

## EFFECTS FROM FINE MUSCLE AND CUTANEOUS AFFERENTS ON SPINAL LOCOMOTION IN CATS

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### SUMMARY

1. The effects of chemically activated fine muscle afferents (groups III and IV) and electrically activated cutaneous afferents on motoneuronal discharges were studied before and during fictive locomotion induced pharmacologically by i.v. administration of nialamide and L-DOPA in high spinal cats. Efferent activity was recorded simultaneously from nerve filaments to ipsi- and contralateral extensor and flexor muscles. In addition, intracellular recordings were made from lumbar  $\alpha$ -motoneurons.

2. After nialamide but before treatment with L-DOPA, in some cases, transient locomotor-like discharges were induced by an increased activity in fine muscle afferents. The response pattern in nerves to both hind limbs could be different showing e.g. only transient alternating activity between knee flexor and extensor of one limb but not of the other one.

3. Treatment with L-DOPA did not always cause fictive locomotion. Often not all motoneurone pools showed rhythmic activity. In these cases stimulation of group III and IV muscle afferents usually caused transient periodic activity. In cases with apparent rhythmic activity, algescic stimulation of the gastrocnemius-soleus muscle caused an accentuation of the rhythm by a more abrupt transition from the active phase to the non-active interval. Again, the response patterns on both sides were not uniform in all cases.

4. A second type of response to activation of fine muscle afferents had a quite different character: the rhythmic activity was more or less completely overridden by a strong transient tonic hyperactivity or the rhythm was transiently blocked. These phenomena did not occur in the same way in all nerves.

5. Electrical stimulation of cutaneous nerves of the hind limb generally induced the same response pattern as chemical stimulation of the group III and IV muscle afferents. The effects varied depending on the stimulus strength and the nerve.

6. The results revealed that cutaneous and fine muscle afferents not only have similar functions in the reflex control of a limb but also in evocation and modulation of locomotion. Therefore, it is assumed that both types of afferents may serve together as a peripheral feed-back to the spinal locomotor centre.

### INTRODUCTION

Experiments with decorticate, thalamic and mesencephalic mammals have shown that a multi-level control system is involved in locomotion (for a review see Shik &

Orlovsky, 1976). Even after a complete isolation of the spinal cord from its connexions with higher centres in a variety of vertebrates, including mammals, locomotor movements may develop to a certain extent (for a review see Grillner, 1975). By treating paralysed spinal preparations with nialamide, a monoamine oxidase inhibitor, and the noradrenergic precursor L-DOPA, rhythmic bursts of motoneuronal discharges have been observed in nerves to hind limb muscles (Jankowska, Jukes, Lund & Lundberg, 1967; Viala & Buser, 1971; Grillner & Zangger, 1974). This activity showed a pattern similar to that observed during locomotion, i.e. a co-ordinated alternation between bursts in nerves to flexor muscles and those to antagonistic extensor muscles. These spinal motoneuronal rhythms are called 'fictive locomotion' since, due to curarization, no actual movements are performed.

Since a walking spinal cat can adapt to the speed of a treadmill, peripheral feed-back signals must act upon the spinal structures controlling locomotion (see Grillner, 1973). Using the technique of fictive locomotion, a powerful peripheral influence on these spinal locomotor structures was found (Andersson, Grillner, Lindquist & Zomlefer, 1978; Viala, Orsal & Buser, 1978; Grillner & Zangger, 1979). But limited information is available about the role of different receptors responsible for this influence. This is especially true for group III and IV muscle afferents. Therefore, it was the intention of the present series of experiments to study the effects of fine muscle afferents on spinal locomotor activity without interference from simultaneously stimulated larger muscle afferents and to compare these effects with the influence of a cutaneous afferent inflow. Preliminary reports have been published (Kniffki, Schomburg & Steffens, 1979*b*, 1980).

#### METHODS

*General procedures.* The experiments were carried out on fifteen adult cats weighing 2.3–4.4 kg. Under general ether–halothane–nitrous oxide anaesthesia they were tracheotomized, anaemically decapitated (cf. Schomburg, Meinck, Haustein & Roesler, 1978), spinalized at C<sub>1</sub>, paralysed with pancuronium bromide (Pancuronium 'Organon'; about 0.1–0.2 mg/kg per hr i.v.) and artificially ventilated. For anaemic decapitation the common carotid arteries were ligated on both sides at low cervical level and were isolated to the level of the carotid bifurcation. All vessels originating from the carotid arteries were ligated bilaterally i.e. external carotid artery, internal and external maxillary arteries, lingual and ascending pharyngeal. A patent internal carotid artery was not observed. Then both vertebral arteries were clamped by compression between the first and second cervical vertebrae. An irreversible interruption of the spontaneous respiration resulted from this procedure together with persistent large and non-reacting pupils and these were taken as a sign for the completion of anaemic decapitation. The ligations and the clamp remained in position throughout the experiment.

