Point: Counterpoint: Afferent feedback from fatigued locomotor muscles is/is not an important determinant of endurance exercise performance

**Point: Afferent Feedback from Fatigued Locomotor Muscles Is an Important Determinant of Endurance Exercise Performance**

We thank Dr. Marcora for suggesting this discussion in which we advance the view that neural feedback from fatiguing limb muscles is a key determinant of endurance exercise performance. Previous findings suggest that muscle afferents affect endurance performance via two routes. First, neural feedback might facilitate peak exercise performance by preventing premature fatigue through optimizing muscle O$_2$ delivery via its influence on circulation and pulmonary ventilation. And second, neural feedback might limit exercise performance via restricting central motor output (CMO) to the locomotor muscles at both reflex and cognitive levels.

Some basics: During sustained exercise, metaboreceptive/nociceptive afferents (group III/IV) originating in working limb muscles are stimulated by intramuscular metabolic byproducts (2, 23) and increase, in parallel to accumulating metabolites, their ensemble input to the CNS. This central projection reflexively augments circulation (i.e., exercise pressor reflex) and ventilation (21), and progressively reduces CMO/voluntary muscle activation (“central fatigue” increases) (16). We explicitly emphasize that muscle afferents are only one of various determinants of the cardiorespiratory response and CMO during exercise.

**Cardiovascular and Ventilatory Response**

Exercise challenges the circulation by a potential enormous reduction in total peripheral resistance and increases the organism’s O$_2$ consumption and CO$_2$ production. Yet blood pressure and alveolar PO$_2$ increase and arterial PO$_2$ remains, in most healthy individuals, close to resting values. Krogh and Lindhard (22) first approached this phenomenon and conducted exercise evoked by electrical muscle stimulation to find similar values for heart rate, blood pressure, and ventilation compared to the same exercise performed voluntarily. It was concluded that the regulation of these cardiorespiratory variables is predominantly influenced by exercising limb muscles. This notion was later affirmed by Alam and Smirk (3) who found that blood pressure, and less clearly also heart rate, maintains following exercise for as long as the previously working muscle is kept ischemic, i.e., trapping intramuscular metaboreceptor stimuli.

In contrast, when electrically induced exercise is carried out in spinal-blocked healthy humans (30) and in paraplegic patients (11), or in spinal cord-transected (or -blocked) animals (18, 20), the circulatory and ventilatory response to exercise is significantly deteriorated, which results in reduced convective O$_2$ transport. Similarly, the cardiovascular response is, compared with control conditions, substantially reduced when voluntary exercise is performed in the absence of afferent feedback from the working limbs (pharmacological spinal block) (14, 30).

Muscle afferents also significantly determine the resetting of the arterial baroreflex with exercise (29), a necessary adjustment to ensure optimized and sustained perfusion pressure to exercising muscles (3) and brain (19). Consequently, when muscle afferents are pharmacologically blocked during exercise, subjects are vulnerable to orthostatic intolerance, which is even more evident in tetraplegic patients (11). Numerous other studies have clearly demonstrated the crucial involvement of muscle afferents in the circulatory and respiratory regulation during exercise (1, 10, 21). Taken together, sensory input from working muscles depicts a prerequisite for achieving individual “optimal” endurance performance since controlled perfusion and peripheral O$_2$ delivery set a limit for how much work a muscle can perform. Indeed, running time to exhaustion in group IV-deficient rats is substantially shorter compared with rats exercising with an intact sensory feedback system (12).

Furthermore, humans competitively bicycling with reduced afferent feedback (spinal anesthesia) rapidly develop severe metabolic/respiratory acidosis, which abnormally deteriorates their muscles ability to respond to neural drive (8).

**Central Motor Output**

During muscle contractions against a fixed load, afferent feedback increases in parallel with intramuscular metabolites and peripheral fatigue, CMO progressively decreases, and the subject eventually reaches task failure, i.e., exercise cannot be continued voluntarily at this intensity. However, if the muscle is then stimulated electrically, exercise continues effortlessly and peripheral fatigue further increases beyond the level observed at task failure (24, 25). These observations indicate that a muscle’s performance is more curtailed than its actual ability to generate force/power and that exercise ceases due to CMO withdrawal rather than the inability of the muscle to contract.

It is well documented that CNS projection of group III/IV muscle afferents significantly determines the reduction in CMO and hence muscle performance (16). For example, when the firing frequency, and thus the CNS projection, of these afferents is kept elevated via occluding blood flow to the fatigued muscle at end exercise, CMO and force output remain low and only begin to recover after circulation is restored, i.e., metaboreceptor stimuli decrease (17).

These findings from isolated muscle studies suggest that the CNS monitors the peripheral state of working limb muscles via sensory feedback and uses this information to adjust the muscles’ neural activation perhaps with the purpose of shielding a muscular reserve capacity. Alternatively, muscle afferents might progressively impair the willingness and/or ability to sustain a high CMO, and thus a high exercise intensity/performance, to avoid the development of peripheral fatigue beyond a “sensory tolerance limit” past which exercise might become “painful” (16). As stated by Gandevia (16), the reduction in CMO, as affected by inhibitory afferent feedback, is “at the expense of truly maximal performance.” This regulatory mechanism has been suggested to also limit whole body endurance performance (16).

