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Stimulating motor wisdom

COMPARED WITH MOST NEUROPHYSIOLOGICAL phenomena, muscle contraction is a slow process. After an action potential has arrived at the muscle fiber membrane, it takes some 30 ms to fully start up the contractile machinery, and it takes even longer to stop it, i.e., to relax force. The contractile muscle properties differ between fast and slow muscle fibers, and they also change during contraction: the durations of contraction and relaxation increase as the muscle fatigues. Because of the asymmetric character of the mechanical muscle response, slowing of relaxation may functionally be far more relevant than slowing of contraction.

To control muscle force, the central nervous system chooses moments of motor unit activation. Obviously, this timing is most relevant in dynamic contractions that require interplay between agonist and antagonist contraction and relaxation. Still, a major part of literature concerning motor control deals with isometric conditions. The reason is that during movement, most experiments become complicated and/or uncomfortable. But, even from isometric contractions, it appears that spinal motorneurons have evolved to match central drive with the contractile properties of their muscle fibers, as shown by Kernell (3).

For the special case of a steady contraction with maximal force, the firing rate of a spinal motorneuron should be such that a steady state of contraction and relaxation processes is just reached. Increasing its firing rate beyond that level then yields no extra force, and it wastes energy for neuronal and muscular membrane activity.

The observation of decreasing firing rate during fatigue to match slowing of relaxation has been termed “muscle wisdom” (1, 4). Although it may be wise to decrease firing rate, it apparently is not the best way to elicit maximum force from a fatigued muscle (2). Stimulation upstream of the muscle can be used to show this as the deficit of muscle activation, expressed as central fatigue. Such stimulus can be given electrically to the peripheral nerve, but also it can be given with transcranial magnetic stimulation (TMS) of the motor cortex (6, 8).

In more general terms: we do know the changing output of the motor system, but it is a challenge to establish if a certain task is limited by mechanical, energetic, or neuronal constraints.

To know how far motor control adjusts optimally to properties of the activated muscles, the muscle’s properties need to be measured during the task. In this issue of the *Journal of Applied Physiology*, Todd et al. (10) present and test a new method to measure muscle relaxation in an active muscle using TMS. The method is elegant in two ways: 1) the intervention is at the motor area of the brain, far away from the target; 2) and it uses a welcome feature of TMS, namely to temporally silence the motor output. The experiments presented have in common that a voluntary contraction is monitored with a single pulse of TMS. During the TMS-induced silent period, motoneuron activity and consequently muscle fiber excitation are suddenly and completely suppressed, much faster than can be done with a voluntary relaxation. The experimental conditions are such that the TMS-induced electrical silence lasts long enough for full relaxation. The nature of TMS makes the relaxation not only complete but also all active motor units relax at the same time. Thus the measured

decline in force reveals the speed of relaxation of the muscle fibers involved in the contraction just before the start of the silent period.

Todd et al. (10) validate the method thoroughly against electrically evoked twitches. Their measurements appear sensitive to parameters known to influence contractile speed: temperature, fatigue, and fiber-type differences between women and men. TMS not only inhibits, but before that it also excites, the muscle. The excitation can be used to demonstrate extra force output in central fatigue. So, by combining TMS with the recording of EMG and force, one estimates from the same single TMS pulse both corticospinal excitation- and inhibition-evoked force and muscle relaxation. In particular, in submaximal contractions of long duration, these multimodal setups demonstrate different rates of fatigue and recovery at the various levels of the motor system (7). This implies that at least in isometric muscle contractions, the cortex, the spinal cord, and the muscle do not share their wisdom.

So, the main advantage of the method used by Todd et al. (10) is that it measures contractile properties during the contraction, and thus it measures muscle fibers that are involved in the contraction. However, there are some restrictions in the interpretation of the data.

1) Obviously, the suppression of muscle excitation, i.e., the silent period, must be long enough to allow measurement of the peak relaxation rate of the muscle, preferably even to allow a full relaxation. This condition can be met easily, but it defines the range of stimulation intensities and thus the amount of excitation.

2) The suppression must involve all relevant muscles and must also be complete. Although this was not addressed explicitly, this seems to be the case considering the complete EMG silence.

3) As stated by Todd et al., in the silent period the speed of relaxation of all active muscle fibers is measured. It must be realized, however, that the measurements do not distinguish between motor units already activated by the task and motor units additionally activated by the stimulus. At a high force in the biceps brachii muscle, the great majority of motor units are already active during the task, and the same units respond to the excitatory effects of TMS. The situation could be more complicated at low forces: voluntary force is produced by low-threshold motor units, but TMS certainly contributes with high-threshold motor units to the motor-evoked potential and the evoked twitch. Then all fibers become silent, and both groups contribute to relaxation speed.

4) A last point to mention is that even without recruitment, motor units can respond with a double discharge to TMS (12). Because doublets can result in substantial and lasting increase of force during low-frequency firing (9), this might complicate the interpretation of the relaxation measured.

Muscle relaxation is prolonged in a number of diseases, which could be studied with the described protocol. In myotonia, muscle relaxation is slow due to an abnormal muscle fiber membrane. Brody’s disease is another example, whereby the abnormal muscle relaxation abnormality is in the sarcoplasmic reticulum. Some myotonic abnormalities are treatable with drugs acting on ion channels, but one of the many difficulties in evaluating

therapeutic interventions is the lack of good measures of muscle relaxation (11). In particular, in patients with neuromuscular disease, the method by Todd and coworkers (10) could show its full advantage: because in these patients the central nervous system does not drive the abnormal muscle maximally (5), voluntary contraction alone is probably insufficient to characterize muscle behavior. If the muscle wisdom resides in the patient's brain, more of it is needed in the neurophysiologist's mind.

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