To prove the reliability of the procedure, selective inspections at the end of several experiments were performed. One hundred millilitres of an Evans Blue solution (0.5 g/100 ml., 2000 i.u. heparin added) was infused over a period of a few minutes. The cat was killed and dissected 5 min after the infusion. No dye was found within the brain and the superficial (pial) or deep brain vessels, while the dye was well distributed in the vessels of the spinal cord and the muscles. This result showed that the technique, as described, adequately blocks the blood supply to the brain, causing an irreversible destruction of its functions.

The anaesthesia was discontinued after spinalization. End-tidal CO<sub>2</sub> concentration was controlled throughout the experiments and respiratory rate was adjusted to maintain it at about 4%. Arterial blood pressure was monitored by a catheter inserted in the external carotid artery and kept above 80 mmHg by infusion of dextran solution if necessary. No infusion of suprarenin was used. Rectal temperature was maintained close to 37.5 °C.

*Preparation.* For intracellular recordings (eight experiments) a laminectomy was performed to

expose the lumbo-sacral spinal cord. In these experiments the ventral roots L<sub>5</sub>-S<sub>1</sub> as well as the following hind limb nerves were cut and mounted for electrical stimulation (abbreviations are given in parentheses): posterior biceps and semitendinosus (PBSt), flexor digitorum and hallucis longus and plantaris (FDL-Pl), interosseous not being removed, anterior biceps and semimembranosus (ABSm), peroneus longus, brevis and tertius (SPM), tibialis anterior and extensor digitorum longus (DP), plantar section of the tibial nerve (Tib), suralis (Sur), and cutaneous section of the superficial peroneal nerve (SPC).

Extracellular filament recordings (seven experiments) were performed as neurograms from nerves to the following muscles: quadriceps (Q) and PBSt on both sides, medial and lateral branch of the gastrocnemius-soleus (GS) contralateral to the side of chemical stimulation (c. MG, c. LGS). In these experiments dorsal and ventral roots remained intact.

In all experiments the nerve to the ipsilateral GS muscle was mounted for electrical stimulation but was left in continuity, otherwise the hind limb was denervated except for a part of the hip region. The animals were rigidly fixed in a spinal frame and over the wounds pools were formed and filled with warm paraffin oil.

*Induction of fictive locomotion.* Fictive spinal locomotion or an enhanced readiness for locomotor-like rhythmicity was induced by i.v. injection of nialamide (Pfizer), 100 mg/kg immediately after the initial preparation, followed by i.v. injection of L-DOPA (Roche), 40-100 mg/kg after 6-7 hr (Jankowska *et al.* 1967; Viala & Buser, 1971; Grillner & Zangger, 1974).

*Recording and electrical stimulation.* Intracellular recordings were made from twenty-four lumbar  $\alpha$ -motoneurons in L<sub>7</sub> using 3M-K citrate micro-electrodes. The motoneurons were identified by antidromic electrical stimulation of the ventral roots and stimulation of group Ia afferents of the corresponding muscle nerve. Electrical stimulation was performed with single rectangular pulses (duration 0.1 msec); the strength is expressed in multiples of the threshold (*T*) for the nerve. Intracellular recordings were performed in a.c. (band width 0.1 Hz-3 or 10 kHz) when the responses to electrical stimulation were tested. The stimulus strength was graded to values of 50 *T*. Latencies of the post-synaptic potentials were measured with reference to the incoming volley recorded from the L<sub>7</sub> root entry zone. Continuous d.c. recording of the membrane potential of the motoneurons was performed during fictive locomotion when the effects of chemically excited fine muscle afferents were studied. In order to identify locomotor activity extracellular recordings were made from filaments of the L<sub>7</sub> and S<sub>1</sub> ventral roots in experiments with intracellular recordings and from muscle nerve filaments in the other experiments. The active units in the ventral root filaments were identified by their response to low threshold stimulation of the appropriate muscle nerve (Schomburg, Roesler & Meinck, 1977).

