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RESEARCH ARTICLE

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Depression of transmission from group II muscle afferents by electrical stimulation of the cuneiform nucleus in the cat

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Abstract The effects of short trains of electrical stimuli applied within the cuneiform nucleus and the subcuneiform region were examined on transmission from group I and group II muscle afferents to first-order spinal neurons. Variations in the effectiveness of transmission from these afferents were assessed from changes in the sizes of the monosynaptic component of extracellular field potentials evoked following stimulation of muscle nerves. Field potentials evoked from group II muscle afferents in the dorsal horn of the midlumbar and sacral segments and in the intermediate zone of the midlumbar segments were reduced when the test stimuli applied to peripheral nerves were preceded by conditioning stimulation of the cuneiform nucleus or the subcuneiform region. The depression occurred at conditioning-testing intervals of 20–400 ms, being maximal at intervals of 32–72 ms for dorsal horn potentials and 40–100 ms for intermediate zone potentials. At the shortest intervals, both group II and group I field potentials in the intermediate zone were depressed. Conditioning stimulation of the cuneiform nucleus depressed group II field potentials nearly as effectively as conditioning stimulation of the coerulear or raphe nuclei. We propose that the nonselective depression of transmission from group I and II afferents at short intervals is due to the activation of reticulospinal pathways by cells or fibers stimulated within the cuneiform area. We also propose that the selective depression of transmission from group II afferents at long intervals is mediated at least partly by monoaminergic pathways, in view of the similarity of the effects of conditioning stimulation of the cuneiform nucleus and of the brainstem monoaminergic nuclei and by directly applied monoamines (Bras et al. 1990). In addition, it might be caused by primary afferent depolarization mediated by non-monoaminergic fibers (Riddell et al. 1992).

Key words Cuneiform nucleus · Synaptic transmission · Spindle afferents · Spinal cord · Cat

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Introduction

The cuneiform nucleus is of particular interest in the analysis of the neuronal mechanisms of locomotion, because electrical stimuli applied in the caudal part of this nucleus are highly effective in evoking locomotion (Shik et al. 1967). However, neurons of the cuneiform nucleus do not project to the spinal cord (Edwards 1975; Steeves and Jordan 1984) and therefore affect spinal neuronal networks of locomotion only indirectly. As judged by the morphologically established projections of cuneiform neurons, their actions might be relayed by a number of descending tract neurons, including reticulospinal (Edwards 1975; Garcia-Rill et al. 1983b; Steeves and Jordan 1984; see also Noga et al. 1988, 1991b), coerulospinal (Edwards 1975; Sotnichenko 1985) and raphespinal (Edwards 1975; Steeves and Jordan 1984). The contribution of the two latter neuronal groups to locomotion has also been indicated by c-*fos* immunohistological labelling of neurons activated by stimulation of the cuneiform nucleus (Dai et al. 1991), and is in keeping with the observations that, in spinal animals, locomotion may be induced or modulated by intravenous or intraperitoneal administration of the precursors or agonists to noradrenaline (NA) or serotonin (5-HT) (for references, see Lundberg 1982; Grillner 1986; Barbeau and Rossignol 1991) and by topical application of these drugs (Kiehn et al. 1992; see also Cazalets et al. 1992). Locomotion may, nevertheless, be induced following depletion of NA and/or 5-HT (Steeves et al. 1980), indicating that activation of the monoaminergic pathways is not conditio sine qua non for activation of spinal locomotor networks. This, together with the recent demonstration that intrathecal administration of excitatory amino acid antagonists blocks locomotion evoked by

stimulation of the cuneiform nucleus (Douglas et al. 1992), indicates that neurons of this nucleus may operate via several parallel pathways. The aim of this study has therefore been to investigate whether electrical stimuli applied in the cuneiform nucleus reproduce the effects of directly applied monoamines (Bras et al. 1990) and of stimulation of the monoaminergic brain stem nuclei (Noga et al. 1992; Skoog and Noga 1991) on transmission from group I and/or group II muscle afferents to spinal neurons (Edgley and Jankowska 1987a,b; Jankowska and Riddell 1993). A replication of the effect of electrical stimulation of the brainstem monoaminergic nuclei by stimulation of the cuneiform nuclei would be evident by the selective depression of transmission from group II muscle afferents to spinal neurons by appropriately timed conditioning stimuli. Preliminary results of this study have been reported in abstract form (Noga et al. 1991a).

Materials and methods

Preparation

Experiments were performed on 20 adult cats anesthetized with chloralose, as described by Noga et al. (1992). Some of the cats were also used for experiments reported by Noga et al. (1992) and Jankowska et al. (1993). The experiments were approved by the local ethics committee and followed the principles of laboratory animal care as specified by the Council of the American Physiological Society. The initial surgical procedures were completed either under a mixture of 70% nitrous oxide, 30% oxygen and 0.5–1.5% halothane or under ether anesthesia. Anesthesia was subsequently maintained with chloralose (initial dose of 60–80 mg/kg, supplemented to a total dose of 6–10 mg/kg/h). The adequacy of anesthesia was assessed by monitoring withdrawal, corneal and pupillary reflexes during surgery and, following paralysis with gallamine triethiodide, by observing the diameter of pupils and the blood pressure during the experimental procedures. The level of chloralose anesthesia has been found to be deep in a series of nonparalysed cats kept under observation for more than 36 h (see Bras et al. 1990). Following paralysis, the animals were artificially ventilated. The end-tidal CO_2 was maintained around 4% and the mean blood pressure between 100–120 mm Hg, by adjusting the ventilation parameters and the rate of infusion of a 100 mM sodium bicarbonate solution in 5% glucose (1–2 ml/kg/h). Body temperature was maintained at approximately 37°C.

The nerves to the quadriceps and sartorius muscles on the left side (ipsilateral to the side of recording) were dissected free and were mounted together in a cuff electrode for stimulation. Other hindlimb nerves were mounted on double electrodes in a paraffin oil pool. The spinal cord was exposed from the second lumbar to the sacral segments. The dura was left intact, except for small holes made for insertion of the recording electrodes, to minimize circulatory disruption and to enhance stability of the spinal cord during intracellular and extracellular recording from spinal neurons. A thoracic laminectomy at the level of the T12-13 segments was made in a few experiments, to allow placement of stimulating electrodes on the surface of the spinal cord above the lumbosacral enlargement for the differentiation of ascending tract neurons from interneurons by their antidromic activation following such stimuli. Craniotomies were performed over the parietal lobe and over the middle part of the cerebellum for the insertion of the brainstem stimulation electrodes.

Stimulation and recording

The effects of brainstem conditioning stimulation on transmission to spinal neurons were assessed from changes in the area or peak amplitude of monosynaptic field potentials evoked by stimulation of muscle nerves and from changes in the responses of individual sacral dorsal horn neurons induced by monosynaptic excitation of group II muscle afferents.

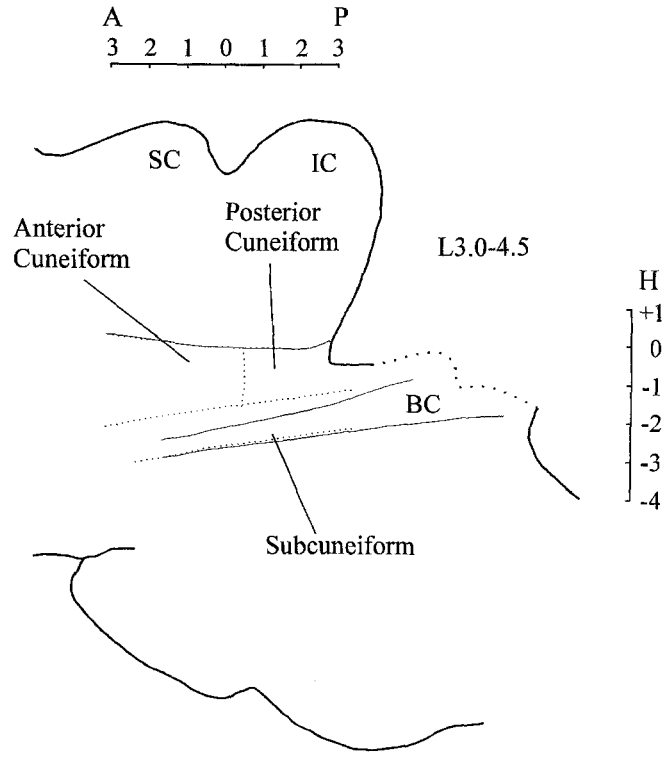

Fig. 1 Boundaries of the cuneiform area considered in the present study illustrated on a representative sagittal plane 4 mm lateral (L) to the midline. The cuneiform area is subdivided into the anterior cuneiform nucleus, the posterior cuneiform nucleus, and subcuneiform region, and ranged from 3.0 to 4.5 mm lateral to the midline. All stimulation sites within ca. 0.5 mm of the boundaries of the various cuneiform regions are considered within each category due to the spread of current at the stimulation sites. *A* Anterior, *P* posterior, *H* horizontal, *SC* superior colliculus, *IC* inferior colliculus, *BC* brachium conjunctivum

