METHOD FOR ASSESSMENT OF STATE OF INHIBITORY APPARATUS IN SPINAL CORD OF MAN

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Our search for a method by which to assess the state of the segmental apparatus in the spinal cord of man began with an attempt to apply the N-reflex method [4, 5]. The essentials of this method are, of course, electrical stimulation of a mixed nerve and recording of the action potentials in the muscle. The muscle response generally consists of 2 elements, the M-response, evoked by stimulation of efferent fibers, and the reflex monosynaptic N-response [4], evoked by stimulation of the afferent fibers. Depending on the position of the stimulating electrode and the characteristics of the stimulating pulse, it may be possible to record only the reflex N-response, without the M-response, in some particular part of the muscle. When the strength of stimulation is increased, the M-response becomes apparent and, as the latter grows, the N-response tends to diminish and ultimately disappear. This is explained [5] by blocking of the reflex response by the oncoming antidromal volley in the efferent fibers or in the motoneurons (first hypothesis: antidromal block only). It is, however, possible that one of the reasons for reduction of the N-response under such circumstances may be central inhibition, evoked both in the motoneurons, the axons of which have been excited antidromically, and in others in the same segment (2nd hypothesis: antidromic block and central inhibition). This central inhibition may be effected through the system of Renshaw cells which are excited by the antidromic volley in the axons of the motoneurons [2, 6], and the system of inhibitory interneurons in Cajal's intermediate nucleus, which are excited by the orthodromic volley in 1c afferent fibers from the tendon organs of Golgi [3]. Involvement of the system of Renshaw cells in the reduction of the N-response on increase of the intensity of stimulation requires that the rate of conduction in the fastest efferent fibers must be somewhat greater than the rate in the slowest, 1a afferent fibers (the volley in these fibers also induces monosynaptic excitation of the motoneurons). Again, involvement of the system of inhibitory interneurons in the Cajal nucleus requires that the rate of conduction in the fastest afferent 1c fibers should be slightly greater than the rate in the slowest afferent 1a fibers.

If the 2nd theory is correct, reduction of the N-response with increase in strength of stimulation of the mixed nerve might be used as an index of the state of the inhibitory system in the spinal cord (Renshaw cells and inhibitory interneurons of Cajal's nucleus) of man. It was postulated in a preceding investigation [1] that feedback inhibition was of considerable importance in the mechanism responsible for the normal functioning of muscle in healthy man. It was also suggested that an abnormal state of the Renshaw cells might be an important element in the mechanism of tremor and rigidity in paralysis agitans.

The present investigation has provided experimental evidence that the depression of the N-response associated with intensification of the M-response is partly due to central inhibition.

METHOD

The investigation was carried out on 8 ostensibly healthy individuals. The subject was seated in a convenient position and superficial electrodes were placed over the medial head of the gastrocnemius, the soleus and the anterior tibial muscle. Stimulation was effected with rectangular pulses 1 msec in length. The active electrode was in the popliteal fossa. The recording instrument was a three-channel electromyograph. As M- and N-responses are both synchromized responses, their amplitudes afford some indication of the number of motor units activated.

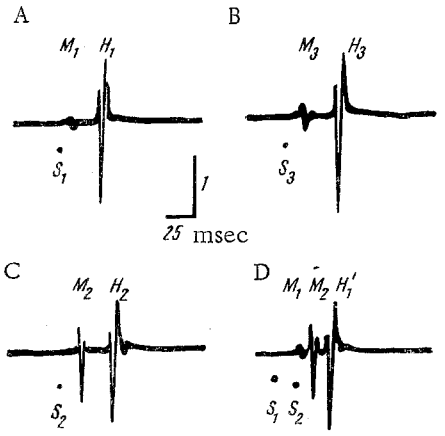

Fig. 1. Responses of gastrocnemius muscle to single and paired stimulations (interval 11 msec). A) S_1 - 25.5 V; B) S_2 - 31 V; C) S_3 - 27 V; D) $S_1 + S_2$.

Only values for N-responses, obtained with M-responses of constant amplitude, were used for comparison, in order to exclude errors arising from displacement of the stimulating electrode.

RESULTS

The stimulation strengths selected were S_1, which produced a reflex response N_1, and S_2, which was stronger than S_1, giving a M_2-response greater than M_1 and a reflex response N_2, which was smaller than N_1 (Fig. 1). The stimuli were then delivered in pairs, S_2 11 msec after S_1, this interval being chosen to ensure that the antidromic volley in the efferent fibers from stimulation S_2 would encounter the reflex volley from S_1 actually in the axons of the motoneurons, and that the responses M_2 and N_2 would not interfere with the response N_1. When the stimulations were paired in this way, the response N_1 was altered, and is denoted by N_1^i.

If it were found possible to select $S_2 > S_1$ so that $N_1^i > N_2$, this would prove the first hypothesis incorrect. In practical terms, if antidromic block were the sole reason for N_2 being less than N_1 (first hypothesis), then N_1^i would be less than or equal to N_2 as (1) the antidromic block was no less complete in the experiment with paired stimulations than with S_2 alone (Fig. 1 shows that, in the experiment with paired stimulations, M_2 had the same amplitude as in the case of stimulation S_2 alone) and (2) stimulation S_1 was purposely selected so that it did not excite more afferent fibers than S_2. It will be seen that the response N_1^i was larger than the response N_2 in the case of single stimulation ($N_1 > N_1^i > N_2$).

