REFLEX EXCITABILITY OF HUMAN SPINAL MOTONEURONS DURING TEMPORARY ISCHEMIC "DEAFFERENTIATION"

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Interruption of the blood flow in the lower limb was caused by application of a constricting cuff proximally or distally to the popliteal fossa. Electrical stimulation of the tibial nerve in the popliteal fossa caused reflex nicotine-like (N) and peripheral muscarine-like (M) cholinergic responses of the gastrocnemius muscles. By comparing changes in the amplitudes of these responses, the sequence of development of the ischemic conduction block in low-threshold afferents of the N-reflex and in efferent motor fibers was determined. During the first 23-25 min of ischemia the conduction block develops mainly in low-threshold afferents. In the case of proximal occlusion, the N response disappears completely by the 23rd-25th minute, while the maximal M response decreases only slightly. The increase in N response discovered after distal occlusion showed that reflex excitability of the "deafferented" motoneurons increases parallel with the development of the afferent block.

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Temporary interruption of the blood flow in a limb produced by application of a pneumatic cuff leads successively to disturbance and loss of sensation, difficulty of movements, and ultimately to total paralysis of the limb [6-9, 11]. After comparing changes in reflex nicotine-like (N) cholinergic and F responses and the peripheral muscarine-like (M) response of muscles, Magladery and co-workers [10] concluded that in the early stages of development of ischemia conduction is mainly blocked in low-threshold afferents of the N reflex while conduction along motor fibers is almost completely preserved. Unfortunately, in the recordings illustrating the paper by Magladery and co-workers (especially those in the left column of Fig. 5) there are considerable differences in size and shape of the stimulation artefacts, rendering it impossible to determine the true time of inhibition of the N and M responses. In addition, in the experiments performed by these workers, the occluding cuff was applied proximally to the stimulating electrodes (proximal occlusion). However, with proximal occlusion the amplitude of the M response does not necessarily reflect development of the efferent conduction block or, consequently, its participation in inhibition of the N response. For example, the conduction block develops primarily in the region of compression by the cuff whereas distally to the cuff ability of the fibers to become excited and to conduct persists longer. In the early stages of occlusion the peripheral M response, generally speaking, may remain unchanged, although at this time conduction along efferent axons in the zone of pressure of the cuff will be blocked, leading to diminution of the N response.

The first object of this investigation was to compare the rates of development of the block in the efferent fibers in the cuff pressure zone and in the distal segments. For this purpose, the decrease in M response was compared after application of the occluding cuff proximally (proximal occlusion) and distally (distal occlusion) relative to the stimulating electrodes.

The second object was to determine the order of development of the conduction block in afferent fibers of the N reflex and in efferent motor fibers. To do this, the decrease in N and M responses during the action of proximal occlusion was compared.

The third object was to determine excitability of the spinal motoneurons during their temporary "deafferentation," and for this purpose distal occlusion was used. During distal occlusion deafferentation occurs as a result of a conduction block in the afferent fibers in the segment lying distally to the cuff, whereas in proximal occlusion conduction along fibers proximally to the cuff is intact.

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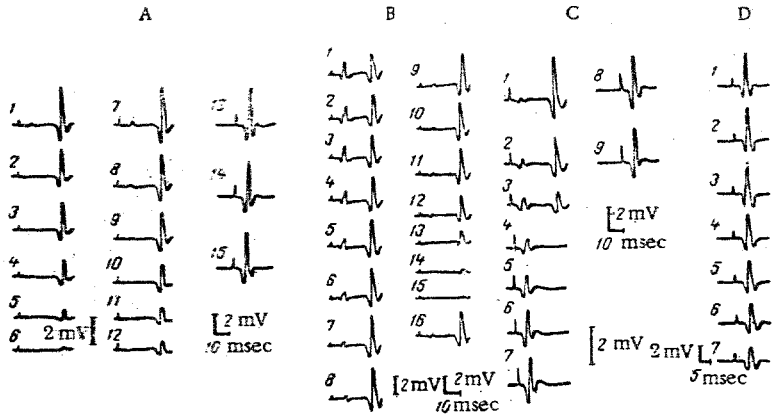