Accumulating evidence indicates that the development of peripheral locomotor muscle fatigue during whole body endurance exercise is also confined to an individual “critical threshold” (or a critical rate of development), and associated sensory
tolerance limit, which is voluntarily never exceeded (4–6, 9, 13, 15, 26–28). This means that, in case of constant-workload trials, exercise is either deliberately terminated, or CMO becomes insufficient to maintain the task, once peripheral fatigue has reached this, presumably task-dependent, critical threshold. For example, following electrostimulation of the quadriceps of healthy humans to induce significant peripheral fatigue, constant-workload bicycling time to task failure was substantially shorter as compared to the identical bicycle exercise but performed without preinduced quadriceps fatigue. However, at task failure in both trials, quadriceps fatigue and perception of leg fatigue were identical (15). These experiments confirm an earlier prefatigue study using time trial, instead of constant-load, bicycling. During the time trial performed with significant preinduced quadriceps fatigue, CMO was significantly lower and time-to-completion longer compared with the same time trial performed without preexisting fatigue. However, end-exercise quadriceps fatigue and perception of leg fatigue were identical in both time trials, insinuating that CMO was adjusted according to the peripheral state of the locomotor muscles (4).

The most compelling evidence for muscle afferents limiting CMO and peripheral fatigue during endurance exercise comes from two recent human studies. When the central projection of lower limb muscle afferents was pharmacologically blocked (L3/L4) during 5-km cycling time trial, CMO was significantly increased compared with the placebo race (7, 8) and the subjects substantially exceeded their critical threshold of peripheral fatigue (8). Compared with the placebo race, exercise performance was 4% faster during the first half of the time trial but, due to missing feedback leading to metabolic/respiratory acidosis (see above), 4% worse during the second half, despite continuous high CMO (8). Blocking muscle afferents apparently released a centrally mediated “brake” on CMO and the CNS “tolerated” locomotor muscle fatigue to develop ~44% beyond the degree observed following the placebo trial. This extreme level of peripheral fatigue was associated with ambulatory problems (8).

In conclusion, during strenuous endurance exercise, somatosensory feedback from locomotor muscles appears to limit performance by imposing inhibitory influences on CMO with the purpose of restricting the development of peripheral locomotor muscle fatigue to an individual “fatigue threshold.”

Given the role of a “double-edged sword,” a clear evaluation of positive vs. negative effects of muscle afferents on endurance performance is an unenviable task. However, one thing is for sure: locomotor muscle afferents significantly determine endurance exercise performance one way or another.

REFERENCES


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COUNTERPOINT: AFFERENT FEEDBACK FROM FATIGUED LOCOMOTOR MUSCLES IS NOT AN IMPORTANT DETERMINANT OF ENDURANCE EXERCISE PERFORMANCE

Since Noakes’ controversial lecture on the central governor (23), brain regulation of endurance performance has been a hot topic in exercise physiology. In this series, Dr. Markus Amann argues that afferent feedback related to peripheral locomotor muscle fatigue is an important determinant of endurance performance. I have two objections to this hypothesis. First, there is no experimental evidence to support it. In fact, in two separate studies, spinal blockade of inhibitory afferent feedback from group III-IV receptors sensitive to fatigue-inducing metabolites did not improve performance in 5-K cycling time trials (5, 6). Actually, in the epidural lidocaine study, there was a significant reduction in time-trial performance (5). Amann and colleagues proposed that this net negative effect is the product of two contrasting effects of epidural lidocaine on exercise performance: 1) the negative effect mediated by the iatrogenic reduction in locomotor muscle strength, and 2) the positive effect of blocking somatosensory feedback from the legs. However, reduced locomotor muscle strength per se has a small effect on endurance performance (21). Therefore, if Amann and colleagues’ proposition is true, afferent feedback from fatigued leg muscles must have an even smaller and, thus, negligible effect on exercise performance.

My second objection to this supraspinal reflex inhibition model of endurance performance (1, 3, 4) is more theoretical. This feedback loop (Fig. 1) is attractive to physiologists because they are familiar with subconscious autonomic regulation (e.g., the exercise pressor reflex) and the mechanisms of central fatigue during maximal voluntary contractions (26). However, it is not a valid representation of what happens during the time trials chosen by Amann and colleagues to test their hypothesis (5, 6). In fact, during endurance exercise, voluntary muscle contractions are always submaximal (8) and, therefore, central fatigue is not a relevant concept (19, 26). Furthermore, during time trials, power output is consciously self-regulated by the subject, e.g., by changing gears. These are not trivial details (2), but considerations that suggest a more relevant question: does afferent feedback from fatigued locomotor muscles affect the brain processes determining conscious self-regulation of submaximal power output during time trials?

To answer this question, it is important to remind ourselves that voluntary actions like cycling as fast as possible for 5-K are the opposite of simple reflexes (13). This is why the feedback loop proposed by Amann and colleagues (1, 3, 4) cannot be an adequate model of endurance performance. I propose a different approach based on the principle that conscious self-regulation, like other mental phenomena, is caused by lower-level neurobiological processes in the brain (25). Therefore, time-trial performance can be understood in psychological terms before investigating the neurobiology underlying the relevant constructs. This is why I call it the psychobiological model of exercise performance (21).

According to this model, conscious self-regulation of submaximal power output during time trials is determined primarily by the following cognitive/motivational factors:

1) Perception of effort;