Driving human motoneurones: recent surprises and possible applications

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Introduction

Motoneurones retain pride of place as the Sherringtonian 'final common pathway'. Conceptually, they integrate the various inputs they receive and convert the input to a frequency code which then is conveyed to the muscle to produce force. Aspects of this conversion by the motoneurone have been the subject of much investigation [for reviews see, for example, 1, 2]). I comment on some of the paradoxes and then discuss some recent investigations of the output from, human motoneurones and studies of the cortical drive to motoneurones.

Background and paradoxes

In the decerebrate cat there can be sufficient extensor tone to support the animal's weight. However, after an acute spinal transection there is minimal tone below the lesion, the 'active' properties of motoneuronal dendrites (see below) diminish, and the synaptic inputs from various sources are not sufficient to produce the motoneurone firing rates necessary to generate substantial forces [3, 4]. Many 'reflex' inputs produce sustained contractions which outlast the stimulus in decerebrate cats [e.g. 5, 6]. Furthermore, high-frequency stimulation of muscle spindle Ia afferents in the decerebrate cat [7] and in humans [8, 9] can lead to the output from motoneurones being rather more randomly organized than tightly locked at monosynaptic latency to each stimulus. Such observations cannot easily be fitted into simple views of the motoneurone soma as a passive integrator. However, these paradoxes might be resolved by recognition of a new element that contributes to motoneuronal output *in vivo*.

The 'gain' of motoneurones *in vivo* is actively boosted by persistent inward currents arising via synaptic inputs acting on the dendrites. This process is state-dependent and is more prominent in small conductance motoneurones [10] (those likely to be of low threshold in voluntary and reflex contractions). The active dendritic properties are subject to neuromodulation via metabotropic receptors (e.g. by serotonin, noradrenaline, and acetylcholine). A number of channels contribute to these currents with the L-type Ca^{++} channel being important in motoneurone dendrites [11]. These persistent inward currents can generate so-called plateau potentials, and in intact humans the threshold for their initiation is probably along the trajectory for action potential generation in static or rhythmic contractions. Through this mechanism, synaptic inputs are assisted to threshold, the initial firing rate of the motoneurone is boosted, and some firing can be maintained in the absence of continuing neural input.

Recent studies

Evidence from a least two sources is consistent with the involvement of some of the non-linear properties described above in determining motoneuronal output in humans. First, the firing pattern of motoneurones (observed singly or in pairs of recordings) has some interesting features. Motoneurones commonly 'jump' to their initial frequency in voluntary contractions. Furthermore, their firing may stop at a lower force than that at recruitment [12-15, cf. 16]. This behaviour and a 'warm up' phenomenon are believed to represent activation of the persistent inward currents on motoneurones. Second, several protocols using surface electrical stimulation at innocuous intensities over lower limb muscles have been used to activate low-threshold afferents and generate unexpectedly large forces [17, 18]. Subjects remain completely relaxed and can even sleep during the stimulation. High-frequency stimulation (up to 100 Hz with wide pulse widths) over ankle plantar or dorsiflexor muscles can evoke sustained centrally-generated forces, which can persist when the stimulation is stopped or its frequency reduced. This extra force is superimposed on that evoked by direct activation of motor axons. This ‘additional’ force is abolished by a complete nerve block proximal to the stimulation and hence it must have a central origin. Furthermore, it can still occur in subjects who have a clinically-complete spinal transection and hence it can probably arise purely from spinal segmental mechanisms (17, see also Nickolls, Collins, Gorman, Burke and Gandevia, this meeting). The maximal force evoked by this mechanism during stimulation for 40 s can be more than 20% of that produced by a maximal voluntary contraction [18]. Compared with classical regulation of the gain of reflexes ‘presynaptically’, alteration of motoneuronal gain through the mechanisms given above provides a much more potent way to change motoneuronal output. It is likely that such mechanisms play a key role in determining the output of motoneurones when they receive sustained inputs as with prolonged fatiguing contractions [19].

Whereas the persistent currents described above reside within motoneurones (and other interneurones), there is increasing evidence for non-linear behaviour in the major descending system which controls movement: the corticospinal connection with motoneurones. While it has long been recognised that the corticospinal system has evolved to aid motor performance, particularly in higher primates, these is now some evidence that the efficacy of the corticospinal connection may itself show strong time- and activity-dependent effects. Thus, when the corticospinal tract is stimulated in conscious human subjects the response in limb muscles can be diminished after previous use of the corticospinal system in a voluntary contraction, but activation of the motoneurone (without the corticospinal system) does not affect the response [20, see also 21]. Recent studies have shown that there may be important plasticity in this system and that it has novel properties which assist repetitive activity in motoneurones during voluntary tasks [22].

Conclusions

The findings on the potential of various patterns of peripheral stimulation to give extra force attributed to activation of persistent inward currents in spinal interneurones and motoneurones are relevant to the way in which contractions may be achieved in muscles via functional electrical stimulation. Any activation of low-threshold motoneurones through this mechanism may be functionally useful (and possibly resistant to fatigue), provided that sufficient force could be generated in a controlled way. The findings on the apparent plasticity of the corticospinal connection with human motoneurones may also be relevant in any attempt to achieve force generation after spinal injury through direct activation of descending pathways.

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