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Research Report

Influence of activity-induced axonal hypoexcitability on transmission of descending and segmental signals

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ARTICLE INFO

Article history:
Accepted 7 December 2009
Available online 22 December 2009

Keywords:
Axonal hyperpolarization
Corticospinal volley
Motoneuron excitability
Voluntary activity

ABSTRACT

In this experiment, the changes in excitability of motor axons produced after natural activity were measured in nine healthy subjects using 1 min of maximal voluntary contractions (MVC) of the abductor digiti minimi (ADM) by studying the relationship between stimulus intensity applied to the ulnar nerve and the size of the ADM compound muscle action potential (CMAP). On cessation of the contraction, there was a prominent right-shift of the input–output curve: the intensity required to produce a control CMAP ~60% of maximum, generated a post-contraction response ~25% of maximum. Similar changes occurred in the input–output curves obtained by recording the ulnar nerve volley evoked by same test stimulus for CMAP. Motor-evoked potential (MEP) and F-waves (and H-reflex in one subject) were recorded from ADM before and after 1 min of MVC. On cessation of contraction, the MEP input–output curves exhibited a significant right-shift: the stimulus required to evoke a pre-contraction maximum MEP (~60% of maximum CMAP) generated a post-contraction response ~65% of initial values. One minute of MVC produced similar decreases of F (~35%)- and H (~30%)-ADM responses. All responses recovered their control value in 15–20 min after the end of contraction. The almost identical depressive effect produced by 1 min of MVC on peripherally and centrally generated muscle responses suggests a common conditioning factor. These findings are discussed within the context of activity-induced motor axonal hyperpolarizion.

1. Introduction

Activity-induced hypoexcitability occurs in human motor and sensory axons when they conduct trains of impulses (Miller et al., 1995; Kiernan et al., 1997; Vagg et al., 1998). Activation of the electrogenic Na^+-K^+ pump is presumably the mechanism responsible for hyperpolarization, as found in animal studies (Bostock and Grafe, 1985; Gordon et al., 1990; Morita et al., 1993). By a computerized threshold-tracking procedure, Vagg et al. (1998) demonstrated that excitability of motor axons in the median nerve innervating the thenar eminence significantly decreased after 1 min of maximal voluntary abduction of the thumb. It was accompanied by appropriate changes in nodal and internodal properties (i.e., increase in rheobase, decrease in strength–duration time constant, and increase in axonal supernormality), indicating that axonal hypoexcitability was

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Abbreviations: ADM, abductor digiti minimi; CMAP, compound muscle action potential; CNAP, compound nerve action potential; CSAP, compound sensory action potential; EMG, electromyography; MEP, motor evoked potential; MVC, maximal voluntary contraction; RMS, root mean square; SD, standard deviation; SE, standard error; TMS, transcranial magnetic stimulation

0006-8993/$ – see front matter © 2009 Published by Elsevier B.V.
doi:10.1016/j.brainres.2009.12.023

actually due to hyperpolarization. Theoretically, hyperpolarization in motor axons following their voluntary activation could be a limiting factor for impulse conduction if it is large enough to overcome the safety margin for impulse conduction (Bostock and Grafe, 1985). Activity-induced axonal hyperpolarization could also involve its proximal segment and, therefore, the trigger zone for action potential, i.e., hillock/first node of Ranvier. If so, the synaptic current transferred to the soma from the set of activated synapses by the same descending or segmental volley could fail to initiate action potential in all the target motoneurons activated before contraction.

Effects of prolonged activity on axonal membrane properties have been more or less ignored in human experiments. For example, after sustained voluntary contraction, the amplitude of both motor-evoked potential (MEP) produced by transcranial magnetic stimulation (TMS) and compound muscle action potential (CMAP) are transiently depressed (Gandevia et al., 1999; Kalmar and Cafarelli, 2004). Decline in MEP amplitude observed during or after voluntary contraction would appear, in the absence of peripheral data, to be evidence of central failure (Brasil-Neto et al., 1993; McKay et al., 1995; Zanette et al., 1995; Gandevia et al., 1996; Liepert et al., 1996; Samii et al., 1996; Taylor et al., 1996; Samii et al., 1997; Pitcher and Miles, 2002). In fact, since peripheral failure may actually confound the interpretation of MEP, the importance of analyzing CMAP before attributing changes in cortically evoked potentials to cortical mechanisms has been stressed (Kalmar and Cafarelli, 2004). Although the extent of activity-induced CMAP failure may be dependent upon the overall demands of the contraction protocol, the mechanism responsible for it has not yet been elucidated. Reduction in sarcolemmal excitability, particularly in fast-twitch muscle fibers (Fowles et al., 2002), has been considered a contributory factor (see also discussion). However, as already mentioned, evidence also exists of prominent activity-dependent hyperpolarization in motor axons lasting many minutes after the end of contraction (Vagg et al., 1998).

