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The use of local anaesthetic microinjections to identify central pathways: a quantitative evaluation of the time course and extent of the neuronal block

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Summary. The time course and extent of local anaesthetic blocks within the spinal cord of cats were evaluated. A monopolar stimulation electrode with the tip lowered into the dorsal columns (DC) 1000 μm below cord surface was used to activate antidromically DC fibers at the T13 level and evoke cord dorsum potentials at the level of the lumbar spinal cord. The amplitude of the negative deflection, the N-wave, was determined for various stimulation intensities (stimulation-response-function, SRF). Lidocaine (1%) was microinjected in volumes of 0.5 or 1.0 μl into the DC from a glass micropipette 1 mm caudal to the stimulation site. Conduction block was characterized by a reversible shift of the SRFs to higher stimulation intensities. The diameter of the blocked area in the transverse plane was evaluated from threshold intensities and was found to be 0.9 ± 0.1 mm 4 to 30 min after the injection of 0.5 μl lidocaine and 1.6 ± 0.36 mm 10 to 45 min after the injection of 1.0 μl lidocaine. In the sagittal plane, the diameter of the blocked area following 1.0 μl lidocaine was found to be up to 2.8 mm. The DC-block was reversible within 92 min following injection of 1.0 μl and 69 min after the injection of 0.5 μl lidocaine. The application of the present findings for blocks in other CNS structures is discussed.

Key words: CNS-blocks – Reversible inactivation – Functional anatomy – Lidocaine

Introduction

The function and anatomy of the central nervous system (CNS) are often investigated by means of interrupting central pathways. Interruptions may be produced irreversibly by surgical or chemical lesions or reversibly by physical or pharmacological blocks of impulse conduction or synaptic transmission. Both lesions and blocks may be differential for various types of neurons or fibers; further they may be circumscribed locally or general in effect. Lesions have been performed by electrical coagulation (Thompson 1971), microknife cuts (Ellison 1972), aspiration (Kimble 1968), ischemia following arterial ligation, X-irradiation (Altman and Anderson 1971; Bayer et al. 1973), cobalt microinjections (Lee and Malpeli 1986) or neurotoxins such as 5,6-Dihydroxytryptamine (Berge et al. 1983) or 6-Hydroxydopamine (Bloom et al. 1969). Reversible block of impulse transmission may be produced by cooling, either focally (Dembowsky et al. 1981; Shefchyk et al. 1984) or totally (Handwerker et al. 1975), by administration of neurotransmitter antagonists (Yezierski et al. 1981; Sagen and Proudfit 1985), implantation of potassium chloride (Green 1971), or focal injection of a local anaesthetic (Delgado and Kitahata 1967; Iakhnitsa et al. 1981; Talman et al. 1981; Flicker and Geyer 1982; Rigdon and Pirch 1984; Sandkühler and Gebhart 1984).

Destructive lesions often produce untoward side effects, apart from their blocking effect. In addition, lesions are irreversible and therefore do not allow comparison with normal function after the interruption. Furthermore, lesions may be accompanied by adaptive or compensatory processes which possibly mask the acute effects when sufficient time has elapsed (e.g. to allow recovery from surgery) (Berge et al. 1983). Most often lesions are performed by electrolytic coagulation or knife cuts, procedures which may not be performed in awake or lightly anaesthetized animals because of strong aversive, motor or autonomic responses, especially when produced in brain stem or spinal cord. These lesions may also cause haemorrhage which may remain undetected initially and be difficult to stop.

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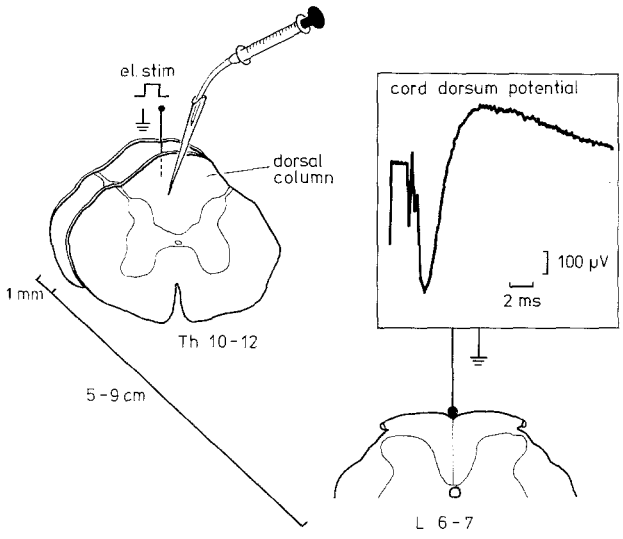

Fig. 1. Schematic diagram of the experimental set up in experiment 1. Frontal section through the lumbar (bottom) and lower thoracic spinal cord are shown. A monopolar tungsten microelectrode was placed in the sagittal plane with the tip 1000 µm below the cord surface. A glass micropipette (30–40 µm tip diameter) attached to the same manipulator was positioned 800–1000 µm caudal to the electrode. A silver ball electrode, placed on the dorsal surface of the L6–L7 segment, was used for recording the cord dorsum potential as shown in the inset. The amplitude of the negative deflection (N-wave) was determined for various intensities of DC-stimulation before and after microinjection of 0.5 or 1.0 µl lidocaine (1%).

In view of the side effects related to CNS-lesions, we used an alternative method of reversible and circumscribed blocks in CNS tissue by microinjection of a local anaesthetic (Gebhart et al. 1983; Sandkühler and Gebhart 1984), a method which has been used by different laboratories (e.g. Proudfit 1980; Iakhnitsa et al. 1981; Thalman et al. 1981; Flicker and Geyer 1982; Minagawa et al. 1983; Rigdon and Pirch 1984). However, no quantitative data were available to describe the time course and extent of blocks following the microinjection of a local anaesthetic in the spinal cord. We now present experimental data and theoretical implications to fully evaluate these blocks. The spinal dorsal columns (DC) were used as an anatomically well-defined fiber bundle (Glees, Livingston and Soler 1951; Scheibel and Scheibel 1969). DC fibers were electrically stimulated at the T10–T13 segmental level, and the dorsum potentials in the lumbar cord were recorded as a sensitive indicator for conducting fibers in the DC. Different models are provided to apply the present findings to blocks in other CNS structures, e.g. the spinal lateral funiculi as described in recent reports (Sandkühler et al. 1987a, 1987b). Blocks by two different volumes of lidocaine are evaluated; 0.5 µl which is often injected in animals like rats and 1.0 µl often used in cats. Parts of the results have been communicated in abstract form (Sandkühler et al. 1985).

