capable of large and complicated movements (36,73, 85). In locomotion they resolve into a cyclical, semilunar movement of the glenoid cavity (Fig. 3.1B), which remains remarkably constant over the velocities and types of gait adopted. A somewhat similar movement of the scapula occurs in the cheetah (73), but the absolute angle of rotation described by the spine is smaller, 26°, in comparison with the cat, approximately 60° (Fig. 3.2). The constant angular excursion of the scapula may be compared with that of the hip (39,49,61,117) (also Miller and Van der Meché, unpublished observations). It is important to specify that the movements of the scapula and hip joint were investigated in all these studies on a level treadmill. If the belt of the treadmill, for example, is tilted in the longitudinal direction the absolute value of the excursions is changed (Graham Brown film (96); Miller and Wetzel, unpublished observations).

The movements of flexion and extension as applied to the scapula can be referred primarily to the direction of rotation of the spine; rostral direction of the glenoid cavity is equivalent to flexion, and caudal direction to extension. As Hildebrand (73) has commented for the cheetah, the range of these movements and therefore the step length of the forelimbs is further increased by the rostrocaudal shifts of the scapula. The above designation of flexion and extension movements of the scapula is contrary to that suggested by Phillippson (117). The association of extension and caudal direction of the glenoid cavity is, however, logical, since it corresponds with the same movements at the shoulder and elbow joint. It is also in agreement with the Sherringtonian concept that antigravity muscles are functional extensors (129), and therefore that movements counteracting gravity fall within the meaning of extension.

The extension period of the scapula, like the hip (39,49,117) does not show the yield phase, which is a prominent feature of the shoulder, elbow and wrist joints. Gurfinkel and Shik (66) and Arshavsky et al. (9) state that there is no yield at the shoulder joint, and compare the shoulder joint with the hip. From the present material it is, however, clear that a yield does occur at the shoulder. It would also seem more meaningful instead to compare the movements of the hip with the scapula. The extension of both joints is delayed in comparison with the more distal joints; the form and range of the movements during stepping on the level treadmill remain rather constant; the extension movement is continuous and is not interrupted by a yield phase. It remains to be shown if the afferents excited by movements of the scapula have a similar effect on the initiation of locomotion as those activated by movement of the hip (60,129).

Phillippson's classical description of the stepcycle (117) provides a general definition of the flexion and extension movements of a limb and their relation to the periods of foot contact and lift-off. However, it suffers from the limitation that it does not take account of the delayed extension of the scapula and hip joint with respect to that of the more distal joints. This delay is essential to confer upon the vertical spring-like movement of the limb a forward, thrusting component. Normal swimming cats and decerebrate cats immersed in water showed that this is not merely a passive feature, since it still occurs in these situations where gravity is negligible. It is elaborated in the spinal cord, since low spinal cats show the same phenomenon (60). It is also independent of local afferent input, since it still occurs in the hindlimbs of decerebrate cats deafferented bilaterally from L_2 to S_2 (107).

From observations of the sequence of activation of forelimb muscles during locomotion (unpublished observations) latissumus dorsi, pectoralis major and pectoralis minor would appear to be amongst those muscles exerting a prime mover action on the scapula. It is probably no coincidence that ascending long propriospinal pathways exert preferential mono- and polysynaptic effects on the motoneurones of these same muscles (13,48,103). These observations would further point to movements of the scapula as having an important role in the generation of locomotion in the forelimbs.

Elbow as an index of forelimb movement

Above 1 m/sec flexion occurs virtually simultaneously at the scapula and shoulder and elbow joints. This is also the moment at which the wrist performs its rapid palmar flexion (Figs. 3.2 and 3.3). Above 1 m/sec the elbow also gives an indication within about 12 msec of the onset of extension at the shoulder joint. The relationship of dorsiflexion of the wrist to the onset of elbow extension is even closer (within 5 msec). Extension of the scapula is delayed, as discussed above. Below 1 m/sec the relationships of flexion and extension are more variable. The discrepancies do not exceed 20 msec, with the exception once more of the scapula. As an estimate of the general distribution of flexion and extension periods of the forelimb, the elbow provides an index for flexion at the scapula and shoulder and palmar flexion at the wrist with an error of less than ± 3% of a step cycle; and for extension at the shoulder and dorsiflexion at the wrist with an error of less than ± 4%.

Movements of the wrist and digits

In the different forms of locomotion the dorsiflexion and palmar flexion movements at the joints of the wrist and digits do not bear a constant relationship with the periods of flexion and extension at the more proximal joints. In swimming, and during stepping in the air of the decerebrate cat, a basic pattern of movements of the wrist and digits can be observed. There are two phases of movement, palmar flexion, associated with the flexion phases of the limb, and dorsiflexion, associated with the first extension phase (Fig. 3.3). This sequence is terminated by a variable period during which the wrist and digits remain approximately straight (Fig. 3.3). Contact of the foot with the ground modifies this basic pattern and releases a powerful 'extensor' (palmar flexion) thrust during the second and third extension phases of the limb. The toes of the hindlimb show a similar phenomenon (40). Anaesthetization of the skin of the footpad did not alter the electromyogram pattern of the muscles acting on the toes, obtained during locomotion. Engberg (40) concluded that "the toe extensor reflex is not necessary for the activation of the muscles in stepping". In decerebrate cats stepping in the air there is no plantar flexion movement during the extension phase of the hindlimb, and on deafferentation of the hindlimbs the movements of the toes are abolished. These observations suggest that afferent input is in some way required for the elaboration of movements of the toes, and that the afferents responsible do not arise exclusively in the region of the footpad (40). Further experiments are required to investigate this problem at the wrist and digits.

From the division of the step cycle at the wrist into different phases of flexion and extension the muscles producing palmar flexion of the wrist are designated physiological extensors and are innervated by median and ulnar nerves (146). Those producing dorsiflexion at the wrist are designated physiological flexors and are innervated by branches of the radial nerve. However, the pattern of the flexor reflex of the distal part of the forelimb would suggest the opposite functional designation of these muscles (101, 105,137). This discrepancy may be resolved in part by the observation that the rapid phase of palmar flexion (i.e. extension of the wrist, as defined in locomotion and by resistance to gravity) occurs at the time of flexion of all the more proximal joints. It is precisely this paradigm of movement which results from noxious stimulation of the distal part of the limb. In other words, the same paradigm of movement is used in both the flexion reflex and the flexion phase of locomotion.

This association of movements is also reflected in the longitudinal columnar association of the motoneuronal cell groups of the intrinsic muscles of the limb, described by Sterling and Kuypers (137). In the flexor phase of locomotion and the flexor reflex, flexion is produced by activity in the muscles innervated by ulnar, median and musculocutaneous nerves. The respective motoneuronal cell bodies lie in a column dorsolaterally in the motoneurone plexus. The first extension in the locomotor cycle involves activity in muscles innervated by proximal and distal branches of the radial nerve. The cell bodies for these muscles lie in a column more ventrally in the motoneuronal plexus. Further association of activity within these columns would presumably be expected on the basis of the longitudinal orientation of the motoneurone dendrites (137). Reflexes and movements involving the toes display a comparable association of plantar flexion with flexion at the knee joint and ankle (40). It is not clear from the studies on motoneuronal cell columns in lumbosacral segments (121,122) whether the motoneurones of the respective intrinsic muscles of the limb are grouped together. All that can be said at present is that the respective motoneurones are contained in the dorsolateral part of the motoneurone plexus of L_6 and L_7 (121), which receives a strong propriospinal projection from fibres in the dorsolateral funiculus (125).

Considerable difficulties exist in the classification of forelimb muscles, but the present observations suggest that it is more meaningful, as others have also suggested (28,66,137) to consider the action of groups of muscles in different types of movements rather than observing their possible reactions in isolation. Willis et al. (146) point out that the muscles acting at the wrist and digits are capable of being employed in a wide variety of functional combinations, which exceed their stereotyped use in locomotion or the flexion reflex. They suggested that this was reflected in the fact that the distribution of Ia afferent convergence extended beyond the designation of motoneurones as physiological or anatomical flexors or extensors.

SUMMARY

In normal cats stepping on a treadmill an analysis has been made of movements of the scapula, shoulder, elbow, wrist and digits. The scapula is capable of making large and complicated movements over the rib cage. In locomotion they may be resolved into a cyclical, semilunar movement of the glenoid cavity in the parasagittal plane of the cat's body. The movements of the scapula are rather constant over a wide range of velocities. They most resemble those of the hip which also shows a delay in the onset of extension and no yield phase. It is suggested that movements of the scapula have an important role in the generation of locomotion in the forelimbs.

The movements at the shoulder tend to parallel those of the elbow. The terms of palmar flexion and dorsiflexion are retained for the movements at the wrist and digits. The rapid phase of palmar flexion corresponds with the flexion phase at the elbow, and the phase of dorsiflexion with the first extension phase at the elbow. Palmar

flexion during the second and third extension phase of the more proximal joints would appear to be initiated by contact of the foot with the ground. The sequences of movement at the wrist and digits allow a comparison of the roles of flexor and extensor muscles of the forearm during locomotion and the flexion reflex, which is compatible with the functional and anatomical organization of cervicothoracic segments. With exception of extension at the scapula the movements of the elbow provide an index of the onsets of flexion and extension at the other joints of the forelimb.

CHAPTER 4.

COORDINATION OF THE FORELIMBS DURING STEPPING UNDER DIFFERENT BEHAVIOURAL SITUATIONS.

INTRODUCTION

Since Muybridge's pioneering cinematographic studies at the end of the last century of locomotion of various species including man (111) much attention has been directed to analyses of the patterns of locomotion. Two main approaches can be recognised:
1) analysis of patterns of gait by reference to sequences of foot contact with the ground (35,50,74,77,111,120); 2) analysis of the movements about the different joints in the limbs (9,105,140,145). Until recently the conclusions of foot contact patterns have dominated the study of locomotion of quadruped mammals.

Muybridge (111) and later Howell (12), Gray (50) and Roberts (120) divided the stepping sequence into eight discrete periods defined by the contact and lift-off of each foot. By numbering the feet they devised numerical footfall formulae to describe the many types of gait observed. By this method Howell (12) distinguished 12 different gaits in mammals. Although these formulae give information about the general locomotor pattern, they contain two severe limitations. As Stuart et al. have commented (140) the division of the step cycle into eight periods obscures the durations and time relations of the different phases and the movements at different joints were ignored.

The footfall formulae were developed by a number of workers into gait diagrams, where the footfall patterns are expressed on a time base (35,74,140). The gait diagrams, however, still give no information of the flexion and extension movements of the limbs.

In the present study attention has been focussed on the flexion and extension phases of the locomotor cycle as these are the basic elements of movement which the nervous system generates. The main questions asked, were:
1) Do the many different types of gait as revealed in studies of foot contact patterns referred to above share simple combinations of the basic elements of flexion and extension movements in each limb?
2) How far can the patterns of interlimb coordination be generated by neural mechanisms within the spinal cord?

The material and methods are described in chapter 2.

RESULTS

Interlimb coordination in alternate gaits

The alternate gaits are defined by strict alternation of movements between the homologous pairs of limbs and is seen in all forms of walking and trotting, and during swimming (107,108). The particular type of alternate gait adopted depends on the coupling of the homolateral limbs and may take the in-phase form, in which the extension movements of the homolateral limbs are in-phase as in pacing, or the out-of-phase form, in which these movements are out-of-phase as in trotting (Fig. 4.1). Further examples of these types of homolateral limb coupling are illustrated in the computed displays of Figures 4.2, 4.3 and 4.4. These were obtained in a decerebrate cat stepping at various constant velocities on a treadmill. In part A of each figure is a display of the successive steps analysed. In part B the movements have been superimposed by reference to the onset in each step cycle of the extension phase of the hip. Below the superimposed movement traces, the durations of the EMG activity from the different muscles are given as solid lines. In Figure 4.2 the cat is stepping at 0.6 m/sec in a pacing gait. Both the flexion and extension phases of the movements at the hip and scapula occur in phase and this is reflected in the EMGs. In Figures 4.3 and 4.4 the cat is stepping at 0.75 and 1.5 m/sec, respectively. The scapula and the timing of the respective EMGs are out-of-phase; extension of the hip is correlated with flexion of the scapula.

Two intervals characterize the two types of homolateral limb coupling described above:

1) The interval between the onsets of extension at the hip and scapula designated by EE. This interval is short in the in-phase type of homolateral coupling, for example the pace (Fig. 4.5A).

2) The interval between the onsets of extension at the hip and of flexion of the scapula, designated by EF. This interval is short in

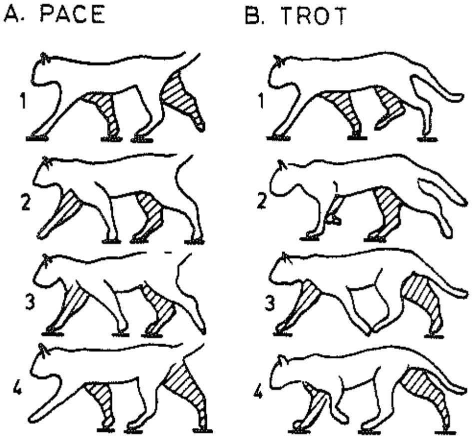

Fig. 4.1. Figurines demonstrating the homolateral forms of coupling in the alternate gaits. The in-phase form of homolateral coupling in the pace (A) and the out-of-phase form in the trot (B). Figurines are traced from 16 mm film of the same cat stepping on a treadmill, in A and B at respectively 1,2 and 1,7 m/sec. The horizontal bar indicates that a foot is in contact with the ground.

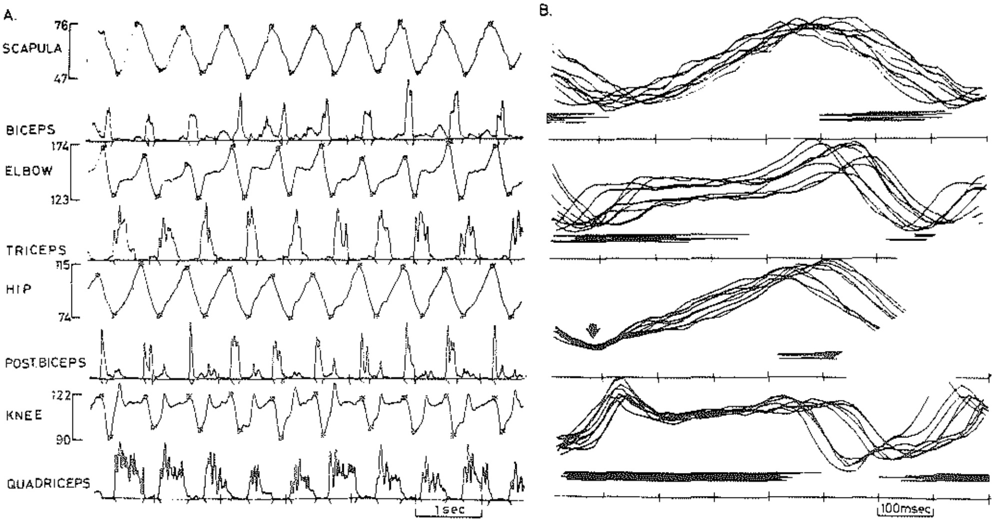

Fig. 4.2. Changes of joint angle and EMGs in homolateral hindlimb and forelimb of decerebrate cat stepping on treadmill at 0.6 m/sec. In the movement traces upward deflection indicates extension, downward flexion. A. Successive steps. B. Superimposition of steps using onset of hip extension as trigger point. The duration of the EMGs is given in the bars under the movement traces. Movements at the knee joint may be slightly distorted in the extension phase by the action of a spring system, partly suspending the hindquarters of the cat.

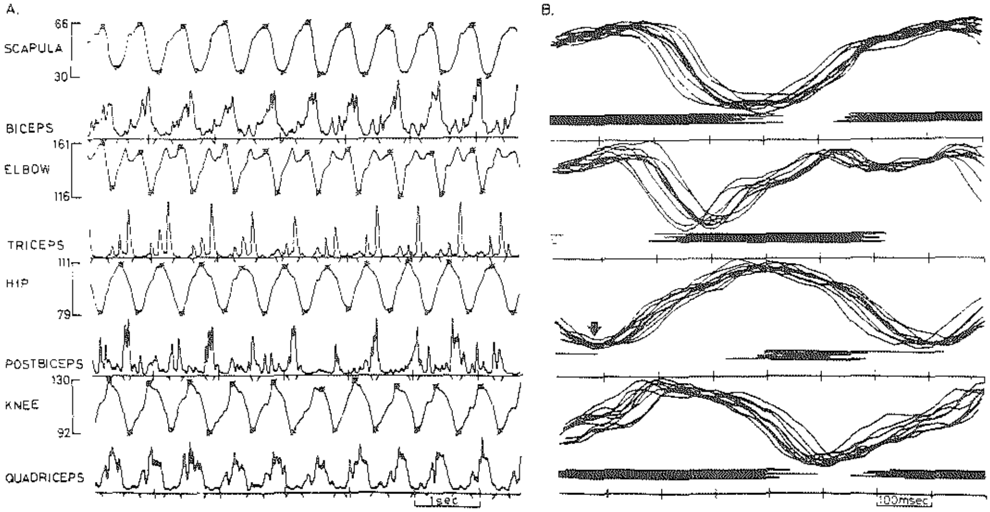

Fig. 4.3. Changes of joint angle and EMGs in homolateral hindlimb and forelimb in decerebrate cat stepping on treadmill at 0.75 m/sec. Other details as in Fig. 4.2.

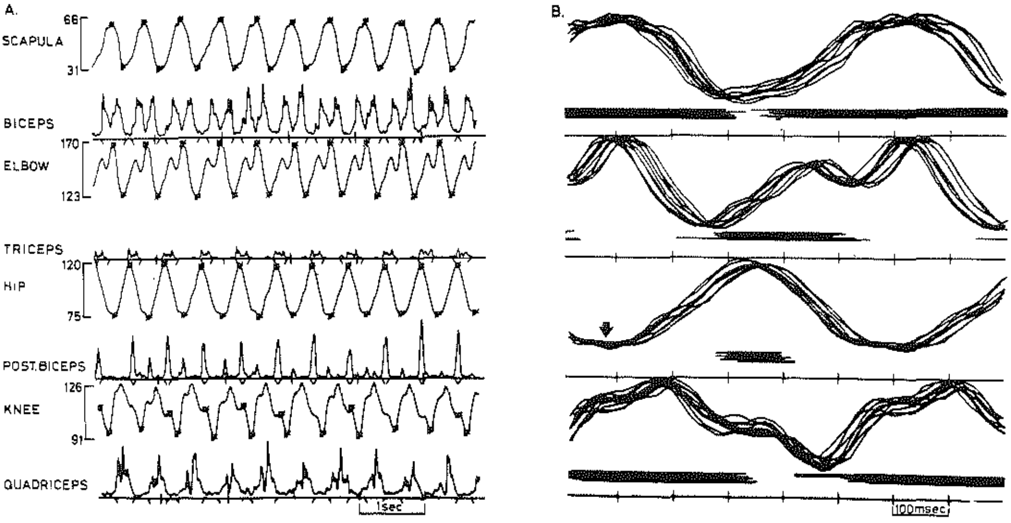

Fig. 4.4. Changes of joint angle and EMGs in homolateral hindlimb and forelimb in decerebrate cat stepping on treadmill at 1.5 m/sec. Other details as in Fig. 4.2.

the out-of-phase type of homolateral limb coupling, for example the trot (Fig. 4.5B). It should be noted that these intervals are always short (< 13% of a step cycle) and rather constant (see below) in relation to the step cycle. The interval can be positive or negative indicating that the hindlimb or the forelimb movement, respectively, begins the first.

In contrast the corresponding intervals, EF in the in-phase homolateral limb coupling and EE in the out-of-phase coupling are considerably longer (Fig. 4.5) and more variable (see below). These intervals are dependent not only on the type of homolateral limb

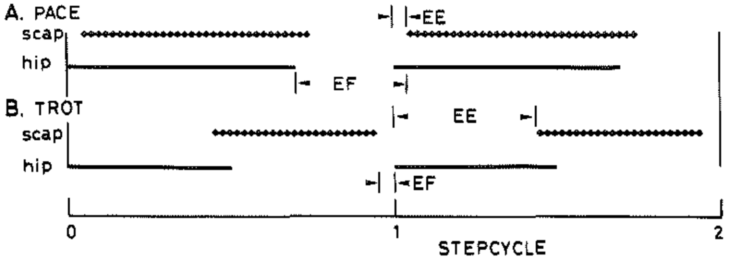

Fig. 4.5. Schematic diagram of the homolateral forms of coupling in alternate gaits. A: the in-phase form of homolateral coupling in the pace and B: the out-of-phase form in the trot. Solid and broken lines indicate periods of extension at hip and scapula, gaps periods of flexion. Two steps are represented. See text for further details.

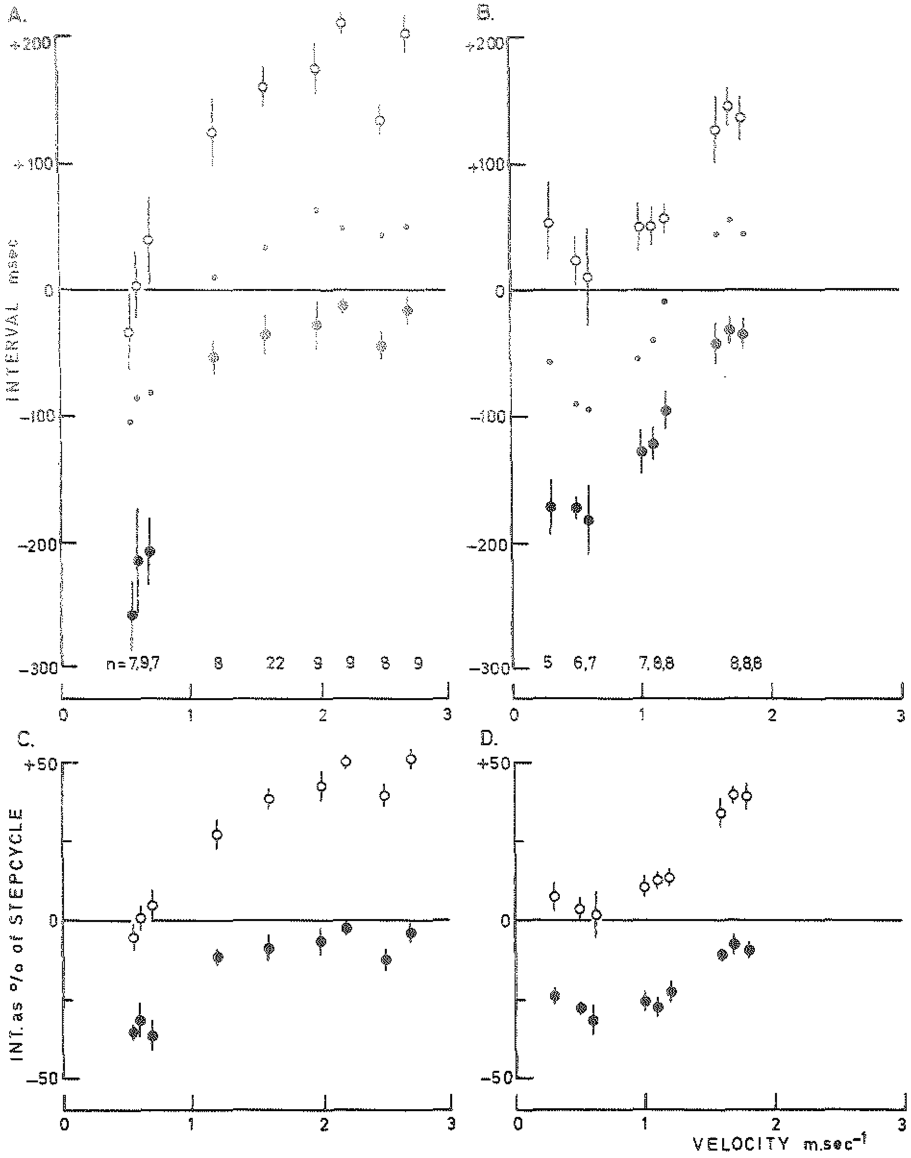

Fig. 4.6. Coupling of movements of homolateral hindlimb and forelimb in normal cats. Open circles: intervals between onsets of hip extension and scapula extension. Large filled circles: intervals between onsets of hip extension and scapula flexion. Small filled circles: intervals between onsets of knee extension and elbow flexion. A and C are from cat F6, and B and D from cat F13. The intervals are in real time in A and B, and expressed as a percentage of the step cycle in C and D. N gives the number of successive steps in each trial.

coupling (in-phase or out-of-phase) but also on the relative duration of the flexion period of the scapula, which tends to vary inversely with the velocity of stepping.

The graphs in Figures 4.6 and 4.8 then show the intervals between the onsets of extension of the hip and extension of the scapula (open circles) and extension of the hip and flexion of the scapula (large filled circles). The coupling intervals during stepping

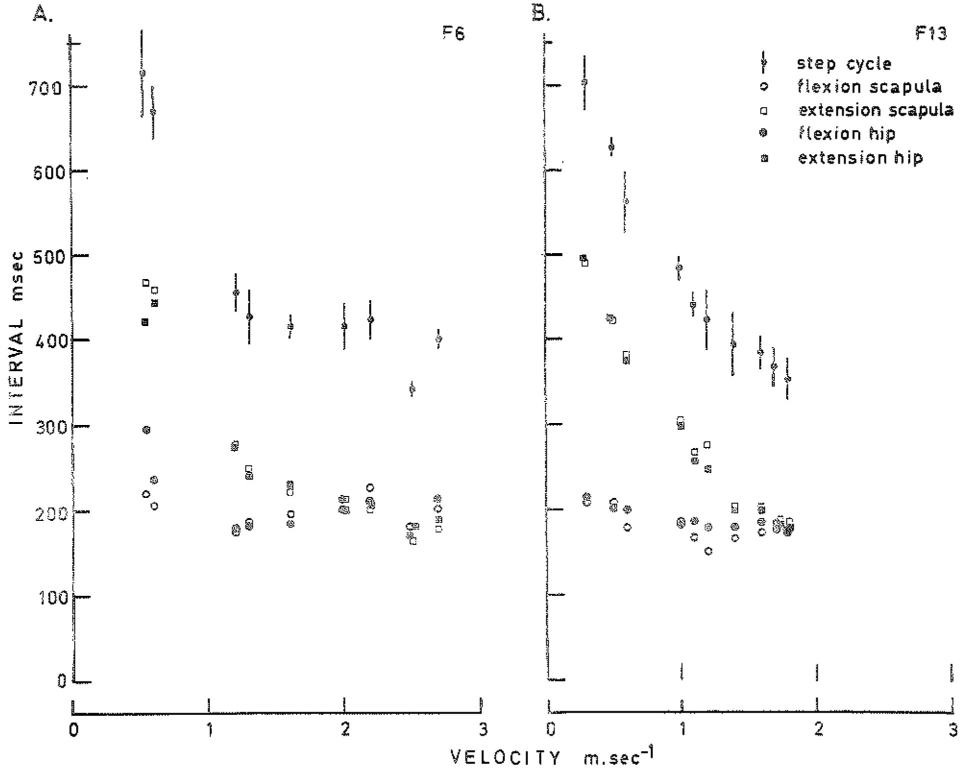

Fig. 4.7. Durations of step cycle and periods of flexion and extension at homolateral hip and scapula in cats F6 (A) and F13 (B) during alternate gaits on the treadmill at various constant velocities. Number of steps as in Fig. 4.6

at different constant velocities on the treadmill are plotted in real time in Figures 4.6A and B and scaled as a percentage of the step cycle in Figures 4.6C and D. Distribution of the intervals as a function of the step cycle is tested in Figure 4.8. The step cycle is measured between the onsets of extension at the hip joint; no significant difference in variance (Fisher test) was obtained by taking other joints or other events in the step cycle. Part of the data of knee-elbow couplings (see below) relating to the same steps in the same cats is plotted as small filled circles in Figures 4.6A and C.