Test stimuli

Field potentials were evoked by electrical stimuli [0.1 ms duration, at five times threshold (T) for the most sensitive fibers, which activated both group I and group II afferents] applied to hindlimb muscle nerves. Field potentials in the L4 and L5 segments were produced by stimulation of the quadriceps-sartorius nerves and those in the S1 and S2 segments by stimulation of the posterior biceps-semitendinosus and gastrocnemius-soleus nerves. Field potentials recorded in the dorsal horn (midlumbar and sacral) were evoked exclusively from group II fibers, at thresholds 2–2.5 T. Field potentials recorded in the intermediate zone included an early component from group I fibers (at thresholds 1–1.4 T) and a later component from group II fibers (at thresholds 2–2.5 T). All these field potentials were evoked at latencies that were within ranges of monosynaptically evoked actions of group I or group II afferents of different nerves established in previous studies (Edgley and Jankowska 1987a,b; Jankowska and Riddell 1993), taking into account a delay in the time of arrival of group II volleys with respect to group I volleys to the spinal cord (depending on the length of the peripheral nerves) and an additional delay due to low conduction velocity of collaterals of group II afferents within the gray matter. For instance, in view of the about 0.8 ms later ar-

rival of group II than of group I volleys in the quadriceps nerve, the latency of a field potential of 1.5 ms from the group I volley would correspond to about 0.7 ms from the group II volley.

Responses of single sacral dorsal horn neurons recorded extracellularly or intracellularly were evoked by stimuli applied to the posterior biceps-semitendinosus and gastrocnemius-soleus nerves at strengths activating group II muscle afferents.

Conditioning stimuli

To activate the ipsilateral or contralateral cuneiform area, electrodes were introduced stereotaxically at an angle of 20° (tip directed caudally) aiming at sites bounded by the coordinates A3–P2.8, L3–4.5 and H–0 to –2.5, according to the atlas of Berman (1968). The cuneiform area was subdivided into three zones (Fig. 1): the anterior cuneiform nucleus, the posterior cuneiform nucleus, and the subcuneiform region. The first two were considered to extend caudal and rostral to P 0.5 level, respectively. The subcuneiform region overlapped with the brachium conjunctivum. The posterior cuneiform nucleus corresponds to the mesencephalic locomotor region in decerebrate cats (see Shik et al. 1967; Noga et al. 1991b). Stimulation sites were considered to be within these zones if they were no more than 0.5 mm from their outer boundaries in view of the spread of current away from the electrode tip with stimuli of 50–100 μA (Gustafsson and Jankowska 1976).

Electrodes were also placed in the red nucleus and in the nuclei of origin of the descending monoaminergic pathways (locus coeruleus/subcoeruleus, Kölliker-Fuse, and/or raphe), according to procedures described previously (Noga et al. 1992). The effectiveness of the conditioning stimuli in reducing midlumbar group II field potentials determined the final location of the coerulear and raphe stimulating electrodes; the electrodes were left at those sites from which the most effective depression was evoked.

At the end of each experiment, the location of each stimulation electrode was verified histologically following electrolytic lesions at selected electrode positions (1 mA, 8–10 s) and perfusion with 10% formalin. Frozen sections of the brainstem (either in the transverse or the sagittal plane, 100 μm thick) were counterstained with toluidine blue or cresyl violet. The various stimulation sites were then defined with respect to the position of the electrode tip (marked by the electrolytic lesion) along the electrode tracks, taking into account the degree of shrinkage indicated by the decrease in distances between individual tracks. Only effects of stimulation at a location within or just outside the nuclei, as subsequently verified histologically, are reported unless stated otherwise. The reconstructed stimulation sites were transferred to standard maps of brain sections (according to Berman 1968).

Conditioning stimuli were delivered through insulated tungsten electrodes with exposed tips of about 100 μm. The stimulation was usually delivered in trains (400 Hz) of six to eight monopolar square wave pulses (0.2 ms long) with intensity of 50-100 μA given every 1 s (Noga et al. 1992). Condition-test intervals were varied between 12 and 375 ms in order to determine the effect of descending fibers of varying conduction velocity.

Recording

A total of 25 intermediate zone field potentials and 19 dorsal horn field potentials in the midlumbar segments and eight dorsal horn field potentials in the sacral segments were tested with conditioning stimulation applied to the cuneiform area (several field potentials being recorded in some experiments). Recordings in the dorsal horn and in the intermediate zone were from sites where the amplitudes of the typical field potentials (Edgley and Jankowska 1987a; Jankowska and Riddell 1993) were largest. A total of 19 sacral dorsal horn neurons were recorded. The field potentials and neurons were recorded using microelectrodes filled with 2 M potassium citrate or 2 M NaCl (1.5–2.0 μm tip, 1–6 MΩ), the negativity being recorded as a downward deflection. The peripheral afferent and descending volleys were recorded using a silver ball electrode placed on the dorsal surface of the L5, L6 or S1 segment, with negativity upward.

Analysis

To determine the effects of conditioning stimulation on the tested field potentials, records of potentials induced by alternating sequences of test (t), test and conditioning (ct), or only conditioning (c) stimuli were averaged in separate quarters of a Nicolet (model 1170) averager memory 20 μs/address time base and eight or 16 averages/waveform). In some experiments (n=4), microelectrode and cord dorsum records were digitized at 5–10 KHz using a 1-MHz analog-digital converter and stored on computer hard disk (Masscomp MC563) for later analysis.

Any changes in the test potentials were assessed by first obtaining a sum of the averaged waveforms evoked by the test and conditioning stimuli alone, and by subtracting from this sum the averaged waveform evoked by the test and conditioning stimuli when they were applied together. A depression of the test responses was then represented as a downward deflection in the difference (diff) waveform (Fig. 2). Changes in the size of the test field potentials were measured from the difference traces as either the area or the peak amplitude contained within a 0.8–2.0 (usually 1.0) ms window from the onset of the field potential (to take into account primarily its monosynaptic components) and calculated relative to the test potential area or peak amplitude within the same measurement window. Measurements obtained by either method were comparable (within 5% in 15 examined field potentials) and were therefore grouped together. The size of the conditioned responses was then expressed as a percentage of the size of the field potential evoked by the test stimulus alone. The assessment was straight forward in the cases of field potentials of exclusively group II origin (in the dorsal horn). However, when midlumbar intermediate zone field potentials were tested, any changes in the overlapping group I and II components of these potentials had to be assessed separately. Changes in group I components were measured for a time period from their onset to the onset of the group II components (but not exceeding a window of 2.0 ms), as illustrated in Fig. 2. Changes in the group II components were then calculated after accounting for the group I components which were assumed to decay in a gradual fashion (as usually seen when only group I test field potentials were recorded). Statistical comparisons were made using a two-tailed Mann-Whitney U-test, since some of the samples were too small for parametric statistical tests.

Results

Effects of stimulation of the cuneiform area on field potentials evoked in the intermediate zone of midlumbar segments

Field potentials of group II origin were depressed in size following conditioning stimulation of the anterior cuneiform nucleus, posterior cuneiform nucleus, or subcuneiform region. The test field potentials were depressed to <85% of the control sizes in all but one case (n=36). The depression is exemplified in Fig. $2B_2$ for stimuli applied within the subcuneiform region. In this example, only the second component of the field potential, that evoked by group II afferents, was depressed. The depression was, therefore, as selective as the depression observed following conditioning stimulation of the monoaminergic nuclei (Noga et al. 1992) and following an intravenous (Edgley et al. 1988) or a local (Bras et al. 1990) application of monoamines.

