Neuromuscular fatigue: interactions between central and peripheral factors

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Over the past years evidence from us and others has accumulated indicating that the development of peripheral locomotor muscle fatigue is confined to a certain limit which varies between humans. Central motor drive to these muscles – and therefore exercise performance – during human athletic activities appears to be regulated to avoid the development of peripheral locomotor muscle fatigue beyond an "individual critical threshold". The existence of a degree of peripheral fatigue that is never exceeded during high intensity endurance exercise prompted us to propose the role of peripheral locomotor muscle fatigue as a carefully regulated variable. In various experiments we have challenged this postulate from different perspectives and our results further verify its validity. Based on the knowledge gained from previous observations we outlined a model linking central motor drive with the metabolic milieu within the working locomotor muscles. Our model suggests that, during high intensity endurance exercise, somatosensory feedback from the working muscles imposes inhibitory influences on the magnitude of central motor drive with the purpose to regulate and restrict the level of exercise-induced peripheral locomotor muscle fatigue. As we also qualified, this proposed feedback mechanism is likely only one of several potential contributors to the modulation of central motor drive and that its relative contribution will change with varying conditions such as, for example, severe hypoxemia. In more recent work, we experimentally tested this model *via* pharmacologically modifying somatosensory pathways originating in the working limbs during whole body exercise. After initial difficulties with the lumbar epidural application of a local anesthetic and the associated loss of locomotor muscle strength we switched to an intrathecally applied opioid analgesic. These experiments were the first ever to selectively block lower limb afferent feedback during cycling exercise without affecting maximal locomotor muscle force output. In the absence of neural feedback from the working limbs, central motor drive was about 8% higher during the opioid trial and end-exercise peripheral locomotor muscle fatigue exceeded, for the first time, the critical threshold by nearly 50%. The outcome of these studies further confirms our hypothesis claiming that afferent feedback inhibits central motor drive and restricts the development of peripheral fatigue to an individual critical threshold.