Thus, the primary purpose of this article is to place our findings of CMAP, MEP, and F-wave changes after 1 min of maximal voluntary contraction (MVC) of the abductor digiti minimi muscle (ADM), within the context of activity-induced motor axonal hyperpolarizion. It was based on the observation that magnitude and recovery time of activity-induced axonal hypoexcitability and those of post-contraction depression of evoked descending (i.e., MEP) and segmental (i.e., F- and H-waves) responses were quantitatively almost identical.

2. Results

2.1. *Excitability of ulnar nerve motor axons innervating the ADM before and after 1 min MVC*

In all subjects, MVC maintained for 1 min reduced output force from 9.12 Newton (N) ± 0.57 standard error (SE) to 6.67 N ± 0.51 SE and electromyographic activity from 0.70 mV ± 0.02 SE to 0.45 mV ± 0.03 SE (data refer to average of first and last 5 min, respectively) (Fig. 1). The time courses of force (N) and EMG root-mean-square (RMS) (mV) showed similar behavior of the trend component of those series, as measured by the Hollander test on linear regression angular coefficients (−0.028534 and −0.004508, respectively): $h = 1.5421$, $P = 0.9371$.

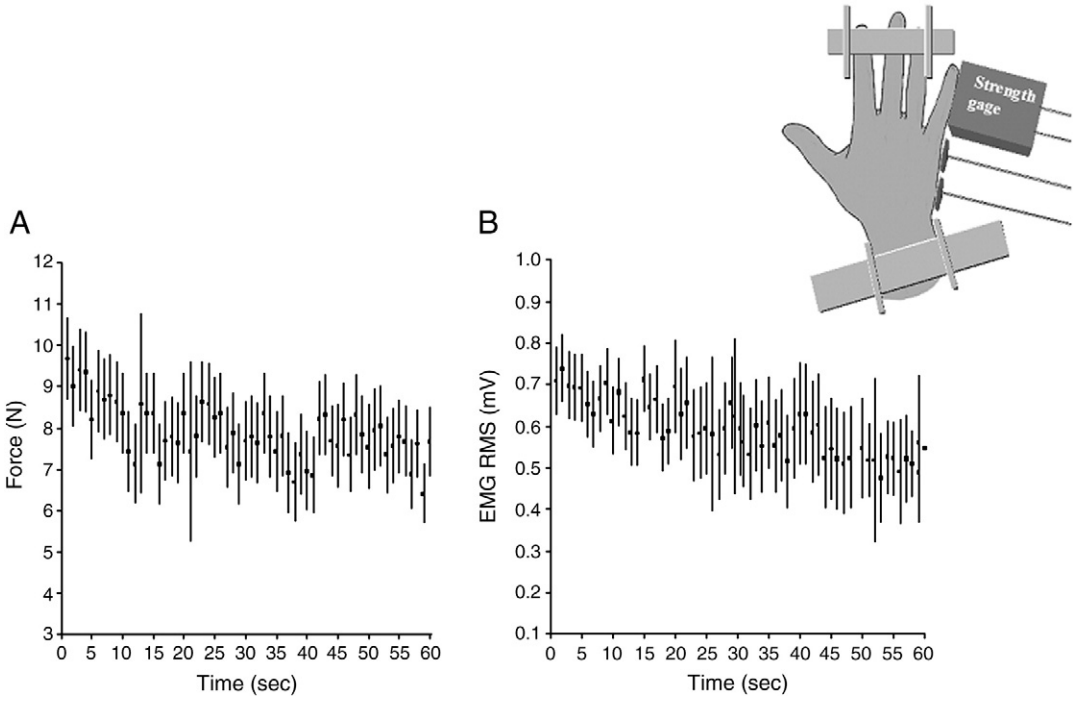

Fig. 1 – Time course of average force (A) and electromyographic activity (EMG) (B) during 1 min of maximal isometric abduction of the fifth finger in eight subjects. Force is expressed in Newtons (N) and EMG, as root-mean-square (RMS). Vertical bars are SE of the mean. Sketch of experimental paradigm is also shown in the figure.