*Chemical stimulation.* A fine cannula was inserted into a branch of the sural artery for i.a. injection of the test solutions into both heads of the GS muscle. The normal blood supply of the muscle was not disturbed by this arrangement. Blood circulation and, thus, the distribution of the test solutions were tested several times in the course of the experiments by i.a. injection of Evans Blue. The chemical substances used were bradykinin triacetate (81  $\mu$ M) and KCl (320 mM). These agents were administered in doses which are known to elicit pain reactions in animals (Guzman, Braun & Lim, 1962) and pain in man (Lindahl, 1961) when injected into the skin (see also Coffman, 1966). Doses used in the present experiments were: bradykinin, 26  $\mu$ g; KCl, 3.8 mg; they were applied at room temperature as single shot injections in a volume of 0.3 ml. within about 10 sec (Franz & Mense, 1975). Using this method only group III and group IV muscle afferents are activated, whereas the activity of spindle and tendon organ afferents is not increased (Mense, 1977). Intravenous injections of the test substances into the jugular vein were performed to exclude possible sites of action of the stimulants outside the GS muscle. In addition, as a control, Ringer solution was applied in the same manner as the test solutions to exclude any non-specific effects or a thermic action of the solutions.

## RESULTS

### *Extracellular recordings*

*Induction of locomotor-like activity.* As a rule recording started 6-7 hr after the pre-treatment with nialamide. At this state (without L-DOPA) in the acute spinal immobilized preparations no alternating rhythmic activity was observed in the neurograms of the nerve filaments of the ipsi- and contralateral hind limb. However,

activation of group III and IV afferents of the left GS muscle by chemical stimulation or cutaneous nerve stimulation induced a transient rhythmic activity which generally passed over to an arrhythmic hyperactivity (Fig. 1). As can be seen in Fig. 1, in principle both chemical agents evoke similar effects but with different latency and duration. In this case in the contralateral hind limb a transient rhythmic alternating

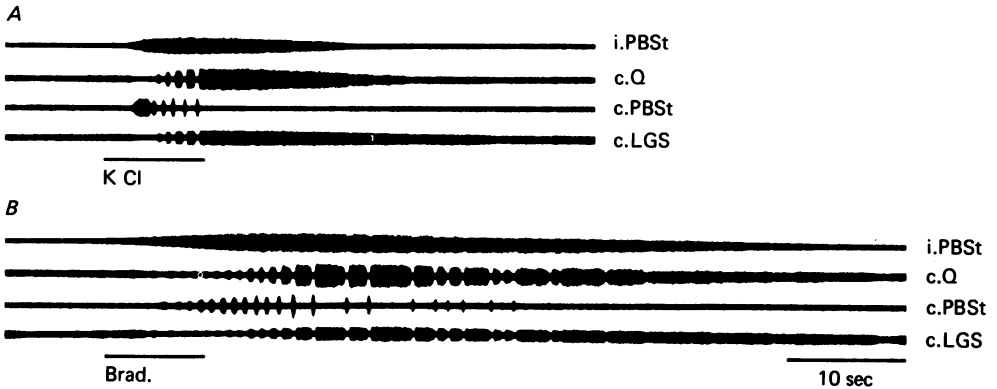


Fig. 1. Responses of various motoneurone pools to i.a. injections of *A*, KCl and *B*, bradykinin triacetate (Brad.) into the gastrocnemius-soleus muscle. The duration of the injections is marked by the bars below *A* and *B*. High spinal cat; pre-treated with nialamide but without L-DOPA. Simultaneous recordings from nerve filaments to ipsi- (i.) or contralateral (c.) quadriceps (Q), posterior biceps and semitendinosus (PBSt) and lateral gastrocnemius-soleus (LGS) muscles.

activity was found in nerves to flexor and extensor muscles of the knee and ankle. In contrast to this effect, a rhythmic activity was almost absent in the ipsilateral knee flexor PBSt which displayed a transient tonic unmodulated hyperactivity. In more than two thirds of the tests the tonic hyperactivity in the PBSt nerve was accompanied by a depression of background activity to the antagonistic quadriceps. If a clear alternating rhythmic activity was induced, the burst duration of the extensors was longer than that of flexors.

After the i.v. injection of L-DOPA, a rhythmic alternating discharge pattern in at least three of the muscle nerves or two ventral root filaments was observed in ten out of the fifteen acute spinal cats. In this preparatory state both the chemical stimulation of fine muscle afferents and the electrically stimulated cutaneous afferents were able to make the rhythm more pronounced or to induce a missing rhythmic activity (Fig. 2).

