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STUDIES OF PRESYNAPTIC INHIBITION IN THE STRETCH REFLEX PATHWAY OF THE HUMAN AND THE CAT

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INTRODUCTION

Presynaptic inhibition of muscle afferent terminals in the spinal cord, including perhaps those of Ib afferents, is a potential and direct mechanism for control of the stretch reflex parameters. Eccles (1964), in reviewing the extensive studies of his group on the cellular basis and network organisation of presynaptic inhibition in the spinal cord, expressed the view that this form of inhibition was in fact more potent than postsynaptic inhibition. Despite this, the functional role of presynaptic inhibition in motor control has, only recently, begun to be studied. Matthews (1972) commented that presynaptic inhibitory mechanisms have not, in general, been incorporated into ideas of how the spinal cord controls movements because of a lack of quantitative measures of its effects. In this chapter we describe the results of two experimental studies bearing on the functional role of presynaptic inhibition during walking in humans and on the biomechanical consequences of presynaptic inhibition of the stretch reflex (s.r.).

In the first experiment, we tested in freely moving human subjects the hypothesis (Morin, Katz, Mazieres & Pierrot-Deseilligny, 1982; Stein & Capaday, 1988) that the decrease of the soleus H-reflex which occurs in going from standing to walking is due, at least in part, to an increase of presynaptic inhibition of the intraspinal terminals of the group Ia muscle afferents. The results of the second experiment address the issue of how presynaptic inhibition of muscle spindle afferents affects the mechanical parameters (stiffness and threshold) of the s.r.

EXPERIMENTS IN HUMANS

It is well known from experiments in the cat that stimulation of flexor nerves at group I strength can induce presynaptic inhibition of the intraspinal terminals of extensor group Ia afferents (reviewed by Rudomin, 1990). Indeed this also seems to be the case in humans,

since we found that in normal subjects a single electrical stimulus to the common peroneal nerve (1 - 1.5 x MT) delivered during quiet standing produces a strong inhibition of the soleus H-reflex, by up to 50%. (Figure 1). The inhibition becomes evident at conditioning - testing (C-T) intervals of about 50ms, and reaches its maximum at C-T intervals of 100 - 120 ms. The conditioning stimulus, when it is given alone, produces little or no change in the background EMG measured at the time of the test stimulus. In fact, based on the relation between the H-reflex amplitude and the mean rectified background EMG during standing, the inhibition of the H-reflex was always greater than could be accounted for by changes in the background EMG. Furthermore, the conditioning stimulus has little effect on the soleus evoked motor response to stimulation of the ankle area of the motor cortex. Taken together, these observations strongly suggest that the inhibition of the H-reflex is due to an increase of presynaptic inhibition of the intraspinal terminals of Ia muscle spindle afferents. When the conditioning stimulus is given in the early part of the stance phase of walking, at a time when the H-reflex is smaller than during standing at similar levels of background EMG (Morin et al., 1982; Stein & Capaday, 1988), it has little if any effect on the H-reflex (average inhibition 45.8% vs. 11.6%, n = 14 subjects). The soleus background EMG, and the soleus and tibialis anterior M-waves were essentially the same in the two tasks. This result is surprising since we had expected that presynaptic inhibition would be greater during walking, because our hypothesis predicts that the presynaptic inhibitory neurons should be more excitable in this phase of the step cycle. There are at least two explanations of this striking, task dependent, modulation of the effects of a conditioning input from a flexor nerve. First, it is possible that the conditioning peripheral input may be itself inhibited during walking, either at the presynaptic or the interneuronal level. Secondly, during walking, the presynaptic inhibitory network may be saturated as a result of central or afferent activity and therefore unresponsive to an added conditioning peripheral input. Thus, while the present experiments did not provide a direct demonstration of an increase of presynaptic inhibition of the soleus Ia-afferents during walking, the results may, nonetheless, be compatible with that idea; and also suggest that in this task the presynaptic inhibitory network is possibly under central control. An important methodological issue is also raised by these results. Neurophysiological studies using C-T paradigms depend on maintaining a

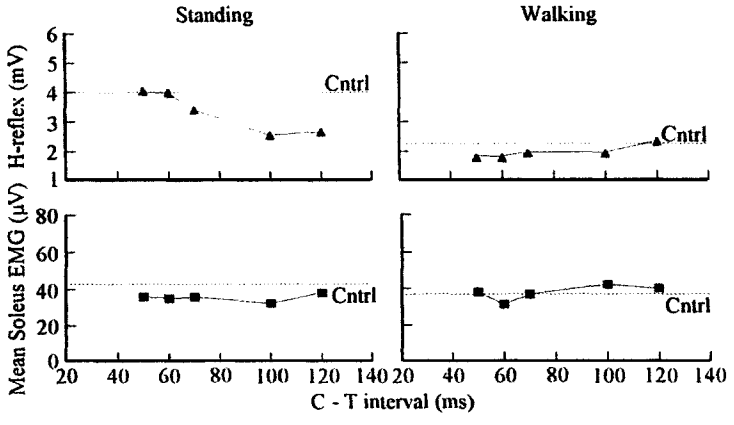

Figure 1. During walking the same conditioning stimulus (1.5 x MT) which produced an inhibition of the soleus H-reflex during standing, at C-T intervals of 100 - 120 ms, did not produce any inhibition during walking. The results were obtained in the same subject during the same experimental session and are shown side by side for each task. Note also that the H-reflex inhibition during standing occurs without a significant change of the background EMG. The natural inhibition of the H-reflex in going from standing to walking is readily apparent, as can be seen from the amplitude of the control H-reflex response in each task.