Fig. 1. Changes in N and M responses of soleus muscle during proximal occlusion. A) suprathreshold control N response. Frame 1) maximal N response in 7th min of occlusion, frames 2-6) control response at 7th, 9th (3), 10th (4), 11th (5), and 12th min (6) respectively. Strength of stimulation increased at 13th min to obtain maximal control N response (7), which subsequently diminished: 15 min (8), 16 min (9), 17 min (10), 18 min (11), 19 min (12). Frames 13-15) maximal M response at 2nd, 13th, and 20th min respectively; B) supramaximal control N response: 1 min (frame 1), 3 min (2), 5 min (3), 6 min (4), 7 min (5), 8 min (6), 9 min (7), 10 min (8), 11 min (9), 12 min (10), 13 min (11), 14 min (12), 15 min (13), 16 min (14), 17 min (15); frame 16) maximal N response at 17th min evoked by increasing strength of stimulation; C) maximal N responses evoked at 16th (1), 20th (2), and 22nd min (3) with increasing strength of stimulation (compare amplitudes of M responses). Frames 4-7) absence of N response at 24th (4 and 5) and 25th (6th and 7th) min during action of stimulation of any strength (see increase in amplitudes of artefacts and M responses). Frames 8 and 9) maximal M response at 16th and 25th min respectively; D) maximal M response at 2nd (1), 11th (2), 24th (3), 29th (4), 31st (5), 32nd (6), and 35th (7) min respectively.

EXPERIMENTAL METHOD

For proximal occlusion the pneumatic cuff of a tonometer, 5 cm wide, was applied to the thigh immediately above the popliteal fossa, and for distal occlusion it was applied to the upper part of the leg at the level of the lower border of the popliteal fossa (about 8-10 cm below the proximal position of the cuff). In both cases air was pumped into the cuff under a pressure of 60-90 mm Hg above the level at which the pulse ceased to be palpable in the dorsalis pedis artery. The tibial nerve was stimulated in the popliteal fossa with square pulses 1 msec in duration. Intervals between stimuli were about 10 sec. The strength of stimulation for the control N response was chosen after air had been pumped into the cuff. The electrical N and M responses of the gastrocnemius muscles were detected with surface electrodes and recorded on a three-channel "Alvar" myocathograph. The amplitude of the test N response was expressed as a percentage of the amplitude of the maximal M response (N/M_{max} [4]). To evoke a supramaximal N response the strength of stimulation was increased until the amplitude of the N response was slightly below maximal [3].

During the investigation the subjects sat in a comfortable resting position. The duration of occlusion did not exceed 42 min.

EXPERIMENTAL RESULTS AND DISCUSSION

Changes in Peripheral M Response during Proximal and Distal Occlusion. Diminution of the M response during the two types of occlusion occurred about equally during the first 25-30 min. The small M response preceding the maximal or supramaximal N response began to diminish 4-6 min after the beginning