The results collected from sixty-one acute high spinal anaemic decapitate cats pre-treated with nialamide of different experimental series with more than 120 injections of L-DOPA (interval 1–4 hr) showed a distinct dependence of the occurrence of fictive locomotion on the dose of L-DOPA. With L-DOPA at a dose of less than 30 mg/kg no stable spontaneous rhythmic activity could be induced. Here, afferent nerve stimulation was required to elicit locomotor activity, which did not outlast the stimulation or at least did not outlast it for more than 5 sec. Doses of more than 100 mg/kg also failed to induce a stable long lasting locomotor pattern, but caused an irregular motor hyperactivity which could be preceded by a short period (less than 1 min to about 20 min) of regular rhythmic activity. In about two thirds of cases, after i.v. injection of 40–100 mg L-DOPA/kg a stable locomotor rhythm was observed occurring about 10–40 min after the injection and lasting for about 2–8 hr (in about 60% of cases; 30% of cases less than 2 hr; 10% up to 4½ hr). After this

period the regular rhythmic activity turned into an irregular hyperactivity in more than two thirds of tests. In this state afferent nerve stimulation caused an increased motor activity which was not regularly modulated. Only in four experiments was it possible to restore a stable regular rhythmicity by a repeated i.v. injection of L-DOPA.

*Effects of fine muscle and cutaneous afferents on fictive locomotion.* One main feature of the responses induced by chemical stimulation of the GS muscle and by electrical

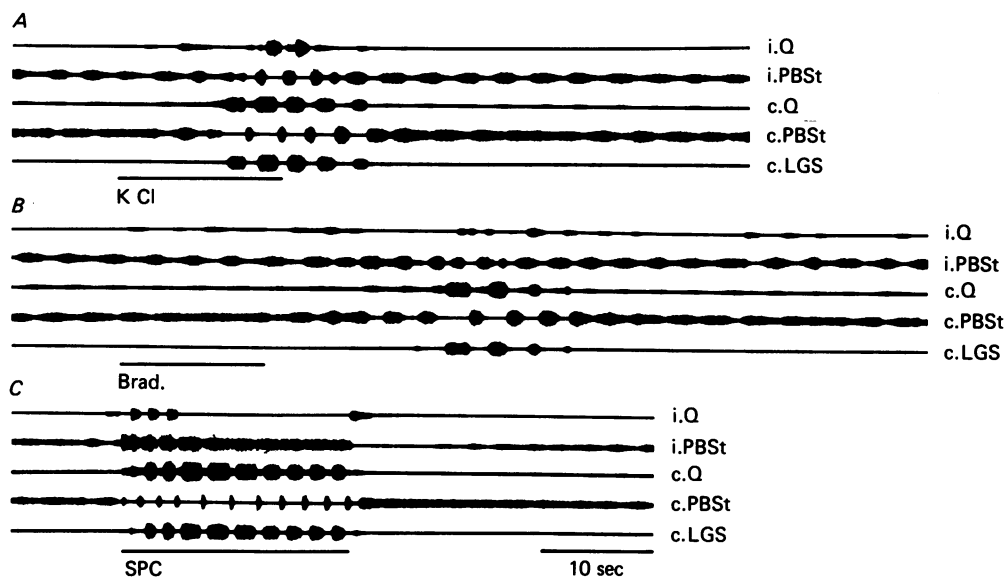


Fig. 2. Modulation of fictive locomotor activity by chemical stimulation of fine muscle afferents (A and B) and electrical stimulation of cutaneous (C) afferents. High spinal cat, pre-treated with nialamide and L-DOPA. Simultaneous recording from nerves to the ipsi- (i.) or contralateral (c.) PBSt, Q and LGS muscles. The duration of the single shot injections of KCl and bradykinin (Brad.) is marked by bars below A and B. The duration of SPC nerve stimulation (50 Hz; 5 times threshold) is marked by the bar below C.

stimulation of cutaneous afferents was that a pre-existent rhythm became more pronounced (Fig. 2). In Fig. 2A, second and fourth traces, it can be seen that the tonic activity which was partly filling the interphasic intervals was completely suppressed during and to a certain extent after application of KCl. Thus, the pre-existent rhythm became accentuated by a more abrupt transition from the active phase to the non-active interval. Except for the time course the i.a. injections of KCl and bradykinin triacetate caused similar effects (Fig. 2A and B). However, after administration of bradykinin triacetate the effects were weaker, i.e. the depression of the tonic background activity was less complete and/or the transition between the active and inactive phases was less sharply defined. Moreover, in about one third of the tests the effects after bradykinin were missing while they were well developed after KCl application.