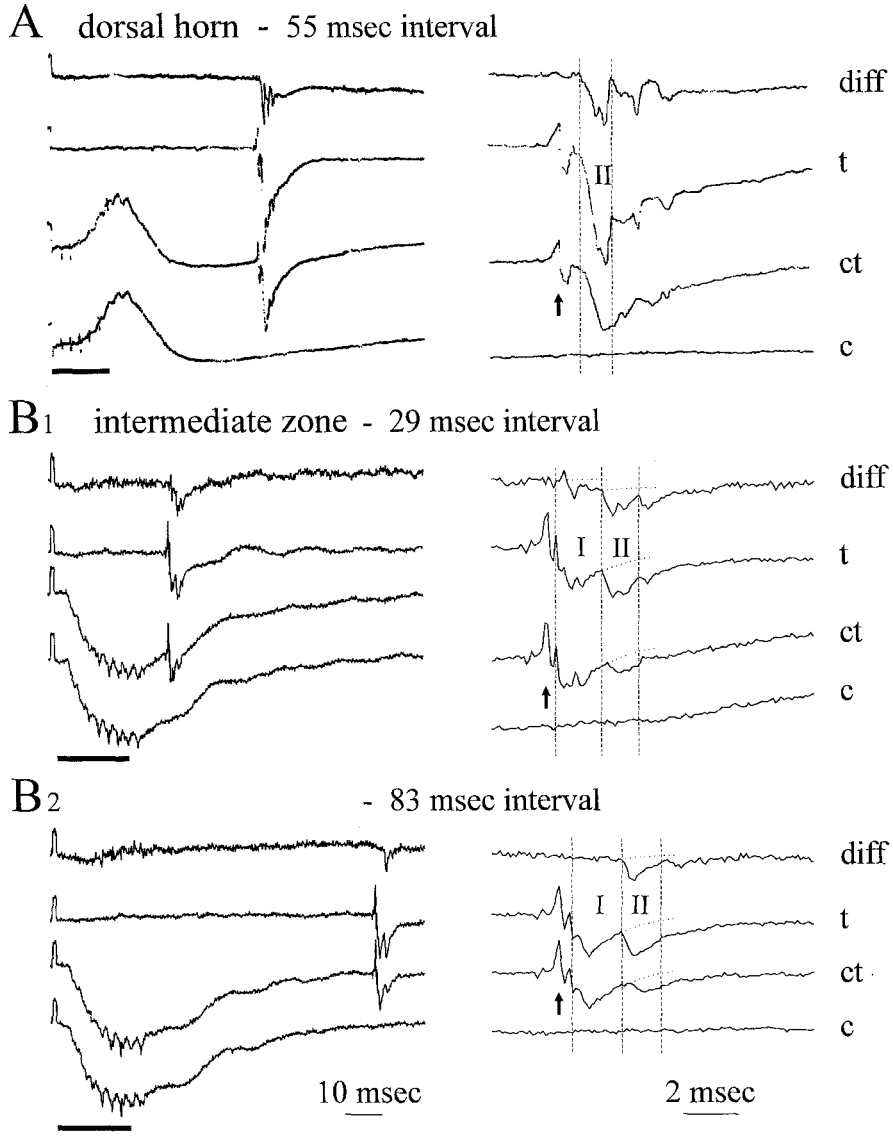

Fig. 2A,B Effect of conditioning stimulation of the cuneiform area on field potentials recorded in the dorsal horn (**A**) and intermediate zone ($\mathbf{B_{1,2}}$) of the midlumbar segments evoked by stimulation of the quadriceps/sartorius nerve (at a strength of five times threshold) activating group I and II muscle afferents. Expanded traces of the field potentials are to the *right*. Averaged responses evoked by test stimuli alone, by conditioning and test stimuli, and by conditioning stimuli alone are labelled *t*, *ct* and *c*, respectively. Traces labelled *diff* have been obtained by subtracting the *ct* trace from the sum of the *c* and *t* traces. Changes in the test potential size following conditioning stimulation were determined from expanded traces for the time periods indicated by *vertical dashed lines*. Any changes in the group I component of the intermediate field potential following conditioning stimulation (as observed in the difference trace) were assumed to decay in a gradual fashion. Stimulation parameters were 100 μA with a train of seven (**A**) or eight (**B**) stimuli at 400 Hz. The period of conditioning stimulation is indicated by the *solid bar*. Condition-test intervals are as indicated. The incoming volleys produced by nerve stimulation are indicated by *arrows*. The labels *I* and *II* indicate the group I and group II components of the field potentials. Note that at the shorter interval (29 ms) both the group I and group II components of the intermediate zone field potential were depressed, while only the group II component was depressed at the longer interval (83 ms). Calibration pulses (in *left traces*) are 1 ms, 200 μV

Time course of the depression of group I and group II components

The depression of group II components was seen over a range of conditioning-testing intervals, usually within 20–30 to over 200–300 ms after the conditioning stimuli, but it peaked at intervals of 40–100 ms and gradually declined over longer intervals (up to about 375 ms), as shown in Fig. 3C. A selective depression of group II field potentials occurred, however, only at conditioning-testing intervals of approximately 60 ms or more, because at shorter intervals it was associated with a depression of group I components (outline symbols in Fig. 3B,D). Thus, the time course of the depression of group I and II components matched that observed following conditioning stimulation of the monoaminergic nuclei (Noga et al. 1992).

Field potentials evoked by group I afferents were depressed at shorter conditioning-testing intervals (Fig. $2B_1$). The depression of group I field potentials was maximal at intervals of approximately 20–30 ms. At

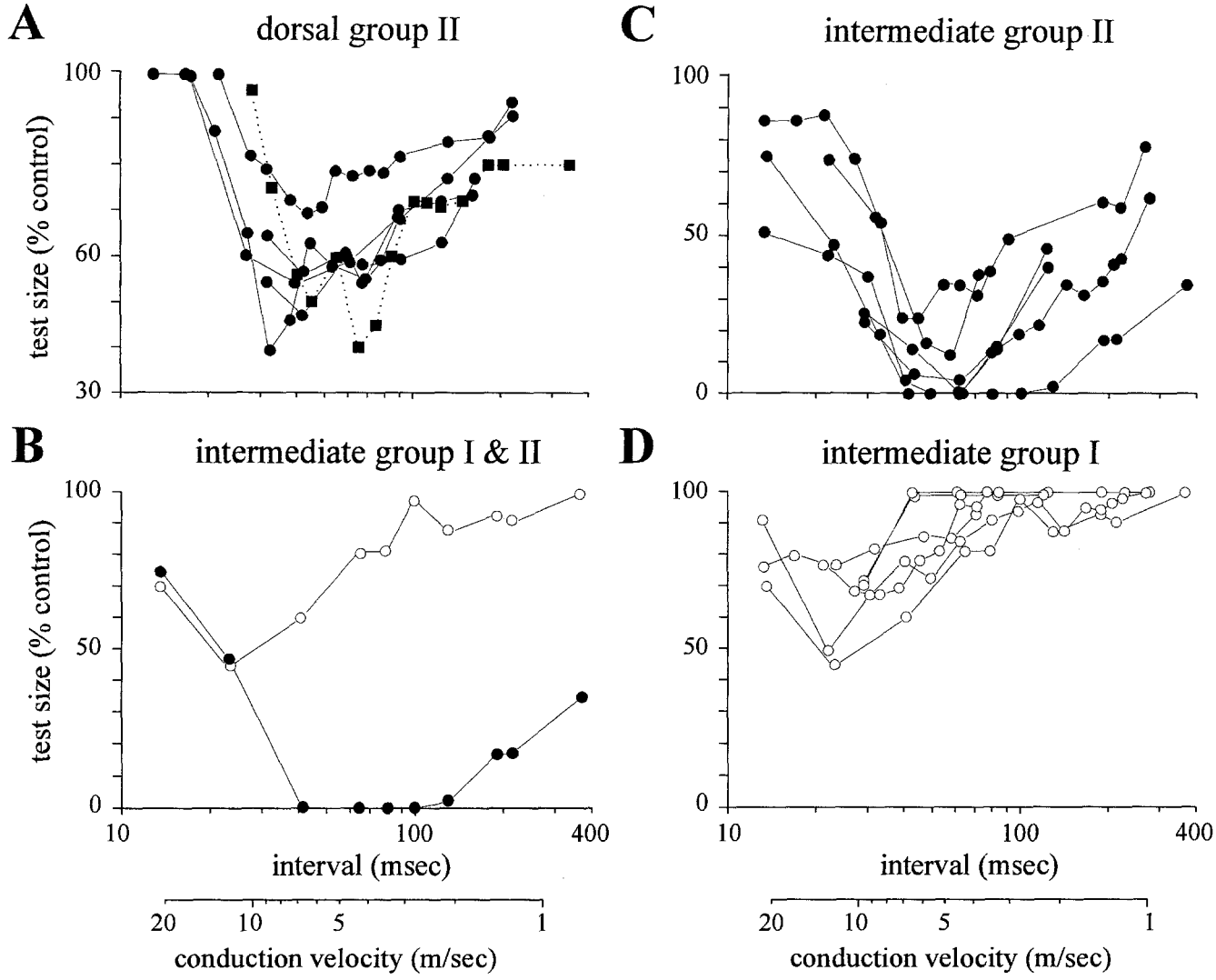

Fig. 3A–D Time course of depression of six dorsal horn and six intermediate zone midlumbar field potentials from the midlumbar segments following conditioning stimulation (trains of six to eight stimuli, 100 μA, 400 Hz) of the cuneiform area. The sizes of group I components (*outline symbols*) and group II components (*solid symbols*) expressed in percentage of their control values are plotted against intervals between the first conditioning stimulus and the test stimulus (note the logarithmic scale). The time course of depression of one sacral dorsal horn field potential in **A** is indicated by the *solid square* symbols and the *dotted line*. The time course of depression of a single intermediate zone field potential (with the group I and II components) is plotted in **B**. Approximate conduction velocities for descending impulses evoked by conditioning stimulation of the cuneiform area and arriving at the lumbosacral enlargement are indicated at the bottom