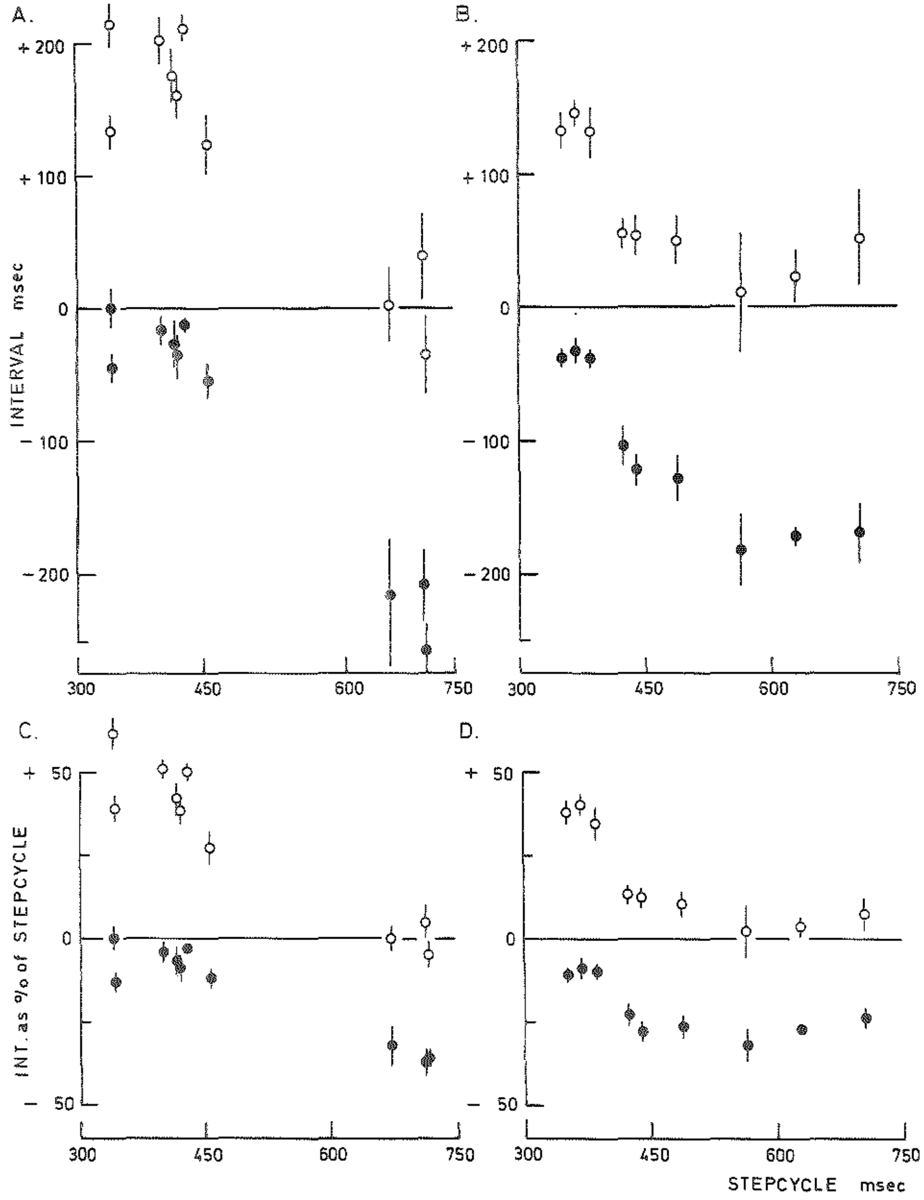

Fig. 4.8. Coupling intervals of homolateral hindlimb and forelimb in real time (A and B) and as percentage of step cycle (C and D) in plots against the step cycle duration. Open circles: intervals between onsets of hip extension and scapula extension. Filled circles: intervals between hip extension and scapula flexion.

As before there are two distinct forms of hindlimb-forelimb coupling below and above a dividing velocity of about 1 m/sec. Note that the dividing velocity refers here to the separation of the in-phase and out-of-phase forms of homolateral limb coupling during alternate gaits, and not to the separation of alternate and in-phase gaits. In one cat (Figures 4.6A and C) the dividing velocity is 1 m/sec, in the other (Figures 4.6B and D) it is 1.4 m/sec. The important features are the following:

1) *Below the dividing velocity* the onsets of hip extension and scapula extension (open circles) are approximately in-phase (Figure 4.6: averaged values, range -6 to 13%). This can also be visualized in the graphs of movement in Figure 4.2. Slight deviations to positive or negative values indicate that either the hindlimbs or the forelimbs, respectively, are leading in the movements.

2) *Above the dividing velocity* it is the onsets of hip extension and scapula flexion (filled circles) which are approximately in-phase (Figure 4.6: averaged values, range -2 to -10%). This can also be visualized in the graphs of movement of Figures 4.3 and 4.4. Note that here all the values tend to be negative indicating that the forelimb flexion leads the hindlimb extension.

3) When the coupling intervals in real time and as a percentage of the step cycle are plotted as a function of the step cycle period (Figure 4.8) the distribution of the two types of coupling of hindlimb and forelimb become even clearer. The long step cycle periods are associated with in-phase coupling of hip and scapula and the shorter (below 450 m/sec) are associated with out-of-phase coupling.

4) The step cycle period decreases with an increase of velocity (Fig. 4.7). For one cat the changes are rather gradual (Fig. 4.7B) for the other the transition is abrupt (Fig. 4.7A). Note, however, by reference to Figs. 6 and 7, that where the homolateral coupling is out-of-phase the periods of extension and flexion tend to be equal.

In conclusion, evidence is presented above which shows that in alternate gaits there are predominantly two types of coupling of the homolateral hindlimb and forelimb 1), in which movements of the hip and scapula are in-phase, with a short EE interval, and 2) in which the movements of the hip and scapula are out-of-phase, with a short EF interval.

Interlimb coordination in different preparations and in different behavioural situations.

Stepping on the treadmill, analyzed in the previous section represents only one type of behavioural situation for locomotion. The conclusions put forward had to be examined in greater detail and tested for their generality in different preparations and situations. The analysis was developed to include normal cats moving freely overground, jumping and swimming, decerebrate cats stepping on the treadmill, in the air and stepping immersed in water. and in high spinal cats stepping on the treadmill and in the air.

For this part of the investigation measurements were made of movements at the knee and elbow rather than at the girdle joints, since with the techniques readily available, observations could be made simultaneously of all four limbs. Because the structure of the stepping movements within a limb remain consistent (9,41,109,117) any observation made of the knee and elbow could be related to movements at the other joints, in particular the hip and scapula. Extensive measurements were made initially in this study of the intervals between the onsets of knee extension and elbow flexion. Wherever these intervals are presented in the following section they are related to the characteristic EE and EF interlimb couplings described above.

Comparison of patterns of interlimb coordination in normal, decerebrate and spinal cats seemed permissible for the following reasons:

1) The structure of the stepping movements within a single limb is consistent for the different preparations (9,60-62,68). For treadmill stepping the step cycle duration varies inversely as the velocity of the belt is changed in the decerebrate (9,68) and spinal cat (60,61) as in the normal cat (Fig. 4.7). The periods of flexion and extension show a similar distribution with velocity in all three cases.

2) The coordination of the homologous limb in normal, decerebrate and spinal cats follows either the alternate or the in-phase pattern of stepping.

3) The patterns of coordination between the homolateral limbs are comparable in the different preparations (see below).

In the in-phase form of homolateral limb coupling there is close association of the onsets of extension at the hip and scapula and the EE interval is short. The interval between knee extension and elbow flexion is negative (Fig. 4.6A and B, small filled circles), implying that the elbow flexes before the knee begins its extension. The out of phase form of homolateral limb coupling is characterized by the association of hip extension and scapula flexion and the EF interval is short. Here the knee extension to elbow flexion interval is positive (Fig. 4.6A and B, small filled circles) indicating that the elbow flexes after the onset of knee extension. In alternate gaits of freely moving cats the homolateral limb coupling was nearly always out-of-phase and therefore the interval between knee extension and elbow flexion was positive (Fig. 4.9A). The in-phase form of homolateral limb coupling (e.g. pacing) was rarely observed in this situation, although two of the three cats sometimes performed this gait (Fig. 4.9A, filled circles, negative value).

In the normal cats stepping on the treadmill the homolateral coupling was in-phase, as seen above, at velocities below, and out-of-phase above, 1.0 to 1.4 m/sec. The knee extension to elbow flexion interval is negative and positive, respectively. The value of the positive plateau was different but consistent for the

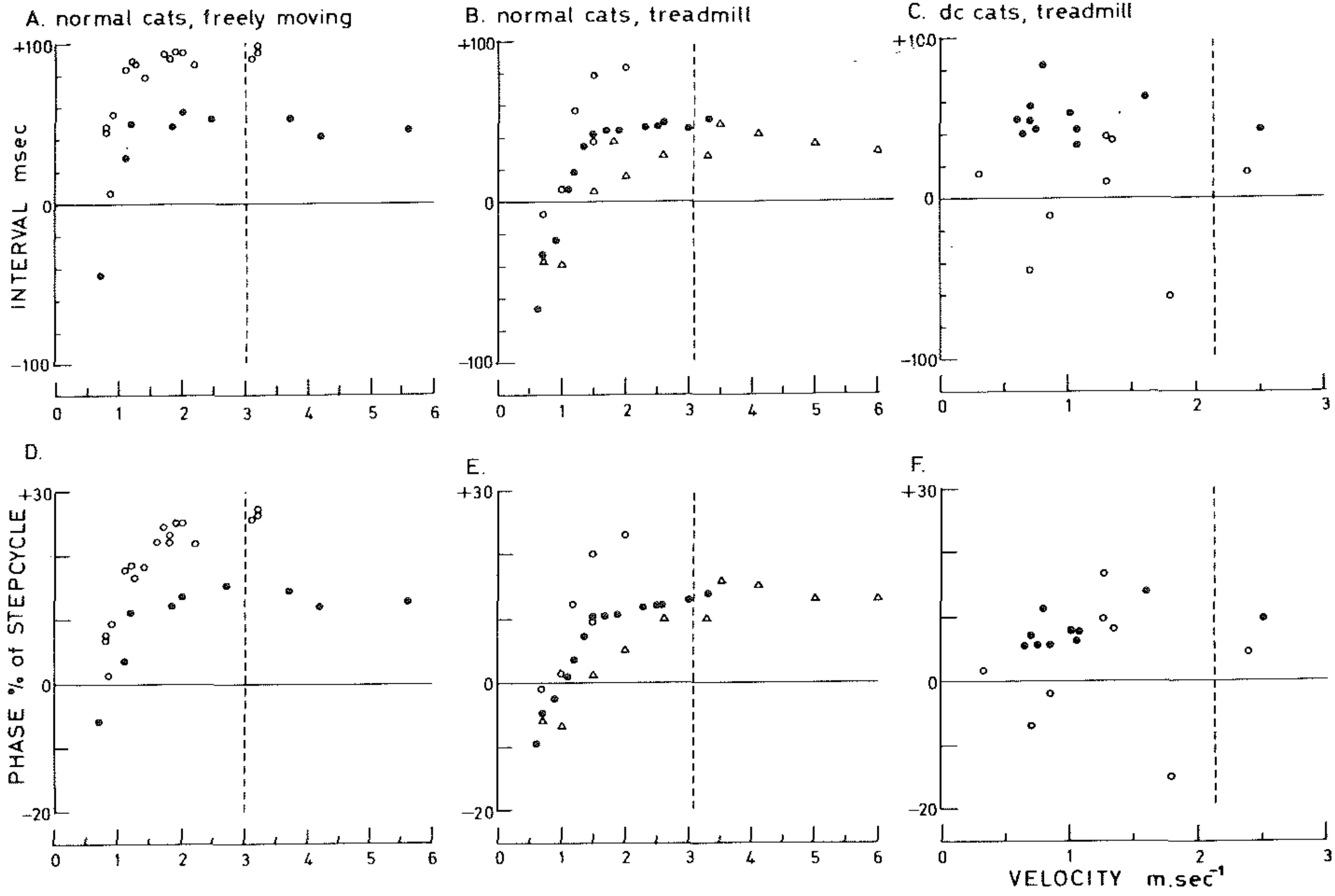

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Fig. 4.9. Variation of the intervals between the onsets of knee extension and homolateral elbow flexion with velocity of locomotion. In A-C the intervals are in real time (msec); in D-F the intervals have been normalised as a percentage of the step cycle. A,B,D and E: filled circles, F6; open circles, F8; triangles, F13. C and F: open circles, DC5; filled circles, DC1. The dotted vertical line represents the separation of alternate (to the left) and in-phase (to the right) gaits. (The dotted line is not related to that of Fig. 4.10). The values obtained from in-phase gaits are discussed below.

individual cats and did not appear to be influenced by training on the treadmill (107).

The decerebrate cats either followed the velocity of the treadmill (cf. 96) or could be induced to walk by stimulation of the mesencephalon (132). The gaits were similar to normal cats but the most common disturbance was an incomplete retraction of the limb during the swing phase so that the dorsum of the foot grazed along the surface of the treadmill. The interval between hindlimb extension and ipsilateral forelimb flexion was in most cases positive and corresponded closely to the coupling of movements in normal cats (68). In 3 of the cats (e.g. Fig. 4.9C, open circles) negative values were obtained in some sequences of stepping.

Coupling intervals as a function of step cycle duration.

The coupling intervals obtained during stepping overground and on the treadmill were normalised by dividing the averaged interval by the averaged step cycle duration for each velocity (phase % step cycle. Fig. 4.9D and F). The step cycle duration was measured between the onsets of extension at one knee joint. The step cycle period shortens with increasing velocity of locomotion (Fig. 4.7), particularly at velocities below 1 m/sec and this tends to compress the phase values in the left hand part of the graphs in Fig. 4.9D and E. In the normal cats freely moving and on the treadmill, normalisation of the coupling intervals appears to have little effect above about 1.5 m/sec (Fig. 4.9D and E). In some cats (filled circles) there is no clear phase shift with velocity, whereas in others (open circles) there is a slight progressive increase. In the decerebrate cats (Fig. 4.9F) normalisation tends to reduce the scatter of the data.

The coupling intervals in the different preparations and under different situations were then compared with the durations of the step cycle (Fig. 4.10). This had the advantage that the observations of the cats swimming and stepping in the air could be included for comparison. At velocities below about 1.4 m/sec the step cycle of normal cats stepping overground and on the treadmill fell in a range of about 800 to 450 msec (Miller and Van der Burg (105), Fig. 6). From 1.4 to 6.0 m/sec there is a smaller absolute decrease from about 450 to 250 msec. The vertical broken lines in Fig. 4.10A and B correspond to the value of the step cycle at a velocity of 1.4 m/sec. (They should not be confused with the vertical broken lines in Fig. 4.9).

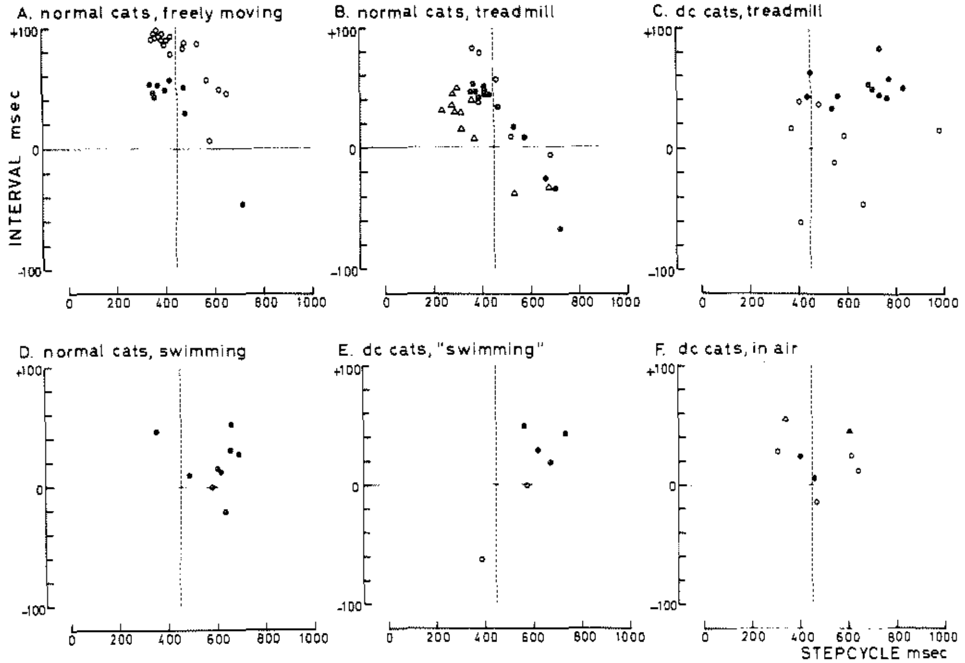

Fig. 4.10. Intervals between onsets of hindlimb extension and homolateral forelimb flexion as a function of the duration of the step cycle. All measurements are in real time (msec). The dotted vertical lines are drawn at a step cycle of 450 msec, see text. (They are not related to those of Fig. 4.9) A-C: the symbols designate the same cats as in Fig. 4.9A-C, respectively. D: each symbol represents the average of 4-20 strokes taken from the different cats indicated in Methods. E: filled circles, HJ1; open circles, HJ2. F: filled circles, HJ1; open circles, HJ2; open triangle, DC2; filled triangle, DC3. Data were obtained from knee and elbow.

The grouping of the points below 450 msec cycle duration in Figs. 4.10A and B corresponds to the plateau seen in Figs. 4.9A and B and represents the out-of-phase type of homolateral coupling. The negative values on the right side of the graphs of Fig. 4.10A and B correspond to the negative values in Figs. 4.9A and B, representing the in-phase type of coupling (see below for transitional values).

The decerebrate cats stepping on the treadmill (Fig. 4.10C) show a much wider scatter, though the values for one cat (filled circles) are clearly distributed about a plateau. The negative values (open circles) correspond to the in-phase form of homolateral coupling. Suspended in the air (Fig. 4.10F) most of the decerebrate cats show the out-of-phase form of homolateral coupling and the coupling intervals are positive, though somewhat less so than in the cats stepping on the ground or on the treadmill. One cat showed the in-phase form in the air and a negative coupling interval. In the group of normal swimming cats the coupling intervals are positive and also generally lower than on the ground (Fig. 4.10D). The one negative point is the average of four strokes where the cat was turning to get out of the bath. The 'swimming' decerebrate cats (Fig. 4.10E) showed a similar picture: all the coupling intervals were positive, except in one case, where an in-phase type of homolateral coupling was adopted.

These results show that it is only in the normal cats stepping on the treadmill or overground that there is a predictable distribution of the coupling intervals in relation to the duration of the step cycle period.

Further support for the correlation of flexion and extension movements as the basis for interlimb coordination

Further confirmation of the coordination of flexion and extension movements in discrete centrally controlled patterns was obtained in normal and decerebrate cats swimming and in decerebrate cats stepping on the treadmill or suspended in the air. Occasionally in these

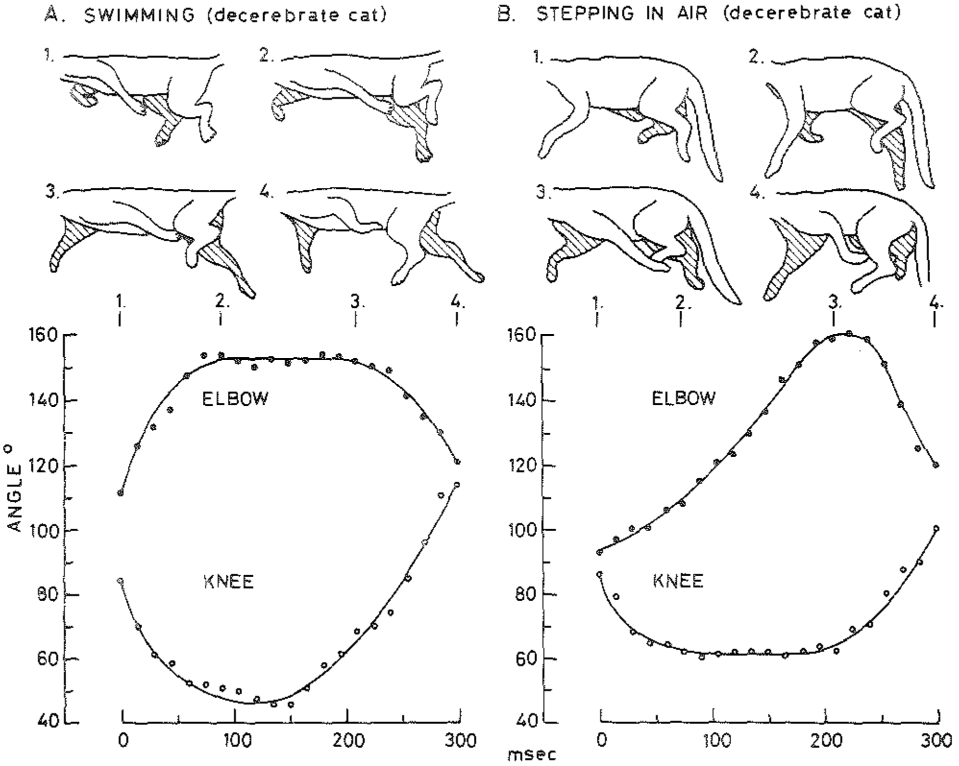

Fig. 4.11. Examples of delayed coupling of movements between hindlimb and homolateral forelimb. A: decerebrate cat HJ2 'swimming'. B: decerebrate cat HJ1 suspended in the air. Data were measured at knee and elbow joints.

preparations one limb could be observed to pause, before beginning its flexion or extension phase, for the other limb of the same side to complete its particular phase of movement. In Fig. 4.11A, for example, the forelimb pauses briefly at the end of its extension phase and continues in flexion as the hindlimb enters extension. Occasionally the reverse was seen: the hindlimb pausing at the end of its flexion and continuing in extension as the ipsilateral forelimb begins to flex (Fig. 4.11B). This does not necessarily imply a trigger function between hindlimb and forelimb movements, but it does underline the tendency for the movements of the homolateral limbs to be correlated in one or other discrete pattern of coupling.

Under natural conditions cats do not step at constant velocity and frequency for more than a few steps. Normal cats and also decerebrate cats may deviate from a regular stepping pattern even while stepping on the treadmill. This occurs particularly at low velocities, below 1 m/sec. Sometimes the forelimbs take one step more than the hindlimbs. This is illustrated in Fig. 4.12A for the homolateral limbs in a decerebrate cat. In the first few steps the cat showed an in-phase coupling of hip and scapula, typical of the pace. Suddenly the forelimb step cycle is shortened and that of the hindlimb lengthened (first arrow). This brings the hip and scapula movement out of phase. The shift is temporary and by the next step of the hindlimbs the same process has repeated bringing the hip and

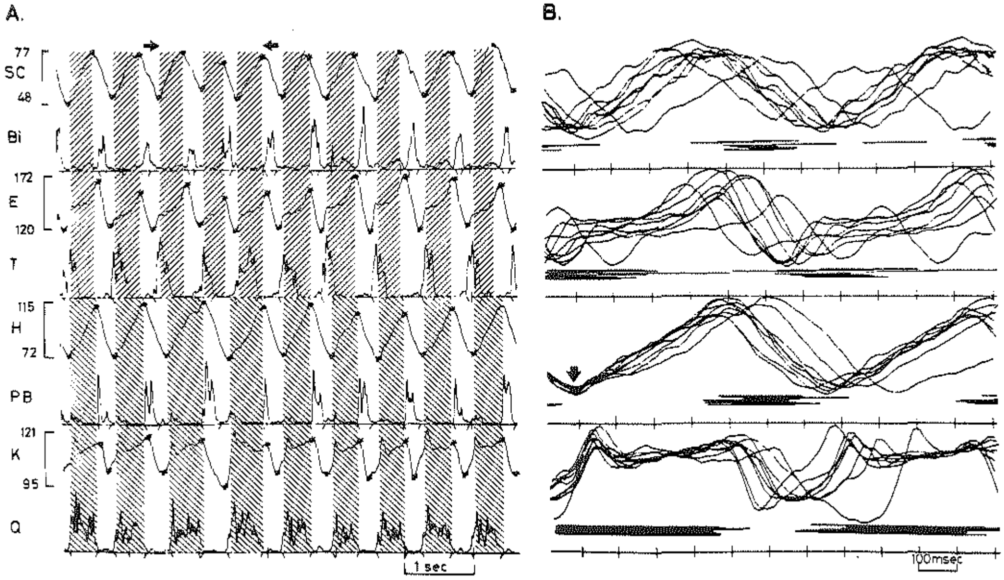

Fig. 4.12. Pacing gait with extra step of forelimbs in decerebrate cat stepping at 0.6 m/sec on treadmill. Arrows indicate occurrence of extra step. SC scapula E elbow, H hip, K knee, Bi biceps brachii, T triceps brachii, PB biceps femoris posterior, Q quadriceps femoris. For other details see Fig. 4.2.

scapula back into phase (second arrow). There are two striking features of this whole process: 1) the homolateral coupling springs abruptly between the coincidence of onsets of extension in hip and scapula to those of hip extension and scapula flexion, and then back again; 2) the flexor and extensor EMGs also show the same type of in-phase to out-of-phase shift. It would appear, therefore, that this is a situation where the frequency of stepping of the forelimbs temporarily exceeds that of the hindlimbs. There is coincidence of the changeover points of flexion and extension in the homolateral limbs in one form or the other, and also correlation of the EMGs of the appropriate flexor and extensor muscles in the limbs. Similar observations for fins of fishes has been made by von Holst (see ref. 62 for discussion).

In five decerebrate cats stepping on the treadmill or in the air it occurred sometimes that the homolateral limb coupling was different on each side of the body: on the left side a positive, on the right side a negative knee extension to elbow flexion interval (Fig. 4.13). Thus on the left side there is the out-of-phase form and on the right the in-phase form of homolateral coupling. This asymmetry is in conflict with a strict alternation of the homologous limbs. The arrows in Fig. 4.13 indicate, where extension should start in the right limbs to obtain strict alternation of the homologous limbs. It can been seen that the deviation of the forelimb from strict alternation is more pronounced than that of the hindlimbs. (A comparable deviation from strict in-phase coupling in the homologous limbs is observed also in the gallop (next section)).

However, it is clear, that the two discrete forms of homolateral coupling can occur simultaneously in alternate gaits and are even strong enough to override partially the homologous coordination, especially that of the forelimbs.

In conclusion, the three examples given above emphasize the underlying principle of interlimb coordination to correlate selected phases of flexion and extension in the limb.

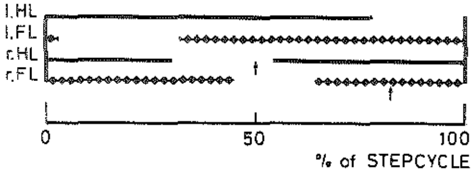

Fig. 4.13. Duration of flexion and extension periods at knee and elbow joints in a decerebrate cat stepping on the treadmill at 1.0 m/sec. Solid and broken lines indicate extension and gaps flexion. Data are averaged from 11 successive steps. l left, r right, HL hindlimb, FL forelimb. Arrows indicate expected onsets of extension in right hindlimb and forelimb: further discussion in text.

Transitions between in-phase and out-of-phase homolateral limb coupling.

The transition of the coupling of the homolateral hind- and forelimb between in- and out-of-phase forms can be achieved in one or two steps. Normal cats stepping overground and using alternate gaits mostly adopt the out-of-phase type of homolateral coupling, so that transitions are rare. However, transitions can be provoked on the treadmill, where the in-phase homolateral coupling occurs, by changing the velocity.

The curves in Fig. 4.9B were obtained by analysing 10-20 successive steps at a constant velocity of the treadmill. In Fig. 4.14A-D the treadmill was accelerated or decelerated at about 0.3 m/sec^2. In each step cycle the coupling interval was related to the instantaneous velocity. At the same time electromyograms (EMGs) were recorded from hindlimb and forelimb muscles. At 1 m/sec the forelimb flexion movement occurs before the extension movement of the hindlimb and is the homolateral coupling in-phase (Fig. 4.14A, open circles). As the velocity increases the phase lead of the forelimb flexion decreases, and within three steps, hindlimb extension leads forelimb flexion by about 10% of a step cycle. A similar curve was followed on slowing down. The timing of the EMGs, however, from hind- and forelimbs does show a much more abrupt phase shift with changing velocity (Fig. 4.14A and B). At low velocities the EMG of pectoralis major (comparable in its onset, at least, to that of flexor muscles such as biceps brachii) falls 40-50% of a step cycle before that of quadriceps and triceps brachii EMG falls 0-10% after that of quadriceps. In other words, the forelimb extensor EMG lies in phase, and the forelimb flexor EMG out of phase, with the hindlimb extensor EMG; this pattern corresponds to an in-phase homolateral coupling. As the velocity increases the forelimb EMGs are suddenly delayed with respect to the hindlimb EMGs by about 30-50% of a step cycle. Pectoralis major EMG now falls 10 to 0% of a step cycle before, and triceps EMG 40-50% after, quadriceps EMG. In other words, the forelimb extensor EMG lies out of phase, and the forelimb flexor EMG in phase, with the hindlimb extensor EMG; this pattern corresponds to an out-of-phase homolateral coupling. The reverse transition occurs during deceleration (Fig. 4.14D). The results from a second cat are shown in Fig. 4.14C and D, where the shifts between the EMGs of triceps brachii and quadriceps are even more abrupt. At constant velocities round about 1.5 m/sec the cat tends to shift back and forth from one form of coupling to another (Fig. 4.14E). This may explain why the coupling intervals of the movements obtained from 10-20 successive steps can lie intermediate between the negative and positive plateau (Fig. 4.9B, filled circles, same cat as Fig. 4.14C-E).