Principally the same pattern of response as induced by chemically activated group III and IV muscle afferents could be observed with cutaneous nerve stimulation (Fig. 2C). The record of Fig. 2C gives another example of a different response pattern of

both limbs. While a distinct alternating flexor–extensor activity occurred on the contralateral side, mainly an arrhythmic hyperactivity of the PBSt was observed ipsilaterally.

If no spontaneous rhythmic activity occurred after premedication with nialamide and L-DOPA in some muscle nerves, it was possible by i.a. injections of the stimulants or by electrical stimulation of cutaneous nerves to induce a transient rhythmic

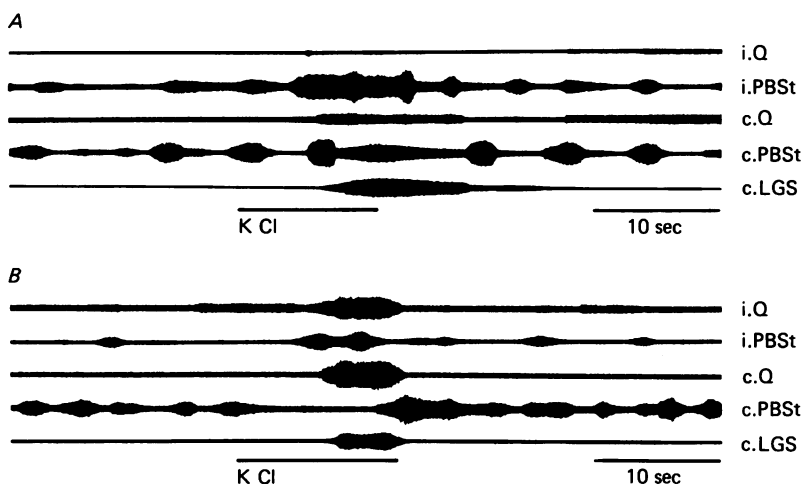


Fig. 3. Modification of fictive locomotion induced by nialamide and L-DOPA in two high spinal cats (*A* and *B*) by chemical stimulation of the GS muscle with KCl while recording from the muscle nerves to PBSt, Q and LGS. The i.a. injections of KCl are marked by bars.

activity, which, however, was restricted to the period of afferent fibre activation and in the case of electrical stimulation did not outlast the end of stimulation for more than 2–10 sec. An example of such a transiently occurring rhythm can be seen in the traces of the c.LGS recordings in Fig. 2 and 4.

The response pattern to chemical stimulation of the group III and IV muscle afferents during fictive locomotion was not stereotyped. Besides the described accentuation of the rhythmic activity another type of reaction was observed; a pre-existent locomotor-like activity was more or less completely overridden by a strong transient tonic hyperactivity (Fig. 3*A*, second and fourth traces). Such a transient tonic activity, which blocked the rhythm, could occur in parallel in nerves to antagonistic muscles (Fig. 3*A*), or was accompanied by a cessation of activity in one or two nerves, similar to the pattern shown in the record of the c.PBSt nerve in Fig. 3*B*.

Both types of response pattern to chemical stimulation, the accentuation or induction of a rhythmic activity and the blockade of the rhythm, were observed in a ratio of about 2 to 1. Since they could occur in the course of one and the same experiment we assume that the response pattern depends on a changing state of the animal and/or on slight differences of the afferent inflow. In order to analyse the influence of varying afferent inflow during weak locomotor activity (see records of ipsi- and contralateral PBSt nerves in Fig. 4), the effects of graded electrical

stimulation of the ipsilateral cutaneous nerves (SPC, Sur) were studied (Fig. 4). It can be seen in Fig. 4 that during weak stimuli the response pattern shows a relatively distinct tonic component. With increasing stimulus strength an increasing rhythmicity occurred: a rhythm which was missing before was established or a weak pre-existent rhythm became more pronounced. The reaction to cutaneous nerve stimulation could