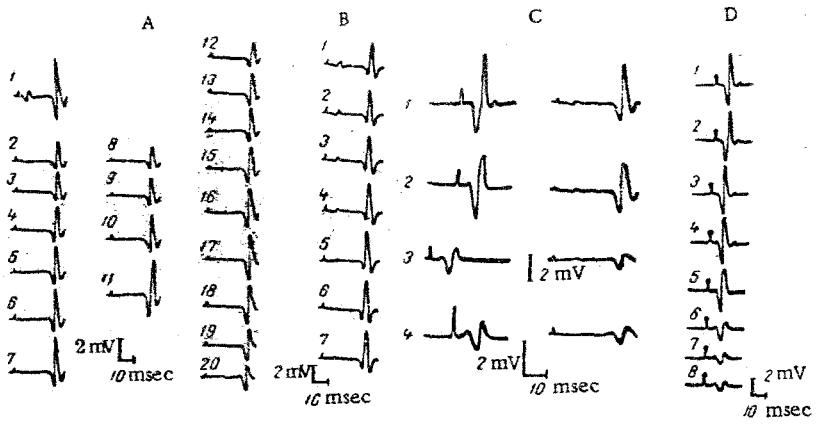

Fig. 2. Changes in N and M responses of the soleus muscle during distal occlusion. A) suprathreshold control N response. Frame 1) maximal N response at 7th min, frame 2) control N response at 7th minute, 9th (3), 10th (4), 12th (5), 13th (6), and 14th min (7). At 16th min strength of stimulation was reduced to obtain a new control N response (8), which subsequently increased: 17 min (9), 18 min (10), 19 min (11). Strength of stimulation reduced at 21st min to obtain new control N response (12), which again increased initially: 22 min (13), 23 min (14), 24 min (15), 25 min (16), 27 min (17), and then began to decrease: 28 min (18), 31 min (19), 32 min (20); B) supramaximal control N response: 5 min (1), 8 min (2), 9 min (3), 10 min (4), 12 min (5), 13 min (6), 15 min (7); C) parallel decrease in maximal M (on the left) and N (on the right) responses in late stages of occlusion: 3 min (1), 27 min (2), 33 min (3), and 36 min (4). Top calibration signal for top 3 pairs, bottom signal for bottom pairs of frames; D) maximal M response: 2 min (1), 9 min (2), 15 min (3), 20 min (4), 26 min (5), 33 min (6), 35 min (7), 39 min (8).

of occlusion (Fig. 1B, frames 1-8; Fig. 2B, frames 1-7). The maximal M response showed a slight decrease only after action of the cuff for 12-15 min, and at this time it was usually about 95% of its initial amplitude (Figs. 1D and 2D). During about the next 10 min the maximal M response continuted to diminish slowly, so that after 23-25 min of ischemia its amplitude was still about 90% of its initial value. From this time the amplitude of the M response began to fall more rapidly, especially during distal occlusion. By 40-42 min the M response had almost completely disappeared.

Hence, in the early stages of occlusion the conduction block in the segment distal to the region of compression by the cuff at least did not develop more slowly than in the region of compression. Meanwhile the pressure in the region of the cuff evidently created conditions aggravating the block, thus explaining the somewhat faster decrease in the M response in the late stages of distal occlusion compared with proximal occlusion (Fig. 3).

Changes in Reflex N Response during Proximal Occlusion. Suprathreshold Control N Response. During the first 7-10 min of occlusion no visible change took place in the suprathreshold N response. After the 7th-10th min the N response began to decrease rapidly (Fig. 1A, frames 2-6). The smaller the amplitude of the control N response, the sooner and more completely the N response was inhibited. However, if the strength of the test stimulus was increased at the 12th-15th min of occlusion, a large, and even maximal N response could again be evoked. The amplitude of the new control N response immediately began to decrease, and the smaller it was initially the sooner it reached zero (Fig. 1A, frames 7-12). Nevertheless, if the strength of stimulation was again increased at the 16th-18th min of occlusion, a large N response with amplitude up to 80% of the maximal control N response could be evoked (Fig. 1B, frame 16). If more than 22-25 min elapsed from the time of application of the cuff, no N response could be evoked whatever the strength of stimulation (Fig. 1C, frames 1-7).

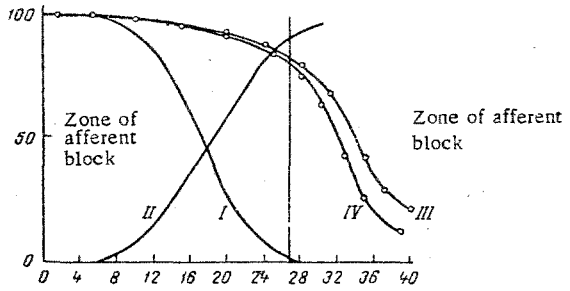

Fig. 3. Reconstructed curves of development of afferent block (I) and increase in reflex excitability of spinal motoneutrons (II) and curves of development of efferent block (III and IV) during action of ischemic cuff. III) decrease in amplitude of maximal M response during proximal occlusion; IV) during distal occlusion. Abscissa, duration of occlusion (in min); ordinate for curves III and IV, amplitude of maximal M response as a percentage of maximal at beginning of occlusion.