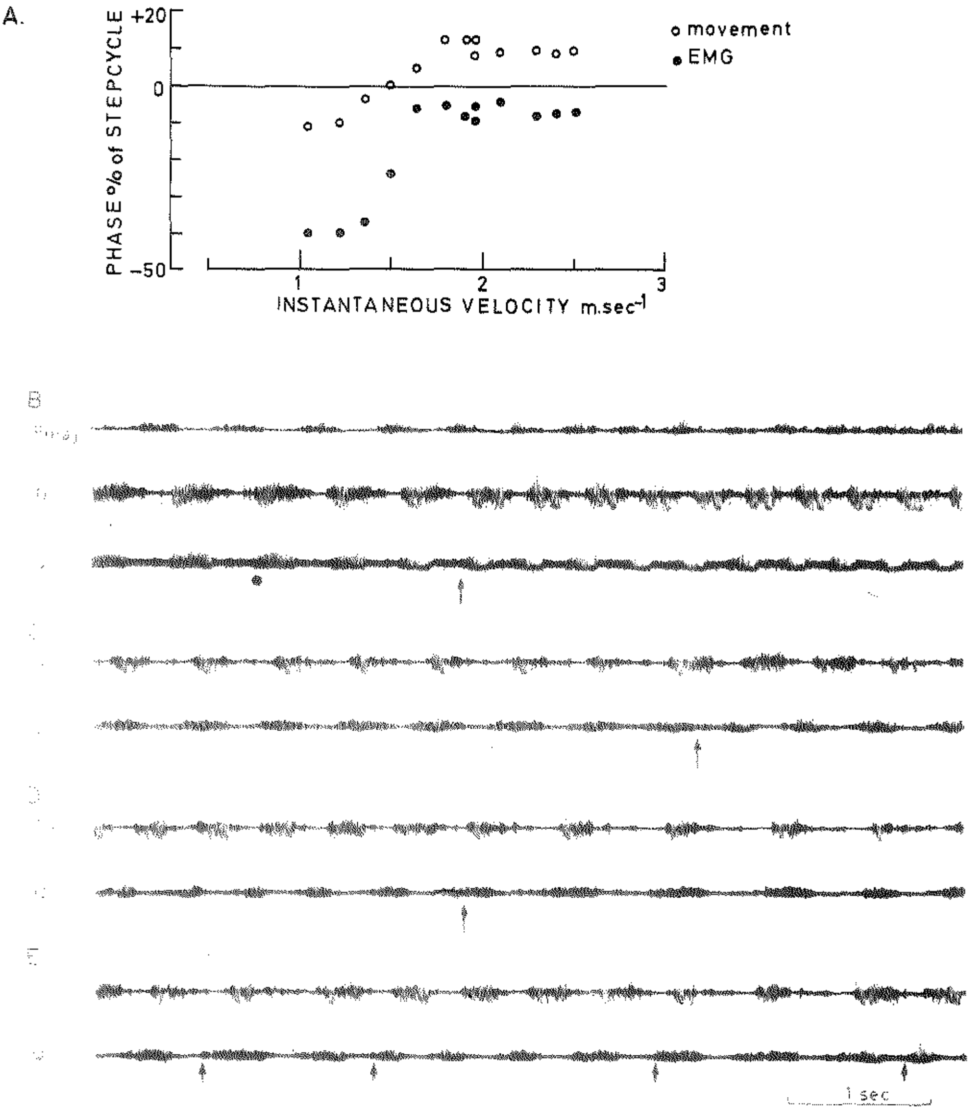

Fig. 4.14. Coupling of homolateral hindlimb and forelimb movements and electromyograms (EMGs). A: variation of intervals between onsets of hindlimb extension and forelimb flexion (open circles), and variation of intervals between onsets of hindlimb extensor EMG and forelimb flexor EMG (filled circles), with velocity of treadmill. EMGs were obtained from quadriceps femoris and pectoralis major. The treadmill was accelerated at approximately 0.3 m/sec^2 and the instant velocity was the average obtained during a step cycle. The points represent successive step cycles. B: EMGs of pectoralis major (Pmaj) and triceps brachii (Tri) from the forelimb, and quadriceps femoris (Q) from the

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hindlimb during acceleration of the treadmill. The filled circles of A were obtained from these traces. The dot indicates the first measured step cycle; cat F5, C and D: EMGs of triceps brachii and quadriceps femoris during acceleration (C) and deceleration (D) between 1 and 2 m/sec; cat F6. B-E the arrows indicate the points at which the coupling of the EMGs changes.

Summary of interlimb coordination in alternate gaits

In alternate gaits there exist two basic and preferred forms of homolateral limb coupling (Fig. 4.15):

1) In-phase, where characteristically the onsets of extension of the hindlimb and forelimb are related and the EE interval is short.

2) Out-of-phase, where characteristically the onsets of extension of the hindlimb and of flexion of the forelimb are related and the EF interval is short. These patterns are further supported by the appropriate correspondance of muscle activity in the different limbs. Transitions between the two forms of homolateral limb coupling occurs abruptly in one or two steps.

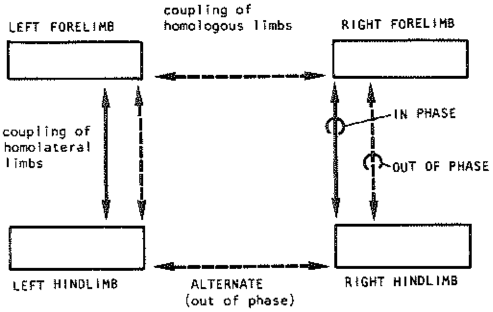


Fig. 4.15. Diagram of the coupling of flexion and extension movements of the limbs.

In phase gaits

All forms of galloping and jumping may be broadly described by a tendency for in-phase coupling of flexion and extension phases of each of the homologous pairs of limbs, combined with either symmetrical or asymmetrical coordination of the homolateral limbs in the in-phase or out-of-phase form. Particular attention has been given to the rotatory, transverse and half bound gallops, where the coordination of the homolateral limbs is asymmetrical. In the present study no full bound was observed, but jumps are described below. These two forms of in-phase locomotion are characterized by a symmetrical homolateral coupling.

In the gallop the sequence of foot contact of the four limbs determines if the gallop is rotatory, transverse or half bound (140 and Fig. 4.16). In this study the same criteria were used initially for classifying the gallops. In addition, the data have been normalized in two ways: (1) by referring all gallops to one side of the body so that the left hindlimb leads with foot contact and (2)

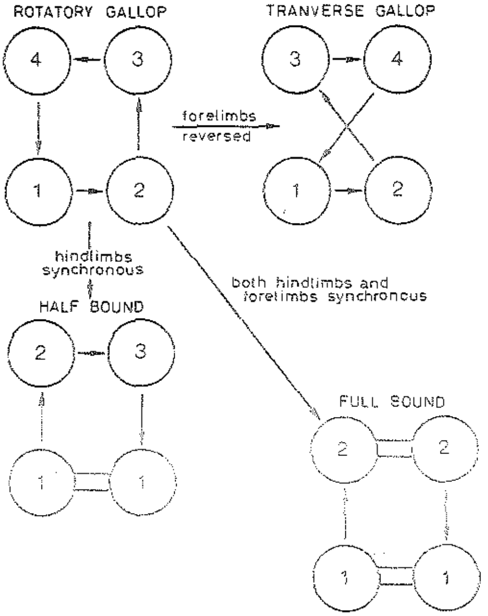


Fig. 4.16. In-phase forms of locomotion defined by foot contact patterns. Numbers indicate the sequence of foot contact referenced to contact of the left hindlimb (140). All forms have mirror images. The rotatory, transverse and half bound gallop are grouped together since they have an asymmetry in the homolateral limb coupling in common (see text).

by dividing the time intervals measured by the duration of the current step cycle to obtain a phase value as a percentage of the step cycle. This implies that the left hindlimb enters extension and makes contact with the ground before, or simultaneously with, the right hindlimb. It is therefore possible to refer to the left hindlimb as leading, and the right hindlimb as trailing.

In all the samples of animals the rotatory was the most common form of galloping. Three normal cats (F8, F11 and F6) were chosen in Fig. 4.17A-D to illustrate the limits of phase lag between the onsets of extension in the hindlimbs. The onsets of flexion are less closely coupled (Fig. 4.17C). In the forelimbs the coupling is negative, since here the right precedes the left in all movements. Once again the onsets of extension are more closely in phase than those of flexion. The difference in phasing of flexion and extension movements is compatible with the asymmetry in the periods of flexion and extension between the homologous limbs in the rotatory gallop (108 and chapter 3).

In the half bound gallop the movements of the hindlimbs are synchronous and symmetrical. This type of gallop was observed in two cats, F12 and DC2. Extension and flexion movements of the hindlimbs are very closely coupled and in DC2 phasing of the forelimb movements is also tighter than in the other cats of this group.

Only 3 cats galloped consistently with the transverse pattern (Fig. 4.17E-H). In normal cats, in particular, transverse steps are often taken during shifts from right to left rotatory gallops or in transitions between trotting and galloping (see below). These transition steps have not been used in the present analysis. In Fig.

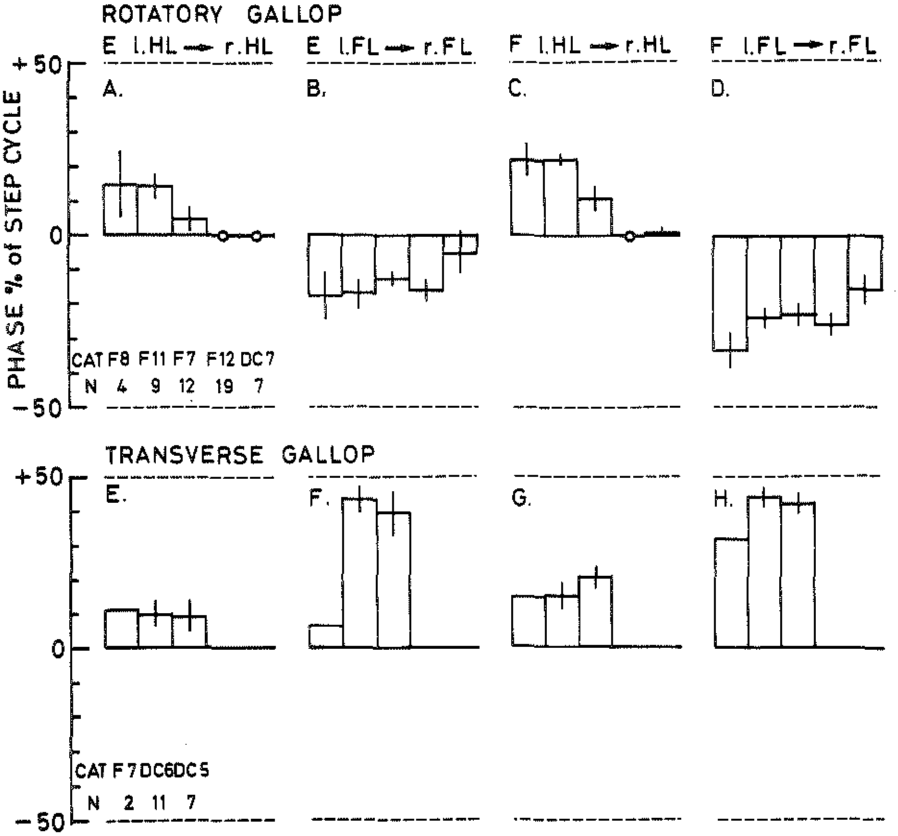


Fig. 4.17. Coupling of movements between the homologous limbs in the in-phase form of locomotion. Intervals were measured between onsets of extension in left and right homologous limbs (A,B,E and F) and between onset of flexion (C,D,G and H). Abbreviations: E, extension; F, flexion; l, left; r, right; HL, hindlimbs; Fl, forelimbs; N, number of observations. Dotted lines are drawn at phase values of 50%. The intervals are normalized as phase % of step cycle. Standard deviations are given by vertical bars. An open circle at 0% phase indicates a mean and a standard deviation of 0. The standard deviation in these cases should be greater than 0: this error results from the low sampling frequency of the film camera (see chapter 2).

4.17E and G the extension and flexion couplings of the hindlimbs remain similar to the rotatory and half bound gallops. In the forelimbs there is an important difference: the coupling order of extension and flexion is reversed so that the left leads the right forelimb. In the two decerebrate cats the phase values of the extension and flexion coupling are increased. This was not observed in the transverse gallop of the normal cat (F7) shown in Fig. E-H, nor in the occasional transverse gallop steps in other normal cats (F6, 8 and 13).

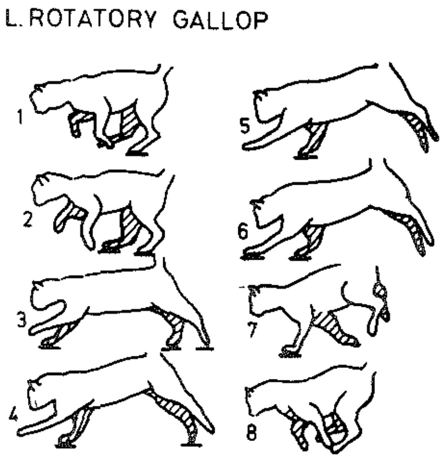


Fig. 4.18. Figurines demonstrating the homolateral form of coupling in the in-phase forms of stepping. The in-phase form of homolateral coupling on the cat's right side (hatched limbs), the out-of-phase form at the cat's left side. The cat stepping on the treadmill was performing a left rotatory gallop at 3.3 m/sec. The horizontal bars indicate that the foot is in contact with the ground.

Homolateral limb coupling in the gallop

In the alternate gaits the coupling of hindlimb and forelimb was shown to follow symmetrically an in-phase or an out-of-phase form. In the normalized left rotatory and half bound gallops the out-of-phase form of homolateral coupling is observed on the left side and in the left normalized transverse gallop on the right side. The out-of-phase coupling in the rotatory gallop is illustrated in the figurines of Fig. 4.18 (open limbs) and in the joint angle measurements of Fig. 4.19B. On the corresponding opposite side of

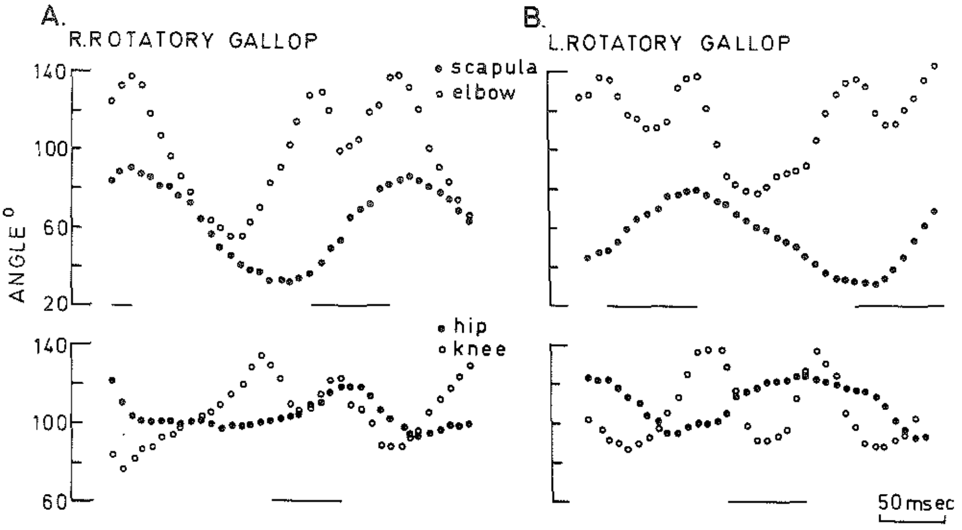


Fig. 4.19. Variation in angle at the forelimb and hindlimb joints of the same side of the body in single steps of right and left rotatory gallops. A. represents the in-phase form of homolateral coupling, B. the out-of-phase form. Cat F6 stepping on the treadmill at 3.3 m/sec. Horizontal bars indicate duration of foot contact with treadmill.

the body the in-phase form of coupling is found (Fig. 4.18, hatched limbs, Fig. 4.19A). The sequences of flexion and extension periods of the homolateral limbs in the in-phase and out-of-phase couplings show striking resemblance in alternate and in-phase gaits. For comparison, the onset of extension and flexion have been measured at the knee and elbow in all four limbs in alternate and in-phase gaits. In the gallop the homolateral limb coupling is asymmetric: the knee extension - elbow flexion interval is negative on the right side and positive on the left in the normalized left rotatory gallop (Fig. 4.20A). The similarities between the homolateral limb couplings in the gallop and in the two forms of alternate gaits is even clearer in Fig. 4.20B-D. The relative durations of the flexion and extension periods at the knee and the elbow joints are set out for a pace, trot and left rotatory gallop in the same cat. Compare the left limbs in the pace with the right limbs in the gallop, and the right limbs in the trot with the left limbs in the gallop. These observations led to the suggestion, that in the in-phase gaits so far described, i.e. in the rotatory, transverse and half-bound gallops, the homolateral limb couplings represent a recombination of the two patterns of homolateral coupling of the alternate gaits.

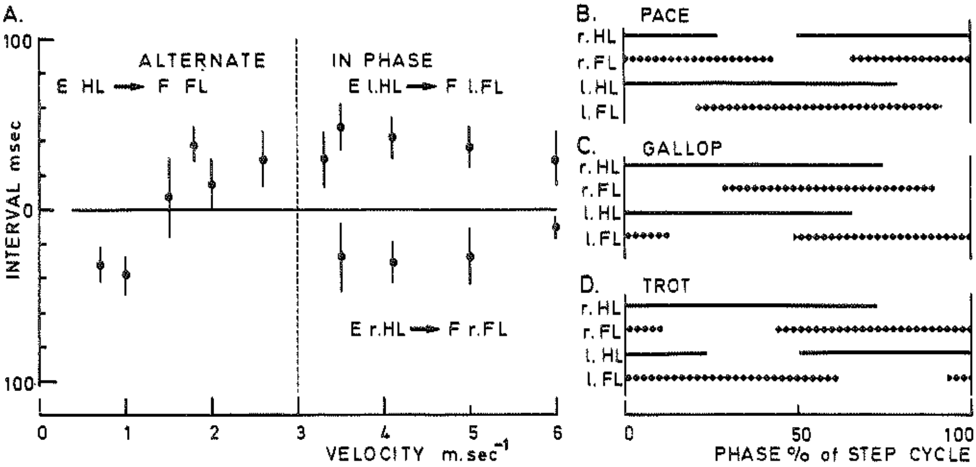


Fig. 4.20. Coupling of the hind- and forelimb of each side in alternate and in-phase forms of locomotion during stepping on a treadmill (cat F13). A: variation of intervals between onsets of hindlimb extension and homolateral forelimb flexion with velocity of treadmill. The vertical dotted line separates alternate and in-phase forms. In the alternate forms the coupling of hind- and forelimbs occurs symmetrically on both sides; in the in-phase form the coupling is different on each side. The points represent the averages from 9-19 successive steps and the vertical bars give the standard deviation of the mean B-D: comparison of patterns of flexion and extension periods in the pace, gallop and trot. Same cat as in A. Solid lines (hindlimbs) and dotted lines (forelimbs) give durations of extension; gaps indicate durations of flexion. The periods have been normalised with respect to the duration of the step cycle.

Further evidence for this suggestion was obtained from the in-phase and out-of-phase homolateral coupling of hip and scapula movements in the gallop. This analysis was restricted with one exception to the rotatory gallop, which is the most common form of gallop in the cat (72,105,140). One series of transverse gallop steps has also been included, indicated by a 't' in the figures. Movements of the hip joint and of the scapula have been measured in five cats stepping on a treadmill. One of these cats was also filmed moving overground and a few steps have been included marked by an 'f' in the figures. Since the cat frequently changes the laterality and type of its gallop (105,140), step cycles have only been selected from sequences of galloping in which the laterality and type remained constant for at least five steps. The first and the last steps of the sequences were discarded to avoid the possible influence of changes in the preceding and succeeding steps. Because of technical limitations movements at the proximal joints were not filmed simultaneously on both sides of the body. Fig. 4.21 therefore represents the pooled observations of the coupling of the hip and scapula on the left side of the cats during both left and right rotatory gallops and during one right transverse gallop. Comparison with results obtained for the couplings between knee and elbow (see below and 107,108) suggests this is a reasonable procedure to obtain estimates of the movements on both sides.

In the left rotatory and right transverse gallops the homolateral coupling on the left side is of the out-of-phase form. This is characterized as discussed for the alternate gaits by a close relation between the onset of extension at the hip and flexion of the scapula: the EF interval (Fig. 4.21A and C, filled circles, hatched zones, averaged values in range -8% to +5% of a step cycle). The interlimb couplings on the other side of the body are represented by the left limbs in the right rotatory gallop. Here there is a coupling resembling the in-phase homolateral coupling obtained in alternate gaits at low velocities. The onsets of hip and scapula extension are more in phase and the EE interval is short (Figs. 4.21A and C, open circles, open zones, averaged values in range 8% to 30%). The in-phase homolateral couplings in alternate and in-phase gaits are compared further in the Discussion section.

Replotting the data as a function of the step cycle period (Figs. 4.21B and D) reveals that the groups of couplings are spread evenly throughout an almost twofold range of stepping frequencies. There is an important difference, however, with the coupling intervals in the alternate forms of locomotion (Figs. 4.8A and B). There it is exclusively at the longer step cycle periods that the hip and shoulder move in-phase, and exclusively at the shorter step cycle periods that the hip and shoulder move out-of-phase. In the gallop the step cycle periods partly overlap the lower end of the range for alternate gaits. Here both types of hip and scapula coupling are found.

In conclusion, observations of movements at the hip and scapula

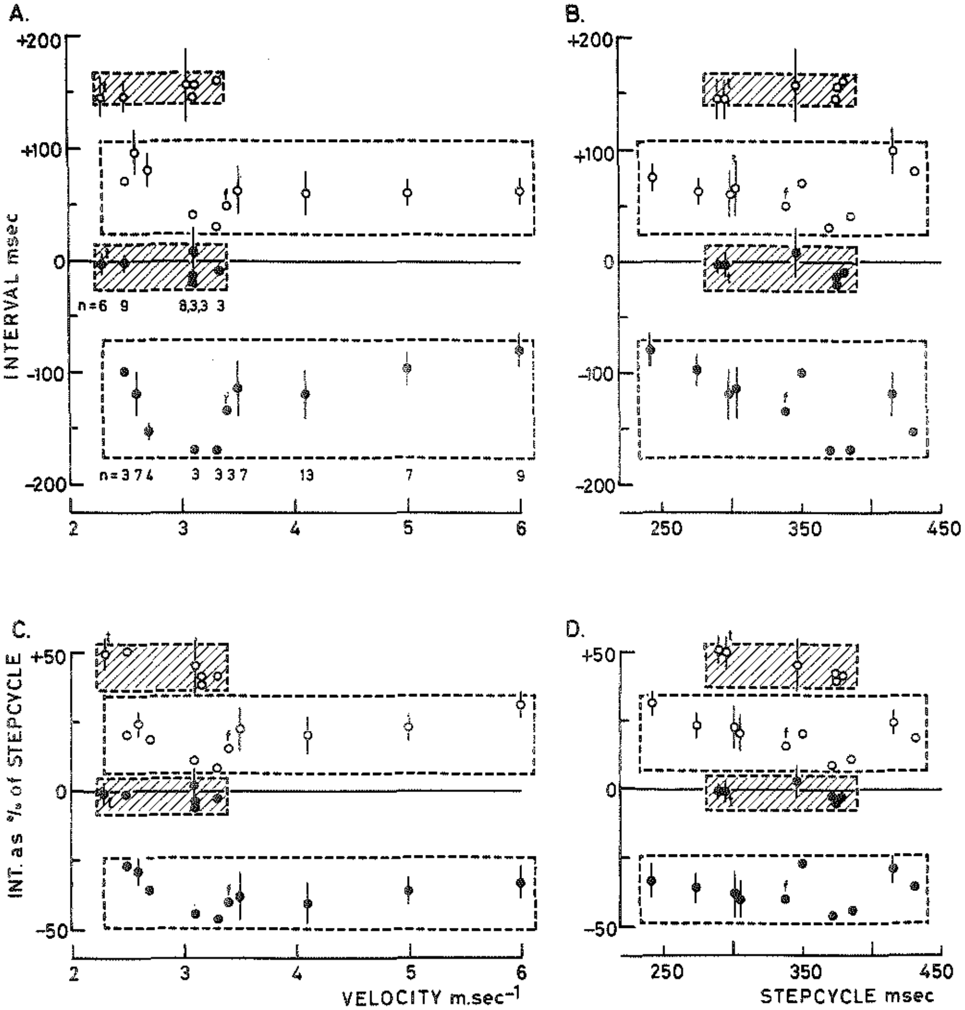


Fig. 4.21. Coupling of movements of homolateral hip and scapula in in-phase locomotion. Open circles: intervals between onsets of hip extension and scapula extension. Filled circles: intervals between hip extension and scapula flexion. Hatched zones: left homolateral limbs in left rotatory and right transverse gallops; open zones: left homolateral limbs in right rotatory gallop. 't' indicates the data referring to the transverse gallop. All the data were obtained in 5 normal cats galloping on treadmill, except in one case, marked 'f' where the cat was freely moving. In A and C the intervals are plotted against the velocity of the treadmill, in B and D they are plotted as a function of the step cycle duration. n = number of trials.

in the rotatory gallop show that the homolateral limb coupling on one side is out-of-phase and resembles the coupling seen in alternate gaits at higher frequencies of stepping. On the other side the coupling is in-phase and resembles the coupling seen in alternate gaits at lower frequencies of stepping. Of the two types of coupling the out-of-phase type is the more consistent.

Jumping

Two cats (F3 and 5) were trained to leap from the ground up onto a 50 cm platform (Fig. 4.22). The commonest sequence of movement was a simultaneous contraction of forelimb extensor muscles (forelimbs push off) throwing the body upwards and the centre of gravity towards the hindlimbs. The hindlimb extensor muscles contract bilaterally (hindlimbs push off) and this is followed by loss of contact (lift off) and flexion of the forelimbs. At the end of their extension period the hindlimbs lose contact (hindlimb lift off) and go into flexion. Then follows a short period when all 4 limbs are in flexion before the forelimbs extend prior to landing.

If the 'step cycle' of the jump is assumed to extend from the onset of active hindlimb extension (hindlimb push off) to the onset of extension of the hindlimbs prior to the hindlimb landing, a comparison can be made with the step cycle of the gallop (Fig. 4.23A and D). The jump illustrated in Fig. 4.22 is reproduced in the upper set of lines in the diagram of Fig. 4.23D. The extension and flexion movements of the homologous pairs of limbs occur in phase, but instead of an asymmetrical coupling of hindlimb and forelimb movements on each side, the coupling pattern is on both sides out-of-phase, with knee extension preceding that of elbow flexion. Other sequences of movement in jumping were also occasionally observed in which one hindlimb led the other in the push off and the forelimbs adopted patterns somewhat comparable to the rotatory or transverse gallops. A further jump has been analyzed in another cat (K1) leaping freely across a stream (lower lines in diagram of Fig. 4.23D). The basic pattern is similar to the cats under laboratory conditions.

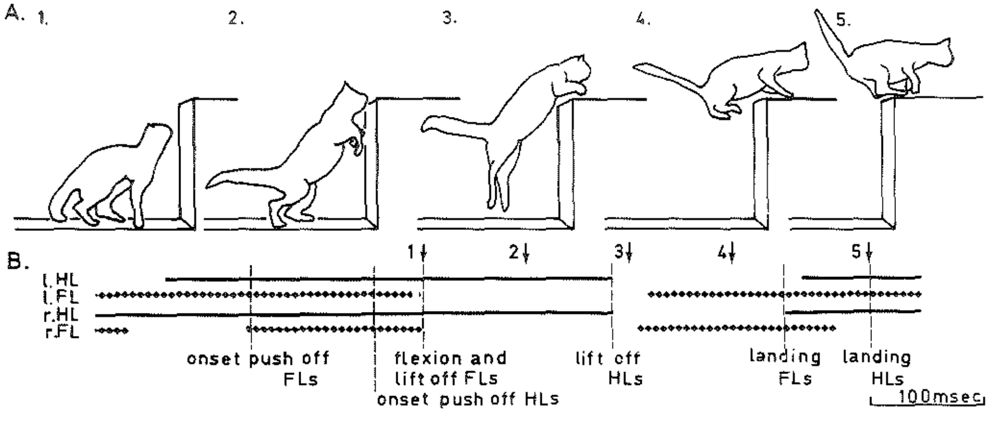
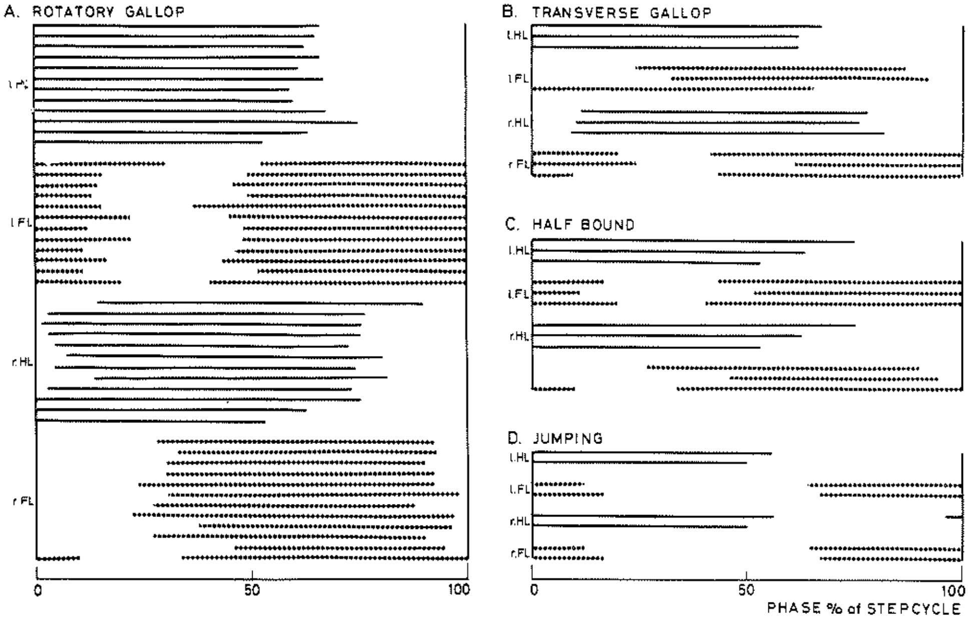


Fig. 4.22. Cat jumping onto a 50 cm platform. The figures in A are indexed by arrows in the diagram of flexion and extension periods in B. Solid and broken lines indicate extension, and gaps flexion. Abbreviations as in Fig. 4.17. Further discussion in text. Cat F3.