The production of such a result, it may be noted, required very careful selection of the parameters of stimulation S_2. The first hypothesis can, however, be proved incorrect even by the results of an experiment which is readily reproducible, in which $N_1 > N_1^i = N_2$, in that - a fact readily verified - S_2 activates a larger number of reflex-producing afferent fibers than S_1 (there is a stimulation value S_3 such that $S_2 > S_3 > S_1$, which produces a response $M_3 > M_1$ and a reflex response $N_3 > N_1$; see Fig. 1).

These experimental findings are thus inconsistent with the first hypothesis. If it is accepted that central inhibition is concerned in the phenomenon under investigation, the fact that N_1^i is greater than N_2 can be explained in the following manner. In the case of paired stimulation the excitation evoked by S_2 is unable to reach the interneurons in the spinal cord, and the reflex discharge will be blocked only in the antidromically excited axons. In the case of solitary S_2 stimulation, the volley evoked by S_2 is able (at any rate by way of the fastest fibers) to reach the Renshaw cells or the inhibitory interneurons in the Cajal nucleus and may, just about the time of arrival of the afferent volley, inhibit more motoneurons than the number of antidromically excited efferent fibers.

Second Proof. This is based on the fact that, when there is antidromic block of the reflex volley, there must be a close connection between the amplitude of the N-response and the number of antidromically excited axons (or, in other words, the amplitude of the M-response). If, then, central inhibition is a factor of real importance, it should be possible, under suitable conditions, to produce a reduced N-response with an unchanged M response as the motoneurons inhibited through the interneurons will not be merely those the axons of which have been antidromically excited.

For the experiment, 2 pairs of recording electrodes were attached to two parts (A and B) of the medial head the gastrocnemius muscle, deliberately chosen for their difference in diameter. S_1 stimulation of the mixed nerve evoked responses M_{A1} and N_{A1} under electrodes A and, at the same time, responses M_{B1} and N_{B1} under electrodes B. A stimulation strength S_2, stronger than S_1, was then selected to give the same M-responses as before ($M_{A2} = M_{A1}$). Under these circumstances, it was always possible to find a part of the muscle (designated B) where the M-response was larger ($M_{B2} > M_{B1}$). In many cases the reflex response under electrodes A was then smaller ($N_{A2} < N_{A1}$). This reduction could not be explained by antidromic block in the axons of motoneurons supplying the muscle segment A, as the M-response in this segment was unchanged. It follows, therefore, that the reduced N-response in segment A was the result of antidromic excitation of addition efferent fibers supplying other segments and muscles (and, in particular, segment B) or orthodromic excitation of additional Ic fibers. These additional fibers, however, can affect

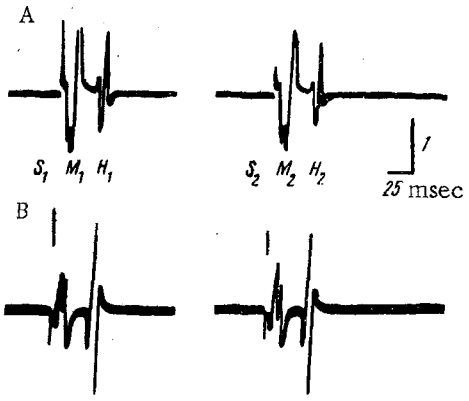

Fig. 2. Responses in two parts (A and B) of medial head of gastrocnemius to stimulation S_1 (22 V) and S_2 (22.5 V).

the volley in axons supplying segment A only through central inhibition (through the system of Renshaw cells or the system of inhibitory interneurons of the Cajal nucleus).

DISCUSSION

The results of animal experiments indicate that feedback collaterals to Renshaw cells come from the stoutest (most rapidly conducting fibers with the lowest thresholds) efferent fibers [7, 8]. This is consistent with the fact that the antidromic volley from stimulation of the mixed nerve was able, through Renshaw cells, to inhibit a number of motoneurons just at the time when the afferent volley was arriving.

The fact that, in the first form of experiment, it was impossible to produce an N_1^1 significantly larger than N_2 may be explained as due to more intense inhibition of the reflex discharge N_1 by the antidromic volley in the axons in the case of paired, as compared with single S_2 stimulation. It has been shown [2] that antidromic stimulation does not result in excitation of the somas of by any means all motoneurons, as in some cases the antidromic impulse fails to enter the initial segment and soma. In that the refractoriness of the axon itself is of short duration, it may be that the reflex discharges of these neurons reach the muscle. In the case of paired stimulation, there is blocking (in the axons) even of those motoneurons, the somas of which have not been excited by the antidromic impulse from S_2 stimulation.

These results indicate that whenever an N-reflex with a preceding M-response is recorded, the magnitude of the reflex has already been reduced by virtue of central inhibition. It is therefore possible to assess the functional state of the inhibitory apparatus in the spinal cord of man on this basis. Further investigation is required to determine what inhibitory system - whether Renshaw cells, inhibitory interneurons in the Cajal nucleus or some other system - is responsible for depression of the N-reflex when the intensity of the stimulation applied to a mixed nerve is increased.

The authors are at present employing a method involving the introduction of central inhibition in a study of the mechanisms for control of spinal cord activity in man and in connection with certain neurological problems.

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