Material and methods

Animal preparation

Experiments were performed on 7 deeply anaesthetized and paralyzed female cats weighing 2.4–2.7 kg. Anaesthesia was initiated with 40 mg/kg pentobarbital given intraperitoneally. Cannulae were inserted into the trachea, jugular vein, common carotid artery and the urethra. When vertebral laminectomy was begun animals were paralyzed with pancuronium bromide (0.4 mg/kg i.v.) and artificially ventilated with a gaseous mixture of 75% N_2O and 25% O_2. Supplemental i.v. doses of pentobarbital (mean 1.5 mg/kg/h) were given to prevent pupillary dilation or increases in blood pressure upon noxious stimulation of cutaneous nerves or the skin. Vital functions were continuously monitored and kept within physiologic limits: end tidal PCO_2 (range: 2.5%–3.5%) by adjusting breath rate between 15–17 breaths/min, central veneous pressure (2–8 cm H_2O), urinary output (10–30 ml/6h) and mean arterial blood pressure (100–150 mmHg) by infusion of a glucose/tyrode solution (4–8 ml/h) and injection of 5 ml Dextrane 40 i.v. if necessary, and rectal temperature (37°–39° C) by means of a feedback controlled heating blanket. The lumbar and lower thoracic spinal cord was exposed by laminectomy (L4–S1 and T10–T13) and the left posterior tibial and superficial peroneal nerves were dissected free and placed on platinum hook electrodes for bipolar electrical stimulation. All exposed nerve tissue was covered with warm paraffin oil.

Recording and stimulation

Epoxylite insulated tungsten microelectrodes with 25 µm exposed tips (Federick Haer) were used for monopolar cathodal stimulation (square pulses 0.1 ms in duration, 5–200 µA every 2.3 s) 1000 µm below the cord surface in the sagittal plane of the dorsal columns (DC) at the T10–T13 level. The N-wave, i.e. the negative deflection of the cord dorsum potential, was recorded from the surface of the lumbar cord at L6–L7 by a platinum ball electrode. The placement of the recording electrode was selected for the maximal N-wave amplitude. The N-wave was monitored on a storage oscilloscope and plotted on a xy-plotter. The N-wave amplitude was determined for various stimulation intensities in the thoracic DC (stimulus response function, SRF). The N-wave deflection represents postsynaptic potentials, probably excitatory (Brown and Ritz 1986), in dorsal horn neurons which are produced by volleys in cutaneous primary afferent fibers (Bernhard and Widen 1953). The DC contain collaterals of these group II cutaneous afferent fibers; thus it is possible to send synchronized volleys of cutaneous fibers antidromically into the caudal dorsal horn (Brown 1968). The amplitude of the N-wave increases with DC-stimulation intensity (stimulus response function (SRF), see Fig. 2 for an example), indicating increasing recruitment of DC fibers and thus increasing the number of excited dorsal horn cells. Typically, SRFs have a steep rise near threshold and level off at higher stimulation intensities.

Lidocaine microinjections

Lidocaine injections into the DC were performed through glass micropipettes (shaft diameter 1.5 mm, tip diameter 20–40 µm)