Survey of patterns of in-phase gaits

The step cycles from all the normal and decerebrate cats in which repeatable sequences of galloping and jumping could be observed are shown in the diagrams of Fig. 4.23. The measurements were taken from knee and elbow on both sides of the body. The step cycles are normalized as described above and are averaged from between 2 and 19 succesive steps. They represent periods of between 250 and 400 m/sec obtained at 1.8-6.0 m/sec. The rotatory gallop was the most common



	A												B			D	
Situation	OG	TM	TM	TM	TM	TM	TM	TM	TM	TM	TM	OG	TM	TM	TM	-	-
Cat	NC	NC	NC	NC	NC	NC	NC	NC	NC	NC	DC	NC	NC	DC	DC	NC	NC
	F8	F13	F13	F13	F7	F7	F10	F11	F13	F12	DC2	K1	F7	DC6	DC5	F3	K1
Velocity m.sec^{-1}	3,2	3,5	4,1	5,0	3,3	3,3	3,3	3,4	6,0	2,5	2,3	4,0	3,3	2,3	2,5	-	-
Number of steps analysed	4	8	10	10	10	12	4	10	10	19	7	1	2	11	8	1	1

Fig. 4.23. Diagrams of normalized patterns of extension (solid or broken lines) and flexion (gaps) in different types of galloping. Each line represents the mean of successive steps; the sequence of lines drawn for each of the 4 limbs is the same. Abbreviations as in Fig. 4.17. Flexion and extension periods are normalized as phase % of step cycle. The lowest 3 sets of lines in A are reproduced in C. Further discussion in text. The material for this figure is as follows. The lines from above downwards in the figure correspond with the columns from left to right in the table below the figure. Abbreviations: OG, stepping overground; TM, stepping on treadmill; NC, normal cat; DC, decerebrate cat.

and is remarkably consistent between the different cats (Fig. 4.23A). The transverse gallops also form a homogeneous group (Fig. 4.23B) and it is striking how closely the pattern mirrors that of the rotatory gallop.

The last 3 gallops in Fig. 4.23A are in fact half bounds and are redrawn in Fig. 4.23C. In the upper two examples the coupling of hind- and forelimbs is typical of the rotatory gallop. In the lowest example the coupling on the right side is also in the out-of-phase form and this pattern of galloping is suggestive of the jumps shown in Fig. 4.23D. In the examples of the half bound in Fig. 4.23C the overlapping periods of extension in the homologous pairs of limbs are particularly clear. The pattern has only to be slightly extended to reach the separation of the hindlimb and forelimb periods of extension shown in the jumps of Fig. 4.23D.

Transition between alternate and in-phase gaits

The transition between trotting and galloping occurred in the present material between 1.8 and 3.5 m/sec. It is always sudden and has been noted to be complete within one or two steps (111,132). The example shown in Fig. 4.24 demonstrates a transition from a right rotatory gallop to a trot and back to a right rotatory gallop. This occurred in successive steps at a constant treadmill velocity of 3.3 m/sec. In the gallop/trot transition (Fig. 4.24A) relatively little change occurs in the hindlimb-forelimb coupling on the right side: these limbs continue in the out-of-phase coupling. It is on the left side where the adjustments have to be made: the left hindlimb undergoes a shorter flexion period to bring the onset of extension earlier and out of phase with that of the right hindlimb. This also helps to re-establish the out-of-phase pattern on the left side.

The transition from trot to gallop (Fig. 4.24B) here involved

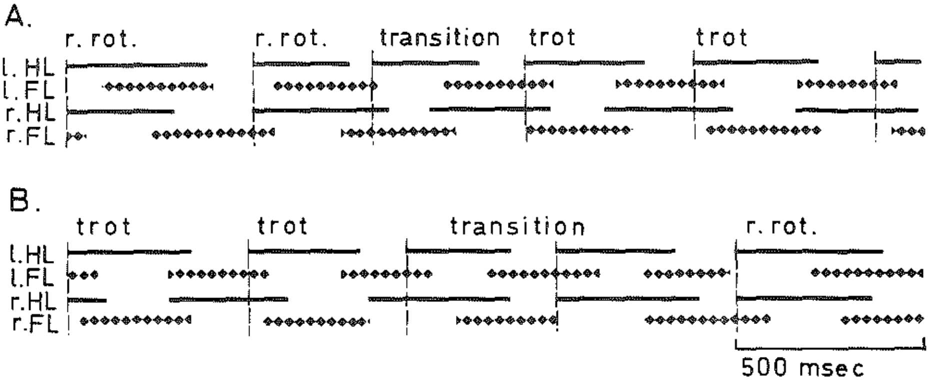


Fig. 4.24. Patterns of flexion and extension periods during transitions between gallop and trot. A: transition between right rotatory gallop (r.rot) and trot. B: transitions between trot and right rotatory gallop. Cat F6, treadmill, 3.3 m/sec. The traces in A and B were obtained from successive steps: the beginning of trace B corresponds to the last complete step cycle of trace A.

two steps, the initial changes occurring as a prolongation of flexion in the right hindlimb and forelimb. The second transition step involves rather uncertain rearrangement of the periods of extension and flexion before a right rotatory gallop is finally achieved. According to the foot contact pattern (140) the transition steps in Fig. 4.24B are right transverse and left transverse respectively, but they have not been labelled in the figure as such, since they are not maintained further. Transverse gallop steps are often observed in the transitions between trot and gallop, and between left and right rotatory gallops.

The transitions illustrated in Fig. 4.24 are not the only strategies used between trotting and galloping. However, all have one feature in common: a shift from a bilaterally symmetrical type of hindlimb-forelimb coupling in the trot, to the asymmetrical in-phase and out-of-phase type of coupling in the rotatory or transverse gallops.

Summary of in-phase gaits

In the in-phase gaits the homologous limbs tend to step in-phase. The homolateral limb coupling is either asymmetrical, in-phase on one side, out-of-phase on the other side, as is observed in the forms of galloping or symmetrically out-of-phase as is common in the jump. The in-phase coupling of the hindlimbs and the out-of-phase coupling of the homolateral limbs are the most consistent. The diagram of Fig. 4.25 summarizes the different patterns of interlimb coupling.

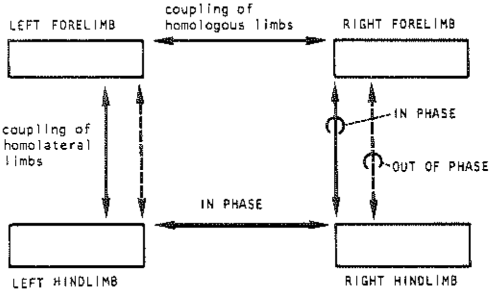


Fig. 4.25. Diagram of the coupling of flexion and extension movements of the limbs.

Spinal mechanisms for interlimb coordination

In the high spinal cat coordinated movements of all four limbs resembling stepping sequences have occasionally been observed (65,97, 105,129). In four experiments on high spinal cats the earlier observations were repeated that the forelimbs occasionally make stepping movements in register with those of the hindlimbs. The cats in these experiments were treated with the monoamine oxidase inhibitor Nialamid (40 mg/kg i.v.) and after a delay of 30 minutes with a further i.v. injection of a mixture of L-DOPA (50-100 mg/kg) and the peripheral DOPA decarboxylase inhibitor Ro 4-4602/1 (Roche; 25-50 mg/kg) dissolved in 0.9% NaCl. The former two drugs have been

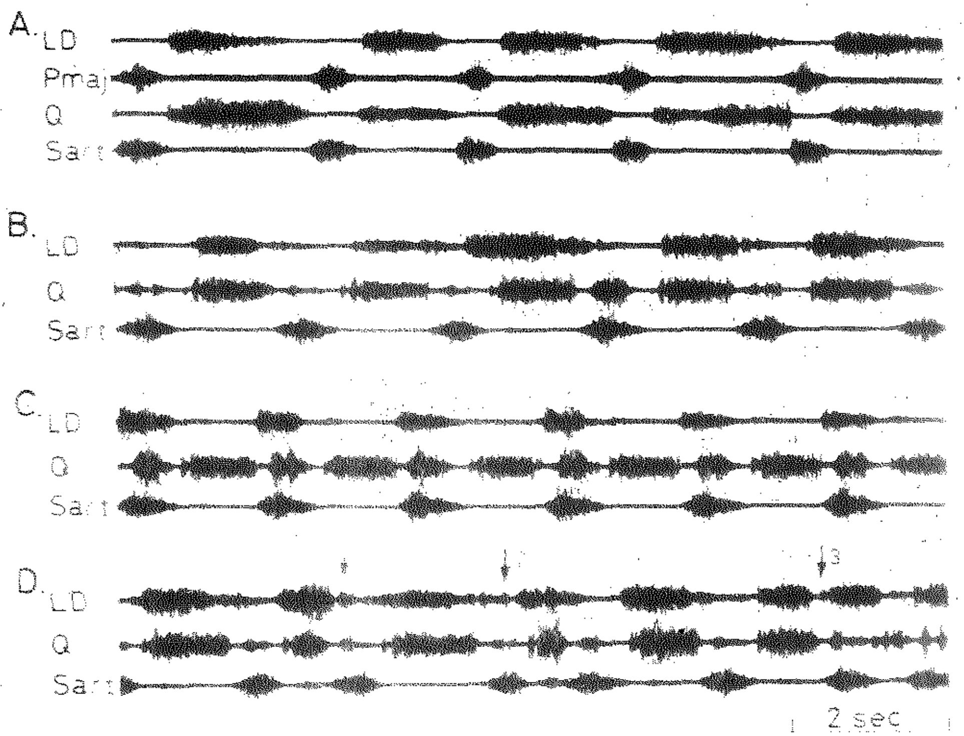


Fig. 4.26. EMGs from homolateral forelimb and hindlimb in a high spinal cat during stepping on treadmill. LD latissimus dorsi, (forelimb extensor), Pmaj pectoralis major, (forelimb flexor), Q quadriceps femoris (hindlimb extensor), Sart sartorius (hindlimb dlexor). B, C and D different preparation to A.

used to activate and potentiate the terminals of the noradrenergic reticulospinal pathways which have been associated with the initiation and maintenance of locomotion in the cat (62,63). When the cat is placed in contact with a motor driven treadmill the hindlimbs begin to step. At first the gait is alternating, but as the velocity increases the hindlimbs can step in-phase as Grillner has reported (62). The forelimbs are retracted caudally with a strong extensor tonus at all joints. In 2 out of the 4 spinal cats and occasionally in a third the forelimbs stepped in time with the hindlimbs moving stiffly forward and backward. Unlike the hindlimbs, the forelimbs are not lifted up well during the swing phase and do not support the weight of the body. The electromyograms in Figure 4.26 illustrate the close register of the homolateral forelimb and hindlimb activity in two of these preparations. In Fig. 4.26A the EMGs of the homolateral limbs display an in-phase coupling: the flexors of the forelimb (Pmaj) and hindlimb (Sart), and the extensors of forelimb (LD) and hindlimb (Q) are closely correlated. Fig. 4.26B shows the same in-phase homolateral coupling obtained in another experiment. Note that the activities of the extensors Q and LD are in register, but that the activity of Sart falls in between. There is occasionally an extra burst in Q corresponding to the flexor activity in Sart. In Fig. 4.26C the homolateral coupling is out-of-phase; the extensor bursts in LD are now matched with the bursts of the flexor Sart. (There is also a brief burst of activity in Q during the activity of Sart).

Transitions between the two forms of homolateral limb coupling have been shown to be abrupt being complete within one or two steps (see above). In Fig. 4.26D the stepping rhythm is irregular. The sequence begins with an in-phase coupling. At the first arrow the gait becomes unstable and there is a brief burst of activity in the forelimb flexor LD with the flexor burst in Sart, but the gait picks up once more in its in-phase homolateral coupling. At the second arrow the EMGs are slightly shifted and the onset of LD overlaps the tail of Sart. The shift is not maintained and the in-phase pattern is re-established. At the third arrow, however, the gait shifts suddenly to an out-of-phase coupling, with correlation of the EMGs of Sart and LD.

These observations are important since it can now be concluded that *coordinated stepping movements of all four limbs in the cat can be generated by spinal mechanisms.*

DISCUSSION

Spinal generation of coordinated movements in all four limbs.

The spinal cord alone can generate coordinated patterns of locomotor movements in all four limbs. Previously the possibility that bulbar centres were in some way necessary for the generation of forelimb locomotor movements coordinated with those of the hindlimbs could not be excluded. Luttrell et al. (97) showed that cats infected with Newcastle virus exhibit coordinated myoclonic movements in all four limbs at about 1 Hz which persist after high spinal section. The homolateral limb coordination could be in-phase or out-of-phase The present results in high spinal cats treated with Nialamid and L-DOPA provide conclusive evidence that the spinal cord can indeed generate forelimb locomotor movements coordinated with those of the hindlimbs. Participation of supraspinal structures in the generation of forelimb movement is not excluded, but it is clearly not essential The patterns of homolateral coupling obtained have been of both the in-phase and out-of-phase types. This conclusion contains important functional specifications for the pathways interconnecting the spinal motor centres controlling each limb (chapter 5).

Basic programmes of interlimb coordination

Observations of the flexion and extension movements and of flexor and extensor EMGs led to the conclusion that the different forms of alternate gaits (e.g., pacing, trotting and swimming) and in-phase gaits (galloping and jumping) result from the interaction of basic patterns, or programmes, for coordinating the homologous limbs and for the homolateral limbs.

In alternate gaits flexion and extension movements of the homologous limbs occur strictly out-of-phase (108). There are two basic forms of homolateral limb coupling, the in-phase and out-of-phase forms, and this simplifies considerably the spinal control of the four limbs under different conditions of locomotion. In all preparations and situations the out-of-phase form is by far the more common. The in-phase form is more frequently seen in normal cats stepping on the treadmill than overground. It is difficult to determine why the mechanics of stepping on the treadmill should be different to the overground situation once a constant velocity is reached. Since pacing does occur naturally, it would seem that in some way the behavioural situation of the treadmill serves to raise the probability for this type of interlimb coordination at low velocities. Both forms of homolateral limb coupling are observed in decerebrate cats stepping on the treadmill, in the air and immersed in water. Under these conditions there was no relationship between the particular form of homolateral limb coupling and treadmill velocity or the duration of the step cycle (Figs. 4.9 and 4.10). Nevertheless in normal, decerebrate and spinal cats the occurrence of alternate and in-phase gaits was determined by the velocity of the treadmill, as others have also reported (42,62,68). Transitions between the patterns of homologous and of homolateral limb coupling usually occur within one or two steps (111,131), emphasizing the discrete character of the patterns.

In-phase gaits e.g. galloping and jumping are characterized by a strong tendency for in-phase coupling of movements of the hindlimbs, and to a lesser extent, for those of the forelimbs. In the different gallops observed coupling of the homolateral limbs is asymmetrical. On one side it is out-of-phase and on the other in-phase. The distribution of the homolateral coupling with respect to the lead order of the hindlimbs, determines whether the gallop is rotatory or transverse (Fig. 4.23). In jumping the homolateral coupling is usually bilaterally in the out-of-phase form; in this situation both pairs of homologous limbs move completely in phase.

These programmes of interlimb coupling represent basic patterns of coordination which occur consistently. They do not exclude variants which may be dictated by external of internal perturbations, by training or by learning. Fig. 4.12 illustrates the situation in which the frequency of forelimb stepping temporarily exceeds that if the hindlimbs. This is in fact a 3:2 change in frequency. It is achieved by a homolateral coupling which shifts by approximately a half cycle from in-phase, to out-of-phase, and back to in-phase. This is somewhat comparable with experiments of Kulagin and Shik (87) where a 2:1 frequency occurred between the two hindlimbs of decerebrate cats stepping on a longitudinally split treadmill. (For further details see ref. 70)

All of these examples serve to illustrate that deviations from the in-phase or out-of-phase patterns of interlimb coupling may occur in response to internal or external demands. There remains, however, a strong tendency to return to the appropriate patterns of interlimb coupling wherever and whenever possible.

Comparison of basic programmes of interlimb coordination with gait patterns derived from foot contact measurements.

Alternate gaits are comparable to the symmetrical gaits described by Muybridge (111). Footfall formulae, gait diagrams as well as the duration of the support phase have been used by different authors for the description of interlimb coordination (33,50,74,77,111,120, 140). Stuart et al. (140) have pointed out, that the criteria used are often arbitrary and that quite dissimilar patterns of interlimb coordination can occur within one category of gait.

For example, the criterion used for walking is defined by a duration of foot contact of more than 50% of a step cycle (74,140). The category of gaits so defined include in-phase and out-of-phase homolateral limbs coupling and all the following gaits: pacing, walking and trotting. It is also a restricted type of classification since it cannot treat swimming and the experimental situation of stepping in the air.

Despite the difficulties encountered in the classification of gaits by foot contact patterns certain comparisons can be made. The in-phase form of homolateral limb coupling is most commonly associated with the pace and the slow walk, where contact of the hindlimb precedes contact of the forelimb by 0-15% of a step cycle (140). The out-of-phase coupling covers the fast walk and the trot, where forelimb contact follows hindlimb contact by 25-50% of a step-cycle (62,74,105,140). Miller and van der Burg showed that the coupling between extension of the knee and flexion of the elbow could remain constant over a wide range of velocities whereas the sequence of hindlimb and forelimb foot contact varied progressively by as much as 35% of a step cycle (105). The reason for this discrepancy is that within a single limb the onset of contact is related to the onset of extension. The interval between contact of the hindlimb and contact of the forelimb is, therefore, analogous to that between the onsets of hindlimb extension and forelimb extension (the EE interval). The phase value of the EE interval does indeed increase in the out-of-phase homolateral coupling (Fig. 4.6) and is not the characteristic index of this pattern. Coincidence of hip extension and scapula flexion (EF) in fact determines this pattern and the EE interval is then dependent on the relative duration of flexion of the scapula.

In the high spinal cat all the changeover points of flexor and extensor EMGs in the homolateral limbs tend to be tightly coupled even where the relative duration of the flexor and extensor EMG periods are unequal (Fig. 4.26D). Similar observations have been made of the coupling of flexion and extension movements in decerebrate cats stepping in the air and immersed in water and in normal cats swimming (van der Meché and Miller, unpublished observations). At high rates of alternate stepping on the treadmill or overground where the periods of flexion and extension are equal, there is also coincidence of all the changeover points (Fig. 4.27A). At lower rates the extension phase is prolonged in both hindlimb and forelimb (109). In the in-phase form of homolateral limb coupling (e.g. pacing) the changeover points are spaced asymmetrically in the step cycle but they occur together (Fig. 4.27B). At low velocities

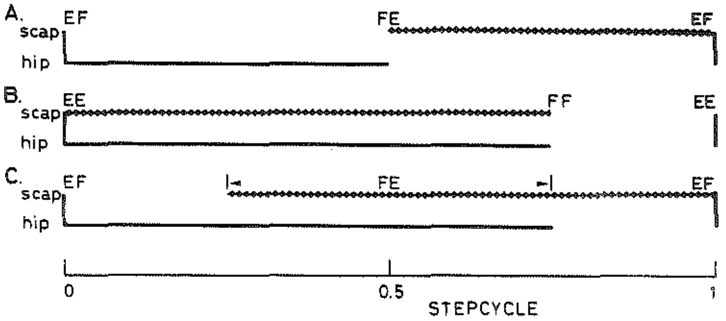


Fig. 4.27. Schematic diagram of the homolateral forms of coupling in alternate gaits. See text for discussion.

of out-of-phase homolateral coupling the long extension periods are not compatible with coincidence of all changeover points and it is only the onsetsof hindlimb extension and forelimb flexion which remain closely related (Fig. 4.27C).

In-phase gaits can be compared with the asymmetrical gaits of Muybridge (111). On the basis of sequences of foot contact several asymmetrical gaits were described (Fig. 4.16 and 140). Hildebrand has proposed on theoretical grounds over 100 different asymmetrical foot contact patterns (International symposium on the Neural Control of Locomotion, Philadelphia, 1975).According to the data presented here, in-phase gaits differ only in the distribution of the homolateral coupling, which is either symmetrically out-of-phase as in jumping of asymmetrically, in-phase and out-of-phase (Fig. 4.23).

Relative dominance of patterns of interlimb coordination

The lack of strict in-phase couplings between the different limbs in the gallop may be explained by the following suggestion. The four limbs are most likely controlled by four individual stepping generators (see general introduction). In the gaits with symmetrical homolateral coupling as the trot, pace and jump there are no conflicts in the mutual phasing of extension and flexion periods in the four limbs. This may explain why for example the trotting gait is so stable. The left forelimb motor centre, for example, would receive mutually reinforcing signals for it phases of flexion and extension from the right forelimb centre and from the hindlimb centres. As a complete system the motor centres of all 4 limbs would therefore be mutually locked to each other. In the rotatory and transverse gallops greater phase shifts occur between the activities of the motor centres, especially between the two forelimbs. This might result from competition between the different programmes for homologous and homolateral limb coupling which converge on each motor centre: in the forelimb centres the asymmetry of the couplings in the pairs of homolateral limbs is not compatible with complete phase locking of forelimb movements.

It is suggested that the relative dominance of the different programmes during a particular locomotor cycle determines the pattern of the gait adopted. Extremes of dominance can be seen in the gallops illustrated in Fig. 4.23A (9th row) and Fig. 4.23B (3rd row). In the first case the forelimbs are almost in phase (8%) with respect to the onset of extension, and in the second case out of phase (44%). In contrast, the coupling between the homolateral limbs in the second case is very close: extension of the left hind- and forelimb is synchronous, and the onsets of extension of the right hindlimb and of flexion of the right forelimb occur simultaneously. The phase shifts between homologous limbs and the frequent change of the laterality of the gallop in some cats represent the facultative qualities of locomotion described by Stuart et al. (140). From the previous discussion it can be seen that this quality could result from the competitive interaction of basic programmes of coupled

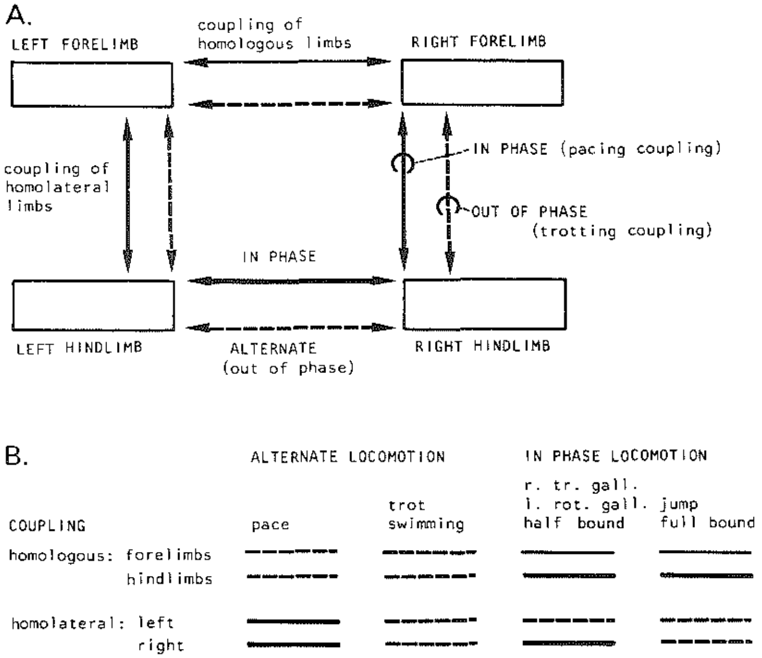


Fig. 4.28. A. Diagram of the coupling of flexion and extension movements of the limbs. B. Distribution of the types of coupling in different gaits. Abbrevations: r.tr.gall. right transverse gallop; l.rot.gall. left rotatory gallop.

movement. The relative dominance of one or other programme during a particular step cycle determines the pattern of gait adopted.

In conclusion, the hypothesis is advanced that there are two basic programmes of *homologous* limb coordination, *alternate* and *in-phase,* and two further programmes of *homolateral* limb coordination *in-phase* and *out-of-phase*. Different combinations of these programmes provide the basis for all the forms of locomotion observed (Fig. 4.28). With the exception, at present, of the in-phase coupling of the forelimbs, the interlimb programmes can all be generated by the spinal cord alone.

SUMMARY

Observations in normal, decerebrate, and high spinal cats of flexion and extension movements of the 4 limbs have led to the conclusion that the different forms of alternate locomotion (e.g. pacing, trotting, swimming) and in-phase locomotion (galloping, jumping) result from the interaction of programmes for the coordination of (1) the homologous limbs (pair of hindlimbs or pair of forelimbs) and (2) the homolateral limbs (hind- and forelimb of the same side of the body). The movements of the homologous pairs of limbs are coupled out of phase in alternate gaits and approximately in phase in the in-phase gaits. The movements of the homolateral pairs of limbs occur approximately out-of-phase (e.g. the trot) or approximately in-phase (e.g. the pace). Transitions between all different forms of coupling occur abruptly over 1 or 2 steps. Therefore, for each type of coupling (homologous or homolateral) there are two distinct forms or programmes of movement.

The observations of stepping in the high spinal cat indicate that with the exception, at present, of the in-phase coupling of the forelimbs, the interlimb programmes can all be generated by the spinal cord alone.

The hypothesis is advanced that (1) all the characteristic patterns of locomotion in the cat result from different combinations of these programmes of homologous and homolateral limb coupling; (b) the programmes are mutually self reinforcing in the gaits in which the coordination of the movements of the 4 limbs is bilaterally symmetrical; (c) the programmes act in competition in certain gaits which are not bilaterally symmetrical giving rise at times to a changing gait pattern, and (d) the temporary dominance of one programme or another can determine the gait of the particular step.

CHAPTER 5.

FUNCTIONAL ORGANIZATION OF LONG ASCENDING AND DESCENDING PROPRIOSPINAL PATHWAYS.

INTRODUCTION

In the high spinal cat coordinated movements of all four limbs resembling stepping sequences have occasionally been observed (65, 97,105,129). From these results Miller et al. (107) argued that the basic elements of coordinated locomotor movements in the four limbs could probably be generated by the spinal cord.

In further experiments on high spinal cats described in chapter 4 regular, coordinated stepping of all four limbs has been obtained and it can, therefore, be concluded that interlimb coordination can be generated by spinal mechanisms. This now carries particular functional specifications for propriospinal connections between the segments controlling locomotion movements of each limb.

Although the spinal segmental reflex systems controlling the hindlimbs in stepping have been investigated in detail (see Lundberg (94) for review), relatively much less is known of the comparable reflex systems of the forelimbs (see refs. 126 and 146) or the organization of long interlimb reflexes in descending (1,2,3,32,33, 92,93,101) or ascending (14,21,44,46,99,100,118,133) directions. In the present chapter an attempt is made to define more precisely the functional organization of long ascending and descending pathways in the high spinal cat.

In the ascending direction particular attention has been paid to the reflexes to motoneurones supplying some of the shoulder girdle muscles (the pectoral muscles and latissimus dorsi), since neuroanatomical studies have revealed ascending projections to these groups of motoneurones (48,138). The reflexes were also examined in median, ulnar and radial nerves supplying muscles of the forearm.

In the descending direction it was shown by Lloyd and McIntyre (93) that extensor and flexor hindlimb motoneurone pools received excitatory changes following distal forelimb nerve stimulation. Short latency inhibition was only observed in flexor digitorum longus, a motoneurone nucleus to which much attention has been paid by these and other authors (7,127). It has been argued that the reflexes to this nucleus are primarily concerned with withdrawal of the claws (7,93). For this reason these particular reflexes have not been examined further in this study.

In Djalali's investigation of descending propriospinal pathways inhibitory effects were described in gastrocnemius motoneurones (32) Recent intracellular studies have in fact shown that all the lumbosacral motoneuronal nuclei tested receive excitatory and inhibitory effects through long descending propriospinal fibres (84, 144).

In this chapter a survey is given of a study of the functional organization of ascending and descending propriospinal pathways.

METHODS

Experiments were performed on 41 cats in the investigation of ascending propriospinal pathways and on 14 cats for the descending propriospinal pathways. The cats weighed 2.0-5.2 kg. and were initially anaesthetized with Fluothane prior to spinalization.

Spinalization at C_1

The carotid arteries were ligated, one being used for blood pressure measurement. The vertebral arteries were compressed bilaterally by a clamp interposed between the transverse processes of C_1 and C_2 vertebrae. The clamp was judged effective if the cat ceased spontaneous respiration. Intermittent positive pressure respiration was started. A small hole was made in the pia mater at the upper border of C_1 (approx. 4 mm below the obex) and a transection made by suction using a glass tube of 1.5 mm outer diameter. As long as the sucker remained within the pia no appreciable bleeding occurred. The separated edges of the cord were held gently apart with a spreader for visual control of the transection. In some later experiments the cat was given curare before spinalization to prevent sudden movements and, by the ganglion blocking effect, to minimize the sudden rises of blood pressure. A blunt probe was passed rostrally into the transection to make completely certain that the brain stem was no longer functioning: the Fluothane was then stopped. The recordings were started between 4 and 10 h after spinalization and the cats generally remained in good condition for a further 8-12 h. Some cats in which the Fluothane anaesthesia lasted several hours developed ECG signs of ventricular fibrillation: some of these cats were given lidocaine 2% (4 mg/kg, w/v) intravenously to restore sinus rhythm. The reflex responses of these preparations differed in no detectable way from those which did not receive lidocaine. During the recordings the cats were paralysed with gallamine (0.2-0.4 mg/kg) rather than curare since this has less ganglion blocking effect. In all experiments rectal temperature was maintained between 36 and 38°C, end-tidal PCO_2 between 4 and 5%, and mean arterial blood pressure in the range 70-90 mm Hg. In a few cases blood pressure had to be raised to these levels by intermittent i.v. infusion of metaraminol, diluted 1:200 in 4% glucose and 0.45% NaCl. Fluids were given i.v. at the rate of

1-3 ml/kg/h of the same glucose/saline mixture. In some experiments (see below) L-DOPA was given intravenously in a dose of 100 mg/kg, dissolved in 0,9% NaCl in a concentration of 10 mg/ml, together with the peripheral DOPA decarboxylase inhibitor, Ro 4-4602/1 from Roche, 25-50 mg/kg.

Dissection of nerves

The following nerves were dissected, often bilaterally, and sectioned for mounting on stimulating or recording electrodes (for explanation of abbreviations see below); in the forelimbs, DR,LD,M, Pmaj,Pmin,SR,U and in a few experiments, Bi and SSc; in the descending experiments LD,Pmaj and Pmin were not dissected, but C1B was tested in most experiments in the hindlimbs, ABSm,G,PBSt, Plantar,Q,Sart,SCI (not including the hamstring nerve), SP,Sur and TA. Plantar and SCI were not used in the descending experiments.