these intervals, the group I field potentials were depressed to 55.8% (SD=29.0, n=8) of the test size with conditioning stimulation of the cuneiform nuclei (6–8 stimuli, 100 μA, 400 Hz). This depression declined significantly ($P \leq 0.01$) over slightly longer (30–60 ms) intervals (outline symbols in Fig. 3B,D) to 88.5% (SD=8.7, n=21) of the test size at intervals at which depression of group II transmission was maximal. The differential sensitivity of group I and group II field potentials at various conditioning-testing intervals suggests that separate descending systems might be involved in producing the effects observed at shorter or longer intervals. This has been previously described for conditioning stimulation of the monoaminergic nuclei, where the effects observed at peak or longer intervals (40–400 ms) were considered to be evoked by the descending monoaminergic fibers (Noga et al. 1992, see also Skoog and Noga 1991). In comparison, the depression of group I field potentials observed with conditioning stimulation of the raphe and coerulear nuclei (data from Noga et al. 1992, and this study) at shorter conditioning-test intervals was 66.3% (SD=23.5, n=28) and 64.6% (SD=28.9, n=22), respectively. This depression was not significantly different from that observed with conditioning stimulation of the cuneiform nuclei.

For intervals of 35–40 ms, at which there was a steep increase in the depression of group II field potentials and an equally steep decline in the depression of group I field potentials, the L4 segment would be reached by descending nerve impulses in fibers conducting at about 7 m/s (Fig. 3, bottom). For conditioning-testing intervals of 300 ms or longer, actions of fibers conducting at <1 m/s

Table 1 Comparison of depression of dorsal horn and intermediate zone group II field potentials following conditioning stimulation (six to eight shocks, 40–170 ms, 100–150 μA) of the indicated nuclei. The depression (grouped data from all experiments) is expressed as a mean percentage (±standard deviation, *SD*) of the area or amplitude of the field potentials after the conditioning stimuli as compared to that evoked by the test stimulus alone. Only the maximum value (one measurement) for each stimulation site for each field has been included (*n* number of measurements). Data for raphe and coerulear nuclei are from Noga et al. (1992) and/or from additional experiments in the present study. CUN_A Anterior cuneiform nucleus, CUN_P posterior cuneiform nucleus, CUN_S subcuneiform region, CUN_{AP} cuneiform nuclei (including anterior and posterior nuclei), *R* raphe nuclei, *COER* coerulear nuclei, *i* ipsilateral, *co* contralateral

	CUN_A	CUN_P	CUN_S	$iCUN_{AP}$	$coCUN_{AP}$	CUN_{AP}	R	COER
Intermediate								
Mean	17.4	48.4	27.1	29.7	36.1	32.2	25.8	28.7
SD	20.1	25.8	17.3	30.3	24.2	27.7	21.7	20.6
n	12	11	13	14	9	23	49	42
Median	8	53	32	28	36	34	23	26
Range	0–61	0–100	0–53	0–100	0–63	0–100	0–66	0–77
Dorsal horn (midlumbar)								
Mean	73.7	66.1	65.0	72.0	68.0	70.1	58.0	61.6
SD	12.2	18.1	11.1	12.6	18.5	15.3	14.4	14.3
n	10	9	6	10	9	19	31	34
Median	73	62	63.5	68.5	63	67	57	62
Range	60–100	47–100	54–80	60–100	47–100	47–100	31–85	32–88
Dorsal horn (sacral)								
Mean	67.8		69.0	67.8		67.8	56.8	
SD	12.9		2.8	12.9		12.9	11.2	
n	7		2	7		7	8	
Median	75		69	75		75	54	
Range	40–76		67–71	40–76		40–76	40–73	

would occur. The conduction velocity of fibers contributing to the selective depression of group II field potentials is, therefore, within the range expected for axons of descending monoaminergic neurons (see Noga et al. 1992). The non-selective depression of group I and II field potentials occurring at shorter conditioning-testing intervals (less than 30 ms) would involve fibers conducting at higher velocities (about 10 m/s or more) (Fig. 3, bottom).

Relative effectiveness of stimuli applied to different parts of cuneiform area

Examination of Table 1 shows that the degree of depression of intermediate zone group II field potentials differed depending on which parts of the cuneiform area were stimulated. Examination of Table 2 shows that the depression evoked from the anterior cuneiform nucleus and subcuneiform region was significantly larger than that evoked from the posterior cuneiform nucleus (to 17.4, 27.1, and 48.4% of the control test field potential, respectively). However, stimulation of the anterior cuneiform nucleus and the subcuneiform region evoked similar effects. Taken together, the ipsilateral anterior and posterior cuneiform nuclei were also as effective as the contralateral anterior and posterior cuneiform nuclei. At long intervals (≥40 ms), the depression of the group II component of the intermediate zone group II field potential peaked at a stimulus intensity of approximately 100 μA (Fig. 4A), indicating that the most effective stimulation sites were localized within the cuneiform nuclei. At these long intervals, very little change in the degree of depression of the group I component was observed with increased stimulus intensity.

Comparison of effectiveness of stimuli applied in cuneiform nuclei and in the monoaminergic nuclei on group II field potentials

Only the values obtained for the cuneiform nuclei proper, the data for the anterior and the posterior nuclei pooled together, were used for this comparison. This was done since the risk of activation of rubrospinal neurones (via current spread to the brachium conjunctivum: see below, Effects of conditioning stimuli applied within the red nucleus...) or subcoerulear neurons (via current spread to the adjacent lateral part of the subcoerulear region with stimuli applied in the caudal aspect of the subcuneiform region) would be greater with stimuli applied within the subcuneiform region.

Different measures were used to compare the effectiveness of stimuli in depressing transmission from group II afferents, as in the previous study (see Noga et al. 1992). The first measure was the mean degree of depression of all the tested field potentials. As shown in Table 1, when six to eight conditioning stimuli of 100–150 μA preceded the test stimuli by 40–170 ms, the test field potential size was reduced to 32.2% of its control size for the cuneiform nuclei stimuli. This may be compared to a depression to 29.0% and 26.2% for coerulear and raphe stimuli, respectively, found by Noga et al. (1992), or to 28.7% and 25.8% after having included a few additional

measurements obtained in this study. The depressions evoked by the cuneiform and monoaminergic nuclei were not significantly different (Table 2).

The second measure was the number of cases in which effects evoked from the various nuclei were similar or different when conditioning stimulation was tested on the same intermediate field potential and at the same stimulation parameters. A comparison revealed that conditioning stimuli applied in the cuneiform nuclei were usually as effective as those applied in either the locus coeruleus or raphe nuclei. A comparison of the effects of conditioning stimulation of the cuneiform and raphe nuclei on the same field potential (n=19) revealed that 11 field potentials were depressed to similar levels (within 15% of each other) by conditioning stimulation of either nuclei, the remainder being more effectively (>15%) depressed by conditioning of the cuneiform (n=2) or raphe (n=6) nuclei. Similar results were obtained in a comparison of the effects of conditioning stimulation of the cuneiform and coerulear nuclei on the same intermediate field potential (n=9): eight field potentials were depressed to similar levels (within 15% of each other) by conditioning stimulation of either nuclei; the remaining field potential being depressed more effectively (>15%) by coerulear stimulation.

The third measure was the proportion of field potentials that were depressed to less than one half of their original size. This was found to be similar following conditioning stimulation of the cuneiform, coerulear and raphe nuclei (70, 86, and 82%, respectively).