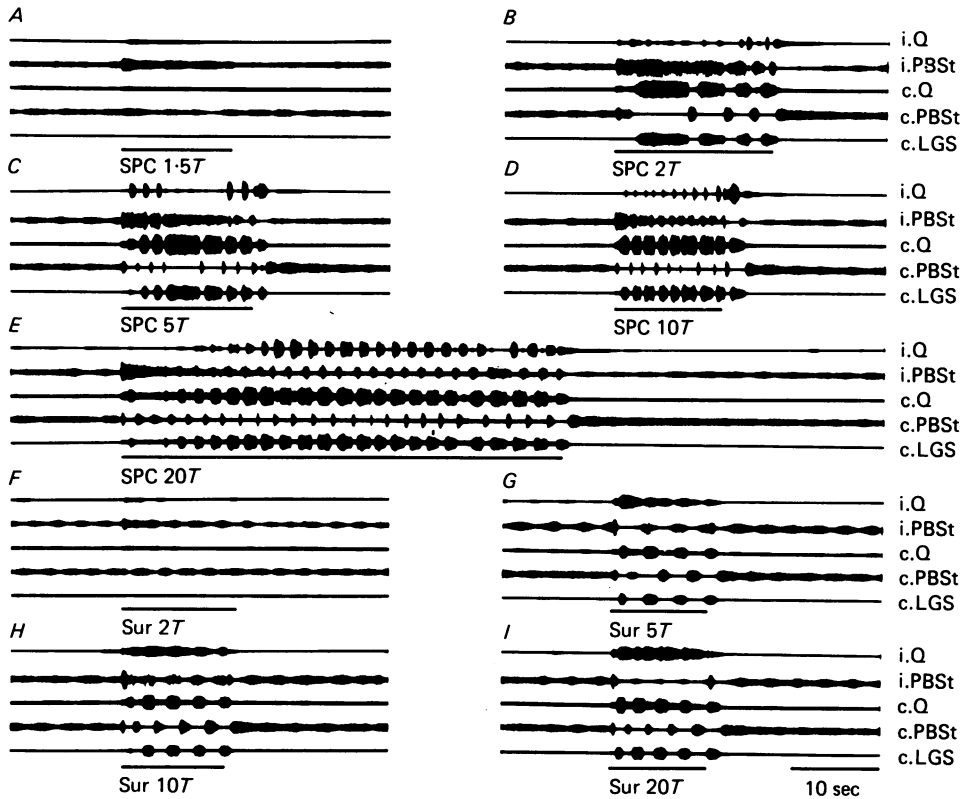


Fig. 4. Effects of electrical stimulation of cutaneous nerves (SPC, Sur) with increasing strength on fictive locomotion. Recording techniques as described in the legends of the previous Figures. Repetitive (50 Hz) electrical stimulation with stimulation strength as indicated in multiples of the threshold ( $T$ ). Duration of stimulation is marked by bars.

be different in both limbs, e.g. stimulating the Sur nerve with 20  $T$  (Fig. 4I) induced a transient tonic hyperactivity with some superimposed cyclic activity in the nerve to the i.Q muscle, whereas a clear accentuated rhythm occurred in the c.Q nerve during the period of stimulation. At the same stimulation strength the SPC nerve (Fig. 4E) evoked a pronounced rhythmic discharge, showing that the action of cutaneous afferents of different origin on fictive locomotion may differ.

#### Intracellular recordings

Intracellular recordings were made from twenty-four ipsilateral identified lumbar  $\alpha$ -motoneurons for which the period of recording was long enough to study the effects of chemically activated group III and IV muscle afferents during fictive locomotion. The cells recorded from belonged to various hind limb muscles as listed (numbers of

cells are indicated in parentheses): PBSt (eight), GS (seven), FDL-Pl (five), and ABSm (four). Recordings from few cells were achieved before administration of L-DOPA. Their responses to the applied algescic agents confirmed our recent results (Kniffki, Schomburg and Steffens, 1980, 1981), i.e. mainly depolarization of the membrane in flexor and hyperpolarization in extensor  $\alpha$ -motoneurones. After treatment with

