Evident difference in the excitability of the motoneuron pool between normal subjects and patients with spasticity assessed by a new method using H-reflex and M-response

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Abstract

The excitability of the motoneuron (MN) pool in the resting state was compared between normal control subjects and patients with spasticity resulting from HTLV-I-associated myelopathy, using a new parameter, Hslp/Mslp, and the conventional parameters Hmax/Mmax and Hth/Mth. Differences in the excitability of the MN pool between these two groups reached a high degree of statistical significance only when assessed with the new parameter. This suggests the methodological advantage of the Hslp/Mslp over both Hmax/Mmax and Hth/Mth for evaluation of the excitability of the MN pool in the resting state.

Keywords: Motoneuron excitability; H-reflex; M-response; Spasticity

For evaluation of the excitability of the motoneuron (MN) pool using H-reflexes and M-responses in the resting state in human subjects, three conventional parameters, the ratio of the maximal size of H-reflex to the maximal M-response (Hmax/Mmax), the ratio of the threshold of the H-reflex to the threshold of M-response (Hth/Mth), and the H-reflex recovery curve, have been adopted [5,12,15]. However, these parameters have some methodological problems. The Hmax/Mmax is assumed to show the maximal percentage of MNs consisting of an MN pool, which are fired by electric stimulation of Ia afferents. However, the Hmax/Mmax could forcibly be suppressed by collision occurring between a descending H-reflex discharge and an ascending antidromic motor volley within the α-motor axons as the strength of the M-response increases. Thus, the Hmax/Mmax does not always show the maximal percentage of MNs within the entire MN pool firing, except when the Hmax is saturated or decreased by Ib inhibition and/or recurrent inhibition before the collision between the H-reflex and M-response occurs. Likewise, a crucial problem with Hth/Mth has been reported. Conditioning stimulus has been suggested not to cause clearly either facilitatory or inhibitory effects on the amplitude of a small test H-reflex, i.e. around its threshold [3]. The conventional notion that Hth/Mth can be regarded as a parameter for estimation of the excitability of the MN pool, therefore, should be reconsidered [6,7]. With respect to the H-reflex recovery curve, it has recently been shown that the second-evoked M-response also decreases in amplitude in parallel with the decrease in the second-evoked H-reflex. This occurs within a stimulus interval of about 200 ms [11]. The early period of the H-reflex recovery curve, therefore, is influenced simultaneously by the changes in excitability of peripheral neural regions as well as the recovery level of the excitability of the MN pool.

As outlined above, we do not yet have a parameter for sufficiently accurate evaluation of the excitability of the MN pool in the resting state. Previously [6], we proposed a new method to evaluate the excitability of the MN pool using the ratio of the developmental slope of the H-reflex to that of the M-response (Hslp/Mslp). This method is apparently not affected by suppression of the H-reflex...
associated with collision between the orthodromic volley for the H-reflex and the antidromic volley occurring with the M-response, and is independent of the H-reflex threshold. Further, we have clearly shown that Hslp/Mslp changes according to the changes in excitability of the MN pool induced by the voluntary contraction of synergist or antagonist muscles. In the present study, we examined the differences in excitability of the MN pool between normal subjects and spastic patients characterized by hyperactivity of the myotatic reflex arc using this new method (i.e. Hslp/Mslp) in comparison with the conventional methods (i.e. Hmax/Mmax and Hth/Mth).

Twenty-eight normal healthy control subjects ranging in age from 19 to 38 years (mean ± SD, 20.4 ± 3.6 years) and five patients ranging in age from 32 to 62 years (mean ± SD, 51.6 ± 13.1 years) with HTLV-I-associated myelopathy (HAM), a progressive spastic disorder associated with the human T-lymphotropic virus 181, participated in this study. All subjects gave their informed consent. The subjects were comfortably seated in an armchair with one foot (right side for the normal subjects and spastic side for the patients) fixed on an immobile pedal, on which the angles of the knee and ankle were maintained at approximately 120° and 100°, respectively.

Paired electrodes were placed on the belly of the soleus muscle. The tibial nerve was stimulated (1 ms duration, once every 3 s) in the popliteal fossa to elicit H-reflexes and M-responses from the soleus muscle. The intensity of these pulses was increased gradually from below the threshold of H-reflex to above the saturated state of the maximal M-response. Seven pulses were administered sequentially at each stimulus intensity. All data obtained were identified. Further, the linear regression line fitting procedures were applied to the development of H-reflex and M-response recorded from a normal subject and a patient with spasticity due to HAM. Two solid lines in each panel (A,B) show the linear regression lines for the development of H-reflex and M-response. Values of Hmax/Mmax, Hth/Mth, and Hslp/Mslp for each example are shown in the box in each panel.