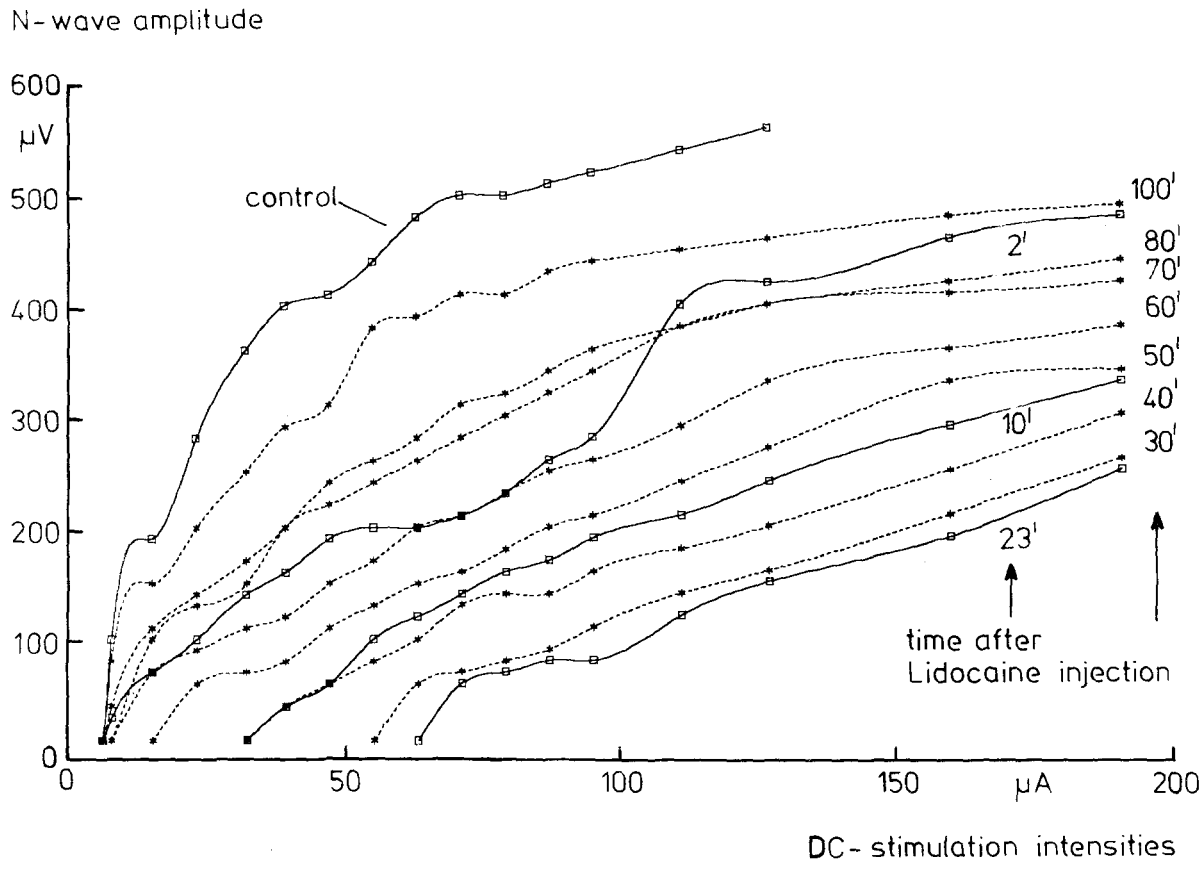

Fig. 2. Experiment 1. Stimulus response function (SRF) before (control) and after microinjection of 1.0 μl lidocaine 1 mm caudal to the stimulation electrode in the DC. Each data point represents the amplitude of the N-wave (ordinate) measured at the L5 segment, plotted vs. the DC stimulation intensity (abscissa). The SRF measured immediately before microinjection of lidocaine is the control curve. Measurements for the other SRFs were begun 2 to 100 min after the injection as indicated, and were completed within 1 to 2 min. Squares connected by continuous lines represent SRFs during increasing conduction block 2, 10 or 23 min after the injection. Dotted lines connecting asterisks are SRFs during recovery from lidocaine block 30 to 100 min after the injection

connected to a Hamilton 10 μl syringe by means of polyethylene (PE 10) tubing. Pipette and tubing were filled with lidocaine hydrochloride 10 μg/μl (1%). Injections were monitored by observing the movement of an air bubble in the tubing. Two experimental protocols were employed.

Experiment 1. The stimulation electrode and injection pipette were glued together with the tips separated by 800–1000 μm and fixed to a micromanipulator. This array was oriented in the midplane with the stimulation electrode cranial to the injection pipette and inserted into the DC at T10–T13 with a stepping motor (1000 μm in 1 min), thus conduction block was performed between the stimulation and the recording electrodes (Fig. 1).

Experiment 2. Two stimulation electrodes were glued to the same side of an injection pipette with tip separations of 800 and 1400 μm, respectively. They were fixed to a micromanipulator in the midplane. In contrast to experiment 1, stimulation electrodes were placed caudal to the injection pipette, thus blocks were made cranial to the stimulation and recording electrodes. In both experiments the geometry of the arrays and the orientation in the midplane was confirmed with a stereomicroscope at a magnification of 50 to verify differences in length of less than 10 μm. Angular deviations from the sagittal plane of were less than 1 degree and thus medio–lateral differences of tip position were less than 18 μm. If more than one experiment was performed in the same cat, the subsequent injections and stimulations were done at least 5 mm caudal to the first. Different electrodes were used in experiment 1, whereas electrodes were not changed in experiment 2. The N-wave amplitude was determined for stimulation in the thoracic DC at various stimulation intensities (stimulus response function, SRF) before and at 5 to 10 min intervals after the injection of lidocaine. The SRFs were measured 2 to 4 times before lidocaine injection to verify stable control values.

Statistical comparisons were made using Student's t-test for paired or grouped data; $p \leq 0.05$ was considered significant. Data are presented as mean values ± S.E.M.

Results

Experiment 1. Transverse spread of conduction block

In 5 experiments, 0.5 μl of lidocaine was injected caudal to the stimulation site. The mean SRFs before (control) and up to 60 min after the injection of lidocaine are given in Fig. 3A. In Fig. 3B the mean SRFs from 5 experiments are plotted before and after