Maximal or Supramaximal Control N Response. After the 3rd-5th min of occlusion, parallel to the decrease in the preceding M response a small increase took place in the amplitude of the maximal and an appreciable increase in that of the supramaximal N response took place (Fig. 1B, frames 1-8). By the 9th-10th min of occlusion the amplitude of the N response sometimes actually exceeded that of the control maximal response. One explanation of the increase in the N response is that because of ischemic exclusion of efferent fibers (shown by the diminution of the M response) the antidromic volley was reduced and this, in turn, led to a decrease in its inhibitory action on the orthodromic reflex response of the motoneuron pool [2]. After a period of increase, the amplitude of the control N response fell rapidly, and by the 16th-20th min the amplitude of the N response was sharply reduced (Fig. 1B, frames 9-15).

Hence, so far as can be judged from the decrease in amplitude of the N response, the most rapid increase in number of blocked afferents of the N reflex occurs between the 10th and 25th min of occlusion. After 23-25 min of proximal occlusion to N response could be evoked whatever the strength of stimulation, although the amplitude of the maximal M response at this period was still about 90% of normal. The results obtained were used to construct the scheme given in Fig. 3 to show the temporal course of development of the ischemic block in the N reflex afferents (curve I).

Changes in Reflex N Response during Distal Occlusion. Suprathreshold Control N Response. In the first 3-5 min of occlusion no appreciable changes occurred in the N response. Later it began to increase, at first gradually and then quickly (Fig. 2A, frames 2-7). If the strength of stimulation was reduced after the increase in amplitude of the N response, the newly diminished N response again began to increase (Fig. 2A, frames 8-11). With the use of a test N response with an initial amplitude of about 50% of maximal, and by recording the time taken to reach maximal amplitude, it was found that the fastest increase in amplitude of the N response took place in the period from the 8th-10th to 20th-23rd min of occlusion. The rate of increase then slowed (Fig. 2A, frames 12-17), and starting from the 27th-30th min of occlusion, the amplitude of the N reflex diminished to a degree which corresponded precisely with the decrease in amplitude of the M response (Fig. 2A, frames 17-20; Fig. 2C, frames 1-4).

Maximal or Supramaximal Control N Response. The first increase in maximal or supramaximal N response was observed 8-10 min after application of the cuff (Fig. 2B, frames 1-7). By the 15th-17th min the amplitude of the N response slightly exceeded the maximal amplitude of the control N response at the beginning of occlusion. In the interval from the 18th-20th to the 23rd-25th min the supramaximal amplitude of the N response showed no appreciable change. After the 23rd-25th min, the decrease in amplitude of the N response was parallel to the decrease in the M response (Fig. 2C, frames 1-4).

Curve II in Fig. 3 was reconstructed from data obtained when test stimuli of different strengths were applied. It will be seen that the increase in excitability of the spinal motoneurons took place parallel to development of the block in the low-threshold afferents of the N reflex (compare curves I and II in Fig. 3). The shape of this curve can be traced reliably only as far as the 25th-30th min of the ischemic block. The subsequent slowing of the rate of increase of the amplitude of the control N response and its subsequent inhibition were evidently of purely peripheral origin – a conduction block in the efferent fibers. This hypothesis is supported by the fact that the decrease in amplitude of the N response in the late stages of occlusion ran strictly parallel to the decrease in the M response, so that the ratio N_{max}/M_{max} remained constant (Fig. 2C).

The increase in reflex excitability of motoneurons undergoing "acute deafferentation" in this way may result either from exclusion of tonic inhibitory influences from the low-threshold afferent fibers of antagonist muscles or of exclusion of homonymous and synergistic tonic facilitatory influences. The latter

may lead to an increase in excitability of "deafferented" motoneurons in accordance with the general mechanism of increase in sensitivity of denervated structures [1, 5].

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