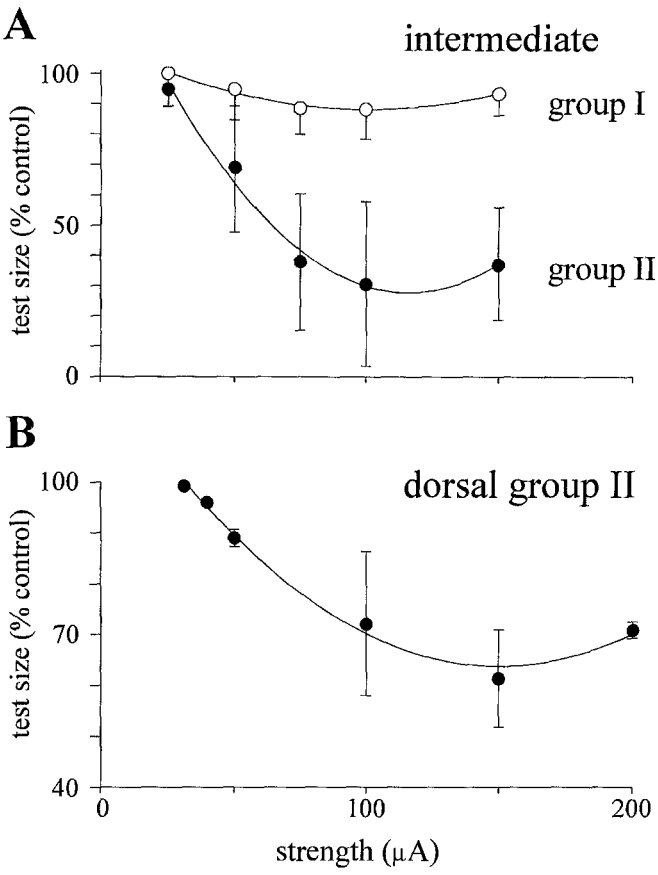

Fig. 4A,B Depression of midlumbar field potentials by conditioning stimuli of different intensity applied in the cuneiform nuclei. **A** mean depression of group I (*outline symbols*) and of group II (*solid symbols*) intermediate zone field potentials (n=25) as a function of increasing intensity of stimuli. Only the maximal value of depression for each stimulus site and field potential at each strength (where measured) and at conditioning-testing intervals ≥40 ms was used in this comparison. **B** effects of increasing intensity of stimulation on dorsal horn group II field potentials (n=19) at conditioning-testing intervals ≥40 ms

Effects of stimulation of cuneiform area on field potentials evoked from group II afferents in the dorsal horn of midlumbar and sacral segments

Conditioning stimulation of the anterior cuneiform nucleus, posterior cuneiform nucleus, or subcuneiform region also depressed field potentials evoked by group II afferents in the dorsal horn. This is illustrated in Fig. 2A (midlumbar segment) for stimuli applied within the contralateral posterior cuneiform nucleus and in Fig. 5A (sacral segment) for stimuli applied within the ipsilateral anterior cuneiform nucleus. The test field potentials were depressed to <85% of the control sizes in all but three of the 34 measurements. No significant differences were found in the degree of depression of group II field potentials in the dorsal horns of the midlumbar or the sacral segments following conditioning stimulation of the anterior cuneiform nucleus/subcuneiform region (Table 3).

Table 2 Statistical significance of differences of effects evoked from different nuclei shown in Table 1. *Int* Group II field potentials in the intermediate zone in midlumbar segments, D_{ML} and D_{SAC} group II field potentials in the dorsal horn of midlumbar and sacral spinal segments, respectively. The significance of the differences was calculated using a Mann-Whitney U-test (two-tailed)

	CUN_A vs CUN_P	CUN_A vs CUN_S	CUN_P vs CUN_S	$iCUN_{AP}$ vs $coCUN_{AP}$	CUN_{AP} vs R	CUN_{AP} vs COER	R vs COER
Int	**	NS	*	NS	NS	NS	NS
D_{ML}	NS	NS	NS	NS	*	NS	NS
D_{SAC}	–	NS	–	–	*	–	–

*P≤0.05
**P≤0.01
***P≤0.001
NS not significant

Time course of the depression

The depression of dorsal field potentials was found to start at slightly longer and peak at slightly shorter conditioning-testing intervals (Fig. 3A) than that of intermediate group II field potentials (Fig. 3C). Peak depression occurred between 32 and 72 ms and gradually declined, so that significant effects were still maintained at prolonged periods (up to 350 ms). Fibers conducting at 9 m/s to about 1.5 m/s would be likely to contribute to the peak depression (Fig. 3, bottom). The time course of the depression observed with conditioning stimulation of the cuneiform area was similar to that observed following conditioning stimulation of the monoaminergic nuclei for dorsal horn group II field potentials in the midlumbar (Noga et al. 1992) and sacral segments (to at least 78% of the control, at intervals between 35 and 350 ms, with peak depression occurring between 55 and 95 ms; n=2).

Relative effectiveness of stimuli applied to different parts of cuneiform area

Dorsal horn group II field potentials were similarly depressed by conditioning stimuli applied to the various subdivisions of the cuneiform area (Tables 1, 2) and when stimuli were applied in the ipsilateral and in the contralateral cuneiform nuclei. The depressions evoked by conditioning stimulation of the different sites ranged from 66.1 to 73.7% of the test field potential. While the depression to at least 80% of the control size required 100 μA or more and five stimuli, its threshold was between 50 and 75 μA, indicating that it was evoked from fairly restricted areas. However, the depression peaked at stimulus intensities of approximately 150 μA (Fig. 4B), intensities at which current spread to the adjacent parts of the cuneiform nucleus and to the subcuneiform and subcoerulear region is more difficult to exclude (Noga et al. 1992).

Relative effectiveness of stimuli applied in the cuneiform and the monoaminergic nuclei on dorsal horn group II field potentials

A comparison was made of the relative effectiveness of stimuli applied in the cuneiform and monoaminergic nuclei [for the latter using data both from Noga et al. (1992) and from additional experiments in this study] in depressing transmission from group II afferents in the dorsal horn at long intervals. Conditioning stimulation (100–150 μA) of the cuneiform nuclei reduced the test field potential size to 70.1% and 67.8% of the control size (Table 1) for midlumbar and sacral segments, respectively. This may be compared to the depression observed with conditioning stimulation of the raphe (to 58.0% and 56.8% of the control size for midlumbar and sacral segments, respectively) and coerulear nuclei (to 61.6% of their control size for the midlumbar segment). Only the depression evoked by the cuneiform and raphe nuclei was significantly different (Table 2). However, examination of the effects of stimuli of the same parameters on the same dorsal field potentials revealed that the depression evoked from the cuneiform nuclei was similar (within 15% of each other) in the majority of cases to that observed with conditioning stimulation of the raphe nuclei (cf. Fig. 5A,B) and the coerulear nuclei (14/22 and 9/12, respectively). Of the remaining field potentials in the comparison, eight were more effectively (>15%) depressed by conditioning stimulation of the raphe nuclei or, in the comparison between conditioning stimulation of either the cuneiform or coerulear nuclei, by conditioning stimulation of either the cuneiform (n=1) or coerulear nuclei (n=2). Finally, only a small proportion of the dorsal field potentials was depressed to less than one half of their original size following conditioning stimulation of either the cuneiform (12%) or coerulear (24%) nuclei. This was lower than that seen following raphe stimulation (38%).

Effects on responses of single neurons

Depression of field potentials of group II origin was associated with a very strong depression of responses evoked by stimulation of group II muscle afferents recorded in individual sacral dorsal horn neurons (interneurons and ascending tract cells) which belonged to the populations of neurons investigated by Jankowska and Riddell (1993, 1994) and Riddell et al. (1994). The parallel depression of field potentials and of EPSPs which were monosynaptically evoked by group II muscle afferents in three intracellularly recorded neurons is illustrated in Fig. 5A and C, respectively. Amplitudes of EPSPs evoked by group II afferents were reduced to 30–70% of the test potential amplitude – the depression to less than 60% occurred at conditioning-testing intervals of up to 300 ms at which PSPs evoked by conditioning stimulation of fast-conducting fibers already declined (Fig. 5E,F). In extracellularly recorded neurons (n=15), the firing index was used as a measure of the depression of responses with conditioning stimulation of the cuneiform nuclei. The neurons responded to practically all stimuli of 4–5 T, but failed to respond when preceded by conditioning stimuli (n=6), or responded with a much lower firing index (25%, n=2; 50%, n=3; 75%, n=4). The decrease in the firing index was associated with a 0.5- to 1.0-ms longer latency of the responses. Conditioning stimuli applied within the cuneiform and raphe nuclei were similarly effective (cf. Fig. 5A,B and Fig. 5C,D). No clear-cut direct synaptic actions were evoked by trains of stimuli applied within either the cuneiform or raphe nuclei in 14 of the 15 extracellularly recorded neurons. An increased firing frequency at a latency of about 20 ms was observed in one cell. Of the intracellularly recorded neurons (n=4), IPSPs were seen in 3 cells (at latencies of 15–20 ms) and small EPSPs in only one cell