Branches of the sciatic nerve were mounted conventionally on silver hook electrodes in a paraffin filled pool formed by skin flaps. Branches of the femoral nerve (Q and Sart) and the distal forelimb nerves (DR,M,SR, and U) were pulled into tunnel electrodes short plastic tubes containing two Pt rings internally for electrical contact with the nerve. The electrodes were stitched to the surrounding muscles and covered with silicon rubber (Dow Corning Medical Silastic 382) to improve electrical insulation. The skin incision was then closed. The nerves of Pmaj,Pmin and LD were approached from the ventral aspect after midline incision of the pectoral muscles. These nerves are generally short and lie on the brachial plexus. Two Pt wires, 100 µm in diameter, held apart on a plastic mould, were wound round the nerves (cf. ref. 119). The nerves were then embedded in silicon rubber. Stable recordings were made for up to 12 h.

Laminectomies

Laminectomies were made at L_{6-7} for recording the hindlimb afferent nerve volleys and to record form the ventral roots, at T_{9-10} for making lesions and at C_{5-7} for measuring the forelimb afferent nerve volleys and for stimulating the dorsal columns to obtain a monosynaptic reflex in forelimb motoneurones. The exposed spinal cord was covered with mineral oil.

Lesions of the spinal cord were made with watch-makers forceps or fine steel hooks. At the end of the experiment the cord was covered for 4-6 h in situ with 10% formalin, then removed and fixed in 10% formalin for at least 24 h. The pia mater was stripped and the cord was immersed in 0.2% toluidine blue. Thin cross-sections were cut with a razor blade and the extent of the lesion was determined under a binocular microscope (x30), the results being drawn to scale on millimetre paper.

Stimulating and recording methods

Conventional stimulating and recording apparatus was used.

Electrical stimuli had the form of rectangular pulses of 0.1 m/sec duration. The signals recorded were passed through differential preamplifiers and displayed on an oscilloscope for photography. Signal averaging and integrating was computed on-line with the aid of neurophysiologically oriented programmes (75). The peak to peak voltages of the signals recorded from the nerves mostly fell in the range 20-400 µV. The recording conditions for each nerve in each experiment remained stable. Since no comparisons are made of the signals from different nerves voltage calibrations are not given.

Abbreviations

c, contralateral; C—T interval, time interval between condition and test stimuli used in investigation of changes of reflex excitability; DC, dorsal columns; i, ipsilateral; T, unit of intensity of electrical stimulating current measured in multiples of the threshold current required to activate the most excitable fibres in a nerve.

Forelimb nerves: Bi, biceps brachii; DR, deep radial; LD, latissimus dorsi; M, median; Pmaj, pectoralis major; Pmin, pectoralis minor; SR, superficial radial; SSc, suprascapular; U, ulnar.

Hindlimb nerves: ABSm, anterior biceps femoris and semimembranosus; G, medial and lateral gastrocnemius; Q, quadriceps; PBSt, posterior biceps femoris and semitendinosus; Plantar, plantar nerve at level of medial malleolus; Sart, sartorius; SCI, sciatic; SP, superficial peroneal; Sur, sural; TA, tibialis anterior.

RESULTS

Discharges evoked over long spinal pathways

In 17 out of 41 experiments (41%) discharges could be evoked in forelimb motor nerves on electrical stimulation of hindlimb nerves (see also Miller et al., 103). This was possible in 8 out of 10 experiments (80%) in hindlimb motor nerves and ventral roots on stimulation of forelimb nerves.

Discharges in forelimb motor nerves were most frequently observed observed in Pmaj (fig. 5.1) and Pmin nerves, and only rarely in LD, M and U. The most effective hindlimb nerves were Q, Sart, SP and Sur nerves. In the descending direction discharges could be observed in both the extensor ABSm (Fig. 5.2 A-F) and the flexor PBSt; in most experiments however discharges were recorded from ventral roots and could not, therefore, be related to flexors or extensors (Fig. 5.2G and H). The following forelimb nerves were effective:C1B,DR, M, SR, SSc, T and U nerves. Of these DR and SR were probably the most effective, but further experiments would be required to establish this. The discharges could be obtained with a stimulation strength between 10 and 50 times the nerve threshold, T. Stimulating with a short train, instead of a single pulse was often more succesful in provoking the discharge. If already present it enhanced the reflex

Fig.5.1

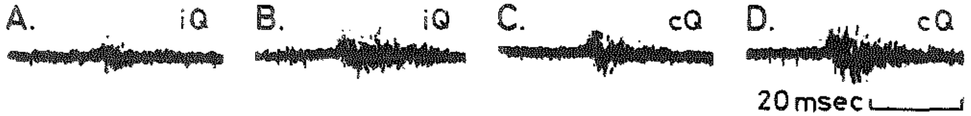


Fig.5.2

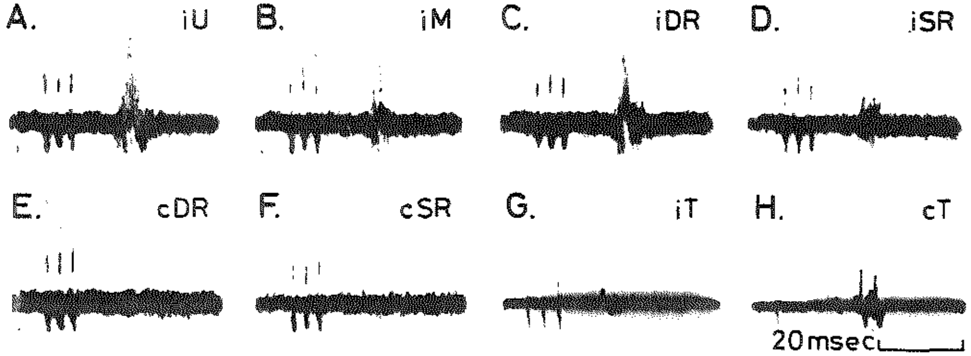


Fig. 5.1. Discharges recorded in the nerve to Pmaj on electrical stimulation of hindlimb nerves; 1 and 3 shocks, 20 T.

Fig. 5.2. Discharges recorded in the nerve to ABSm (A-F) and ventral root, L7 (G and H) on electrical stimulation of forelimb nerves. A-F, one experiment, 25 T, 3 shocks G and H, one experiment, 10 T; iT, 3 shocks; cT, 1 shock.

and shortened the latency (Fig. 5.1). In the original publication this was attributed to strong temporal facilitation. Detailed microelectrode studies will be required to distinguish this from spatial convergence or even transmitter potentiation.

The latencies are in general rather variable, as has been reported for ascending (14,46,100) and descending (92,93) propriospinal systems. In the ascending direction it varied in the present experiments from 8-25, and in the descending direction from 12-27 msec. Taking the different afferent and efferent delays into consideration these ranges are comparable with the latencies mentioned by other investigators (21,92). Stimulating the ipsilateral side was in general more effective than the contralateral, although occasionally the reverse occurred (Fig. 5.2G and H). The latencies also were 1-3 msec. longer, suggesting extra synapses or less temporal facilitation or spatial convergence.

Changes of segmental reflex excitability evoked over long spinal pathways

Direct discharges only give information about excitatory changes which result in massed firing of groups of motoneurones. A more sensitive index is required to detect the patterns of weaker excitatory changes and also inhibitory changes evoked over the long propriospinal pathways. The influence of electrical stimulation of hindlimb and forelimb nerves was therefore investigated on the transmission of local segmental monosynaptic and polysynaptic reflexes to forelimb and hindlimb motoneurones, respectively.

Monosynaptic reflexes were evoked in forelimb motoneurone pools by stimulation of group Ia fibres within the dorsal columns, and recorded in the central cut ends of the motor nerves (see also McDonald (100)). The stimulus was applied between a remote indifferent electrode in the surrounding muscles and a tungsten electrode in the dorsal columns about two segments above the level of the motor nucleus of the particular motor nerve; e.g. stimulating electrode at C_6, two segments above upper limit of Pmaj nucleus at C_8. The electrode was driven to a depth of about 1 mm since the group Ia fibres occupy an intermediate position in the dorsal columns (123,143). In most of the experiments, including all those illustrated in the figures, the dorsal columns were sectioned at the lower border of C_8 to prevent activity evoked by the dorsal column stimulation being conducted antidromically to lower segments. When the strength of the stimulus of the dorsal columns was increased 3 groups of waves could be distinguished after the stimulus artefact (Fig. 5.3A). The first wave occurred at the lowest stimulus strengths and at a similar latency to the first elevation of the afferent volley at the spinal cord, evoked orthodromically on stimulation of the motor nerve (about 0.7 msec for Pmaj). The first wave was therefore assumed to result from antidromic activation of large, primary afferent fibres in the dorsal columns, including group Ia afferents. The second peak occurred for Pmaj at

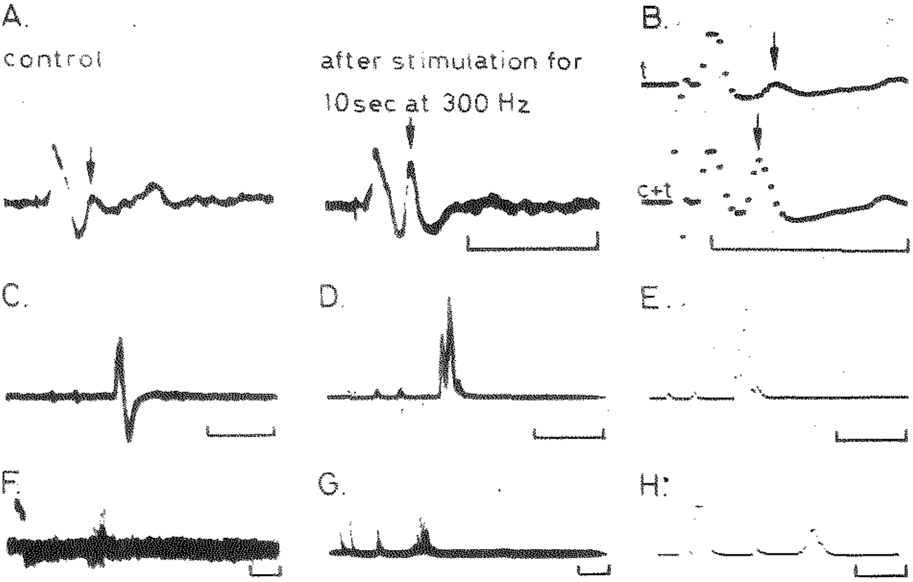


Fig. 5.3. Examples of mono- and polysynaptic reflexes. A; monosynaptic reflex in Pmaj evoked by stimulation of DC. The reflex (arrows) is potentiated after stimulation for 10 sec at 300 Hz. B: facilitation of monosynaptic reflex in Pmaj by iQ; 3 shocks, 10 T, C-T interval 15 msec, 8 samples averaged for each signal; t, test response; C+T, conditioned response. C-E: monosynaptic reflex stimulating Q, 1.5T, recording ventral root, L_7, at the same side; raw (C), rectified (D) and 8 samples averaged (E). F-H: polysynaptic reflex stimulating Sur, 1.75T, recording ventral root, L_7, on the same side; raw (F), rectified (G) and 8 samples averaged (H). At the beginning of each trace a pulse is used for identification. A-H, time scales 5 msec.

about 1.6 msec after the stimulus and was attributed to the monosynaptic activation of the alpha motoneurones (arrowed in Fig. 5.3A). The third wave was irregular and represented polysynaptic activation of the motoneurones. The latency of the second peak (1.6 msec, Pmaj) could be accounted for by a minimum efferent conduction delay of about 0.7 msec and a presumed synaptic delay for the monosynaptic reflex of 0.5-1.0 msec (38). Although the timing mentioned above is in accord with monosynaptic activation of the motoneurones, post-tetanic potentiation of the group Ia synapses (100,146) was used as further confirmation (Fig. 5.3A).

Monosynaptic reflexes in hindlimb motoneurone pools were evoked by stimulating either Ia fibres in hindlimb motor nerves and recording ventral roots or stimulating dorsal roots and recording from the motor nerves. To obtain a larger and more adjustable monosynaptic reflex, two test volleys separated by 1 to 3 msec were often used according to the method of Eccles and Lundberg (37).

The polysynaptic reflexes were evoked by skin or motor nerve stimulation and recorded in motor nerves or ventral roots. All reflexes could be averaged and integrated on-line during the experiment and the integral of the test reflex and the conditioned reflex compared graphically (75). For examples of these techniques see Fig. 5.3.

Changes of excitability in forelimb segmental reflexes through long ascending propriospinal pathways.

On hindlimb nerve conditioning the monosynaptic reflexes to Pmaj and DR were facilitated (Fig. 5.4A and B) with a peak at 15-20 msec C-T interval and a duration of 50-100 msec. Polysynaptic segmental reflexes to both Pmaj and DR were initially facilitated at about 10 msec, then profoundly depressed (Fig. 5.4D), with a peak of depression at about 45 msec and a duration often exceeding 400 msec. All hindlimb nerves tested could produce these effects, irrespective of being flexor or extensor muscle nerves or skin nerves. There were however differences in effectiveness (see Miller et al. ref: 103). Stimulating contralateral nerves gave qualitatively the same but usually less potent results. The early excitatory conditioning effects on DR reflexes are in agreement with the observations of Gernandt and Megirian (46).

The effects of hindlimb nerve conditioning of reflexes to LD were studied in 6 experiments. In contrast to Pmaj, where the conditioning effects were obtained from nerves to flexors and extensors and skin nerves alike, LD received a more definitive reciprocal pattern. Contralateral hindlimb extensor nerves produced a facilitation of both monosynaptic and polysynaptic reflexes, while ipsilateral hindlimb extensor nerves evoked depression (e.g. knee extensor, Q (4 experiments); Fig. 5.4C. Conversely, the knee flexor PBSt (2 experiments) produced ipsilaterally some slight. (about 15%) facilitation, and contralaterally similar slight depression. Ths skin nerves SP and Sur (4 experiments) showed weak effects and no clear pattern; they were not tested on monosynaptic reflexes. At C-T intervals of 15 msec the skin nerves bilaterally evoked predominantly facilitation of polysynaptic reflexes; at intervals of 50 msec predominantly depression.

The median and ulnar nerves were investigated in 22 and 13 experiments, respectively. In the median nerve there was no unequivocal facilitation of monosynaptic reflexes and no depression. Ulnar monosynaptic reflexes were unaltered. Polysynaptic reflexes, evoked by ulnar or median nerves, appropriately, or by the SR, were generally depressed after a C-T interval of about 20 msec with a peak depression at about 50 msec and a time course of 100-150 msec. In comparison with Pmaj the depression of polysynaptic reflexes was less intense and of shorter duration (Fig. 5.4E and F). Slight facilitation (about 20%) of polysynaptic reflexes to M could occasionally be observed (Fig. 5.4E), and this is in agreement with

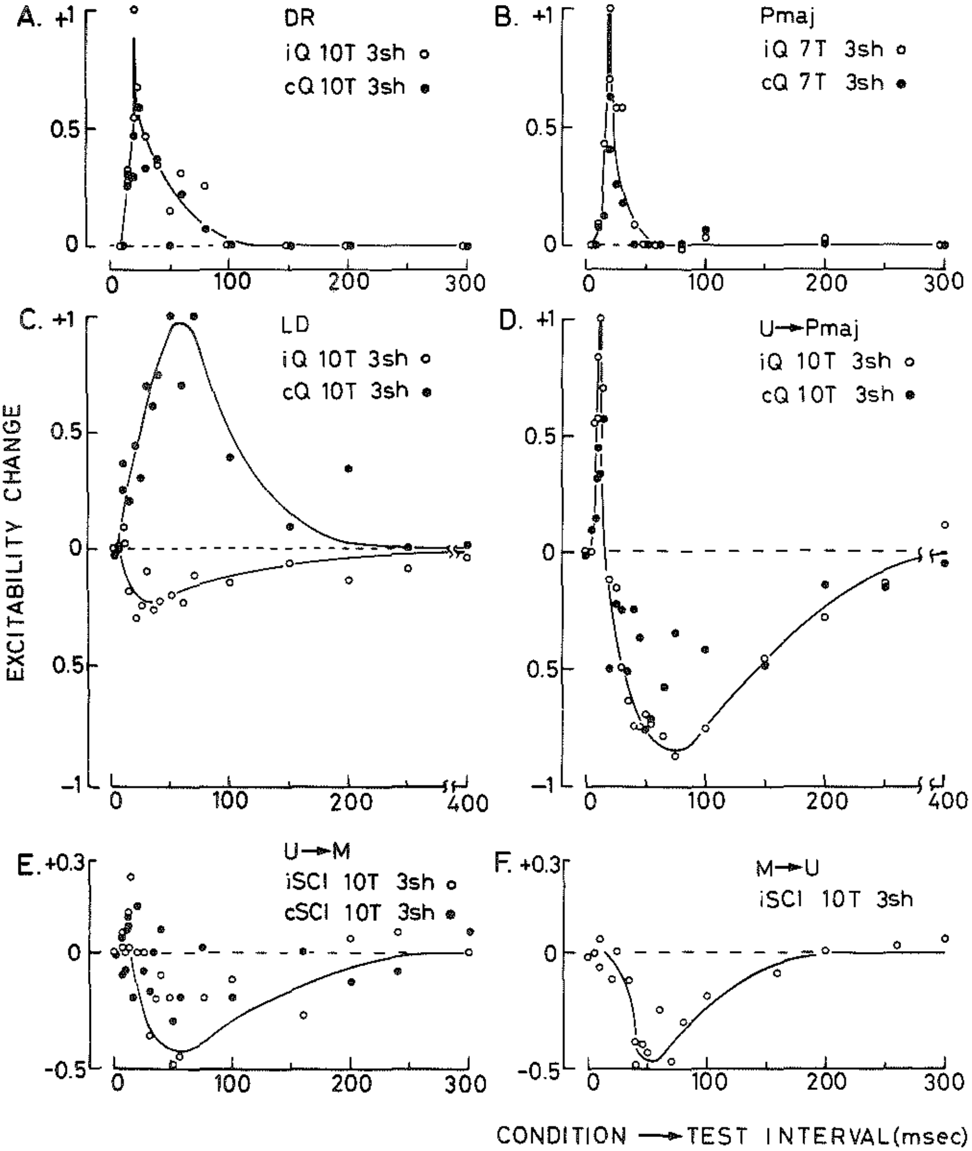


Fig. 5.4. Time course of excitability changes evoked in forelimb reflexes on stimulation of hindlimb nerves. A,B and C: changes in monosynaptic reflexes evoked by stimulation of DC. D,E and F: changes in polysynaptic reflexes evoked by nerve stimulation; in D:U at 2.4 T, in E: U at 1.5T; in F: M at 1.7 T. D same experiment as B. Test responses were generally set at 30-50% of their maximum values. In all graphs the changes of excitability have been estimated by dividing the amplitude of the conditioned response by that of the test response. In the polysynaptic reflexes (D, E and F) only the first

(Legend continued on following page).

peak of the response has been measured. The values of the maximum facilitation in the various graphs ranged from +2 - +5. They have been normalized in the scale of positive excitability changes such that the strongest facilitation for each forelimb motor nerve in each experiment is assigned the value of + 1.0. Zero indicates no change. The depression is scaled such that no change and complete depression are represented by 0 and -1.0, respectively.

the brief and weak facilitation described by McDonald (99,100) to flexor carpi radialis and components of flexor profundus digitorum, which are innervated by the median nerve.

Changes of excitability in hindlimb segmental reflexes through long descending propriospinal pathways

On forelimb nerve conditioning a variety of motor nuclei tested in the lumbar cord, received comparable excitability changes. Below a C-T interval of 10 msec there is usually some inhibition followed by excitation with a peak around 20 msec. After this rather consistent response a more variable phase of inhibition with a peak around 50 msec and excitation around 100 msec can occur. Central latencies between 2.8 and 4.8 msec for the earliest excitation and inhibition are suggestive of mono- or disynaptic

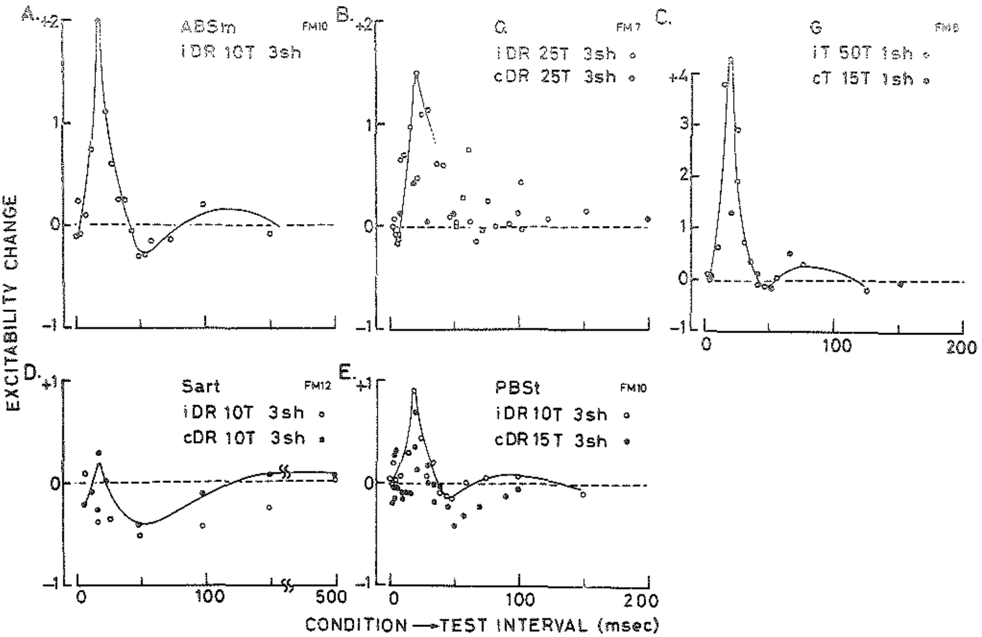


Fig. 5.5. Time course of excitability changes evoked in hindlimb monosynaptic reflexes on stimulation of forelimb nerves; 8 trials each of test and conditioned responses were averaged and integrated. The integral of the conditioned response was compared with the integral of the test response. Zero indicates no change, positive value excitation and negative value depression with reference to the test reflex.

activation of lumbar motor neurons by long propriospinal fibres as Jankowska et al. have recently shown with intracellular recordings (84). This pattern was in general more pronounced in the extensors tested, ABSm, Q and G, in 4,3 and 5 experiments, respectively, (Figs. 5.5A,B and C). The flexors, Sart and PBSt, showed a similar wave form of excitatbility changes but less pronounced, in 2 and 3 experiments (Figs. 5.5D and E). The facilitation of flexors and extensors about a C-T interval of 20 msec. is in agreement with the findings of Lloyd and McIntyre (93) and the excitability changes of G is in agreement with Djalali (32).

Polysynaptic reflexes in the lumbar segments are depressed by forelimb nerve conditioning, although occasionally an initial phase of excitation was observed in PBST (Fig. 5.6)

All forelimb nerves tested (CIB,DR,M,SR,SSc,T and U nerves) could evoke the described effects; DR and SR, however, were very consistently effective. On stimulating the contralateral forelimb nerves, less potent effects were usually evoked, although this difference was less marked compared with the ascending propriospinal pathways (see above).

A considerable variation of these effects between experiments was observed, although the main features of the temporal course of the excitability changes could be recognized in all experiments. The initial inhibition to ABSm for example could vary considerably

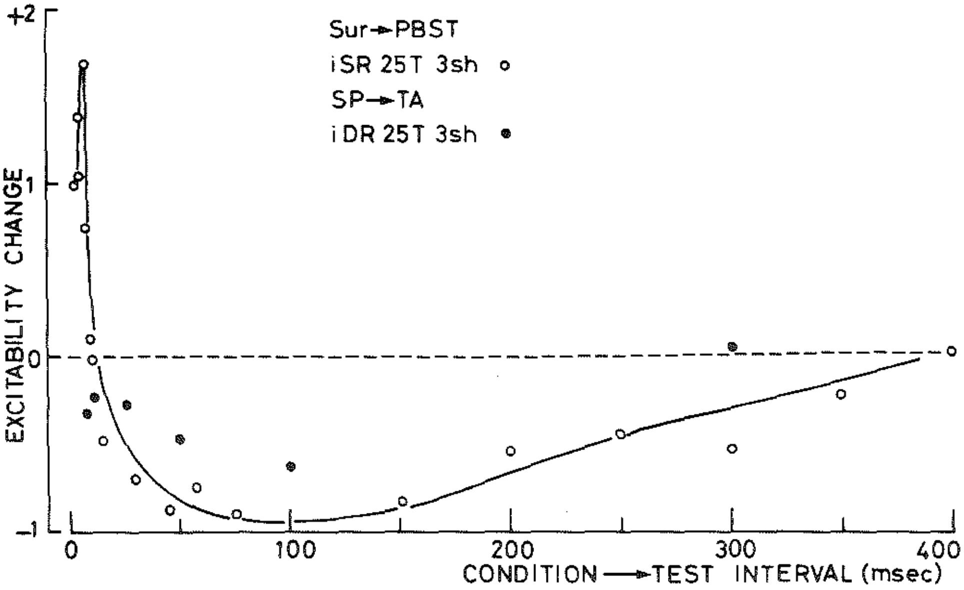


Fig. 5.6. Time course of excitability changes evoked in hindlimb polysynaptic reflexes on stimulation of forelimb nerves. The complete reflex has been averaged and integrated; Sur at 1.75T; SP at 2.0T (See Fig. 5.5. for further details).

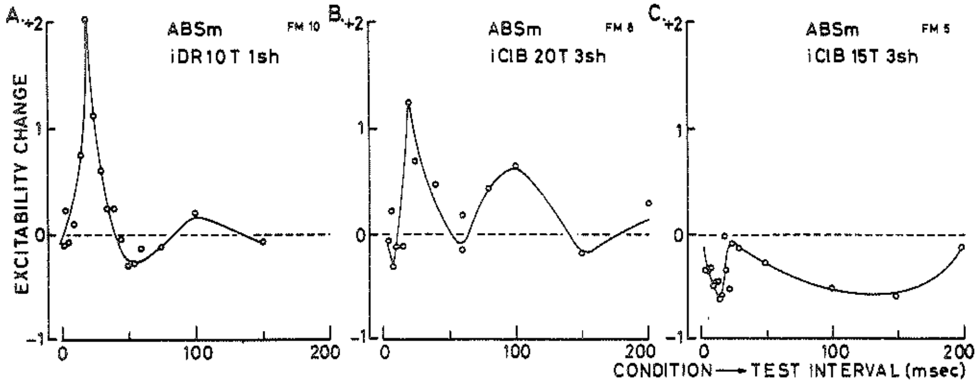


Fig. 5.7. Time course of excitability changes evoked in ABSm monosynaptic reflexes on stimulation of forelimb nerves. (See for further details Fig. 5.5.).

(Fig. 5.7A-C) and the facilitation around 20 msec could even disappear (Fig. 5.7C), leaving only an suggestion of the facilitatory process. These observations suggest that long descending propriospinal pathways may evoke mixed excitatory and inhibitory effects in these motoneurone pools which may vary in strength during and between different experiments (see further discussion).

In conclusion: excitatory and inhibitory effects are evoked through the long ascending and descending propriospinal pathways, possibly superimposed upon each other. In the ascending direction reciprocal effects were evoked only in LD motoneurones from flexor and extensor hindlimb muscle nerves. This was not observed at all in the descending direction. In the ascending direction hindlimb muscle nerves were slightly more effective than skin nerves in evoking facilitation or depression. In the descending direction there were no clear differences.