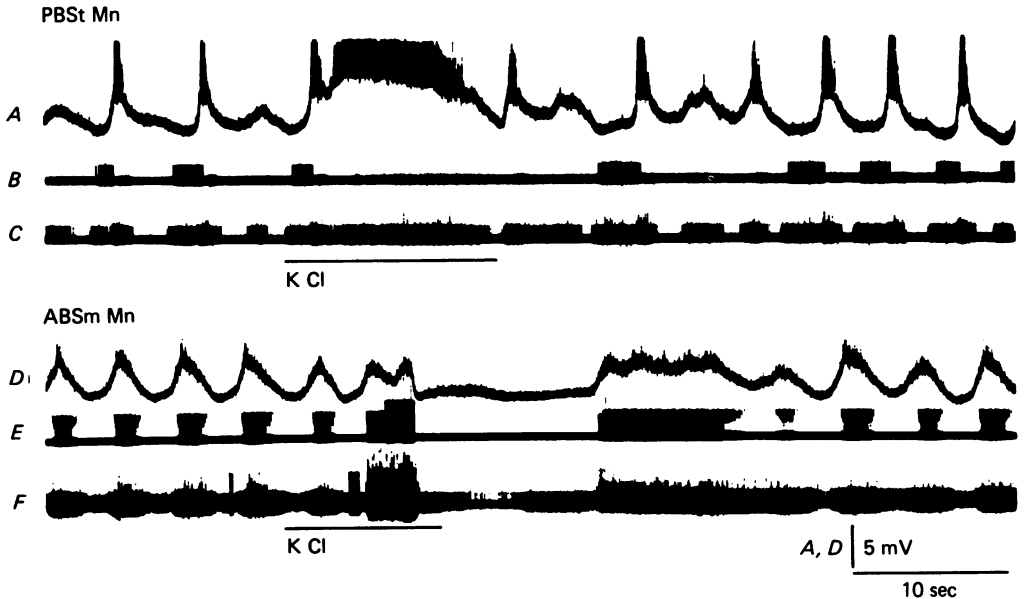


Fig. 5. Responses of an ipsilateral knee flexor motoneurone (PBSt, *A*) and a hip extensor motoneurone (ABSm, *B*) to i.a. injection of KCl into the GS muscle. Intracellular recordings in *A* and *D*. In *B*, *C*, *E* and *F* extracellular recordings from filaments of the ventral roots  $L_7$  and  $S_1$  are shown. *B*: activity of an axon to the GS muscle (large fibre); *E*: activity of an ABSm fibre (large spontaneously rhythmically active unit; larger unit and smaller unit activated in the course of stimulation not identified); *C* and *F*: unidentified multifibre recordings. The duration of the injections is marked by bars.

L-DOPA almost all motoneurones revealed, at least for a certain period, distinct oscillations of the membrane potential. Fig. 5 shows examples of a PBSt (*A*) and a ABSm (*D*) motoneurone; the oligo- (*B* and *E*) and multifibre (*C* and *F*) ventral root recordings together with the cyclic oscillations of the motoneuronal membrane potential reflect a clear locomotor activity; the large unit in *B* was identified as a GS efferent fibre, the large spontaneously active one in *E* as an ABSm fibre. By i.a. injection of KCl, i.e. by the activation of fine muscle afferents, the cyclic alternations of the membrane potential of the recorded PBSt motoneurone (Fig. 5*A*) are completely overridden by a transient prolonged depolarization, very similar to the behaviour of the i. PBSt neurogram in the experiment shown in Fig. 3*A*. On the other hand, the membrane of the ABSm motoneurone (Fig. 5*D*) shows a tonic hyperpolarization followed by a period of stable depolarization. An equivalent phenomenon is seen in the c. PBSt trace in Fig. 3*B*. The results from intracellular recordings agreed with those from extracellular recordings. However, they showed that the cyclic membrane depolarization may often remain well below the firing level,



indicating for example that a missing spontaneous rhythm in the neurogram of the c. LGS nerve in Figs. 2 and 4 does not necessarily mean that the corresponding motoneurons are not periodically modulated. Less than one third of about eighty motoneurons to hind limb muscles which were intracellularly recorded from during fictive locomotion, in this and a former series of experiments, showed a spontaneous burst activity during the phase of depolarization.

### *Response characteristics*

Due to irregularities of the locomotor rhythm and to the length of the fictive step cycles an exact measurement of the time course of the effects was difficult to determine. However, two general features coincided with the observations of former experiments: the responses to bradykinin triacetate appeared with a longer latency and had a longer duration than those to KCl. The latencies were comparable to those measured in previous experiments on recordings from motoneurons under static conditions (mean latency: KCl 3.4 sec, bradykinin 15.4 sec; Kniffki *et al.* 1981), while the mean durations tended to be slightly longer (KCl 15 sec, bradykinin 57 sec). As described above, the effects after injection of bradykinin were less pronounced than those after KCl and in about one third of tests they were even missing. This is in agreement with a recent finding (Hong, Kniffki, Mense, Schmidt & Wendisch, 1979) where the effectiveness of both chemical stimuli was studied on neurones of the spinocervical tract. The differences are probably due to the different input pattern of group III and IV afferents to the spinal cord (Fock & Mense, 1976).

