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Escape of the extensor monosynaptic reflex from presynaptic inhibition

Excitation of the Group I afferent fibers of the nerve of the knee flexor muscles induces inhibition of the monosynaptic reflex response evoked by stimulating the nerves of the gastrocnemius and soleus muscles (GS). It has been found that during this kind of inhibition there is no hyperpolarization of the postsynaptic membrane and the excitability of GS motoneurons is unchanged when tested with stimuli applied directly through microelectrodes[6]. According to further investigations by Eccles *et al.*[5], the inhibition results from decreased presynaptic spike during depolarization of GS Ia afferent endings induced by stimulated flexor afferent fibers. The time course and amount of inhibition following brief trains of stimuli applied to knee flexor nerves have been described[3].

The purpose of this communication is to report the effect of longer trains of conditioning stimuli at physiological rates, applied to the nerve of the posterior biceps-semitendinosus muscle (PBST), on the mono- and polysynaptic responses evoked by single shocks to the GS nerve. The effects of this interaction on the EPSP of a GS motoneuron was noted by Eccles *et al.*[1]. Disinhibition occurs during the conditioning stimulation and the time course and amount of recovery of the monosynaptic reflex have been found to be a function of the frequency of the conditioning stimulation.

The experiments were carried out on adult cats, anesthetized with pentobarbital sodium (35 mg/kg) administered intraperitoneally and spinalized at the lower thoracic level. The lumbar enlargement of the spinal cord was exposed and the ventral roots on the left side were cut distally. The nerves to gastrocnemius, soleus and PBST muscles of the left side were also exposed and cut distally. Stimulating electrodes were applied both to GS and PBST nerves. Recording electrodes were applied to S1 or L7 dorsal roots and S1 ventral root as shown in the diagram (Fig. 1). When required, the original dose of anesthetic was supplemented with an additional 30 mg. The spinal cord as well as the isolated nerves were kept under warm mineral oil and the rectal temperature was maintained at 37°C $\pm$ 1.

The experimental procedure was as follows: Maximal electrical stimuli for Group I fibers were applied continually to the GS nerve at low frequency, usually once every 1.5–3.0 sec in different animals. The resulting mono- and polysynaptic reflex responses were recorded from S1 ventral root while the incoming impulses to the spinal cord were recorded from S1 or L7 dorsal roots. Intermittently, long trains of stimuli were applied to PBST nerves at an intensity supramaximal for Ia and Ib fibers. The duration of a single train was about 30 sec and the interval between them at least 40–50 sec. During a 30 sec train the frequency of the stimuli was maintained at one of the following frequencies for 3 or 4 trials: 50, 100, 200 or 300 c/sec. In a subsequent train the frequency was then shifted to one of the other values.

As expected the amplitude of the GS monosynaptic reflex was found to decrease during conditioning stimulation of the PBST nerve[3]. However, a tendency to recover along an exponential time course occurred in the first 10–15 sec (Fig. 2). Although the control amplitude was not reached, the amplitude of the monosynaptic reflex in the