Mslp between normal control subjects and patients with spasticity were analyzed using the unpaired t-test after confirming the equal variance of each group by the F-test. To decrease the experimental error rate due to the repeated use of t-tests on multiple dependent variables (i.e. Hmax/Mmax, Hth/Mth, and Hslp/Mslp), we adjusted the a priori statistical probability (i.e. the alpha of 0.05) using the Bonferroni method (i.e. dividing the alpha level by the number of t-tests conducted) resulting in a corrected alpha of 0.0167 [16].

Fig. 1A,B shows the typical recruitment curves of H-reflex and M-response recorded from a normal subject and a patient with spasticity due to HAM, respectively. To clarify the measurement criteria adopted in the present study, the horizontal dashed line (Hmax/Mmax), the vertical dashed line (Hth/Mth), and two solid regression lines fitted to the development of H-reflex and M-response are shown. Values of each variable (i.e. Hmax/Mmax, Hth/Mth, and Hmax/Mmax) are cited in boxes in each diagram. Fig. 2A–C shows the differences in excitability of the soleus MN pool in the resting state between the normal control subjects (white bars) and patients with spasticity (dark bars) assessed by Hmax/Mmax, Hth/Mth, and Hslp/Mslp (means ± SD). Respectively. We detected no significant differences in the excitability of the MN pool between the normal control subjects and the patients with spasticity using the conventional parameters, i.e. Hmax/Mmax (t = -2.549, P = 0.0160, just marginal) and Hth/Mth (t = 0.532, P = 0.5986). In contrast, Hslp/Mslp clearly showed a significant difference (t = -8.668, P < 0.0001) between the normal control subjects and patients with spasticity.

The theoretical background for the use of Hslp/Mslp was as follows. Given the experimental evidence that the Ia afferents have monosynaptic synapses to almost all of the homonymous MNs [9], the Hslp is defined as the ratio of the increase in the number of recruited MNs against the
the amplitude of the M-responses during muscle contraction in the monosynaptic reflex loop, e.g. changes in innervation of the effects of possible changes in the peripheral region in the monosynaptic reflex loop. Thus, Hslp is a parameter for evaluation of the excitability of the MN pool and for exclusion of the effects of possible changes in the peripheral region in the monosynaptic reflex loop, indicating the output efficiency of soleus MNs provided with Ia synaptic input induced by electrical stimulation. Such an output efficiency is likely to be modified by the intrinsic properties of MNs, which receive natural synaptic input other than Ia input in the resting state. Mslp, however, is defined as the ratio of the increased number of recruited a-efferents (i.e. the axons of soleus MNs which innervate the corresponding muscle fibers) involved in the nerve trunk at the stimulus site to the increase in stimulus intensity on Ia afferent nerves. The large fibers (i.e. high threshold fibers) which could originate from comparatively large MNs (i.e. high threshold MNs) are thought to be excited first, and the fibers with relatively high threshold are recruited subsequently as the intensity of the stimulus increases. In contrast, MNs which contribute to the Hslp would be recruited from small to large cells, according to the 'size principle' theory. That is, the recruitment order of a-efferents, which innervate the corresponding muscle fibers, showed a reversed relationship between the Mslp and Hslp. Nevertheless, the values of the regression slope are calculated regardless of whether the recruitment order depends on the size of MNs (for Hslp) or on the diameter of MN axons (for Mslp). Therefore, the Mslp can reasonably be used as a reference property of MNs to evaluate the reflexive Hslp. Thus, Hslp/Mslp is a more effective parameter for evaluation of the excitability of the MN pool and for exclusion of the effects of possible changes in the peripheral region in the monosynaptic reflex loop, e.g. changes in the amplitude of the M-responses during muscle contraction which would also affect the amplitude of the H-reflex.

Despite the marked difference in age between the two groups tested in the present study, the between-group difference was not significant (or marginal) in either the Hmax/Mmax or Hth/Mth. This result is similar to the findings of a previous study [1] which showed non-significant differences in both Hmax/Mmax and Hth/Mth between age-matched normal control subjects and patients with spasticity. The difference in age between the two groups in the present study, therefore, would probably have no effect on the fundamental characteristics of the recruitment of the H-reflex and M-response. The neural mechanisms of spinal spasticity, which is characterized by hyperactivity of the myotatic reflex arc, have been analyzed [4,10,13]. In addition, it has been reported that neither static nor phasic γ-activity is augmented in spastic patients [2,17]. These results suggest that the excitability of the MN pool of spastic patients is higher than that of normal subjects. However, the higher excitability of the MN pool of spastic patients relative to that of normal subjects has not always been clearly observed in terms of either the Hmax/Mmax or Hth/Mth [1,14]. Hslp/Mslp, in contrast, can detect obvious differences in excitability of the MN pool in the resting state between normal subjects and patients with spasticity. Therefore, the present results suggest a methodological advantage of the use of Hslp/Mslp as a parameter for evaluating the excitability of the MN pool in the resting state rather than the use of either Hmax/Mmax or Hth/Mth.

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