Afferent fibres responsible for facilitation and inhibition over long propriospinal pathways

By means of graded electrical stimulation the threshold for facilitation and depression were determined in various nerves in both the ascending and descending direction. In 10 experiments hindlimb nerves (ABSm, G, PBST, Q, Sart, SP, Sur, bilaterally), and in 5 experiments forelimb nerves were investigated (ClB,DR,SSc and SR, bilaterally. Not all nerves were taken in each situation. The C—T intervals for each graph were selected appropriately with respect to the maxima of facilitation and depression in all experiments. Below 2T for muscle nerves no consistent excitability changes were observed. Above this stimulation strength either facilitation or inhibition was observed depending on the C—T interval. A plateau was reached for both facilitation and inhibition between 5 and 10T (Fig. 5.8 and 5.9 for ascending and descending

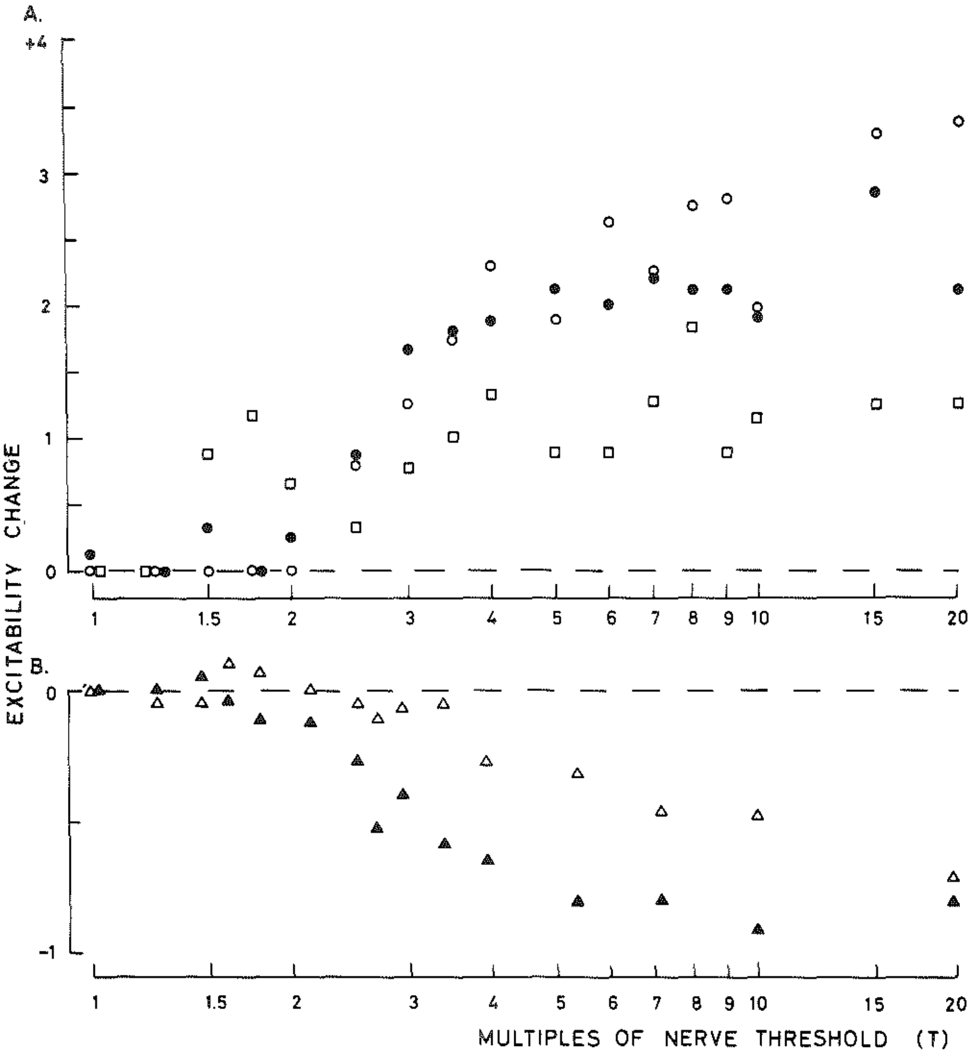


Fig. 5.8. Input-output relations of hindlimb nerve conditioning of forelimb reflexes. A: facilitation of Pmaj monosynaptic reflex. Open circles iQ, filled circles cQ, open squares iSP. Hindlimb nerves 3 shocks, C——T interval 20 msec. B: depression of U to M reflex (open triangles) and U to Pmaj reflex (filled triangles) by iQ: 3 shocks, C——T interval 50 msec.

direction,respectively). This implies that most of the effects are mediated by group II muscle afferents.

Sometimes the increase of either facilitation of inhibition did not follow a smooth, progressive curve (Fig. 5.9A, filled circles at 2 to 4T). At 3T the reflex is in fact depressed by about 40% In other experiments there was no depression at this point and the facilitation was detectable at 2 to 3T. This suggests either that

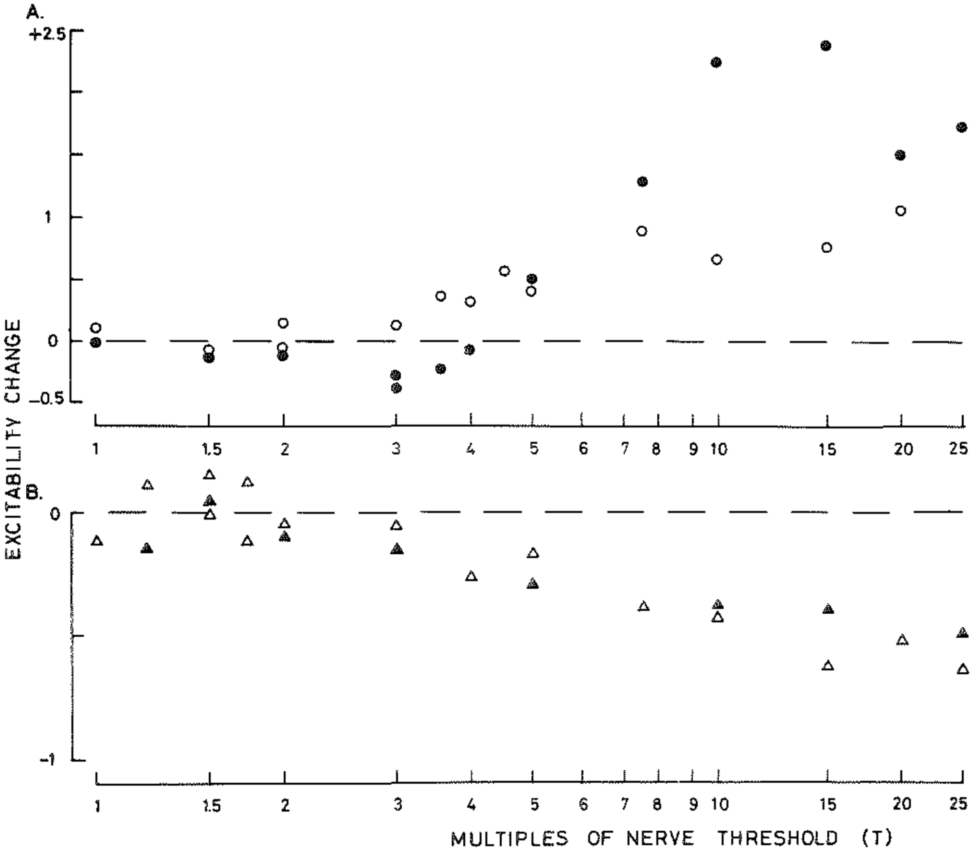


Fig. 5.9. Input-output relation of forelimb nerve conditioning of hindlimb reflexes. A: facilitation of Q (open circles) and PBST (filled circles) monosynaptic reflexes by iDR, C——T interval 20 msec, 3 shocks. B: depression of polysynaptic SP to PBSt reflex by iDR (open triangles) and cDR (filled triangles), C —— T interval 40 msec, 3 shocks.

different fibres can exert different actions or that centrally the balance between excitation and inhibition is in some way dependent on the intensity of the afferent information. From skin nerves effects were usually obtained between 1,5 and 2,0T and generally reached a plateau at 3T, for both facilitation and depression in the descending and ascending directions (Fig. 8A, open squares). The results presented here for the descending direction are in accordance with the results of Lloyd and McIntyre (93) and Djalali (32).

The effects of L-DOPA on transmission in long descending propriospinal pathways

Monoaminergic reticulospinal pathways terminating predominantly in the cervical and lumbar enlargements of the spinal cord have been demonstrated by fluorescence microscopy to contain either noradrenaline or 5-hydroxytryptamine (in the rat (24,29)). The noradrenergic terminals in the spinal cord may be selectively activated by intravenous injection of the cat catecholamine precursor DOPA, L-3,4-dihydroxyphenylalanine (6). This results in profound changes of reflex excitability in lumbo-sacral segments, in particular a depression of short latency reflex responses in motoneurones, evoked by the flexor reflex afferents (FRA), and an unmasking of a prolonged, long latency reflex discharge evoked by the same afferents (6,81). It was suggested that these long latency reflex responses might reflect the activity of mechanisms involved in the control of stepping, and further support for this hypothesis has been obtained in mesencephalic (63) and spinal cats (43). It was also concluded that the noradrenergic reticulospinal pathway is involved in the initiation and maintenance of locomotion. Bergmans et al. (13) described long lasting discharges in Pmaj and DR motoneurons on stimulation of hindlimb nerves after intravenous injection of L-DOPA. They considered these reflex changes to reflect activity in neuronal systems involved in the control of stepping.

In 3 experiments, therefore, a study was initiated to determine the effect of L-DOPA on the transmission of descending propriospinal pathways. In all 3 experiments long lasting discharges have been observed in hindlimb motoneurone pools following forelimb

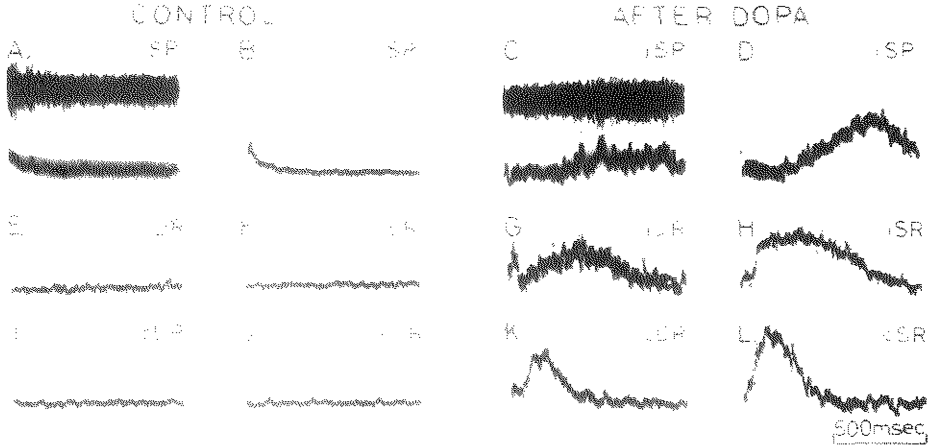


Fig. 5.10. Discharges evoked in PBSt. A-D: on stimulation of SP, 5T, 3 shocks; A and B before C and D after DOPA. A and C: top: raw response; below: response rectified and filtered with a time constant of 30 msec. B and D: 16 rectified and filtered samples averaged. E-L: discharges in PBSt on stimulation of different forelimb nerves, 25T, 3 shocks. E,F,I and J before and G,H,K and L after DOPA; the traces represent averages of 16 samples. The stimulus is given at onset of each trace.

nerve stimulation, lasting often over 700 msec. Both ipsilateral and contralateral muscle and skin nerves were effective. In 2 experiments recordings were made from ventral roots, and in one experiment only could the activity be related to flexors and extensors. Figs. 5.10E-L give examples of this experiment where the flexor PBSt and not the extensor ABSm was activated from ipsilateral and contralateral forelimb nerves. As in the ascending pathways the early discharge at 12-25 msec is unmasked or enhanced and the late discharge occurs at approximately 50-100 msec. The early discharges evoked at the lumbar segmental level (Fig. 5.10A-D) is depressed after DOPA and the late response appears after a delay of 50-200 msec. This is in agreement with the experiments of Andén et al. (6).

Location of long propriospinal fibres in the spinal cord

As Lloyd (92) has pointed out the fibres mediating effects between the cervical and lumbar enlargements are so "diffuse and dispersed that the experimental approach by the use of microelectrodes has failed to yield significant results". Therefore many investigators have used the method of selective lesions. The ascending effects described in this chapter are mediated at the thoracic level mainly via the ventrolateral fasciculus although part of the ventral funiculus could not be entirely excluded (see further Miller et al. Ref. 103). Under L-DOPA, however, it is possible to evoke long discharges in forelimb motoneurone pools by stimulating the ventral quadrant at mid-thoracic levels (13). This is also consistent with the anatomical experiments of Sterling and Kuypers (138), who demonstrated that in the brachial segments long propriospinal fibres were mainly located in the ventrolateral and ventral funiculi. The descending effects reported in this chapter are greatly depressed, but still present if only the ventral funiculi are spared indicating, that both the lateral and ventral funiculi are involved. This is in agreement with Lloyd's (92) findings, who also mentioned, that the ventral funiculi were especially involved in the mediation of bilateral effects. Only fibres in the lateral funiculus, however, mediate mono- and disynaptic effects (84,144). The ascending and particularly the descending effects are exerted bilaterally and this is in agreement with anatomical studies (48,138). Molenaar and Kuypers (110) have demonstrated using the retrograde horseradish technique that the cell bodies of these long propriospinal fibres, both ascending and descending, are located mainly in the ventromedial part of the intermediate zone. A large proportion of these cells, especially in the descending direction are located contralateral to the location of the fibres. This recent anatomical evidence together with earlier neurophysiological studies (46,92,103) emphasize the reciprocity of the long fibres connecting the segments innervating each limb. The possibility that some of the effects are conducted by chains of shorter fibres should not be neglected (13,48,103,138).

In conclusion, the long propriospinal fibres are located in the ventrolateral and ventral funiculi. Fibres in the ventral funiculi also exert their effects bilaterally. There is a reciprocity of long fibres connecting the segments innervating each limb.

DISCUSSION

As part of the study of interlimb coordination the functional organization of the propriospinal connections between the lumbar and cervical enlargements has been investigated. In both the ascending and descending direction strong effects are mediated by these pathways, often strong enough to elicit discharges in the motoneurones (41 and 80% of the experiments, respectively). Excitatory and inhibitory changes in reflexes to different groups of motoneurones were also observed after stimulation of nerves in the remote girdle.

In the ascending direction the direct excitation and the facilitation of mono- and polysynaptic reflexes evoked by hindlimb nerves is distributed predominantly to the physiological flexors of the forelimb: to Pmaj and the muscles innervated by DR (the present study, and after DOPA, Ref. 13); to biceps and deep radial nerve (99,100). By contrast, amongst the physiological extensors (muscles innervated by M and U nerves in this study; triceps brachii in the studies of McDonald, Ref. 100; and Bernhard and Therman, Refs. 14 and 15) hindlimb nerve stimulation predominantly evokes depression of segmental reflexes. In mediating the facilitation and depression the ipsilateral nerves were usually more effective than the contralateral, and muscle nerves sometimes more effective than those from skin. The conditioning of LD, also an extensor, showed a reciprocal pattern (Fig. 5.4C) with facilitation from ipsilateral flexors and inhibition from ipsilateral extensors, and a reverse pattern from the contralateral side.

In the descending direction direct excitation and modulation of segmental reflexes are distributed to both extensors and flexors. Extensors are more strongly influenced than the flexors (present study and Refs. 32,33 and 93). Here also contralateral nerves are effective and the difference between ipsi- and contralateral effects even less pronounced (cf. Ref. 93). The classical excitability changes are a short period of slight inhibition followed by excitation with a peak at about 20 msec, followed more variably by inhibition maximal at 50 msec and a further phase of excitation. Polysynaptic reflexes are sometimes initially facilitated but always characterised by a long period of depression. Djalali (32) has demonstrated that this depends upon presynaptic mechanisms.

The degree of facilitation and inhibition of the monosynaptic hindlimb reflexes varied considerable between experiments (Fig. 5.7). It was already suggested in the Results section that this could be produced by a balance of excitatory and inhibitory influences. From intracellular studies it is known that flexor and extensor motoneurones can receive mono- or disynaptic excitatory and inhibitory postsynaptic potentials (83,84), confirming this suggestion for the initial excitability changes. With reference to the later changes Djalali (32,33) has shown, that the inhibition of the monosynaptic reflexes is of a postsynaptic nature; when this inhibition was blocked with strychnine, not only did the phase of inhibition disappear, but the phase of excitation was increased in parallel in both strength and duration, suggesting further the superimposition of facilitatory and inhibitory mechanisms. This could also explain the occurrence of preparations displaying different states of excitability as described by Lloyd (92).

The fibres involved in both the ascending and descending direction are mainly group II muscle fibres and low threshold skin fibres. Group III muscle fibres can also contribute to the effects and in a single experiment group I muscle fibres could not be excluded (cf. Ref. 103). There was not always a gradual increase of the effects by increasing the stimulus. Sometimes the reversed action was seen at low intensity compared with high intensity stimuli (Fig. 5.9). This indicates either that different fibres produce different effects, or that at low intensity stimulation the balance between inhibition and excitation is still unstable.

In comparison with the long propriospinal pathways the short crossed connections between the two lumbar halves are also able to produce strong excitatory and inhibitory changes to both extensor and flexor motoneurones, as shown by Holmqvist (76). Furthermore, by making successive lesions caudally in the brainstem she revealed a differential supraspinal control of the inhibitory and excitatory effects. First the crossed inhibition appears, replaced after a more caudal lesion by a massive crossed excitatory effect.

Although long ascending (103) and descending (84) propriospinal pathways can exert their excitatory effects monosynaptically, it should not obscure the more complex and polysynaptic organization of the long connections between different functional regions of the spinal cord revealed by anatomical (48,110,138) and physiological (13,84,100,103) studies. Recent studies have revealed both convergence of short crossed and long propriospinal influences on interneurones (83) and radiation of projections from groups of interneurones in one spinal enlargement bilaterally to comparable regions in the other enlargement (110).

It is, therefore, likely to be of more relevance functionally to consider the direct or indirect connections between lumbosacral and brachial segments as *intrinsic links between the spinal motor centres controlling the hindlimb and forelimb* (see Refs. 103, 105,107). Studies in various vertebrates and insects indicate that coordinated stepping of the limbs may occur in the absence of afferent feedback from peripheral receptors, and that the basic neural programmes responsible for this activity are laid in the neuraxis (61,64,107,113,115,147,148). The role of afferents may be to provide optimal regulation of the ongoing movements as they are elaborated by the central programmes (19,94) (for review see Grillner, Ref. 62). Within this concept of the control of movement, propriospinal pathways would serve primarily as coordinative links between the intrinsic activities of the segmental neuronal systems controlling the limbs, trunk and neck.

Transmission in the pathways would also be expected to be powerfully influenced by supraspinal centres, as has been shown for segmental reflexes and various ascending pathways (8,78,94,95,102, 112). Further, convergence of corticospinal and rubrospinal fibres upon propriospinal cells giving rise to long descending fibres located in the cervical cord has been demonstrated recently (79). It is also of considerable significance that the transmission in both ascending (13) and descending propriospinal pathways can be strongly influenced and modulated by L-DOPA, a drug which imitates the action of noradrenergic reticulospinal pathways, which have been considered to be involved in the initiation of locomotion (43,63).

It is striking that the same excitability changes in hindlimb motoneurone pools are described after a variety of other sensory stimuli, e.g. auditory (149), visual (139), vestibular (26,71), tactile (86) as well as to direct reticular formation stimulation (25). Wright and Barnes (149) even describe the same variation of the effects on auditory stimuli as has been described here for the descending propriospinal effects. These effects are involved in the "startle" response (89,124,149) and have, as reviewed by Thomas (141), elements in common with the spino-bulbo-spinal reflex (135, 136,142) and the "chloralose jerk" phenomenon studied extensively by a number of investigators (4,5,10,22,23,30,31,135,136). These effects are mediated through the medullary and pontine medial reticular formation (141,149), although on vestibular stimulation the effects are in part produced by the vestibulospinal tracts (71). A reciprocal effect has also been described. Stimulation of lumbar dorsal roots gives rise to initial excitation followed by depression of reticulo-spinal neurones (116) similar in sign and timing as that described here for the lumbar monosynaptic reflexes. On anatomical grounds Kuypers (88) has claimed that the medial reticular formation forms a continuous neural column with the ventromedial part of the intermediate zone of the spinal grey matter. It receives the same distribution of the descending pathways and sends its fibres into the same funiculi. It is interconnected throughout its course from sacral segments to pontine levels. Taking these observations together, it seems that irrespective by what sensory system an experimental stimulus is transmitted to this "column" it produces approximately the same sequence of excitability changes in the lumbar cord, in particular under the immobilised condition of the preparations. It is therefore suggested that startle reflexes, chloralose jerk, spino-bulbo-spinal and long spinal reflexes represent components of one, heavily interconnected system.

SUMMARY

In high spinal cats propriospinal pathways linking the lumbosacral and cervical enlargements can mediate strong excitatory and inhibitory effects to different pools of motoneurones.

In the ascending direction monosynaptic reflexes to pectoralis major and deep radial motoneurones supplying the physiological flexor muscles were strongly facilitated by hindlimb nerve stimulation, ipsilateral nerves being more effective than contralateral. Monosynaptic reflexes to latissimus dorsi, a physiological extensor, showed a reciprocal pattern of conditioning, being depressed by ipsilateral and facilitated by contralateral hindlimb extensor nerves, the flexor nerves giving the reverse pattern. Monosynaptic reflexes to median and ulnar nerves supplying distal physiological extensor muscles were not significantly affected by hindlimb nerve conditioning.

Polysynaptic reflexes to pectoralis major and deep radial motoneurones received initial, strong facilitation followed by prolonged depression, ipsilateral hindlimb nerves being more effective than contralateral. In latissimus dorsi a reciprocal pattern similar to that for monosynaptic reflex testing was found. Polysynaptic reflexes to median and ulnar motoneurones received only prolonged depression.

In the descending direction monosynaptic reflexes to physiological flexors and extensors are strongly influenced by long propriospinal pathways. After an initial inhibition a period of excitation follows with a peak around 20 msec. After this, there is a more variable period of inhibition, with a peak at 50 msec and a second period of excitation with a peak around 100 msec. Superimposition of parallel processes of excitation and inhibition has been suggested to account for the variation of responses within and between preparations. Polysynaptic reflexes to flexor nerves were depressed, although PBSt was sometimes initially facilitated. All excitatory and inhibitory effects were obtained from ipsilateral and contralateral forelimb nerves, the ipsilateral nerves usually being more effective.

The afferents responsible for the effects in ascending and descending direction include group II and to a lesser extent group III muscles afferents and group II skin afferents. The hypothesis is suggested, that long propriospinal paths primarily represent intrinsic links between the segments generating locomotor movements in the hindlimbs and forelimbs.

The similarity between propriospinal reflexes and reflexes mediated by the medial reticular formation is discussed.

CHAPTER 6.

REVERSAL OF REFLEXES BETWEEN HINDLIMB AND FORELIMB DEPENDENT ON THE PHASE OF THE STEP CYCLE.

INTRODUCTION

In Chapter 5 it was shown that activation of in particular long descending propriospinal pathways in high spinal cats results in varying mixtures of excitatory and inhibitory effects in lumbosacral motoneurones. The evidence was obtained from reflex studies (see Chapter 5) and from intracellular investigations (84,144). In some preparations the balance of the effects lay towards excitation and in others toward inhibition. Bergmans, Miller and Reitsma (13) showed that certain excitatory effects could be unmasked by injection of the preparation with L-DOPA or by stimulation of an as yet unidentified pathway lying in the ventral funiculus at C_1. The effects with L-DOPA injection were particularly interesting since this manoeuvre mimics the activity of a noradrenergic reticulospinal pathway involved in the initiation of locomotion (42,63).

Apart from latissimus dorsi no other motor nuclei in either of the spinal enlargements have been shown to receive reciprocal excitatory or inhibitory effects over long propriospinal pathways following peripheral nerve stimulation (Chapter 5). This is unexpected since spinal connections can evidently mediate the coordination of the flexor and extensor periods of hindlimbs and forelimbs during locomotion (Chapter 4).

Electrical stimulation of distal skin nerves was effective in most high spinal preparations in eliciting excitatory and inhibitory responses in motoneurones over long propriospinal pathways. This type of stimulation was therefore repeated, not in the immobilized high spinal cat, but in the decerebrate cat during locomotion, to test if the long spinal reflexes might be reversed in sign according to the phase of the step cycle.

Reflex reversal dependent on the phase of the step cycle has been described since these experiments were started for tactile placing in the chronic low spinal cat (43), cutaneous reflexes in the hindlimb in thalamic cats (34) and startle reflexes in normal human subjects (124). There is also a brief and incomplete report on the reversal of the hindlimb flexion reflex in thalamic cats and normal human subjects and hemiplegic patients (91).

METHODS

The experiments were performed on 13 cats decerebrated at precollicular, mammillary level under Fluothane anaesthesia by the method described in chapter 2. The cats were placed on a motor driven treadmill in a normal posture for locomotion. The weight of the body was partially born by a headholder and by strings attached to the lumbar fascia and the spine of C7. All of the cats used stepped spontaneously, following the velocity of the treadmill and did not require electrical stimulation in the mesencephalon to elicit locomotion (132). Experiments were also performed on the four high spinal cats described in Chapter 4.

Electromyograms (EMGs) were recorded from hindlimb and forelimb muscles by the method of Engberg and Lundberg (39). The muscles included T, Bi, Pmaj and LD in the forelimbs and PB, AB, Q and Sart in the hindlimbs. The bipolar electrodes were made of enamelled copper transformer wire of 150 µm diameter. A reliable index of correct electrode placement was obtained if palpable contraction of the respective muscle occurred on stimulation of each electrode with pulses of 1 msec duration, at 5 Hz and at currents below 500 µA. The EMGs were high pass filtered at 30 Hz (-3dB) and recorded on magnetic tape. After full wave rectification the EMGs were written out off-line on paper and in some cases averages were computed after low pass filtering at 100 Hz (-40 dB) (70). 16 mm films were also made of each cat to check the type of gait, but these were not synchronized with the EMG recording.

Electrical stimuli were applied to the skin or to exposed cutaneous nerve trunks in the limbs at varying times within the step cycle by the use of a delay triggered from one of the EMGs. A pulse corresponding to the end of the delay was stored in one channel of the tape recorder and the stimulus was fed to another channel. By this means the point of occurrence of the stimulus in the step cycle could be determined for comparison with that of the preceding step. For skin stimulation the stimuli were applied through bipolar electrodes over the dorsum of the forepaw, and hindpaw. The electrodes consisted of two 5 mm convex brass discs glued at 20 mm centres onto the skin with celloidin. Electrode paste was injected through a central hole in each disc. For nerve trunk stimulation the superficial peroneal nerve in the hindlimb and the superficial radial nerve in the forelimb were exposed by a small skin incision. The cut end of each nerve trunk was then drawn into a 15 mm plastic tube in which two rings of platinum wire had been set 8 mm apart for electrical stimulation. The tube was then stitched to surrounding fascia and the electrode wires were brought to the outside through the skin incision. With both types of stimulation 3 - 5 current pulses at 300 Hz, of 1 msec duration and 1-10 mA were given generally every fourth step. The effects on the EMGs obtained in the step cycle where the stimulus occurred were compared with those of the preceding step.

The following abbreviations are used: Bi biceps brachii, LD latissimus dorsi, Pmaj pectoralis major, T triceps, AB biceps femoris anterior, Q quadriceps femoris, PB biceps femoris posterior, Sart sartorius, EMG electromyogram.

RESULTS

Type of gait analyzed

In all the experiments the gait spontaneously adopted in response to movement of the treadmill was almost exclusively an alternate gait with an out-of-phase homolateral limb coupling (e.g. the type most commonly seen in fast walk and trot, chapter 4). The velocities used were in the range 0.3 to 1.5 m/sec but for most tests the range 0.6 to 1.0 m/sec was used. No attempt was made to analyze in-phase gaits as it is difficult to detect small stimulus linked changes against the large, peaky signals of the EMG in the gallop.

Influence of stimulation of skin on dorsum of the foot in EMGs in the limbs

Electrical stimulation of the skin on the dorsal surface of the forepaw evokes changes of activity in the flexor and extensor EMGs of the ipsilateral hindlimb (Fig. 6.1). In each case the vertical bar indicates the onset of the stimulus and the dot indicates the equivalent moment in the preceding step. Short trains of stimuli were selected rather than trains lasting up to 300 msec (34) to provide stimuli comparable to those used in the neurophysiological experiments on long propriospinal pathways and to enable reliable estimates to be made of the latencies of the changes evoked in EMG activity.

The criteria for excitation were an increase of at least 50% in amplitude of the current EMG lasting at least 15 msec and occurring within 30 msec of the stimulus. Inhibition of EMG activity could only be detected during the period of activity of the muscle. The criteria adopted here were a reduction of the EMG, for a period of more than 15 msec starting within 30 msec of the stimulus, to less than 50% of its current value. Abolition of the EMG to baseline levels at the beginning and end of the period of activity of the EMG, predicted from the preceding step, was also considered as inhibition if it occurred within 30 msec of the stimulus.

Figure 6.1B shows an example of the effects evoked by stimulating the forelimb at 10 mA. If the stimulus is applied during the hindlimb extensor activity (quadriceps, row 2) there is clear excitation. Similarly, if the stimulus is applied during the hindlimb flexor activity (sartorius, row 3) it is the flexor which is excited. All these excitatory effects are brief. There is no disturbance of the rhythm of stepping nor interruption of locomotor movements detectable from the films in the limbs distant to the

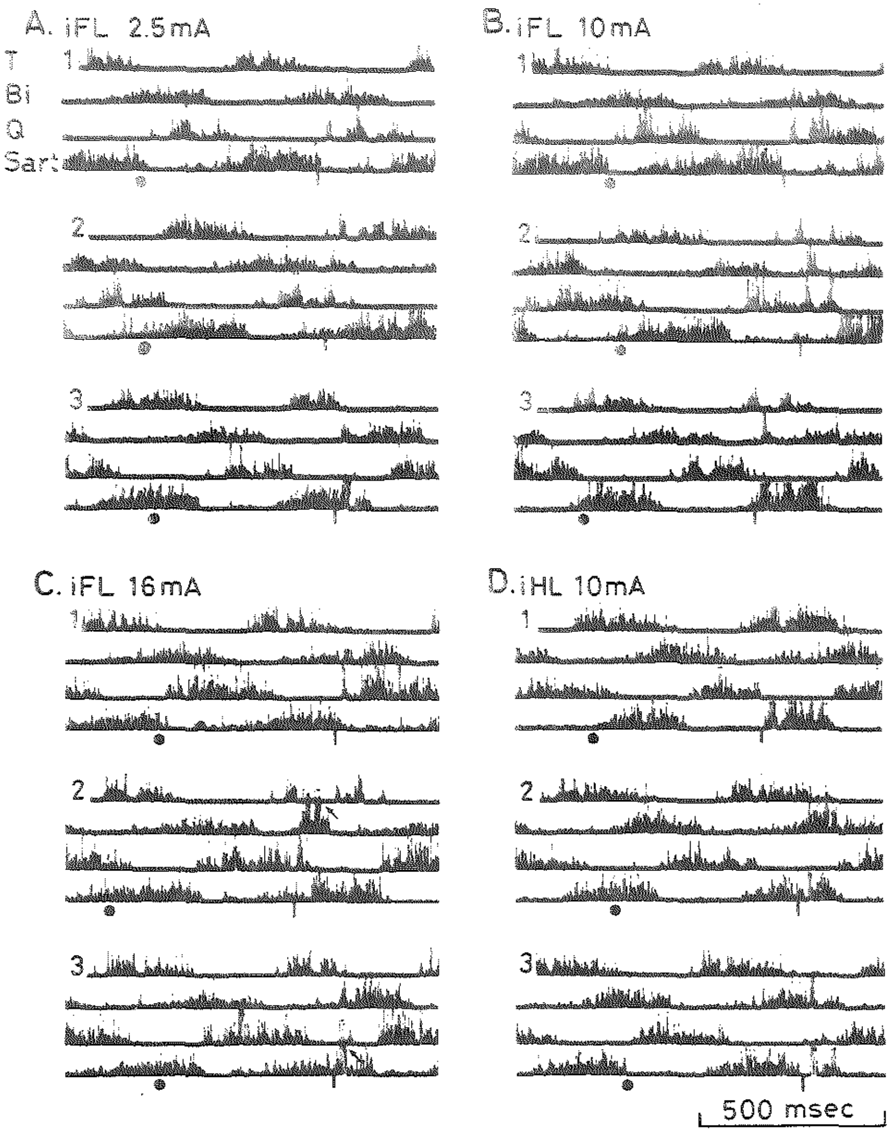


Fig. 6.1. Effect of electrical stimulation of the skin on the dorsal surface of the forepaw or hindpaw on the EMG activity of flexor and extensor muscles in the ipsilateral hindlimb and forelimb. Decerebrate cat stepping at 1.0 m/sec. The stimulus is indicated by a vertical bar, the corresponding point in the preceding step by a filled circle. The stimulus consists of 3 pulses at

(Legend continued on following page).

the currents indicated and is applied to the forelimb (iFL) in A,B and C and to the hindlimb (iHL) in D. Small arrows indicate places where the response in the lower trace overshoots the baseline of the trace above.

stimulus. Inhibition was observed in 3 experiments and then only when the activity of muscle overlapped with that of its antagonist. This is illustrated in Fig. 6.1B, row 2, where inhibition of sartorius occurs reciprocally with excitation of quadriceps. It was always the extensor activity which was enhanced and the flexor activity which was depressed; the reverse did not occur. The reciprocal effects in flexor and extensor EMGs during their period of overlap is important since it is the only indication of the inhibition of activity in one muscle during excitation of the other.