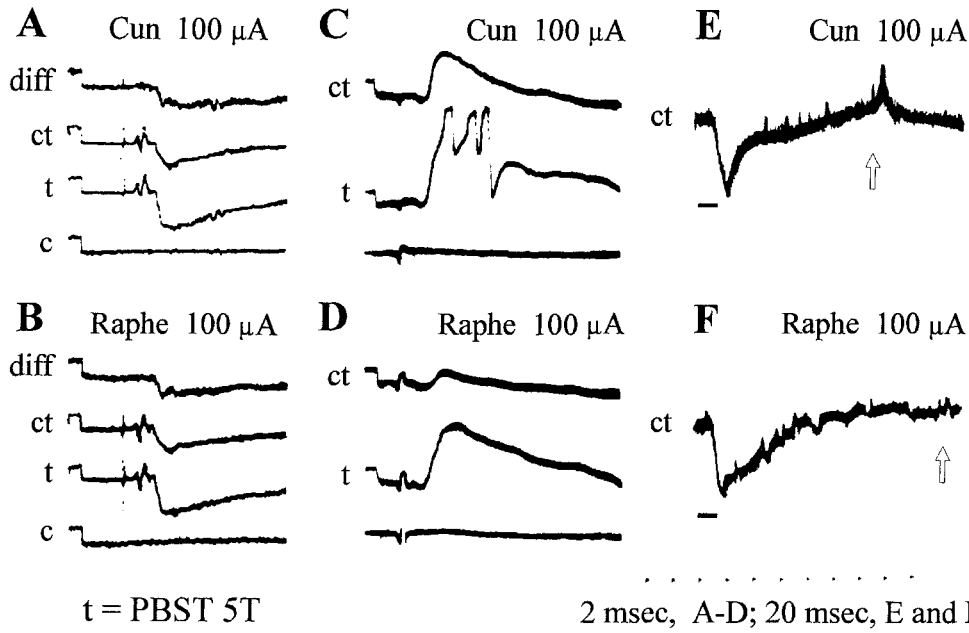

Fig. 5A–F Effect of conditioning stimulation of the cuneiform (**A,C**) and raphe nuclei (**B,D**) on a dorsal horn group II field potential (**A,B**) and on postsynaptic potentials in an ascending (most likely spino-cervical) tract neuron (**C,D**), both recorded in the S2 segment and evoked by stimulation of group II afferents of the posterior biceps-semitendinosus nerve (*PBST*). Conditioning-test intervals: **A,B** 75 ms; **C** 132 ms; **D** 185 ms. **E** and **F** show when the **C** and **D** test stimuli (*arrows*) were applied with respect to the short-latency IPSPs evoked by the conditioning stimuli in the illustrated neuron (single DC records at a slow time base). The period of conditioning stimulation is indicated by the *solid bar*. Conditioning stimulation parameters are seven stimuli, 100 μA, 400 Hz. Calibration pulses: **A,B** 200 μV; **C–F** 0.5 mV. Time calibration is indicated by the *dotted line*

Table 3 Statistical significance of the differences in the degree of depression of group II field potentials recorded at different sites within the spinal cord. The differences were calculated a Mann-Whitney test (two-tailed)

	CUN_A	CUN_P	CUN_S	CUN_{AP}	$coCUN_{AP}$	CUNAP	R	COER
Int vs D_{ML}	***	NS	***	***	**	***	***	***
Int vs D_{SAC}	***	–	*	**	–	***	***	–
D_{SAC} vs D_{ML}	NS	–	NS	NS	–	NS	NS	–

(at latencies of 42–47 ms from *both* the cuneiform and raphe nuclei).

Relative effectiveness of brainstem conditioning stimulation on dorsal horn and intermediate zone group II field potentials

Group II field potentials in the intermediate zone of the midlumbar segments were significantly more depressed than those recorded in the dorsal horn following conditioning stimulation of all brainstem areas, except the posterior cuneiform nucleus, when data from all experiments were grouped together (Table 3). However, intermediate zone group II field potentials (n=5) were more effectively depressed (>15%) than dorsal horn group II field potentials (n=6) in 9 of 11 comparisons with conditioning stimulation (same parameters) of the same site within the posterior cuneiform nucleus in three experiments. The intermediate zone field potentials were depressed by an additional 42.7±12.8% in this group. In the remaining (2 of 11) comparisons, the dorsal horn and intermediate zone group II field potentials were depressed to the same degree (within 15%) by conditioning stimulation of the posterior cuneiform nucleus. Similar results were obtained in comparisons of the relative effectiveness of the anterior cuneiform nucleus/subcuneiform region in depressing either the dorsal horn or intermediate zone group II field potentials: intermediate zone group II field potentials were more effectively depressed (>15%) in 9 of 11 comparisons (by an additional 40.6±13.6%); the remaining two comparisons were within 15% of each other.

Comparison of effects of stimuli applied within and outside the cuneiform area

The extent of the brainstem areas from which the depression of transmission from group I and II muscle afferents was most pronounced was estimated by comparing the degree of the depression of intermediate zone group I and II field potentials. At conditioning-testing intervals ≥40 ms (Fig. 6), the group II field potentials were most effectively depressed by stimuli applied within the anterior and posterior cuneiform nucleus and subcuneiform

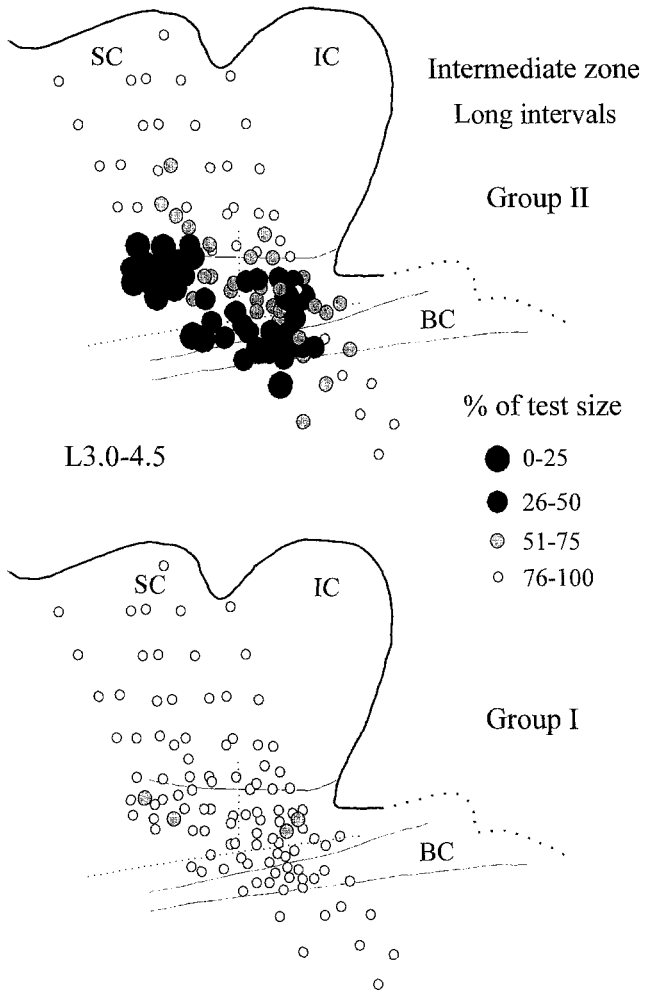

Fig. 6 Map of effectiveness of conditioning stimuli applied at various stimulation sites in and around the ipsilateral and contralateral cuneiform area in depressing midlumbar intermediate group I and group II field potentials at long (≥40 ms) condition-test intervals. The effectiveness of the depression is indicated according to the given scale. Effective sites for the depression of group II field potentials were clustered around the cuneiform nuclei and subcuneiform region. Note the lack of effect on group I field potentials at these intervals from most stimulation sites. In this and the following figures, the maximal effect of stimulation of each site is plotted for all field potentials (more than one site could be used for any given field potential)