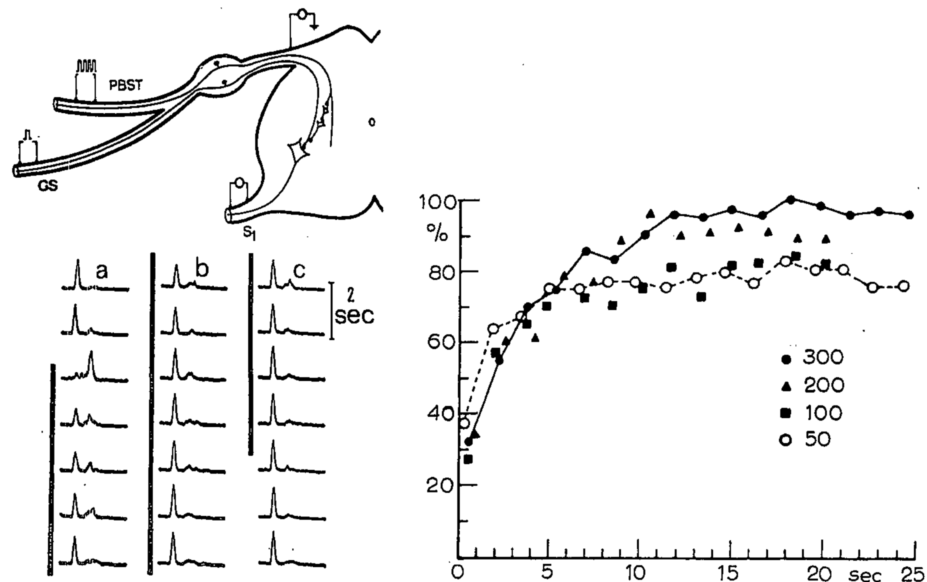

Fig. 1. The upper part of the diagram illustrates the experimental arrangement in which single test shocks were delivered to gastrocnemius-soleus nerves (GS) and conditioning stimulus trains were delivered to posterior biceps-semitendinosus nerves (PBST). Recordings were obtained from S_1 ventral root and the corresponding dorsal root.

The continuous series of records a, b, and c show mono- and polysynaptic responses evoked by stimulating GS at 1.6/sec. The heavy vertical lines indicate the period of conditioning stimulation of PBST at supramaximal intensity for Ia + Ib fibers and at 300/sec. The first two responses in record a represent the termination of the control period. Inhibition of the monosynaptic and augmentation of the polysynaptic responses occur throughout the conditioning period. However, the intensity of the effect decreases as a function of time. The duration of each trace is 8.5 msec.

Fig. 2. The recovery of the GS monosynaptic response from inhibition by conditioning stimulation of PBST at 4 different stimulus frequencies. The mean amplitude of 3 trials at each frequency is plotted as percent of the mean control value. The degree of recovery depends on the conditioning frequency, maximum recovery seen here for 300 c/sec (solid line) and minimum for 50 c/sec (broken line). All data for Figs. 1 and 2 were obtained from the same cat.

following 15–20 sec stabilized at a level dependent on the frequency of conditioning stimulation. Related changes have been reported by Eccles *et al.*[1,4] for the excitatory postsynaptic and dorsal root potentials. During the inhibition of the monosynaptic response there was an increase in the area of the polysynaptic reflex. No attempt, however, has been made to analyse this phenomenon quantitatively.

According to Eccles *et al.*[2], the inhibition of GS monosynaptic reflex following the stimulation of the PBST nerve results from the excitation of special interneurons, which in turn depolarize the GS primary afferent endings. The increase of the polysynaptic response suggests that the depolarizing action is specific to the Ia endings which are in monosynaptic contact with the motoneurons. As a result, when the presynaptic terminals involved in the monosynaptic reflex are depolarized, greater responsiveness of motoneurons can be expected through polysynaptic chains.

Our results do not reveal the mechanisms involved in the disinhibition of the

monosynaptic reflex. Since there was no diminution of the afferent volleys at different frequencies, the input from the PBST nerve can be considered constant. Therefore, the mechanism of disinhibition must be within the spinal cord. Either accommodation or depletion of chemical transmitter in the inhibitory pathway or active disinhibition may be responsible.

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1 ECCLES, J. C., ECCLES, R. M., AND MAGNI, F., Central inhibitory action attributable to presynaptic depolarization produced by muscle afferent volleys, *J. Physiol. (Lond.)*, 159 (1961) 147–166.
2 ECCLES, J. C., KOSTYUK, P. G., AND SCHMIDT, R. F., Central pathways responsible for depolarization of primary afferent fibres, *J. Physiol. (Lond.)*, 161 (1962) 237–257.
3 ECCLES, J. C., SCHMIDT, R. F., AND WILLIS, W. D., Presynaptic inhibition of the spinal monosynaptic reflex pathway, *J. Physiol. (Lond.)*, 161 (1962) 282–297.
4 ECCLES, J. C., SCHMIDT, R. F., AND WILLIS, W. D., The location and the mode of action of the presynaptic inhibitory pathways onto Group I afferent fibres from muscle, *J. Neurophysiol.*, 26 (1963) 506–522.
5 ECCLES, J. C., SCHMIDT, R. F., AND WILLIS, W. D., The mode of operation of the synaptic mechanism producing presynaptic inhibition, *J. Neurophysiol.*, 26 (1963) 523–538.
6 FRANK, K., AND FUORTES, M. G. F., Presynaptic and postsynaptic inhibition of monosynaptic reflexes, *Fed. Proc.*, 16 (1957) 39.

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