No responses were induced by systemic i.v. application of bradykinin triacetate or KCl. Therefore, no different site of action of these algescic agents could be found, as was established for example for 5-HT (Hong *et al.* 1979). The control injections of Ringer solution into the muscle artery failed to detect a possible unspecific or thermic action of the applied solution. Moreover, the responses to the i.a. injection of the algescic agents were abolished by cutting the ipsilateral GS nerve. Thus it can be presumed that the observed effects were due to a specific activation of receptors within the muscle itself.

### DISCUSSION

In 1913 Sherrington concluded from experiments with peripheral nerve stimulation in decerebrate cats, that the spinal cord is capable of generating an alternating flexor-extensor activity, which he named 'reflex stepping'. His conclusions were questioned by later experiments of Egger & Wymann (1969). Recently, it has been shown that the spinal cord deprived of both its supraspinal control and peripheral feed-back can generate long lasting co-ordinated rhythmic activity in motoneurons to limb muscles of curarized animals, provided the preparation is pre-treated with nialamide and/or L-DOPA (Jankowska *et al.* 1967; Viala & Buser, 1971; Grillner & Zangger, 1974). This severely reduced preparation proved the existence of spinal structures generating a locomotor-like activity, which remains 'fictive' in paralysed animals. The provocation of fictive locomotion in spinal animals may be quite problematical, e.g. in five out of fifteen experiments we failed to induce a stable locomotor activity. Presumably, a certain optimal level of spinal activity, which is variable between animals, has to be reached and kept for co-ordinate operation of

the locomotor centres. If the level of activity is too low it fails to trigger locomotion. If it is too high, a co-ordinated function is no longer maintainable and an irregular motor hyperactivity will be the consequence. This conclusion resulted from the observation that fictive locomotion can only be evoked by a limited range of L-DOPA dosage, and that changes of the afferent input, e.g. by varying the stimulus strength, or changes of the conditions of the preparation, may alter the response pattern to stimuli from a more tonic to a more rhythmic feature or vice versa.

Locomotor activity occurring in motoneurons of one limb was not always accompanied by a corresponding activity in the contralateral limb. Sometimes not even all motoneurone pools to the muscles of one limb were engaged in the rhythmic activity. These findings confirm the assumption that separate locomotor centres exist for each limb and that these centres in their turn are divided into subcentres for the control of movements about each joint (Edgerton, Grillner, Sjöström & Zangger, 1976). In spinal cats these subcentres often show an interjoint and interlimb co-ordination, but as demonstrated they can be decoupled even by spinal mechanisms. The possibility of uncoupling a rigid connexion between the locomotor centres by descending motor commands appears to be necessary for the performance of voluntary goal directed limb movements. However, it cannot be excluded that there is no uncoupling of the centres in this case but that a new pattern of co-operation is formed.

The results revealed an extensive correspondence between the locomotor effects evoked by fine muscle afferents and those from cutaneous afferents, similar to that observed with the synaptic effects evoked by these groups of afferents in  $\alpha$ -motoneurons (Kniffki, Schomburg & Steffens, 1979*a*, 1981). Since cutaneous afferents and probably also part of the fine muscle afferents (Kniffki, Mense & Schmidt, 1978, 1981; Mense, 1978) are activated during normal movements, these fibres – as a part of the flexor reflex system (Eccles & Lundberg, 1959) – may function as a peripheral feed-back to the spinal locomotor centres similar to the feed-back mechanism assumed to be performed by the flexor reflex system in other movements (Lundberg, 1979).

Thus, the locomotor centres and different afferent fibres form a complex control system: on one hand the locomotor centres are modulated by the afferent input, on the other hand they exert a potent control of the transmission in reflex pathways from cutaneous and muscle afferents to motoneurons (Forssberg, Grillner & Rossignol, 1975, 1977; Schomburg *et al.* 1977; Andersson, Forssberg, Grillner & Lindquist, 1978; Schomburg & Behrends, 1978*a, b*; Forssberg, 1979). At present it cannot be estimated to what extent the nociceptive component of the chemically activated group III and IV muscle afferents was participating or even dominating in the effects on locomotor activity. This nociceptive component could be of a quite different functional relevance since it is missing during normal locomotion.

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