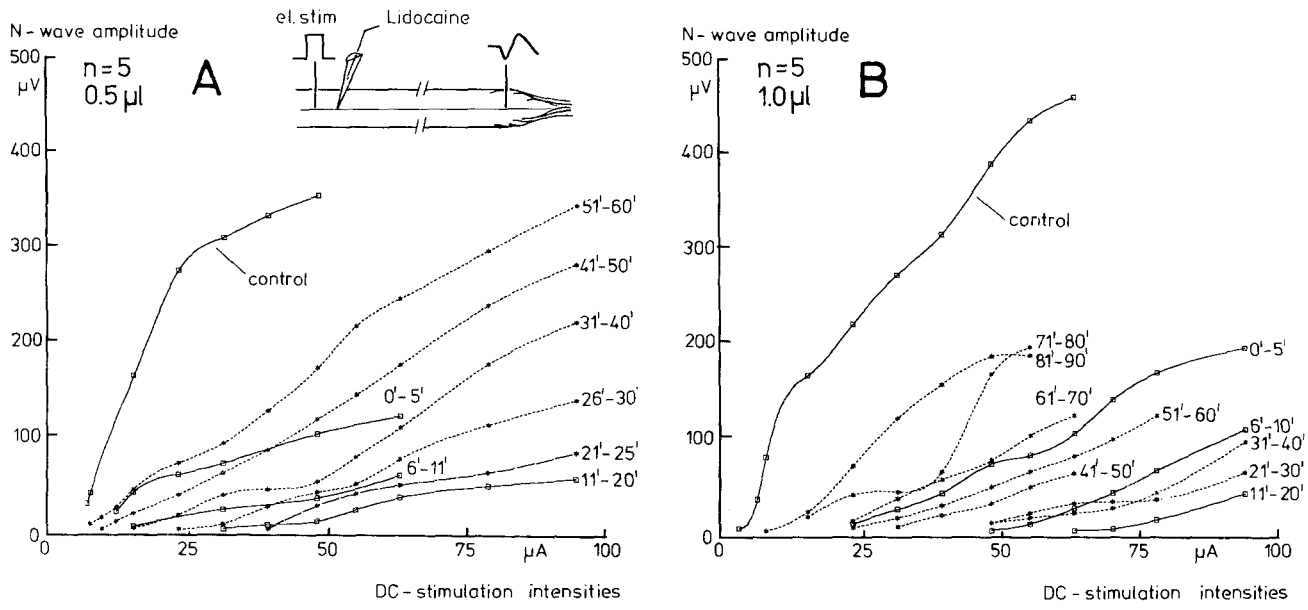

Fig. 3A, B. Stimulus response functions (SRF) before and after intraspinal microinjection of 1% lidocaine. Experiment 1. The amplitude of the N-wave (ordinate) is plotted versus the stimulation intensity in the DC (abscissa). All SRFs represent means of 5 experiments. SRFs were measured before (control) and at 5 to 10 min intervals after the injection of 0.5 μl (**A**) or 1.0 μl (**B**) lidocaine 900 μm caudal to the stimulation site (see inset in **A**). Solid lines represent SRFs during increasing conduction block, broken lines SRFs during the decay of the block. The time (min) after the injection is given for each SRF at the right

the injection of 1.0 μl lidocaine caudal to the injection site. An example of these experiments is given in Fig. 2. After the injection of lidocaine, SRFs were progressively shifted to higher stimulation intensities and the slopes of the initial rise were significantly reduced (Figs. 2 and 3). The extent of the conduction block was maximal at 16.0 ± 2.2 min after 0.5 μl lidocaine and at 21.3 ± 2.7 min after the injection of 1.0 μl lidocaine as revealed by the increase in threshold for the N-wave (T_s). Figure 4 shows the mean change of T_s in these experiments following the injection of 0.5 or 1.0 μl lidocaine. Mean thresholds for N-wave before lidocaine (T_o) were elevated from control (6.6 ± 0.9 μA) to a maximum of 70.4 ± 14.2 μA, i.e. 10.7 times T_o (mean of 5 experiments ± S.E.M., t = 4.055, $p \leq 0.02$) 15 min after the injection of 0.5 μl lidocaine. 30 min post injection thresholds were still elevated to 48.0 ± 5.1 μA and returned to 3 × T_o values 48.6 ± 2.9 min post injection (Fig. 4). Thresholds 4 to 30 min after the injection were elevated to 59.0 ± 4.2 μA (mean of 7 threshold measurements in each of the 5 experiments). The slope of the initial rise of the averaged SRFs was reduced from 15.2 μV/μA (control) to 0.5 μV/μA 11-21 min after the injection and did not return to control values 51-60 min. post injection (4.2 μV/μA).

In 5 experiments 1.0 μl lidocaine was injected into the DC (Fig. 3B). Stimulation thresholds for the N-wave were elevated from 6.7 ± 1.0 μA before injection to a maximum of 120.0 ± 13.6 μA (t = 8.036, $p \leq 0.002$, n = 5), i.e. 17.9 times T_o, 25 min after the injection (Fig. 4). Averaged thresholds 10 to 45 min post injection were elevated to 103.8 ± 4.8 μA (n = 8 threshold measurements in each of the 5 experiments) and returned to 3 × T_o values within 81.5 ± 2.7 min post injection. Slopes were reduced from 10.8 μV/μA to 1.3 μV/μA during 11–20 min post injection and were still reduced at 81–90 min after the injection (6.1 μV/μA).

Experiment 2. Longitudinal spread of conduction block

Stimulation thresholds for N-wave before lidocaine (T_o) were 10.2 ± 1.5 μA for stimulation 800 μm caudal to the injection site and 6.9 ± 1.5 μA 1400 μm caudal. Following lidocaine injection (1 μl), mean thresholds were elevated maximally 20 min post injection to 95.6 ± 25 μA (t = 3.847, $p \leq 0.02$, n = 5) 800 μm caudal to the injection site (n = 5). At 1400 μm caudal to the injection site, elevation of thresholds was less pronounced but significant (t = 3.195, $p \leq 0.05$, n = 5) and the maximum was reached later (25.5 ± 11.7 μA 30 min post injection, Fig. 6). Thresholds returned to 3 × T_o values 800 μm caudal within 80.2 ± 9.9 min.

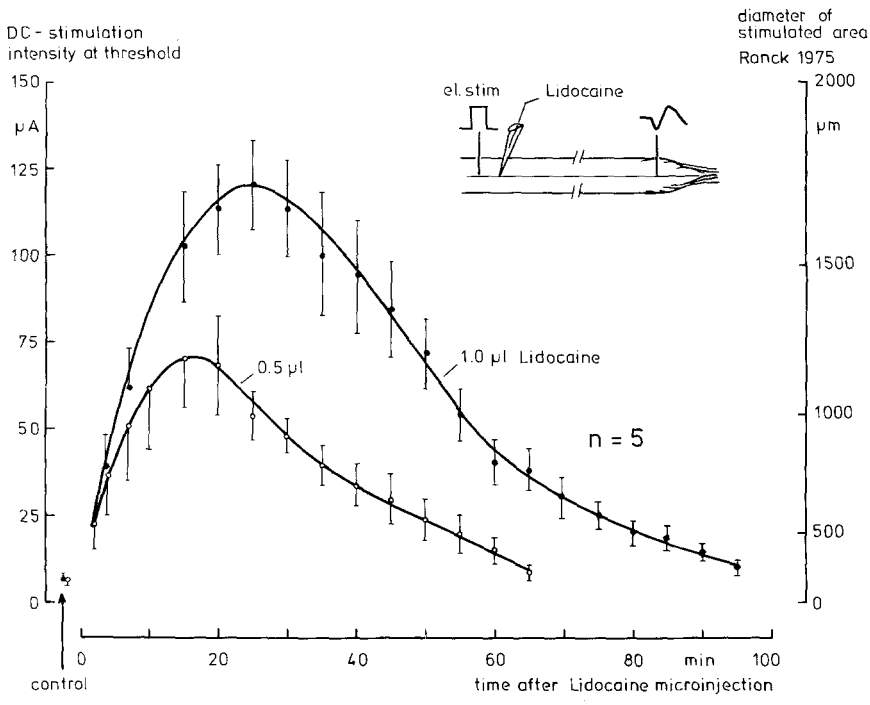

Fig. 4. Experiment 1. Time course and extent of conduction block in the DC after microinjection of lidocaine were determined by the DC stimulation thresholds for N-wave. Experimental set up as in Fig. 1 and indicated in the inset. Stimulation intensities at threshold (ordinate) for N-wave are plotted versus time after injection of lidocaine, 0.5 μl (○) or 1.0 μl (●), respectively; all data points represent means of 5 experiments, ±S.E.M.. The cross sectional area of stimulated fibers in the DC were calculated for threshold intensities according to Ranck (1975), right hand scale