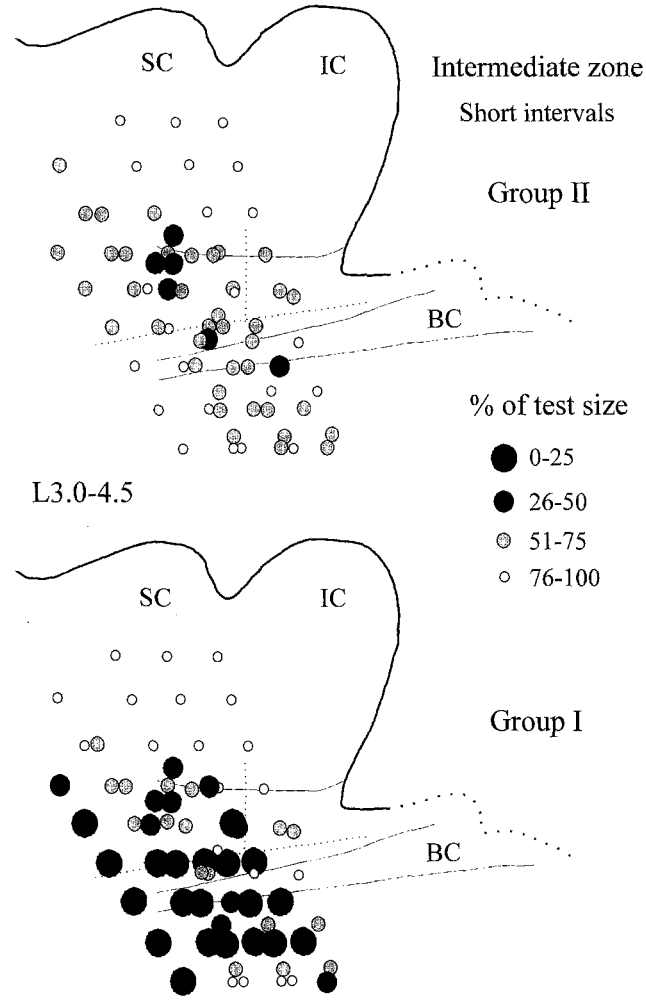

Fig. 7 Map of effectiveness of conditioning stimuli applied at various stimulation sites in and around the ipsilateral and contralateral cuneiform area in depressing midlumbar intermediate group I and group II field potentials at short (≤35 ms) condition-test intervals. Note the much larger depression of group I field potentials at these intervals. Effective sites for the depression of group I field potentials were found throughout the central tegmental field surrounding the brachium conjunctivum (*BC*)

region. Little effect was observed on the group I field potentials by the same stimuli at the various locations.

At conditioning-testing intervals ≤35 ms, the distribution of effective brainstem sites was different (Fig. 7). Group II field potentials were only moderately depressed by stimuli applied throughout the cuneiform and subcuneiform areas. In contrast, group I field potentials were depressed most effectively by stimuli applied within a larger part of the central tegmental field ventral to the cuneiform area. Increasing the strength of conditioning stimulation applied to the cuneiform area at short intervals depressed group I field potentials additively (not shown), probably due to a spread of current to the central tegmental field.

The effectiveness of stimuli applied in and around the cuneiform nucleus in depressing midlumbar and sacral dorsal horn group II field potentials is illustrated in Fig. 8. At conditioning-testing intervals of ≥33 ms, the group II field potentials were most effectively depressed by stimuli applied within the anterior and posterior cuneiform nucleus and subcuneiform region. This distribution of effective sites was similar to that seen for intermediate zone field potentials at long conditioning-testing intervals (Fig. 6).

Actions of raphespinal and reticulospinal pathways have previously been associated with the production of negative and positive cord dorsum potentials, respectively (Jiménez et al. 1989). Stimuli applied at the most effective sites within the cuneiform area also evoked the largest negative cord dorsum potentials. The latency of these potentials ranged between 4 and 6 ms. They were

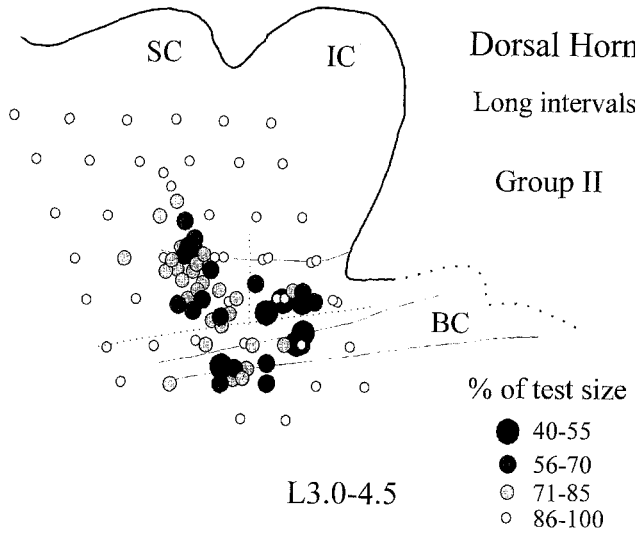

Fig. 8 Map of effectiveness of conditioning stimuli applied at various stimulation sites in and around the ipsilateral and contralateral cuneiform area in depressing midlumbar or sacral dorsal horn group II field potentials at long (≥33 ms) condition-test intervals. Note that effective sites for the depression of group II field potentials were found within the cuneiform nuclei and subcuneiform region

larger than the negative cord dorsum potentials evoked from the locus coeruleus (3–5 ms latency) and smaller than those evoked from raphe nuclei (3–4 ms latency). These short-latency, negative cord dorsum potentials were earliest observed following the third (cuneiform) or the first (raphe and coeruleus) stimulus in the train. The duration of these negative potentials was difficult to determine, since they were interrupted by a large positive cord dorsum potential (observed following stimulation of all sites) which lasted approximately 10–30 ms. A negative cord dorsum potential was usually observed following this positive potential, possibly being the decaying remnant of the short-latency negative potential. This potential gradually decayed over a period of up to 100 ms. Stimulation of the cuneiform nuclei also evoked short-latency positive cord dorsum potentials (3–4 ms latencies; 60% of cases) which preceded the negative cord dorsum potentials. Similar potentials were evoked by stimuli applied in the coeruleus and raphe nuclei, although much less frequently (≤20% of cases). Group II field potentials were depressed when stimulation of the cuneiform nuclei evoked only the negative cord dorsum potential uncontaminated by this early positive potential. Stimuli applied at these three sites might thus activate the same descending pathways, but involvement of separate descending pathways with similar actions at the spinal level could not be excluded.

Effects of conditioning stimuli applied within the red nucleus on field potentials evoked in midlumbar segments

The effects of conditioning stimulation of the contralateral red nucleus were examined in three experiments to determine the possible contribution of rubrospinal pathways (which may be activated by interpositorubral fibers stimulated within the ipsilateral brachium conjunctivum) to the effects of stimulation of the ipsilateral subcuneiform region. At intervals ≤35 ms, intermediate zone group I field potentials were powerfully depressed, while group II field potentials were either depressed or unaffected. The depression of both group I and II field potentials (when present) declined to less than 20% within 100 ms. At longer intervals, the rubrospinal neurons would thus not likely contribute to the depression of transmission from group II afferents induced by stimulation of the subcuneiform region and even less to that evoked by stimulation of more dorsal sites. Rubrospinal neurons could however, contribute to the depression evoked at shorter intervals.

Discussion

Comparison of effects of stimuli applied within the cuneiform, locus coeruleus, and raphe nuclei on transmission from group I and II muscle afferents

The results of this study show that conditioning stimuli applied within the cuneiform nuclei may depress transmission from group II muscle afferents nearly as effectively as conditioning stimuli applied within the nuclei of origin of the descending monoaminergic pathways, the effects of which have been reported previously (Noga et al. 1992). As shown in Tables 1 and 2, only small differences were seen between them. It should also be noted that stimuli applied in all of these nuclei produced a larger percentage decrease of the intermediate zone group II field potentials than of dorsal horn group II field potentials (Tables 1, 3). However, this depression was similar in magnitude (see Noga et al. 1992) since the dorsal field potentials are larger than their intermediate counterparts (Edgley and Jankowska 1987a).

Maximal depression of group II field potentials induced from either the cuneiform or monoaminergic nuclei occurred, furthermore, at similar conditioning-testing intervals and may be attributed to actions of similarly slowly (less than 5–10 m/s) conducting nerve fibers. The depression occurring at these intervals was not combined with any marked depression of intermediate zone field potentials evoked by group I afferents showing a high degree of specificity in effects of conditioning stimuli applied in all these nuclei.

Which descending pathways might be responsible for the depressive actions evoked from the cuneiform nuclei?

Similar effects of stimuli applied in different nuclei may be used to indicate that they were secondary to activation of the same neuronal system(s). This might include axons of the same descending tract neurons passing through, or in the neighborhood of, the various brainstem

nuclei or axons of neurons providing shared input to these nuclei (Cedarbaum and Aghajanian 1978; Ennis and Aston-Jones 1986).