In some cases the threshold for excitatory effects was between 1 and 2 mA and clear effects could generally be observed at 2.5 mA (Fig. 6.1A). Raising the stimulus current led to an increase in the magnitude and duration of the excitatory and inhibitory effects, but it did not alter their pattern or sign (Figs. 6.1A,B and C). With currents between 2.5 and 10 mA consistent effects could be evoked in all experiments (Figs. 6.1A and B). When the stimulus current was still further increased a ringing effect with periods of alternating activity at about 12 Hz could sometimes be observed in the antagonist muscles (Fig. 6.1C, row 3, Q and Sart).

Electrical stimulation of the skin on the dorsal surface of the hindpaw evoked similar excitatory changes in the forelimb muscles as described above for those in the hindlimb. If the

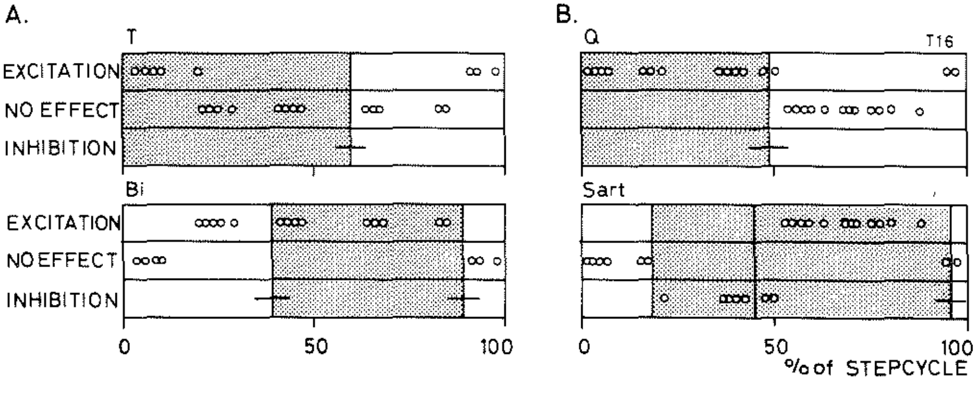


Fig. 6.2. Distribution of excitatory and inhibitory effects. The step cycle has been normalized and expressed as a percentage. Stippled areas indicate averages of the periods of EMG activity in the step preceding the stimulus. Horizontal bars indicate standard deviation. The vertical line within the stippled area of Sart indicates where activity was invariably present. The area at the left represents, therefore, a period where activity did not always occur. A. Stimulation of the skin of the ipsilateral hindpaw with 3 shocks at 10 mA. B. Stimulation of the skin of the ipsilateral forepaw with 3 shocks at 10 mA. Same experiment as Fig. 6.1.

stimulus fell during the activity of an extensor (e.g. T, Fig. 6.1D, row 1) excitation occurred. Similarly, stimulation during flexor activity also evoked appropriate excitation (e.g. Bi, Fig. 6.1D, row 2). Clear inhibitory effects have not been observed although reciprocal bursts of activity often occur (Fig. 6.1D, row 1). Despite the lack of inhibition there were often examples of excitation to one muscle together with lack of extra activity to its antagonist, e.g. Bi and T in Fig. 6.1D, row 2.

The distribution of the effects within the step cycle is shown in the diagrams of Fig. 6.2. Excitatory effects occur in general throughout the period of EMG activity (stippled zone) and during the last part of the inactive period of the muscle. Triceps is not excited throughout its period of activity but the periods of excitation alternate in a remarkably tight reciprocal pattern between the pair of antagonist forelimb muscles (Fig. 6.2A). The excitation is generally spread over a greater proportion of the step cycle to flexors of the forelimb. Sartorius is inhibited during the period in which its activity overlaps with that of quadriceps.

When the stimulus was applied to different regions of skin in the limb the pattern and the sign of the responses were the same as those already described (Compare Figs. 6.1 and 6.3. which are from the same cat). The only difference was that stimulation of the

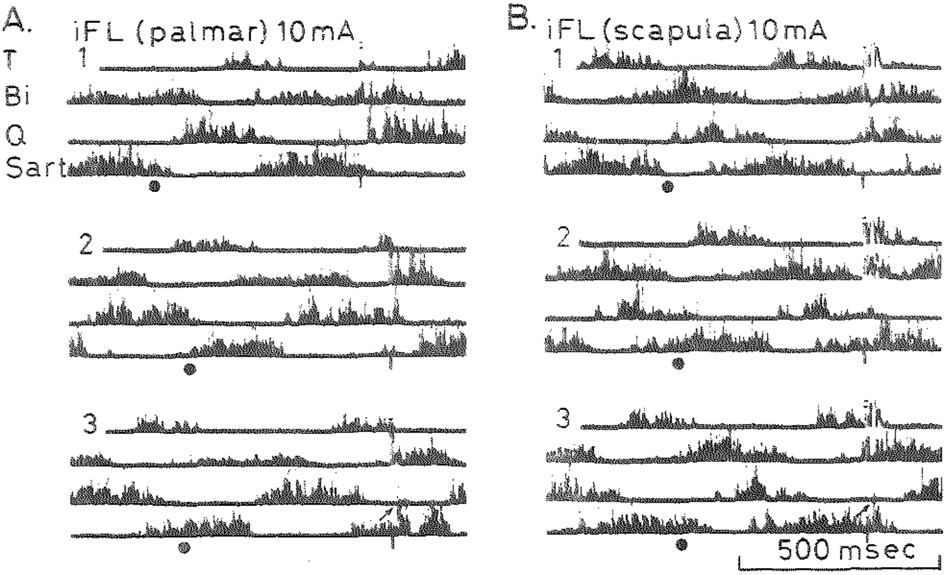


Fig. 6.3. Effect of electrical stimulation of the skin on the palmar side of the forefoot and over the scapula on the EMG activity of muscles in the ipsilateral hindlimb and forelimb. Same experiment as Fig. 6.1. For further details see legend of Fig. 6.1.

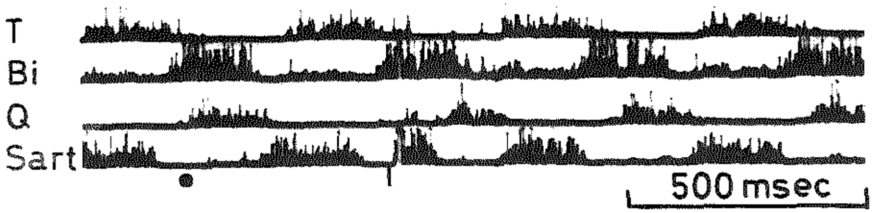


Fig. 6.4. Effect of stimulation of skin of hindpaw on EMG activity in the ipsilateral hindlimb and forelimb. Stimulus is 3 shocks at 10 mA. Same experiment as Fig. 6.1. For further details see legend of Fig. 6.1.

proximal areas of skin, for example over the scapula as in Fig. 6.3, resulted in less marked responses.

Within the limb stimulated the effects evoked in the EMGs followed the pattern of the flexion reflex, which might be expected considering the noxious intensity of stimulation used (24,128,130). The flexion reflex could in fact be strong enough to disrupt the step cycle of the limb stimulated (Fig. 6.4). Despite this the rhythm of the ipsilateral forelimb is hardly disturbed.

In five experiments the EMGs were averaged to obtain more precise estimates of the excitatory effects and estimates of the latencies. In this procedure the EMGs of the step cycle conditioned with the stimulus were compared with those of the preceding test step. Fig. 6.5 illustrates results obtained in one experiment from Sart on stimulation of the skin on the dorsum of the forepaw. The upper two rows in A,B and C show the EMGs of the control and the stimulated step, respectively, at three different points in the step cycle, as arrowed in D. Row 3 of A,B and C shows the responses of the stimulated step on an expanded time scale. The small vertical bar under each trace indicates the onset of the stimulus. In this case no inhibition was obtained and the excitatory effects in Sart begin before the onset of EMG activity (part D of Fig. 6.5). Here the magnitude of the excitation was calculated by comparing the integrals of the control and stimulated EMGs in the period 9 to 40 msec after the point corresponding in each case to the stimulus in the step cycle. The latencies of the excitation are seen to decrease as the muscle becomes active, the shortest latencies in this experiment being 20 msec. A more extensive analysis of the latencies of the excitatory effects in three experiments is given in the histograms of Fig. 6.6. All these points represent values derived from averages of 16 samples irrespective of whether the excitation occurred during or before muscle activity. The range of latencies for excitation in forelimb muscles was 18 to 29 msec and in hindlimb muscles 13 to 25 msec.

Stimulation of the skin of the dorsum of the hindpaw and forepaw, comparable to that described above, was tested in the four high spinal cats described in Chapter 4. No consistent excitatory or inhibitory effects were obtained over long spinal pathways.

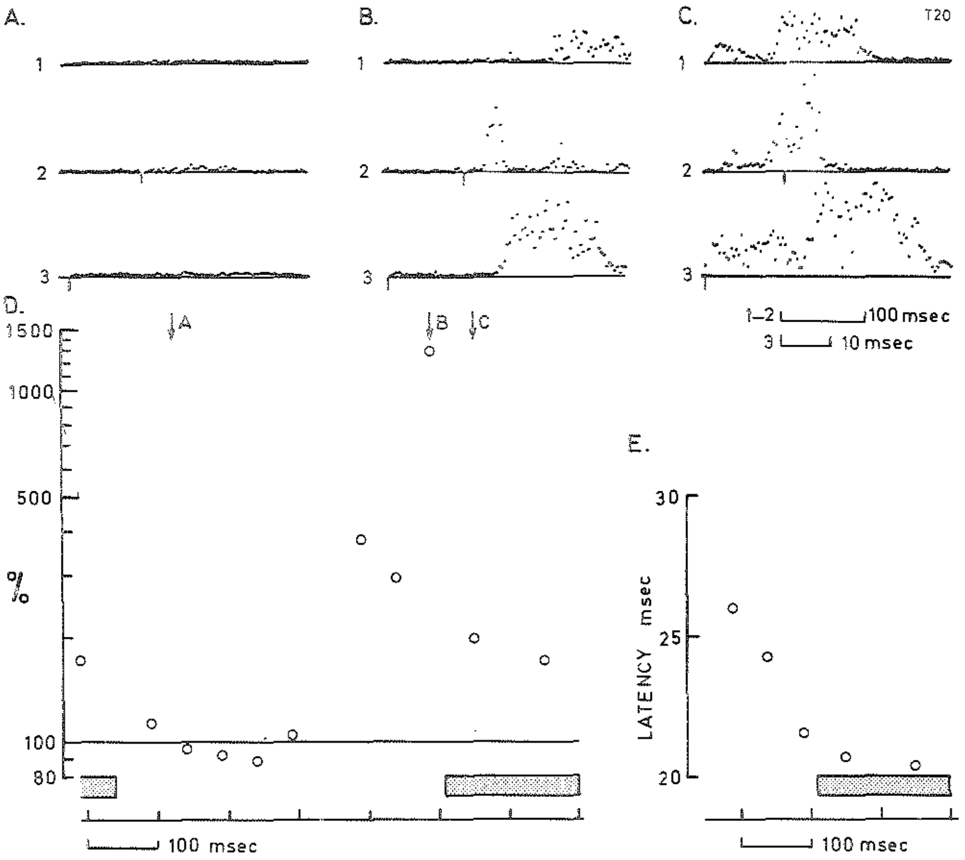


Fig. 6.5. Analysis of long reflex effects to sartorius following stimulation of skin of ipsilateral forepaw. Decerebrate cat stepping on treadmill at 1. m/sec. A,B and C: averages of 4 samples each of control step cycles (row 1) and stimulated step cycles (rows 2 and 3). In each of the stimulated step cycles the vertical bar indicates the onset of the stimulus. In rows 1 and 2 the averages last 300 msec and begin 100 msec before the stimulus; in row 3 the averages last 50 msec and start with the stimulus. The vertical gain is arbitrary, but is the same in A,B and C. In D integrals of the averages between 9 and 40 msec from the stimulus or from the corresponding point in the preceding step were obtained and expressed in a logarithmic scale in the ordinate as the ratio: (stimulated integral/control integral) x 100. The abscissa indicates in real time the step cycle; shaded bars give the duration of EMG activity of sartorius. The arrows indicate the points in the step cycle at which the samples in A,B and C were obtained. In E the latency of the excitatory effects is shown for the same points as D in relation to the EMG activity of sartorius.

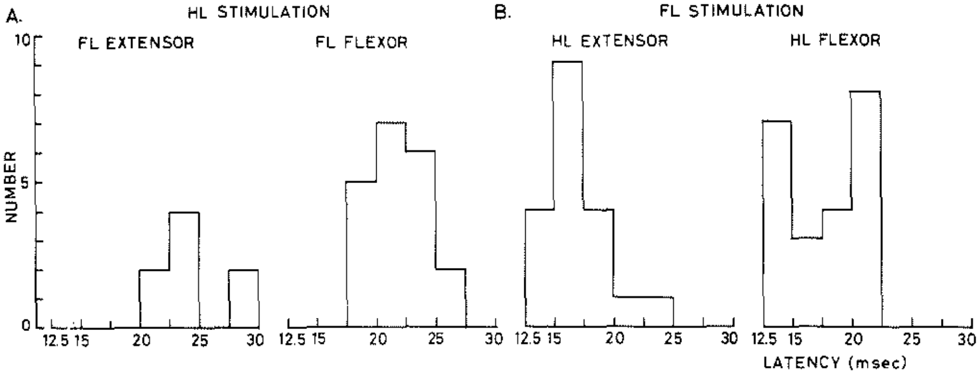


Fig. 6.6. Histograms of the latency distribution of the excitatory effects evoked over long reflexes. The latencies are from three experiments and were derived from averaged signals (n=16). Stimulus: 3 shocks at 3-10 mA. Velocity of stepping 1.0 $m.sec^{-1}$. A. Latencies in forelimb extensor, T, and forelimb flexors, Bi and Pmaj. Bi and Pmaj were observed in 1 and 2 experiments, respectively: there was no systematic difference between their latencies. B. Latencies in hindlimb extensor, Q, and flexor, Sart.

Influence of stimulation of skin nerves on EMGs in the limbs

In four cats the effects of electrical stimulation of the superficial radial nerve and the superficial peroneal nerve were investigated on the EMGs of the limbs in an attempt to obtain more information on particularly the inhibitory effects. The results were puzzling since the effects varied, not only between experiments, but also within the same experiment. Two main patterns emerged: excitation occurred during activity of the muscle (Fig. 6.7A) or during the period of inactivity (Fig. 6.7B). The homolateral coupling in A was out-of-phase and in B in-phase. An

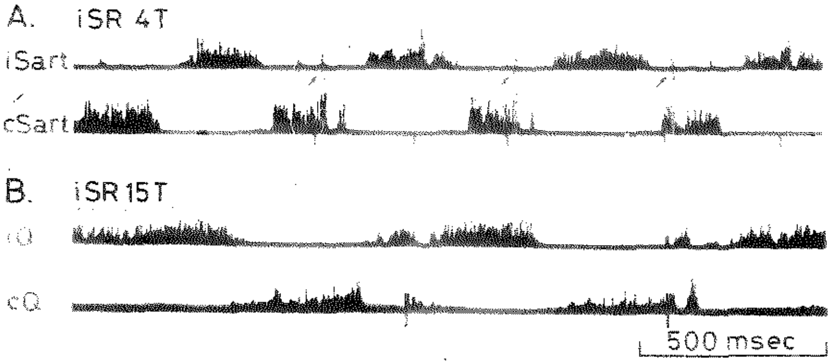


Fig. 6.7. Effect of electrical stimulation of superficial radial nerve on ipsilateral (i) and contralateral (c) hindlimb EMGs. Stimulus is indicated by vertical bars. A. Stimulus 3 shocks at 4 times nerve threshold (T). Velocity 1 m/sec. B. Stimulus 4 shocks at 15 times nerve threshold. Velocity 1 m/sec. Different experiment to A.

attractive conclusion would be that the sign of the reflex reversal was determined by this interlimb linkage. Unfortunately, in the results obtained in other cats this correlation of gait pattern and of excitatory EMG changes were not consistently confirmed. Latencies of excitatory effects were measured from single trials and were comparable to those obtained on skin stimulation. In both the ascending and descending directions they could be as low as 12 msec.

DISCUSSION

Reversal of the sign of long ascending and descending spinal reflexes dependent on the phase of the step cycle has been demonstrated in the high decerebrate cat. The reflexes were evoked by electrical stimulation of skin over the dorsum of the forepaw or hindpaw. In all the experiments stimulation evoked an increase in EMG activity in flexor or extensor muscles shortly before, and during activity of the muscle. Such cyclical changes of excitability are not necessarily an expression of a mechanism gaiting the effect of distant skin stimulation to one or other muscle group. They could well result from non-specific summation of subliminal facilitation evoked by distant skin stimulation with subliminal excitation of motoneurones before activity and during the active period itself of the motoneurones. However, active gating of the effects between antagonist muscle groups and, therefore, reflex reversal, is strongly suggested by the reciprocal inhibition seen in three experiments (Fig. 6.1B, row 2), the increase of EMG activity in only one of a pair of antagonist muscles when they are simultaneously active (Fig. 6.1D, row 2), the alternating bursts of activity evoked on high intensity stimulation (Figs. 6.1C, row 3, and 6.1D, row 3) and the reciprocal curves of excitation between Bi and T in Fig. 6.3A. Reciprocal inhibition of the activity of the antagonist motoneurone nuclei has not been described in other examples of reflex reversal dependent on the phase of the step cycle (43,124). This may in fact be difficult to demonstrate and may require intracellular recording.

Stimulation of nerve trunks gave distinct, but inconsistent effects. An explanation may be, as other authors have pointed out (67,71), that such stimulation evokes antagonistic actions in the central nervous system resulting in net responses which vary in strength and sign.

In the limb stimulated a flexion reflex was always evoked. Its intensity was modulated over the step cycle, being strongest during the inactive period of the flexor muscles when it could disrupt the step cycle, particularly in the hindlimb. Under these circumstances the rhythm of the corresponding homolateral limb (i.e. distant to the stimulated) remained constant. The effects evoked in the limb stimulated in the decerebrate and high spinal cats used in this study differ considerably from those of the chronic low spinal cat (43). Although the stimulus parameters are very similar no comparable reflex reversal has been observed.

In some cases the latencies of the excitatory effects were as short as 13 msec. Allowing 5 to 7 msec for afferent, efferent and synaptic delays (103) this suggest a central latency of 6 to 8 msec. It can therefore be concluded that at least the early part of the responses, occurring below about 18 msec is due to effects conducted over long propriospinal pathways. The question is at present open whether the longer latencies reflect activity over spino-bulbo-spinal pathways (70,133,134). The shortest latencies, however, are comparable to those obtained in neurophysiological experiments in immobilized high spinal cats. The results, therefore, are suggestive that long propriospinal pathways may evoke cyclical effects during locomotion, but it still remains to be shown if the phase dependent reflex reversal utilizes the same spinal pathways as those which are concerned with interlimb coordination.

SUMMARY

Reversal of the sign of long ascending and descending spinal reflexes dependent on the phase of the step cycle has been demonstrated in the high decerebrate cat. The reflexes were evoked by electrical stimulation of skin over the dorsum of the forepaw or hindpaw. Stimulation generally evoked an increase in activity in flexor or extensor muscles shortly before, and during, activity of the muscle. Reciprocal inhibition of a muscle occurred when the activity of the antagonist pair of muscles overlapped. In the stimulated limb the response was always a flexion reflex, modulated somewhat in intensity during the step cycle. From the latencies it was concluded that the early responses at least are due to spinal mechanisms. No consistent responses were obtained in high spinal cats during stepping. Electrical stimulation of cutaneous nerve trunks during stepping gives variable, phase dependent reflex effects.

CHAPTER 7.

GENERAL DISCUSSION.

The programmes of interlimb coupling (Chapter 4) represent basic patterns of coordination which occur consistently and they are supported further by the abrupt transitions of coupling seen in the electromyograms. If these basic patterns are organized at a spinal level, as suggested by the observations in high spinal cats a conceptually simple model emerges. Coordinated locomotion of all four limbs is achieved by intrinsic spinal programmes which may be modulated to suit the requirements of the cat by the activity of segmental afferent input and supraspinal descending control (62,108)

This model provides in turn relatively simple principles for the underlying neural organization responsible. It is possible that there are spinal interneurones concerned with the generation of periods of flexor and extensor activity in one limb which also compare the phase of the step cycle in that limb with the corresponding phase in another limb. Neurones with comparator functions have been described, for example, in the visual cortex for signalling the optimal orientation of the eyes for binocular vision (18) and in the inferior olive for comparing cortical and spinal influences (102). In the context of interlimb coordination it is particularly interesting that Jankowska et al. (83). found interneurones in lumbar segments receiving excitatory convergence from long descending propriospinal pathways and from the contralateral segmental flexor reflex afferents. Long propriospinal pathways also evoke powerful inhibitory effects (Chapter 5). The possibility should not be excluded that interlimb coordination is partly achieved by inhibitory signals, as has been shown in insects (115).

The association of the coupling of movements of the homolateral pairs of limbs and the prepotent ipsilateral influences of long propriospinal pathways seems logical. However, it has yet to be reconciled with the observations from a recent neuroanatomical study using the horse radish peroxidase technique (110) that a large proportion of the axons ascending or descending between the spinal enlargements have their cell bodies on the opposite side of the spinal cord. If these connections are concerned with interlimb coordination it could mean that each spinal motor centre would receive direct information concerning the other three limbs.

The results of long spinal reflex reversal dependent on the phase of the step cycle are suggestive that long propriospinal pathways may evoke cyclical effects during locomotion. This is apparent particularly since the peripheral skin nerves in the limbs evoke potent effects in these pathways of the immobilized high spinal preparation. It still remains to be shown if the phase dependent reflex reversal utilizes the same spinal pathways as those which are concerned with interlimb coordination.

A further generalization of the programmes of interlimb coordination described is that they are used in other behavioural situations, where coordination of the four limbs are required. It is therefore of interest that in the postural adjustments of the limb during the tactile placing reaction of one forelimb in intact cats, flexion of the forelimb performing the placing and reinforcement of the extensor tonus of the ipsilateral hindlimb occur simultaneously (98). This has also been observed in dogs during conditioned movements (80). This pattern corresponds strikingly to the out-of-phase and dominant pattern of homolateral limb coupling.

In man Bates (12) has suggested that basic patterns of movement are organized at the spinal level. His arguments were drawn from varied sources such as studies of movement in the newborn and from observations of the similarity of movements evoked by stimulation of the cerebral cortex and by stimulation of the internal capsule after hemispherectomy.

Tightly linked patterns of arm and leg movements have in fact been described in man. The coupling of the arm movement with stepping may be so strong that even if the arms are firmly bound to the body phasic EMGs in the arm muscles in time with stepping movements are still recorded (11). At velocities for comfortable walking the coordination pattern of the arm and the ipsilateral leg follows an out-of-phase sequence which corresponds to the most commonly occurring pattern of homolateral limb coupling in normal cats (27). Long propriospinal fibres somewhat comparable to those in the cat (48) are found in the monkey (Brinkman and Kuypers, personal communication) and in man (47). It would be tempting to speculate that they also play a role in the control of basic patterns of interlimb coordination.

Patterns of movements of the limbs coordinated with the trunk and head have been used for some years as the basis for physiotherapeutic techniques (17). It would be interesting to establish by EMG and movement recording how far these patterns are founded upon simple neural strategies, and if features of such patterns could also be used for the retraining of patients with central motor disorders using biofeedback retraining techniques (16).

SUMMARY.

1. An analysis has been made of movements of the forelimbs in normal cats stepping on a treadmill. Movements of the scapula and at the joints of the shoulder, elbow, wrist and digits show consistent time relationships over a range of velocities. The movements of the scapula are comparable to those of the hip and remain rather constant during locomotion. The sequence of the movements of the wrist and digits follows a different pattern to those of the more proximal joints. The role of flexor and extensor muscles of the forelimb during locomotion and the flexion reflex were shown to be compatible with the functional and anatomical organization of motoneurone nuclei in brachial segments of the spinal cord (Chapter 3).

2. Observations in normal, decerebrate and high spinal cats of flexion and extension movements of the four limbs have led to the conclusion that the different forms of alternate locomotion (e.g. pacing, trotting, swimming) and in-phase locomotion (e.g. galloping and jumping) result from the interaction of programmes for the coordination of (1) the homologous limbs (pair of hindlimbs or pair of forelimbs) and (2) the homolateral limbs (hind- and forelimb of the same side of the body). The movements of the homologous pairs of limbs are coupled out-of-phase in alternate gaits and approximately in-phase in the in-phase gaits. The movements of the homolateral pairs of limbs occur approximately out-of-phase (e.g. trotting) or approximately in-phase (e.g. pacing). Transitions between all forms of coupling occur abruptly over one or two steps. Therefore, for each type of coupling, homologous or homolateral, there are two distinct forms or programmes of movement.

The hypothesis is advanced that (a) all the characteristic patterns of locomotion in the cat result from different combinations of these programmes of homologous and homolateral limb coupling; (b) the programmes are mutually self-reinforcing in the gaits in which the coordination of the movements of the four limbs is bilaterally symmetrical; (c) the programmes act in competition in certain gaits which are not bilaterally symmetrical giving rise at times to a changing gait pattern, and (d) the temporary dominance of one programme or another can determine the gait of the particular step.

The observations of stepping in the high spinal cat indicate that, with the exception at present of the in-phase coupling of the forelimbs, the interlimb programmes can all be generated by the spinal cord alone (Chapter 4).

3. In high spinal cats propriospinal pathways linking the lumbosacral and brachial enlargements can mediate strong excitatory and inhibitory effects to different motoneurone nuclei. Reciprocal

long spinal effects to flexor and extensor motoneurones were rarely observed: only the motoneurones of latissimus dorsi received differential effects on stimulation of hindlimb flexor and extensor nerves. In long spinal reflexes to motoneurones mixtures of inhibitory and excitatory changes are superimposed. The afferents responsible for the effects in both the ascending and descending directions include group II and to a lesser extent group III muscle afferents, and group II skin afferents. The ipsilateral nerves were in general more effective than the contralateral. The hypothesis is suggested that long propriospinal pathways form an integrated system of connections between the segments generating locomotor movements in the hindlimb and forelimb (Chapter 5).

4. Reversal of the sign of long ascending and descending spinal reflexes dependent on the phase of the step cycle has been demonstrated in the high decerebrate cat. The reflexes were evoked by electrical stimulation of skin over the dorsum of the hindpaw and forepaw. On the basis of the latencies of the effects it was concluded that at least the initial part of the reflex is conducted exclusively over spinal pathways (Chapter 6).

SAMENVATTING.

In dit proefschrift zijn de resultaten neergelegd van een onderzoek naar de coordinatie van de vier poten van de kat onder verschillende omstandigheden van voortbewegen. Het bevat naast een studie van de bewegingen van de voorpoot en de mogelijke coordinatiepatronen van de vier poten, een onderzoek naar de onderliggende neurale mechanismen. Een samenvatting van deze onderwerpen volgt hieronder.

1. Tijdens het lopen op een lopende band zijn voorpootbewegingen bij normale katten geanalyseerd. Bewegingen van het schouderblad en van het schouder, elleboog, pols en carpofalangeale gewricht vertonen een vaste tijdrelatie over al de gemeten loopsnelheden. De bewegingen van het schouderblad zijn vergelijkbaar met die van heup en zijn eveneens tamelijk konstant tijdens het lopen. De bewegingen van de pols en het carpofalangeale gewricht volgen een ander patroon dan die van de meer proximale gewrichten. Het werd aangetoond, dat de functie van buig- en strekspieren van de voorpoot tijdens het lopen en tijdens de terugtrekreflex verenigbaar is met de functionele en anatomische opbouw van motorkernen in de cervicothoracale intumescentie van het ruggemerg (hoofdstuk 3).