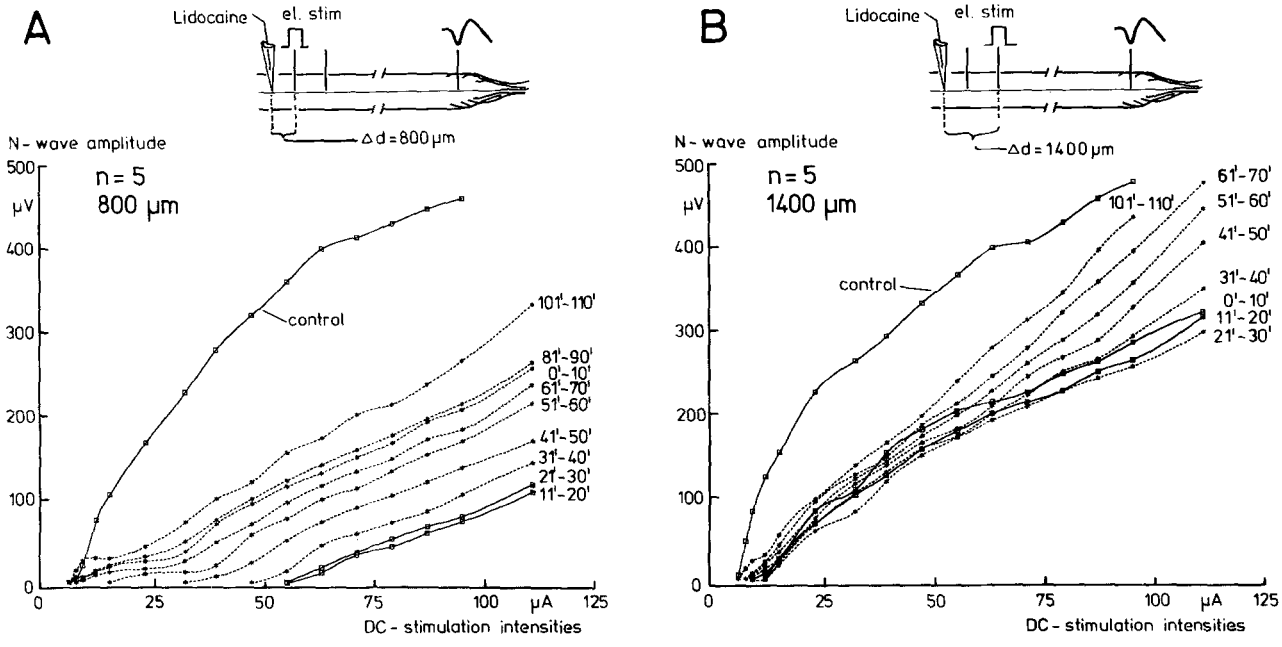

Fig. 5A, B. Experiment 2. The N-wave amplitudes are plotted on the ordinate versus DC-stimulation intensities on the abscissae (SRF). In 5 experiments stimulation electrodes were positioned 800 and 1400 μm caudal to the injection pipette (see insets in **A, B**). **A** Mean SRFs are plotted for stimulation 800 μm caudal to the injection site before (control) and after the injection of 1.0 μl lidocaine. Solid lines represent SRFs during increasing DC block, broken lines represent SRFs during the decay of the block. **B** Same experiments as for **A** but stimulation site 1400 μm caudal to the injection site. The time after injection is given for each SRF at the right

Thresholds did not exceed $3 \times T_o$ values 1400 μm caudal in three experiments and returned to $3 \times T_o$ values within 62 and 37 min after the injection in two other experiments. The slopes of the averaged SRFs 800 and 1400 μm caudal to the injection site (Fig. 5) were reduced from control values (12.6 and 16.0 μV/μA, respectively) to 1.9 μV/μA 11–20 min post injection 800 μm caudal and to 4.9 μV/μA 21–30 min