An alternative, although not exclusive, possibility might be that stimuli applied in the cuneiform nucleus acted via noradrenergic or serotonergic neurons and that their effects were secondary to activation of these neurons. For example, stimuli applied in the subcuneiform region could activate nearby located catecholamine-containing neurons (Steeves et al. 1975). Monoaminergic neurons could also be activated by cuneiform neurons projecting to the locus coeruleus (Edwards 1975; Sotnichenko 1985) and raphe nuclei (Edwards 1975; Steeves and Jordan 1984; Behbehani and Zemlan 1986). Actions of raphe-spinal pathways have previously been associated with the production of negative cord dorsum potentials (Jiménez et al. 1989 and personal communication) and their induction with stimulation of the cuneiform nucleus, the locus coeruleus, and the three raphe nuclei explored in this study is in keeping with these possibilities.

Indications for contribution of monoaminergic neurons

The depression of transmission from group II afferents by stimuli applied in either the cuneiform or monoaminergic nuclei was evoked at conditioning-testing intervals that were long enough for actions of slowly conducting monoaminergic fibers but too long for actions of more rapidly conducting reticulospinal fibers (see discussion in Noga et al. 1992). The selectivity of the depression of transmission from group II, but not from group I afferents at sufficiently long conditioning-testing intervals is in keeping with the selectivity of actions of directly applied monoamines (Bras et al. 1990). However, the two groups of observations provide only a circumstantial evidence for the involvement of the monoaminergic neurons and do not exclude the possibility that slowly conducting non-monoaminergic neurons are involved in effects evoked from either of the stimulated nuclei, or the possibility that the actions of fast-conducting reticulospinal pathways on transmission from group II afferents could require more time to develop than that observed on transmission from group I afferents.

More direct evidence for the contribution of monoaminergic fibers has been obtained by interfering with the depression of group II field potentials evoked from the cuneiform nucleus by NA antagonists. The NA antagonists idazoxan, yohimbine and phenoxybenzamine have been found to reduce depression of intermediate zone field potentials (Skoog and Noga 1991; Noga et al. 1991a). Yohimbine and idazoxan were applied locally (ionophoretically) while phenoxybenzamine was administered intravenously (2 mg/kg). The depression of the intermediate zone field potentials was reduced by 20–50%. Monoaminergic neurons might thus be involved in the depression of transmission from group II afferents following stimuli applied in the cuneiform nucleus, although not necessarily exclusively.

Indications for contribution of non-monoaminergic neurons

The contribution of non-monoaminergic fibers to the long-latency depression of transmission from group II afferents would be in keeping with the partial interference between the NA antagonists and the depression evoked by the conditioning stimuli (Skoog and Noga 1991). However, effects of monoaminergic antagonists are often incomplete (Griersmith et al. 1981) and could not be expected to be much stronger, even if the depression were evoked exclusively by monoaminergic neurons, because of technical limitations (e.g., the synaptic sites may be too distant to be sufficiently accessed by a locally applied antagonist – see Curtis 1976; Zhao and Duggan 1988). The contribution of non-monoaminergic fibers would also be in keeping with the recently reported presynaptic depolarization of group II afferents evoked by stimulation of the coerulear and raphe nuclei (Riddell et al. 1992) at conditioning-testing intervals effective in the present study. There is little evidence of a direct depolarizing action for either NA or 5-HT upon terminals of sensory fibers (Riddell et al. 1992; see, however, Sillar and Simmers 1994) and direct excitation of spinal neurons (which could induce primary afferent depolarization) by monoamines appears to be seen only exceptionally (Alhaider et al. 1991; see also Riddell et al. 1992 for references). Primary afferent depolarization would thus be more likely evoked by non-monoaminergic neurons and such neurons might be activated, directly or indirectly, by stimuli applied in either the cuneiform, coerulear or raphe nuclei.

Actions mediated by slowly conducting fibers were not the only actions of stimuli applied in the cuneiform nuclei. The same stimuli also induced depression of group I field potentials which was evoked at much shorter conditioning-testing intervals and is therefore attributable to fast-conducting fibers. Such a short-latency depression of group I field potentials was evoked in parallel by stimuli applied within the cuneiform and within other nuclei, but was often most pronounced when evoked from within the reticular formation or the brachium conjunctivum. It is, therefore, attributed primarily to reticulospinal neurons which could have been activated by cuneiform neurons projecting to the medial reticular formation (Garcia-Rill et al. 1983b; Steeves and Jordan 1984; Garcia-Rill and Skinner 1987). The fact that the short-latency, positive cord dorsum potentials usually evoked by stimulation of the cuneiform nucleus (see also Noga et al. 1995) occurred at latencies similar to that seen with direct stimulation of the reticular formation adjacent to the raphe magnus (Jiménez et al. 1989) is in keeping with this suggestion (taking into account an additional synaptic delay required to activate the reticulospinal neurons). The depression may also have been due to activation of reticulospinal neurons by a spread of current to the neighboring parts of the reticular formation or by the stimulation of collaterals of reticulospinal neurons within the cuneiform nucleus (Bayev et al. 1988).

Of other fast-conducting descending tract fibers, rubrospinal fibers might contribute to the depression of transmission from group I afferents at short intervals. Field potentials evoked by group Ib afferents would be likely to be more effectively depressed by stimuli applied in the contralateral red nucleus if the depression were induced by presynaptic inhibition of rubral origin (Hongo et al. 1972), and cells in the contralateral red nucleus could be activated by stimulation of interpositorubral fibers within the brachium conjunctivum (Shinoda et al. 1988). Effects of rubrospinal fibers by stimuli encroaching upon the brachium conjunctivum would, on the other hand, be unlikely to add to the depression of group II field potentials in the intermediate zone at longer intervals, because stimuli applied directly within the red nucleus were less effective.

Functional consequences

In view of a potent depression of intermediate zone field potentials evoked by group II afferents by stimuli applied within the cuneiform nucleus, it is not surprising that midlumbar last-order intermediate zone neurons (Edgley and Jankowska 1987b) are less effectively activated by group II afferents during fictive locomotion evoked by stimulation of this nucleus (Shefchyk et al. 1990). The phasic character of this inhibition (much more pronounced during the stance phase of the locomotory cycle) has been interpreted as a reflection of oscillatory locomotor drive potentials induced in them by rhythmically active spinal locomotor networks (Shefchyk et al. 1990). Such oscillatory potentials were seen in two intracellularly recorded interneurons with group II input recorded in the same area, and might explain both the lower excitability of group II interneurons during stance phase and their higher excitability during the swing phase. More recently, monosynaptic group II field potentials recorded from the midlumbar segments have been found to be tonically depressed during fictive locomotion evoked by tonic stimulation of the mesencephalic locomotor region (Perreault et al. 1994), thus supporting our data in another preparation. A small phasic depression during extension was sometimes superimposed on this tonic depression. Monoaminergic neurons could account for this type of depression of group II monosynaptic transmission providing that the activity of the descending monoaminergic neurons increases tonically during locomotion and/or becomes locked to a specific phase of the step cycle (Noga et al. 1992). The fact that both rhythmically active and tonically active neurons are observed within the mesencephalic locomotor region (Garcia-Rill et al. 1983a) and the raphe pallidus (Veasey et al. 1993) during spontaneous locomotion strengthens this possibility. Alternatively, release of monoamines in the spinal cord could be controlled locally by neurons of the central rhythm generator by presynaptic regulatory mechanisms involving excitatory amino acids (e.g., Wang et al. 1992; Desce et al. 1992).

Any tonically or rhythmically occurring depressive actions of monoaminergic neurons would, nevertheless, be superimposed on both the oscillatory locomotor drive potentials and any other rhythmic descending influences. Depression of inhibitory synaptic actions of group I afferents that are mediated by midlumbar intermediate zone spinal neurons (Shefchyk et al. 1990) could not be attributed to the same monoaminergic neuronal systems that depress transmission from group II afferents, because transmission from group I afferents to these neurons is not subject to depressive actions of monoamines (Bras et al. 1990). It might not be either likely to be mediated by the same slowly conducting non-monoaminergic neurons, because of the different time course of the depression of field potentials of group I and group II origin, as described in Results. It could, however, be mediated by fast-conducting reticulospinal neurons activated by stimuli applied within the cuneiform nucleus, or by spinal interneuronal networks activated by them.

Provided that descending tract fibers mediating depression of synaptic actions of group I and II afferents contribute to the phase-locked changes in activity of spinal interneurons with input from group I and II afferents, one may further postulate that the activity of fast- and slow-conducting descending tract fibers is very efficiently synchronized with the rhythmic activity of spinal interneuronal networks during locomotion.

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