2. Waarnemingen van buig- en strekbewegingen in normale, gedecerebreerde en hoog spinale katten hebben tot de konklusie geleid, dat verschillende vormen van *alternerend* lopen (bijv. telgang, draf, zwemmen) en *in-fase* lopen (bijv. galopperen, springen) het resultaat zijn van interaktie tussen de coordinatieprogramma's van (1) de homologe poten (het paar achterpoten of het paar voorpoten) en (2) de homolaterale poten (achter- en voorpoot aan de zelfde kant van het lichaam). De bewegingen van de beide paren homologe poten zijn uit fase gekoppeld tijdens *alternerend* lopen en bij benadering in fase tijdens het *in-fase* lopen. De homolaterale poten bewegen bij benadering *uit-fase* (bijv. in de draf) of *in-fase* (bijv. in de telgang). Overgangen tussen al deze vormen van koppelingen vinden in 1 à 2 stappen plaats. Er zijn daarom voor ieder type koppeling, homoloog of homolateraal, twee duidelijke vormen of programma's voor de beweging.

De hypothese is voorgesteld, dat (a) al de karakteristieke looppatronen in de kat het resultaat zijn van verschillende combinaties van deze programma's voor de koppeling van de homologe en homolaterale poten; (b) de programma's elkaar onderling versterken in die vormen van lopen, waar de coordinatie van de bewegingen van de vier poten tweezijdig symmetrisch is; (c) de programma's in kompetitie met elkaar zijn in die vormen van lopen, die niet tweezijdig symmetrisch zijn, hetgeen soms aanleiding kan geven tot een veranderend looppatroon, en (d) het tijdelijk overwicht van het ene programma op het andere de vorm van een bepaalde stap bepaalt.

Waarnemingen aan loopbewegingen in hoog spinale katten duiden aan, dat met uitzondering momenteel van de *in-fase* koppeling van de voorpoten, al de coordinatie programma's door het geisoleerde ruggemerg kunnen worden geproduceerd.

3. In hoog spinale katten kunnen lange propriospinale verbindingen tussen de lumbosacrale en cervicothoracale intumescenties sterke excitatoire en inhibitoire effecten uitoefenen op verschillende motorkernen. Reciproke lange spinale effecten naar motorneuronen van buigers en strekkers werden zelden waargenomen: alleen de motoneuronen van latissimus dorsi werden verschillend beïnvloed door stimulatie van zenuwen van buigers en strekkers. In lange spinale reflexen naar motoneuronen vindt in wisselende verhouding een overdekking plaats van excitatoire en inhibitoire effekten. De afferenten verantwoordelijk voor deze effekten in zowel de ascenderende als de descenderende richting omvatten groep II en in mindere mate groep III spier afferenten en groep II huid afferenten. De ipsilaterale zenuwen waren in het algemeen effectiver dan de contralaterale. De hypothese is voorgesteld, dat lange propriospinale verbindingen een geintegreerd systeem van verbindingen vormen tussen de spinale segmenten die de loopbewegingen in de achterpoot en voorpoot veroorzaken (hoofdstuk 5).

4. Omkering van het teken van lange ascenderende en descenderende spinale reflexen afhankelijk van de fase van de stapcyclus is aangetoond in de gedecerebreerde kat. De reflexen werden opgewekt d.m.v. elektrische prikkeling van de huid over het dorsale aspect van de metacarpalen en metatarsalen. Op basis van de latenties van de effekten werd gekonkludeerd, dat tenminste het eerste gedeelte van de reflex exclusief over spinale verbindingen werd voortgeleid.

REFERENCES.

1. Abrahams, V.C., Spino-spinal mechanisms in the chloralose anaesthetized cat, J. Physiol., 215 (1971) 755-768.
2. Adamovich, N.A., Borgest, A.M. and Evdokimov, S.A., Influence of afferent impulses from the nerves of the anterior limbs on the insertion neurones of the lumbar section of the spinal cord, Neirofiziologiya, 1 (1969) 235-242. (English translation).
3. Adamovich, N.A., Borgest, A.M., Evdokimov, S.A. and Kiselev, P.A., Influence of forelimb afferents on the activity of lumbar spinal-cord motoneurons, Neirofiziologiya, 3 (1971) 58-67. (English translation).
4. Adrian, E.D. and Moruzzi, G., Impulses in the pyramidal tract, J. Physiol., 97 (1939) 153-199.
5. Alvord. E.C., Jr. and Fuortes, M.G.F., A comparison of generalized reflex myoclonic reactions elicitable in cats under chloralose anesthesia and under strychnine, Amer. J. Physiol., 176 (1954) 253-261.
6. Andén, N.E., Jukes, M.G.M. and Lundberg, A., The effect of DOPA on the spinal cord. II, Acta Physiol. Scand., 67 (1966) 387-397.
7. Aoki, M. and McIntyre, A.K., Cortical and long spinal actions on lumbosacral motoneurons in the cat, J. Physiol., 251 (1975) 569-587.
8. Arshavsky, Y., Berkinblit, M.B., Fukson, O.I., Gelfland, I.M. and Orlovsky, G.N., Origin of modulation in neurones of the ventral spino-cerebellar tract during locomotion, Brain Research, 43 (1972) 276-279.
9. Arshavsky, Y.I., Kots, Y.M., Orlovsky, G.N., Rodionov, I.M. and Shik, M.L., Investigation of the biomechanics of running by the dog, Biofizika, 10 (1965) 665-672 (English translation).
10. Balis, G.U. and Monroe, R.R., The pharmacology of chloralose, a review, Psychopharmacologia (Berl.), 6 (1964) 1-30.
11. Ballesteros, M.L.F., Buchthal, F. and Rosenfalck, P., The pattern of muscular activity during the arm swing of natural walking, Acta physiol. scand., 63 (1965) 296-310.
12. Bates, J.A.V., The significance of complex motor patterns in the response to cortical stimulation, Int. J. Neurol., 4 (1963) 92-99.
13. Bergmans, J., Miller, S. and Reitsma, D.J., Influence of L-DOPA on transmission in long ascending propriospinal pathways in the cat, Brain Research, 62 (1973) 155-167.
14. Bernhard, C.G. and Therman, P.O., Alternating facilitation and inhibition of the extensor muscle activity in decerebrate cats, Acta physiol. scand., 14, Suppl. 47, No. 3 (1947) 1-9.

15. Bernhard, C.G. and Therman, P.O., Reciprocal facilitation and inhibition following a single afferent volley, Acta physiol. scand., 14, Suppl. 47, No. 5 (1947) 1-17.
16. Blanchard, E.B. and Young, L.D., Clinical applications of feedback training, a review of evidence, Arch. Gen. Psych., 30 (1974) 573-589.
17. Bobath, B. and K., The Facilitation of Normal Postural Reactions and Movements in the Treatment of Cerebral Palsy, Physiotherapy, 50, 8, (1964) 246.
18. Burns, B.D. and Pritchard, R., Cortical conditions for fused binocular vision, J. Physiol., 197 (1968) 149-171.
19. Brown, T.G., The intrinsic factors in the act of progression in the mammal, Proc. roy. Soc. B, 84 (1911) 308-319.
20. Brown, T.G., On the nature of the fundamental activity of the nervous centres; together with an analysis of the conditioning of rhythmic activity in progression, and a theory of the evolution of function in the nervous system, J. Physiol., 48 (1914) 2-45.
21. Budakova, N.N. and Shik, M.L., Effect of brain stem stimulation evoking locomotion on ascending reflexes in the mesencephalic cat, Bull. exp. Biol. Med., 69 (1970) 5-8.
22. Buser, P., Ascher, P., Bruner, J., Jassik-Gerschenfeld, D. and Sindberg, R., Aspects of sensorimotor reverberation to acoustic and visual stimuli. The role of primary specific cortical areas. In G. Moruzzi, A. Fessard and H.H. Jasper (Eds.), Brain Mechanisms, Progress in Brain Research, vol. 1 (1963) 294-322-
23. Buser, P., St. Laurent, S. and Menini, C.H., Intervention du colliculus inferieur dans l'elaboration et le contrôle cortical specifique des décharges cloniques au son chez le chat sous chloralose, Exp. Brain Res., 1 (1966) 102-126.
24. Carlsson, A., Falck, B., Fuxe, K. and Hillarp, N.A., Cellular localization of monoamines in the spinal cord, Acta physiol. scand., 60 (1964) 112-119.
25. Chan, S.H.H. and Barnes, C.D., Brain stem reticular effects on lumbar monosynaptic reflexes, Physiology, 13 (1970) 164.
26. Cook, W.A., Jr., Gangiano, A. and Pompeiano, O., Vestibular control of transmission in primary afferents to the lumbar spinal cord, Arch.ital. Biol., 107 (1969) 296-320.
27. Craik, R., Herman, R. and Finley, F., Human solutions for locomotion II, Interlimb coordination, In: R. Herman, S. Grillner, P.G. Stein and D.G. Stuart (Eds.), Neural control of locomotion, Plenum Press, New York. In Press
28. Creed, R.S. and Sherrington, C.S., Observations on concurrent contraction of flexor muscles in the flexion-reflex, Proc. roy. Soc. B., 100 (1926) 258-267.
29. Dahlström, A. and Fuxe, K., Evidence for the existence of monoamine neurons in the central nervous system. II, Experimentally induced changes in the intraneuronal amine levels of bulbospinal neuron systems, Acta physiol. scand., Suppl. 247

(1965) 1-36.

30. Devanandan, M.S., Eccles, R.M., Lewis, D.M. and Stenhouse, D., Responses of flexor alpha-motoneurons in cats anaesthetized with chloralose, Exp. Brain Res., 8 (1969) 163-176.
31. Devanandan, M.S., Eccles, R.M., Lewis, D.M. and Stenhouse, D., Responses of extensor alpha-motoneurons in cats anaesthetized with chloralose, Exp. Brain Res., 8 (1969) 177-189.
32. Djalali, E., Relations Neurophysiologiques Brachio-Lumbaires chez le Chat Spinal. Contribution à la Connaissance de la Physiologie de la Moelle Epinière. Thèse. Faculté des Sciences de l'Université d'Aix-Marseille. I, Index no. C.N.R.S.A.O, 4674 (1970) 150 pp.
33. Djalali, E. and Hugon, M., Influence de la stimulation de nerfs du membre antérieur du Chat sur divers réflexes lombaires, J. Physiol. (Paris), 61, Suppl. 2 (1969) 270.
34. Duysens, J. and Pearson, K.G., The role of cutaneous afferents from the distal hindlimb in the regulation of the step cycle of thalamic cats, In preparation.
35. Easton, T.A., On the normal use of reflexes, Amer. Scientist, 60 (1972) 591-599.
36. Eaton, Th.H.Jr., Modifications of the shoulder girdle related to reach and stride in mammals, J. Morphol., 75 (1944) 167-171.
37. Eccles, R.M. and Lundberg, A., Supraspinal control of interneurons mediating spinal reflexes, J. Physiol., 147 (1959b) 565-584.
38. Eccles, J.C., The Physiology of Synapses, Springer, Berlin (1964) 316 pp.
39. Eccles, R.M. and Lundberg, A., Integrative pattern of Ia synaptic actions on motoneurones of hip and knee muscles, J. Physiol. (Lond.), 144 (1958) 271-298.
40. Engberg, I., Reflexes to foot muscles in the cat, Acta physiol. scand., 62, Suppl. 235 (1964) 1-64.
41. Engberg, I. and Lundberg, A., An electromyographic analysis of muscular activity in the hindlimb of the cat during unrestrained locomotion, Acta physiol. scand., 75 (1969) 614-630.
42. Forssberg, H. and Grillner, S., The locomotion of the acute spinal cat injected with clonidine i.v., Brain Research, 50 (1973) 184-186.
43. Forssberg, H., Grillner, S. and Rossignol, S., Phase dependent reflex reversal during walking in chronic spinal cats, Brain Res., 85 (1975) 103-107.
44. Fröhlich, A. and Sherrington, C.S., Path of impulse for inhibition under decerebrate rigidity, J. Physiol., 28 (1902) 14-19.
45. Furnée, E.H., Halbertsma, J.M., Klunder, G., Miller, S., Nieukerke, K.J., Van Der Burg, J. and Van Der Meché, F.G.A., Automatic analysis of stepping movements in cats by means of a television system and a digital computer, J. Physiol., 240 (1974) 3-4P.

46. Gernandt, B.E. and Megirian, D., Ascending propriospinal mechanisms, J. Neurophysiol., 24 (1961) 364-376.
47. Giok, S.P., The fasciculus intermediolateralis of Loewenthal in man, Brain, 81 (1958) 577-587.
48. Giovanelli Barilari, M. and Kuypers, H.G.J.M., Propriospinal fibers interconnecting the spinal enlargements in the cat, Brain Research, 14 (1969) 321-330.
49. Goslow, G.E., Reinking, R.M. and Stuart, D.G., The cat step cycle: hindlimb joint angles and muscle lengths during unrestrained locomotion, J. Morphol., 141 (1973) 1-42.
50. Gray, J., Animal Locomotion, Weidenfeld and Nicolson, London (1968) 479 pp.
60. Grillner, S., Locomotion in the spinal cat. In R.B. Stein, K.G. Pearson, New York (1973) 515-536.
61. Grillner, S., On the spinal generation of locomotion. In S. Batuev (Ed.), Sensory Organization of Movements, Akademia Nauk Press, Leningrad (1974)
62. Grillner, S., Locomotion in vertebrates: Central mechanisms and reflex interaction, Physiol. Rev. 55 (1975) 247-306.
63. Grillner, S. and Shik, M.L., On the descending control of the lumbosacral spinal cord from the mesencephalic locomotor region, Acta physiol., scand., 87 (1973) 320-333.
64. Grillner, S. and Zangger, P., Locomotor movements generated by the deafferented spinal cord, Acta physiol. scand., 91 (1974) 38A-39A.
65. Guillebeau, A. and Luchsinger, B., Fortgesetzte Studien am Rückenmarke, Pflügers Arch. ges. Physiol., 28 (1882) 61-69.
66. Gurfinkel, V.S. and Shik, M.L., The control of posture and locomotion, In A.A. Gydikow, N.T. Tankov and D.S. Kosarov (Eds.), Motor Control, Plenum Press, New York (1973) 217-234.
67. Hagbarth, K.E., Excitatory and inhibitory areas for flexor and extensor motoneurones, Acta physiol. scand., suppl. 94 (1952) 1-58.
68. Hak, P., Klootwijk, R., Miller, S. and Van Der Burg, J., Stepping patterns of normal and decerebrate cats, Acta physiol. scand., 396 (1973) 69A.
69. Halbertsma, J.M., Registratie en analyse van bewegingen en spierpotentialen voor het onderzoek naar de neuronale besturing van het lopen bij de kat. Thesis for Degree in Engineering. Department of Applied Physics, University of Technology, Delft, Netherlands (1975).
70. Halbertsma, J.M., Miller, S. and Van Der Meché, F.G.A., Basic "programs" for the phasing of flexion and extension movements of the limbs during locomotion in the cat, In: R. Herman, S. Grillner, P.G. Stein and D.G. Stuart (Eds.), Neural Control of locomotion, Plenum Press, New York, In Press (1975).

71. Hassen, A.H. and Barnes, C.D., Bilateral effects of vestibular nerve stimulation on activaty in the lumbar cord, Brain Res., 90 (1975) 221-233.
72. Hildebrand, M., Motion of the running cheetah and horse, J. Mammalogy, 40 (1959) 481-495.
73. Hildebrand, M., Further studies on locomotion of the cheetah, J. Mammalogy, 42 (1961) 84-91.
74. Hildebrand, M., Analysis of the symmetrical gaits of tetrapods, Folia Biotheoretica, 6 (1966) 9-22.
75. Hillegers, L.T.M.E. and Miller, S., LAB-8 Advanced averager program (Rotterdam Version), Decuscope 11, No. 3 (1972) 17.
76. Holmqvist, B., Crossed spinal reflex actions evoked in somatic afferents, Acta physiol. scand., 52, Suppl. 181 (1961) 1-67.
77. Howell, A.B., Speed in Animals, University of Chicago Press, Chicago, Ill., (1944) 270 pp.
78. Hultborn, H., Convergence on interneurones in the reciprocal Ia inhibitory pathway to motoneurones, Acta physiol. scand., Suppl, 375 (1972) 1-42.
79. Illert, M., Lundberg, A., Padel, Y. and Tanaka, R., Convergence on propriospinal neurones which may mediate disynaptic corticospinal excitation to forelimb motoneurons in the cat, Brain Res., 93 (1975) 530-534.
80. Ioffe, M.E. and Andreyev, A.E., Inter-extremities coordination in local motor conditioned reactions of dogs, Zh. vyssh. nerv. Deyat. Pavlova, 19 (1969) 557-565. (In Russian)
81. Jankowska, E., Jukes, M.G.M., Lund, S. and Lundberg, A., The effect of DOPA on the spinal cord. 5. Reciprocal organization of pathways transmitting excitatory action to alpha motoneurones of flexors and extensors, Acta physiol. scand., 70 (1967a) 369-388.
82. Jankowska, E., Jukes, M.G.M., Lund, S. and Lundberg, A., The effect of DOPA on the spinal cord. 6. Half-centre organization of interneurones transmitting effects from the flexor reflex afferents, Acta physiol. scand., 70 (1967) 389-402.
83. Jankowska, E., Lundberg, A. and Stuart, D., Propriospinal control of last order interneurones of spinal reflex pathways in the cat, Brain Research, 53 (1973) 227-231.
84. Jankowska, E., Lundberg, A., Roberts, W.J. and Stuart, D., A Long Propriospinal system with direct effect on motoneurones and on interneurones in the cat lumbosacral cord, Exp. Brain Res., 21 (1974) 169-195.
35. Jenkins, F.J., Jr., The movement of the shoulder in claviculate and aclaviculate mammals, J. Morphol., 144 (1974) 71-84.
36. Kubota, K., Kidokoro, Y. and Suzuki, J., Postsynaptic inhibitions of trigeminal and lumbar motoneurons from the superficial radial nerve in the cat, Jap. J. Physiol., 18 (1968) 198-215.

87. Kulagin, A.S. and Shik, M.L., Interaction of symmetrical limbs during controlled locomotion, Biofizika, 15 (1970) 164-170. (English translation).

88. Kuypers, H.G.J.M., The descending pathways to the spinal cord, their anatomy and function, In J.C. Eccles and J.P. Schadé (Eds.), Organization of the Spinal Cord, Progr. Brain Res., Vol. 11, Elsevier, Amsterdam (1964) 178-202.

89. Landis, C. and Hunt, W.A., The startle pattern. New York: Farrar and Rinehart (1939)

90. Lawrence, D.G. and Kuypers, H.G.J.M., The functional organization of the motor system in the monkey. II, The effects effects of lesions of the descending brain-stem pathways, Brain, 91 (1968) 15-36.

91. Lisin, V.V., Frankenstein, S.J. and Rechtmann, M.B., The influence of locomotion on flexor reflex of the hindlimb in Cat and Man, Exp. Neurol., 38 (1973) 180-183.

92. Lloyd, D.P.C., Mediation of descending long spinal reflex activity, J. Neurophysiol., 5 (1942) 435-458.

93. Lloyd, D.P.C. and McIntyre, A.K., Analysis of forelimb-hindlimb reflex activity in acutely decapitate cats, J. Neurophysiol., 11 (1948) 455-470.

94. Lundberg, A., Reflex control of stepping, Nansen Memorial Lecture V, Universitetsforlaget, Oslo (1969) 42 pp.

95. Lundberg, A., Function of the ventral spinocerebellar tract. A new hypothesis, Exp. Brain Res., 12 (1971) 317-330.

96. Lundberg, A. and Phillips, C.G. , Graham Brown's film on locomotion in the decerebrate cat, J. Physiol. (Lond.), 231 (1973) 90-91P.

97. Luttrell, C.N., Bang, F.D. and Luxenberg, K., Newcastle disease encephalomyelitis in cats. II, Physiological studies on rhythmic myoclonus, Arch. Neurol. Psychiat., (Chic.), 81 (1959) 35/285-41/291.

98. Massion, J. and Smith, D.M., Ventrolateral thalamic neurones related to posture during a modified placing reaction, Brain Research, 71 (1974) 353-359.

99. McDonald, W.I. and McIntyre, A.K., Observations on ascending long spinal reflexes, Proceedings of the Otago Medical School (Dunedin), 34 (1956) 5-6.

100. McDonald, W.I., An Electrophysiological Investigation of Hindlimb-Forelimb Activity in Acutely Decapitate Cats, B. Med. Sci. Thesis, Otago University Medical School, Dunedin, New Zealand, 117 pp.

101. Miller, R., Studies on mammalian reflexes, Trans. roy. Soc. Canada, 17 (1923) 29-32.

102. Miller, S. and Oscarsson, O., Termination and functional organization of spino-olivocerebellar paths, In W.S. Fields and W.D. Willis, Jr. (Eds.), The Cerebellum in Health and Disease, Warren H. Green, St. Louis, Mo., (1969) 172-200.

103. Miller, S., Reitsma, D.J. and Van Der Meché, F.G.A., Functional organization of long ascending propriospinal pathways linking lumbo-sacral and cervical segments in the cat, Brain Research, 62 (1973) 169-188.
104. Miller, S., Van Berkum, R., Van Der Burg, J. and Van Der Meché, F.G.A., Interlimb coordination in stepping in the cat, J. Physiol. (Lond.), 230 (1973) 30-31P.
105. Miller, S. and Van Der Burg, J., The function of long propriospinal pathways in the co-ordination of quadrupedal stepping in the cat. In R.B. Stein, K.G. Pearson, R.S. Smith and J.B. Redford (Eds.), Control of Posture and Locomotion, Plenum Press, New York (1973) 561-578.
106. Miller, S., Van Der Burg, J. and Van Der Meché, F.G.A., Locomotion in the cat: a hypothesis for interlimb coordination, Brain Research, 85 (1975) 189-190.
107. Miller, S., Van Der Burg, J. and Van Der Meché, F.G.A., Coordination of the hindlimbs and forelimb in different forms of locomotion in normal and decerebrate cats, Brain Research, 91 (1975) 217-237.
108. Miller, S., Van Der Burg, J. and Van Der Meché, F.G.A., Locomotion in the cat: basic programmes of movement, Brain Research, 91 (1975) 239-253.
109. Miller, S. and Van Der Meché, F.G.A., Movements of the forelimbs of the cat during stepping on a treadmill, Brain Research, 91 (1975) 255-269.
110. Molenaar, I. and Kuypers, H.G.J.M., Identification of cells of origin of long fiber connections in the cat's spinal cord by means of the retrograde axonal horseradish peroxidase technique, Neuroscience Letters, 1 (1975) 193-198.
111. Muybridge, E., Animals in Motion, Chapman and Hall, Ltd., London, (1899) 264 pp. (Republished with minor changes in L.S. Brown (Ed.), Dover Publications Inc., New York (1957) 74 pp).
112. Orlovsky, G.N., The effect of different descending systems on flexor and extensor activity during locomotion, Brain Research 40 (1972) 359-371.
113. Pearson, K.G., Central programming and reflex control of walking in the cockroach, J. exp. Biol., 56 (1972) 173-193.
114. Pearson, K.G. and Duysens, J., Reflex control of stepping in cockroach and cat, In: R. Herman, S. Grillner, P.G. Stein and D.G. Stuart (Eds.), Neural Control of Locomotion, Plenum Press, New York. In Press
115. Pearson, K.G. and Iles, J.F., Nervous mechanisms underlying intersegmental co-ordination of leg movements during walking in the cockroach, J. exp. Biol., 58 (1973) 725-744.
116. Peterson, B.W. and Felpel, L.P., Excitation and inhibition of reticulospinal neurons by vestibular cortical and cutaneous stimulation, Brain Res., 27 (1971) 373-376.

117. Phillippson, M., L'autonomie et la centralisation dans le système nerveux des animaux, Trav, Lab. Physiol. Inst. Solvay (Bruxelles) 7 (1905) 1-208.
118. Pi-Suñer, J. and Fulton, J.F., The influence of the proprioceptive nerves of the hindlimbs upon the posture of the forelimbs in decerebrate cats, Amer. J. Physiol., 83 (1928) 548-553.
119. Pomeranz, B., Wall, P.D. and Weber, W.V., Cord cells responding to fine myelinated afferents from viscera, muscle and skin, J. Physiol. (Lond.). 199 (1968) 511-532.
120. Roberts, T.D.M., Neurophysiology of Postural Mechanisms, Butterworths, London (1967) 354 pp.
121. Romanes, G.J., The motor cell columns of the lumbo-sacral spinal cord of the cat, J. comp. Neurol., 94 (1951) 313-359.
122. Romanes. G.J., The motor pools of the spinal cord. In J.C. Eccles and J.P. Schadé (Eds.), Organization of the Spinal Cord Progr. Brain Res., Vol. 11, Elsevier, Amsterdam (1964) 93-116.
123. Rosén, I., Localization in caudal brain stem and cervical spinal cord of neurones activated from forelimb group I afferents in the cat, Brain Research, 16 (1969) 55-71.
124. Rossignol, S., Startle responses recorded in the leg of man, J. of EEG (1976) In Press.
125. Rustioni, A., Kuypers, H.G.J.M. and Holstege, G., Propriospinal projections from the ventral and lateral funiculi to the motoneurons in the lumbosacral cord of the cat, Brain Research, 34 (1971) 255-275.
126. Schmidt, R.F. and Willis, W.D., Intracellular recording from motoneurons of the cervical spinal cord of the cat, J. Neurophysiol., 26 (1963) 28143.
127. Schomburg, E.D., Meinck, H.M. and Haustein, J., A fast descending propriospinal pathway for inhibition, Exp. Brain Res., 23 (1975) 185.
128. Sherrington, C.S., Qualitative difference of spinal reflex corresponding with qualitative difference of cutaneous stimulus, J. Physiol., 30 (1904) 39-46.
129. Sherrington, C.S., Flexion-reflex of the limb, crossed extension reflex, and reflex stepping and standing, J. Physiol (Lond.), 40 (1910) 28-121.
130. Sherrington, C.S. and Sowton, S.C.M., Reversal of the reflex effect on an afferent nerve by altering the character of the electrical stimulus applied, Proc. roy. Soc., 83B (1911) 435-446.
131. Shik, M.L. and Orlovsky, G.N., Co-ordination of the limbs during running of the dog, Biofizika, 10 (1965) 1148-1159 (English translation).
132. Shik, M.L., Severin, F.V. and Orlovsky, G.N., Control of walking and running by means of electrical stimulation of the mid-brain, Biofizika, 11 (1966) 659-666. (English translation)

133. Shimamura, M. and Akert, K., Peripheral nervous relations of propriospinal and spino-bulbo-spinal reflex systems, Jap. J. Physiol., 15 (1965) 638-647,

134. Shimamura, T. and Livingstone, R.B., Longitudinal conduction systems serving spinal and brain-stem coordination, J. Neurophysiol., 26 (1963) 258-272.

135. Shimamura, M., Mori, S. and Yamauchi, T., Effects of spino-bulbo-spinal reflex volleys on extensor motoneurons of hindlimb in cats, J. Neurophysiol., 30 (1967) 319-332.

136. Shimamura, M. and Yamauchi, T., Neural mechanisms of the chloralose jerk with special reference to its relationship with the spino-bulbo-spinal reflex, Jap. J. Physiol., 17 (1967) 738-745.

137. Sterling, P. and Kuypers, H.G.J.M., Anatomical organization of the brachial spinal cord of the cat. II, The motoneuron plexus, Brain Research, 4 (1967) 16-32.

138. Sterling, P. and Kuypers, H.G.J.M., Anatomical organization of the brachial spinal cord of the cat. III, The propriospinal connections, Brain Research, 7 (1968) 419-443.

139. Stratten, W.P. and Barnes, C.D., Modifications of monosynaptic reflex by visual stimulus, Physiologist, 10 (1967) 317.

140. Stuart, D.G., Withey, T.P., Wetzel, M.C. and Goslow, G.E., Jr. Jr., Time constraints for inter-limb co-ordination in the cat during unrestrained locomotion, In R.B. Stein, K.G. Pearson, R.S. Smith and J.B. Redford (Eds.), Control of Posture and Locomotion, Plenum Press, New York (1973) 537-560.

141. Thomas, J.S., The mechanism and distribution of the startle response, Ph.D. thesis, Department of Anatomy and Physiology Indiana University, Bloomington, Indiana (1971)

142. Thomas, J.S. and Barnes, C.D., Contralateral conditioning of lumbar MSRs as a paradigm of a generalized afferent 'on response', Physiologist, 13 (1970) 321.

143. Uddenberg, N., Differential localization in dorsal funiculus of fibres originating from different receptors, Exp. Brain Res., 4 (1968) 367-376.

144. Vasilenko, D.A., Propriospinal pathways in the ventral funiculus of the spinal cord: their effects on lumbosacral motoneurons, Brain Res., 93 (1975) 502-506.

145. Wetzel, M.C., Atwater, A.E., Wait, J.V. and Stuart, D.C., Neural implications of different profiles between treadmill and overground locomotion timings in cats, Journal of Neurophysiology, 38 (1975) 492-502.

146. Willis, W.D., Tate, G.W., Ashworth, R.D. and Willis, J.C., Monosynaptic excitation of motoneurons of individual forelimb muscles, J. Neurophysiol., 29 (1966) 410-424.

147. Wilson, D.M., Insect walking, Ann, Rev. Ent., 11 (1966) 103-122.

148. Wilson, D.M., The nervous control of insect flight and related behaviour, Advanc, Insect Physiol., 5 (1968) 289-337.

149. Wright, C.G. and Barnes, C.D., Audio-spinal reflex responses in decerebrate and chloralose anesthetized cats, Brain Res., 36 (1972) 307-331.

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