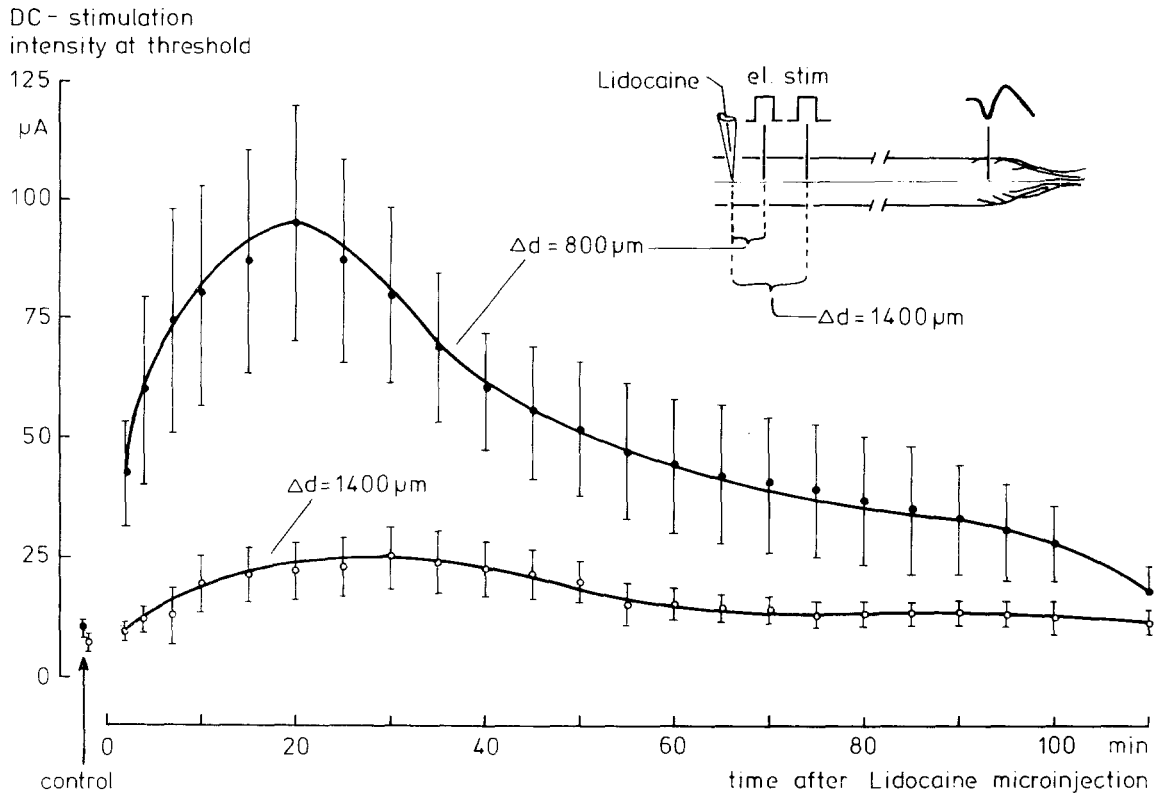

Fig. 6. Experiment 2. Threshold elevation of DC-stimulation to elicit an N-wave on the lumbar cord dorsum following microinjection of 1.0 µl licocaine cranial to the stimulation electrodes. The experimental set up is shown in the inset: Stimulation electrodes were positioned 800 (●) and 1400 µm (○) caudal to the injection site. Mean values ±S.E.M. are given from 5 experiments. Control values as indicated by the arrow

post injection 1400 µm caudal to the injection site. Thus, 1 µl lidocaine microinjected into the DC affects nerve conduction at sites up to 1400 µm caudal to the injection site.

Control experiments

Control experiments were performed to estimate the effect of supplemental i.v. doses of the anaesthetic (pentobarbital sodium) used in this study (n = 4), to estimate the effect of systemic lidocaine (n = 3) and the effect of microinjections of physiologic saline (n = 3) into the DC. Neither pentobarbital (0.5 or 1.0 mg/kg) nor lidocaine (10 µl, 1%) given intravenously affected the N-wave deflection evoked by either DC-stimulation or peripheral nerve stimulation. Injections of 1.0 µl physiologic saline 1000 µm caudal to the stimulation electrode were performed in three cats to evaluate the effect of volume in experiment 1. Mean thresholds were enhanced from 10.2 ± 2.3 µA to 12.9 ± 2.3 µA and mean slopes of the initial rise were 3.6 ± 1.3 before and 3.5 ± 1.5 µV/µA after the injection. None of these changes was statistically significant ($p > 0.05$).

Discussion

Several questions require consideration. To what extent are the results influenced by known sources of error? What is the relation between DC stimulation intensity, recruitment of DC fibers, N-wave amplitude diameter of the block? Are the results found for the DC also relevant for blocks in other CNS structures?

Does lidocaine act locally when microinjected?

Lidocaine was selected for this study because it is a local anaesthetic with well known pharmacodynamic properties (e.g. Heavner and de Jong 1974; Staiman and Seeman 1976; Hille 1977; Denson et al. 1983; Fink and Cairns 1983; Fink and Cairns 1984) and an intermediate duration of action, features which may be suitable for many experiments designed to study central pathways. The observed conduction block in the spinal cord is likely due to a specific pharmacological action of lidocaine, since injection of an equal volume of vehicle (saline) had no significant

effect on the amplitude of the N-wave. Furthermore, the onset and duration of the lidocaine block closely corresponds to data for peripheral nerve blocks (Fink and Cairns 1983; Fink and Cairns 1984). Questions arise concerning the spread of the injected lidocaine and thus the spatial extent of the block. The critical determinant for the spread of an injected substance into CNS tissue is the injected volume. This has been directly assessed by autoradiographic studies (Lomax 1966; Grossman and Stumpf 1969) and dye injections (Myers 1966; Flicker and Geyer 1982). It has been concluded that lipid solubility and diffusion may not be important contributing factors (Grossman and Stumpf 1969). This conclusion is confirmed by Lomax (1966), who reported that 90% of a radiolabelled solution (of morphine) injected in a volume of 1 µl had spread less than 1 mm from the site of injection. The profile of the distribution was indistinguishable when determined immediately after the injection or 60 min later. Clearance of the injected substance is therefore predominantly dependant upon transportation by blood (Lomax 1966; Grossman and Stumpf 1969; Clark and Ryall 1983). Entrance into the circulation may account for the systemic effects of highly lipophilic substances such as the opioid etorphine after intracerebral injection (Clark and Ryall 1983). A significant contribution of possible lidocaine redistribution by the circulatory system after intraspinal microinjection of up to 1.0 µl can be excluded in the present study since the amplitude of the N-wave evoked by electrical stimulation of the superficial peroneal nerve or posterior tibial nerve remained unchanged, while the DC conduction block was maximally effective (not shown). Direct evidence against a detectable effect of systemic lidocaine arises from the failure of injection of a 10-fold higher volume of lidocaine (1%) injected intravenously, to affect the N-wave amplitude evoked either by stimulation of the DC or peripheral nerve stimulation.

Known sources of error

Because of the quantitative character of the present study the effects of known sources of error need to be discussed in some detail.

