Can supraspinal/central fatigue explain the lesser muscle endurance of men compared with women?

Several studies have shown that women can present with greater muscle endurance (less fatigability) compared with men (3, 5, 10, 12), although this is not always the case (4, 8). Most of these studies have focused on peripheral physiological mechanisms, mostly those within the muscle, to explain this effect of sex on fatigue. For example, reported differences in muscle fiber-type composition between men and women have been suggested to explain the lesser changes in electromyographic (EMG) signal variables of women compared with men when performing a sustained contraction (11). Because the effect of sex can be eliminated under ischemic conditions (5, 12), a predominant role for muscle metabolism or perfusion in explaining the sex-related differences in muscle fatigue has been suggested. This is also consistent with studies showing no difference in muscle fatigue when men and women are matched for strength (6, 8), which implies similar levels of perfusion. However, sex differences in muscle fatigability can still exist even when subjects are matched for strength (9). Although the mechanism(s) responsible for the sex differences could still involve peripheral structures, differences in the descending drive from higher centers of the brain to motoneurons (9) could also influence how well men and women are able to sustain a required force output.

The ability to maximally activate a muscle or muscle group under volition, also termed “voluntary activation,” can be assessed by delivering a pulse of electrical stimulation to a muscle (or the motor cortex via magnetic stimulation) during a maximal contraction. Any additional force produced by the stimulation above the voluntary force implies a submaximal level of voluntary activation. A decrease in the level of voluntary activation with sustained activity is referred to as “central fatigue.” The presence of significant central fatigue could lead to the early termination of a sustained contraction, even when the muscle(s) can still generate the required force. Central fatigue has been a research topic of increased interest in the past 10 yr. It appears to be task and muscle dependent (1, 2), which means that results of individual studies are difficult to generalize, and underlines the importance of testing hypotheses using multiple experimental protocols and muscle groups. Nevertheless, the presence of a possible impairment in the ability of the central nervous system to drive a muscle to produce maximal force should be measured when a given task involves volitional activity. It is reasonable to think that this type of fatigue could explain differences between men and women in the performance of a given fatigue task.

The paper in this issue of the *Journal of Applied Physiology* entitled “Supraspinal fatigue does not explain the sex difference in muscle fatigue of maximal contractions” by S. K. Hunter, J. E. Butler, G. Todd, S. C. Gandevia, and J. L. Taylor (7) aims at assessing the significance of central fatigue in explaining a sex difference in muscle fatigue observed during repeated intermittent maximal contractions. A novel aspect of the study is that these authors are evaluating “supraspinal” fatigue, which because of the use of transcranial magnetic stimulation allows the implication of structures “at or above the level of the motor cortical output.” This is in contrast to stimulation of the motor nerve, which does not allow the differentiation between the relative contributions of structures/mechanisms upstream of the motoneuron pool (including influences at the spinal level). In addition to the force/torque response to transcranial magnetic stimulation, Hunter et al. also monitor the EMG response to the stimulation to provide further insight into specific mechanisms related to motor cortical activity. Two variables are reported: 1) the size of the motor-evoked potential (MEP), the EMG response recorded from the biceps brachii, which is an estimate of cortical excitability; and 2) the silent period in the EMG signals after the stimulus, an indicator of intracortical inhibition changes.

Both men and women had to perform six sustained maximal elbow flexion contractions lasting 22 s each, with a 10-s rest period between contractions. Overall fatigue was quantified as the decrease in maximal force at the end of this fatigue protocol compared with prefatigue values. The main results were that men exhibited greater fatigue than women and that this was not explained by a difference in supraspinal (central) fatigue but rather by greater peripheral fatigue. The fatigue protocol did lead to the development of supraspinal fatigue; however, the extent was similar between men and women. There were also no differences in the estimates of motor cortex excitability (MEP size) and intracortical inhibition (silent period) between men and women, ruling out a significant sex difference in these processes. The lack of a sex difference in supraspinal fatigue is in contrast to findings from a recent study by Russ and Kent-Braun (12) showing greater central fatigue in men compared with women also for an intermittent maximal fatigue protocol. A brief discussion of three key differences between the present study by Hunter et al. (7) and the Russ and Kent-Braun (12) study will help identify some of the current challenges in the field.

First, the muscle groups tested were different, with Russ and Kent-Braun (12) studying the ankle dorsiflexors muscles. As mentioned earlier, central fatigue may be muscle dependent, and a significant effect of sex on central fatigue is more likely to be observed in a muscle group prone to central fatigue. However, whether this is the case for elbow flexors vs. ankle dorsiflexors is not established. Second, even though both fatigue protocols involved intermittent maximal isometric contractions, the overall duration of the task was longer in Russ and Kent-Braun’s study [4 min compared with ~3 min in Hunter et al.’s study (7)], but their lower work-to-rest ratio (5 s on, 5 s off vs. 22 s on 10 s off for Hunter et al.) led to about the same total “on” time. Although a varying work-to-rest ratio does not seem to influence the extent of central fatigue (13), a longer task duration (1) [mostly with no rest periods (2)] can lead to more central fatigue and could thus favor the development of varying levels of central fatigue between subjects, including men vs. women. In fact, Hunter et al. conclude: “it is conceivable that the site for the sex difference in muscle fatigue varies not only with the task performed but also with the muscle being assessed.” Third, the different methods used to quantify central (or supraspinal) fatigue, with different stimulation sites implicating different structures/mechanisms,
could also influence the outcome of a study. However, the use of motor nerve stimulation with the fatigue protocol in Hunter et al.’s study would have likely resulted in the same conclusion of no sex difference in central fatigue.

Thus, Hunter and colleagues (7) assessed the role of supraspinal fatigue, a form of fatigue that is often not tested, in explaining sex differences in muscle fatigue. They concluded that the greater fatigue of men was, in fact, explained by peripheral differences. The fact that their results contradict those of others (12) is an indication that the issue of the importance of central fatigue is not resolved. This is not surprising considering the complex, muscle- and task-dependent nature of fatigue. Consequently, further research is needed in this area to increase our general knowledge base on muscle fatigue, and more specifically on central fatigue and its significance in limiting performance across different groups of subjects or patients.

REFERENCES


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