Estimation of persistent inward currents in proximal vs. distal muscles in the upper extremity

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HYPEREXCITABLE stretch reflexes are often observed following stroke and spinal cord injury (SCI), and they can contribute to debilitating muscle spasms and increased muscle tone that adversely affect mobility. Previous studies have suggested that increased activation of persistent inward calcium and sodium currents (PICs) in spinal motor neurons may contribute to hyperexcitable stretch reflexes in these pathologies [1,2].

The excitability of motor neurons can be modulated by brainstem projections releasing serotonin and norepinephrine. Binding to motor neuron receptors, these monoamines facilitate PICs, which are capable of increasing the gain of synaptic input. PIC activation includes self-sustained firing behavior in which a recruited motor unit (MU) will continue to fire even in the absence of additional synaptic input. These observations have led to a hypothesis that in able-bodied individuals, PICs may be an important component in postural control when muscles must be activated for prolonged periods. Following stroke or SCI, alterations in monoaminergic modulation may underlie the proposed increased activation of PICs.

We hypothesize that in able-bodied individuals, brainstem modulation of spinal motor neurons via PICs will be higher in proximal muscles, which carry more postural load and have a higher proportion of brainstem projections than distal muscles. This difference in PIC activation between proximal and distal muscles may differ following stroke or SCI.

PICs can be estimated in humans by calculating the difference in firing rate of a low-threshold control unit at the time of recruitment and de-recruitment of a second higher threshold test unit [1]. This difference in firing rate, termed delta-F (ΔF), is thought to be proportional to PIC amplitude. *In vivo* studies of PIC activation in humans have used intramuscular (IM) electrodes to directly record from MU. In the current study, high-density surface EMG and a recently presented decomposition algorithm [2] were used to isolate individual MU with the hope of improving MU yield. The purpose of this study is twofold: 1) to evaluate the feasibility of surface EMG arrays to study PIC activation, and 2) to test the hypothesis that proximal muscles will have higher ΔF values than distal muscles, suggesting greater PIC activation.

Three able-bodied participants (mean age: 52 years) performed isometric ramp contractions to 10-20% MVT in shoulder abduction, elbow flexion, elbow extension, and finger flexion. Surface EMG was recorded from 4 64-channel matrices placed on anterior deltoid, biceps, triceps, and extrinsic finger flexors and was decomposed into MU discharges using the Convolution Kernel Compensation technique [4]. For each contraction, ΔF was calculated for control and test unit pairs receiving similar synaptic drive, determined by r values of $\geq$ 0.85.

The yield of appropriate MU pairs for ΔF calculation was substantially higher than the conventional intramuscular method, where an average of 2-3 pairs are typically isolated per subject. In total, 22 pairs of deltoid, 30 pairs of biceps, 18 pairs of triceps and 43 pairs of finger flexor MU were isolated. ΔF values for the proximal flexors—deltoid and biceps—were 6.05 +/- 1.53 and 5.92 +/- 1.01, respectively, whereas the distal flexors were lower, averaging 4.09 +/- 1.36 SD. The biceps value was similar to previously published values [5]. The triceps value was higher than all of the flexors, at 7.21 +/- 0.29 SD.

The increased yield of MU pairs found with the current method illustrates the viability and increased efficiency of high-density surface EMG decomposition in estimating PIC amplitude. In addition to revealing differences between flexors and extensor, these results suggest greater PIC amplitude in proximal versus distal muscles, supporting the hypothesis that PIC-related MU firing behaviors may be instrumental in brainstem-mediated postural control in able-bodied individuals. This distinction has implications for the underlying mechanisms of hyperexcitable motor neurons in individuals post-stroke or SCI where changes in monoaminergic neuromodulation have been postulated. Calculation of ΔF may be an appropriate outcome measure to evaluate interventions aimed at reducing hyperexcitable stretch reflexes or brainstem modulatory activity.

REFERENCES

[1] K. C. Murray, et al., “Recovery of motoneuron and locomotor function after spinal cord injury depends on constitutive activity in 5-HT2C receptors,” *Nat Med*, 2010.

[2] J. McPherson, et al “Evidence for increased activation of persistent inward currents in individuals with chronic hemiparetic stroke.” *J Neurophys* 2008.

[3] M. A. Gorassini, et al., “Self-sustained firing of human motor units,” *Neurosci Lett,* 1998.

[4] A. Holobar, and D. Zazula, “Multichannel Blind Source Separation Using Convolution Kernel Compensation,” *IEEE Trans on Signal Process,* 2007.

[5] C. J. Mottram, et al., “Origins of abnormal excitability in biceps brachii motoneurons of spastic-paretic stroke survivors,” *J Neurophysiol,* 2009.

This work was supported in part by NIH grants R01HD039343, T32EB009406, and T32HD057845, and ERC Advanced Grant DEMOVE (No. 267888).
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