The interpretation of data from experiment 1 (i.e. stimulation electrode cranial to the injection site) relay on the observation that the fibers do not change their relative position in the dorsal columns over the distance required by the experimental procedure. Scheibel and Scheibel (1969) reported that groups of DC fibers (microbundles) maintain their course quite rigorously along the dorsoventral axis with virtually no communication between adjacent microbundles. The figures by Glees, Livingston and Soler (1951) derived from degeneration studies of single dorsal roots suggest that variability in position may be less than 50–100 µm over a length of 1000 µm. In stimulation experiments BeMent and Ranck (1969) found variations of less than 100 µm for longitudinal distances of up to 2500 µm.

At least three factors concerned with the physiological state of the animal may account for variability in the results: first, the general anaesthetic pentobarbital used in this study affects both nerve conductance (Blaustein 1968; Staiman and Seeman 1974) and the release of transmitters as shown for spinal motor neurones (Weakly 1969) and the neuromuscular junction (Thomson and Turkanis 1973). Since the N-wave reflects postsynaptic activity, it is thus possible that both factors may have influenced the results. However, great care was taken to provide a deep and constant level of anaesthesia (see methods) and supplemental doses of pentobarbital (1 mg/kg i.v.) did not affect the SRFs. The second factor concerned is the temperature within the DC and lumbar spinal cord, which affects nerve conductance (Krnjevic 1959; Paintal 1965) and the excitability of spinal neurons. In the present study core body temperature was kept constant at 38.0 ± 1.0° C (see methods) and varied not more than ±0.35° C during the recording intervals of up to 110 min (mean change ±0.23° C). Finally, the local concentration of carbon dioxide may influence conductance of DC fibers and the excitability of spinal neurons. BeMent and Ranck (1969) reported that increases in the respiration rate of 5 breaths/min from basal rates of 19–22 breaths/min affected the conductance of DC fibers by less than 10%, as evaluated by measurements of compound action potentials. Kitahata et al. (1971) found a specific suppression of lamina V cells by doubling the respiration rate. In the present experiments end-tidal CO_2 was continuously monitored and constant within narrow limits (see methods). Without adjusting respiration parameters during the recording intervals CO_2 did not change by more than ±0.3 vol% (mean ±0.15 vol%). None of these changes affected the SRFs significantly (not shown).

Stimulation thresholds versus diameter of the blocked area

To evoke a detectable N-wave deflection stimulation intensities of 6.7 µA were needed in the absence of lidocaine. At this intensity, DC fibers up to a distance of r_O = 150 µm within an area A_o may be

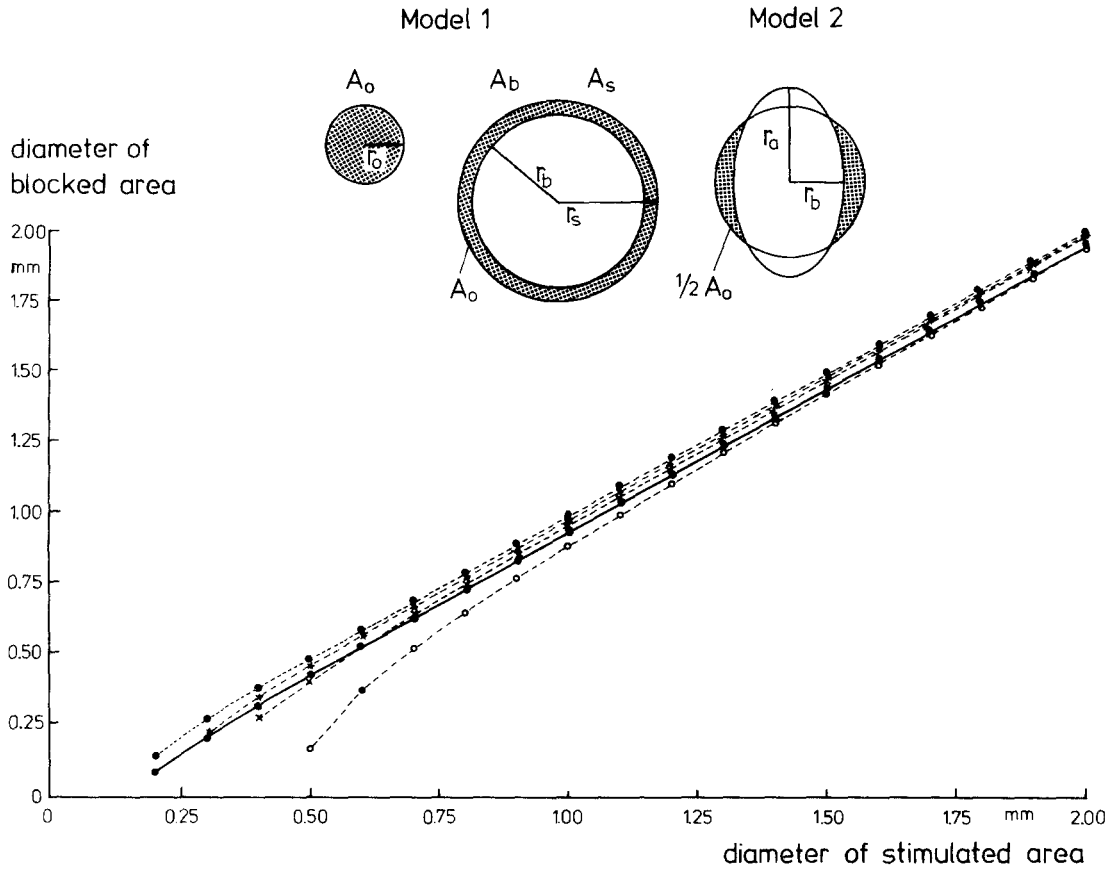

Fig. 7. Calculation of block size from size of the stimulated area at threshold (T_s) in experiment 1. The diameter of the blocked area ($2r_b$) is plotted on the ordinate versus diameter of the stimulated area ($2r_s$) on the abscissa. In model 1 both stimulated area and blocked area have circular symmetry and are concentric in the transverse plane. The completly blocked area is surrounded by a sheet of partially blocked tissue, where only 1/n of all fibers are conducting. Graphs are plotted for model 1 with dotted lines and n = 1 (i.e. all fibers are conducting in the outer sheet) with filled circles for n = 2 (i.e. half of the fibers are conducting) with stars and for n = 4 and n = 10 (crosses and open circles, respectively). Model 2: stimulated area is radially symmetric but the blocked area is more extended along the vertical axis parallel to the injection pipette, resembling an ellipse with a long radius (r_a) and a short radius (r_b) with $r_b = mr_a$. The diameter of the blocked area ($2r_b$) is shown as a function of the diameter of the stimulated area ($2r_s$) with solid lines for m = 0.5