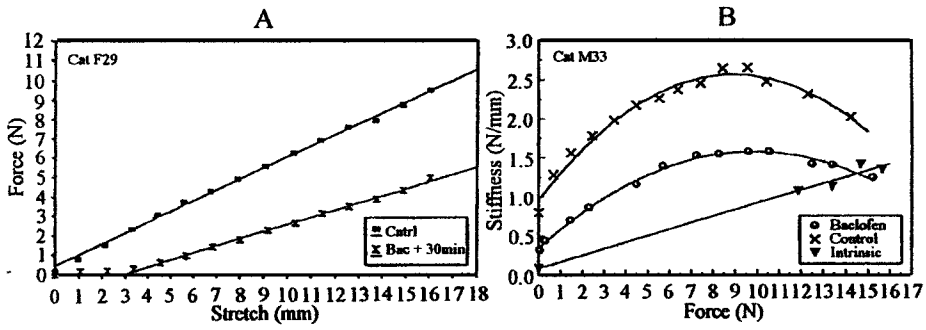

Figure 2. Examples of the effects of Baclofen on the length-tension (A) and stiffness-force (B) relations of the cat stretch reflex. There are two main points summarised in these figures. Firstly, the decrease of the stiffness of the tonic stretch reflex (A) following the injection of Baclofen is always accompanied by an increase of its threshold. Secondly, Baclofen can decrease the stiffness of the stretch reflex, measured "dynamically", at all background forces (B).

constant conditioning stimulus. This criterion can usually be met when dealing, for example, with anaesthetised animal preparations. However, when this paradigm is used during natural motor tasks, as in the present study, it is always tacitly assumed that the task itself would not affect the conditioning stimulus. This is clearly not a tenable assumption without direct corroborating experimental evidence.

EXPERIMENTS IN CATS

These experiments were done in cats decerebrated at the precollicular postmammillary level to determine how a tonic increase of presynaptic inhibition of the intraspinal terminals of muscle spindle afferents changes the mechanical properties of the soleus s.r. Baclofen, a specific $GABA_B$ receptor agonist, was injected i.v. (1 mg/kg) so as to induce a tonic increase of presynaptic inhibition (Edwards, Harrison, Jack & Kullman, 1989). The effects of Baclofen on the stiffness and threshold of the s.r. were determined from plots of stiffness vs. background force and length vs. force, respectively. Baclofen, at these doses, had no effect on the excitation-contraction coupling properties of muscle, nor on the intrinsic stiffness-force relation. Changes of the soleus background force, required to obtain the stiffness vs. force plots, were produced by stimulation of the contralateral common peroneal nerve or the posterior tibial nerve. The stiffness of the s.r. as a function of the background force level was determined by stretching the muscle with a square pulse of 1 - 2 mm amplitude and 200 - 300 ms duration. The stiffness at each force level was calculated by dividing the change in force by the change in length, at a point where the force trace had stabilised. The length-tension relation of the soleus stretch reflex was determined by stretching the muscle 14 - 17 mm at a constant rate of 1 - 2 mm/sec. Baclofen produced a significant decrease (25 - 40% or more) of the s.r. stiffness, at all force levels, within 10 - 15 min. of injection as determined from the stiffness-force plots (Figure 2B). The length-tension plots revealed that the decrease of s.r. stiffness was always accompanied by an increase of the s.r. threshold, typically 2 - 3mm (Figure 2A). Since the fusimotor system, reciprocal inhibition, and activation of descending motor pathways, mainly change the s.r. threshold with little effect on its stiffness (see Matthews, 1959; 1972), we suggest that the effects of Baclofen on the stretch reflex stiffness occur as a result of an increase of presynaptic inhibition of the muscle afferent terminals. Thus, it is concluded that it may be

possible for the CNS to adaptively modify the s.r. stiffness via presynaptic inhibition of the of the intraspinal terminals of muscle afferents, and thereby modify the mechanical impedance at a single joint. However, any such change of s.r. stiffness will be accompanied by a change of the s.r. threshold. Therefore, the s.r. threshold is not an independent variable, it depends on the level of presynaptic inhibition of the muscle spindle afferent terminals.

CONCLUSION

Presynaptic inhibition of muscle spindle afferent terminals in the spinal cord is potentially a direct and independent neural mechanism specific for the control of stretch reflex parameters. The findings in the cat describe what would be expected if a change of presynaptic inhibition were to occur during a motor task. The challenge will be to identify clearly such tasks, which can be fraught by unexpected complications as described above, and to correlate the neurophysiological changes with the biomechanical changes.

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