excited according to current distance relations summarized for stimulation in the DC by Ranck (1975). Current may flow radially in all directions in spherical symmetry (Ranck 1975) since stimulation was performed with monopolar electrodes in the DC, which consist of relatively homogeneous tissue (Glees, Livingston and Soler 1951). Assuming that both, the stimulated (A_s) and the blocked area (A_b) have circular symmetry and are concentric in the transverse plane (see inset in Fig. 7), the radius (r_b) of the blocked area may then be calculated by the equation:

$A_b = A_s - A_o$ after solution:

$$r_b = \sqrt{r_s^2 - 0.15^2}$$

This relationship is plotted as model 1-1 in Fig. 7. In an extended model with a completely blocked area surrounded by an incompletely but homogeneously blocked annular sheet with 1/n fibers conducting, the stimulated area needs to be larger than the blocked area by $n \times A_o$, thus:

$A_b = A_s - n \times A_o$ after solution:

$$r_b = \sqrt{r_s^2 - n0.15^2}$$

This relationship is plotted for various values of n in Fig.7 as the models 1–n. If one takes into account that the distribution of the injected solution may not be of radial symmetry, but rather more extended parallel to the injection canal (Myers and Hoch 1978), thus resembling an ellipse in the transverse plane with two radii r_a and r_b (inset in Fig. 7), the relationship between the radius of the stimulated area r_s at threshold and those of the blocked area is given by the following equation: (solution at the authors)

$$A_0 = 2r_s^2 \arctan \frac{K}{n} - 2r_a r_b \arctan K$$

$$K = \sqrt{\frac{r_s^2 - r_b^2}{r_a^2 - r_b^2}}$$

The relation between r_b and r_s was calculated numerically and is shown in Fig. 7 as model 2.

Ten to 45 min after the injection of 1.0 µl lidocaine, stimulation thresholds were elevated to 103.8 ± 4.8 µA; thus, the mean diameter of the stimulated area is 1570 ± 366 µm. The corresponding diameter of lidocaine block vary from 1500 µm for model 1–10 to 1563 µm for model 1–1. Mean diameters of block 4 to 30 min after the injection of 0.5 µl lidocaine were elevated to 59.0 ± 4.2 µA, exciting fibers at a distance of up to 990 ± 100 µm. Thus, calculated diameters of lidocaine block vary from 869 µm (model 1–10) to 979 µm (model 1–1).

The assumption that an area of complete block is surrounded by a sheet of partial block is supported by the effects of the conduction block on the slope of the SRFs in Experiment 1 (i.e. the increase in the N-wave amplitude per increase in stimulation intensity). Although the mathematical relationship between the N-wave amplitude and the number of recruited DC fibers is not known, a monotonic relation is most likely. Thus an increasing N-wave amplitude indicates an increasing number of recruited DC fibers. Correspondingly, a steeper slope of the SRF indicates a stronger recruitment of DC fibers.

A_s may be linearly related to the number of DC fibers recruited by stimulation since the density of fibers within the DC (Glees et al. 1951) as well as the T_o values (unpublished observations) are fairly constant. The slopes of the SRFs may therefore be expressed as the change in N-wave amplitude (µV) per change in A_s (mm^2). In experiment 1, the slopes of the initial rise were reduced from 743.3 µV/mm^2 to 14.4 µV/mm^2 after the injection of 0.5 µl lidocaine and to 17.9 µV/mm^2 after 1.0 µl. Thus, recruitment of DC fibers was dramatically reduced when stimulating just above threshold. When stimulation thresholds for N-wave returned to near control values (i.e. $3 \times T_o$), slopes were still reduced to 248.9 and 219.5 µV/mm^2 respectively, indicating that a widespread partial block still exists when the size of the complete block is reduced or completely abolished.

Blocks in other CNS structures

The dorsal columns were choosen for study because of their well defined anatomy and physiology. It may, however, be desirable to apply the present findings to blocks in other CNS structures, which may be different in respect to their physical properties (e.g. cell density, vascularization) and their content of neuronal elements (e.g. cell bodies, axons, glia cells). Neuronal transmission in different classes of axons, dendrites or cell bodies as well as synaptic transmission may be blocked. The blocking concentrations for all these neuronal elements do not exceed those for large myelinated fibers (0.8–1.0 mM licocaine), which were blocked in the present study (see, however, Fink and Cairns (1983) for a sensitivity to local anaesthetic which is not related to the axon diameter) and thus are considerably lower than the concentration of the injected solution (40 mM). It is therefore concluded that the blocks produced in other CNS structures will also be complete. However, the size of the lateral sheet of partially blocked tissue may differ according to different sensitivity to the local anaesthetic. The spatial extent of the incomplete block should be largest for the most sensitive neuronal structure i.e. synapses with blocking concentrations of 0.1 mM (Kuno and Matsuura 1982) and smallest for the least sensitive fibers which are the large myelinated ones (blocking concentration 1.0 mM, Staiman and Seeman 1977). Thus, blocking concentrations differ by factor of 10, which is also the range provided by the models 1–1 to model 1–10 in Fig. 7. The present results may only strictly apply to the first lidocaine injection made at a site. Possibly, subsequent blocks might be influenced by changes in the local circulation e.g., which should be considered when several injections are made at the same site.

To identify central pathways, the microinjection of a local anaesthetic may provide a reliable tool, with known time course and extend of the block produced. The size of the block is fairly predictable for various structures within the CNS when applying one of the different assumptions discussed above and may not differ by more than 15%. However, a partial block of conductance may persist for longer than two hours, which should be taken into account when comparing parameters before and after the production of local anaesthetic blocks.

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