PERSPECTIVES

The rate of fatigue accumulation as a sensed variable

Jose A. L. Calbet
Department of Physical Education, University of Las Palmas de Gran Canaria, Spain

Email: lopezcalbet@terra.es

How can an athlete regulate the rate of fatigue accumulation during a time trial competition? How is muscle contractile activity regulated to maintain the highest work rate possible without precipitating fatigue precociously? At the end of exercise will the level of central fatigue coincide with the level of peripheral fatigue, even if the conditions of exercise have changed dramatically? Previous investigations have used either 'open-loop' designs in which the influence of a given factor on fatigue is studied by measuring its effect on endurance time (time to exhaustion) or 'closed-loop' designs in which power output and time to task completion is assessed. In this issue of *The Journal of Physiology*, Amann *et al.* (2006) use different levels of arterial oxygen content (C_{aO_2}) to manipulate the rate of fatigue accumulation during 'open-' and 'closed-loop' tasks. With this unique experimental approach Amann *et al.* (2006) show that peripheral locomotor muscle fatigue development is a significant determinant of the magnitude of central motor output (central command) during exercise. This is demonstrated by showing that during exercise at a given fixed intensity, the lower the C_{aO_2}, the greater was the rate of development of peripheral fatigue and the greater the time-dependent rise in the integrated electromyography (iEMG). During the time trial performance test ('closed-loop') in which the subject tries to cover a given distance in the shortest time possible, the iEMG is enhanced during the conditions with high C_{aO_2} and vice versa. A unique aspect of the study is that at exhaustion, the degree of peripheral fatigue was the same in all conditions meaning that the CNS should receive information which then is used to up- or down-regulate motor output, and to optimize the rate of fatigue accumulation to the exercise conditions. This allows a delay in the attainment of the level of fatigue that would impede the continuation of exercise (Gandevia, 2001).

With this study the group led by Jerome Dempsey makes an important contribution showing that fatigue is a signal useful to regulate motor output in order to optimize the rate of fatigue accumulation to the available functional reserve (capacity for exercise). Thus, from a classical view in which fatigue is perceived as something negative and catastrophic Amann *et al.* (2006) present a new vision in which peripheral muscle fatigue acts as a signal required for the optimal regulation of exercise intensity in order to attain the greatest level of performance achievable.

These findings, however, should not be interpreted as meaning that fatigue, i.e. any exercise-induced reduction in the ability to exert muscle force or power, regardless of whether or not the task can be sustained (as it was defined by Bigland-Ritchie & Woods, 1984) is caused by peripheral sensory feedback. For example, at the end of an incremental exercise to exhaustion in severe acute hypoxia, but also in chronic hypoxia, the incremental exercise can be continued by allowing the subjects to breath a normoxic (or mild hyperoxic) gas mixture (Calbet *et al.* 2003*a*,*b*). Both conditions (acute and chronic hypoxia) are rather different. In severe acute hypoxia C_{aO_2} is rather low but in chronic hypoxia maximal exercise C_{aO_2} is the same as during normoxia without altitude acclimatization. According to Amann *et al.* (2006), neuromuscular fatigue should be similar at the end of an incremental exercise regardless of the inspired O_2 fraction (F_{IO_2}). Nevertheless the studies by Calbet *et al.* indicate that in severe acute and chronic hypoxia fatigue can be easily overcome by raising arterial P_{O_2}, something that is not possible when subjects perform the incremental exercise in normoxia and on exhaustion breath hyperoxic gas (Calbet J, Boushel R and Lundby C, unpublished observations). How can these divergent findings be reconciled? Potentially hypoxia may attenuate the metabolically elicited sensory feedback causing fatigue (this will fit with the observation of a higher accumulation of muscle lactate during all-out exercise with hypoxia). Moreover, during sprint-like exercise to exhaustion of short duration, such as a Wingate test (Calbet *et al.* 2003*c*) exercise performance is not affected by moderate or severe hypoxia, despite the fact that anaerobic energy release is increased during the hypoxic sprint to compensate for the reduction of the aerobic ATP production. Why is fatigue not occurring sooner during an all-out exercise (sprint) with hypoxia, or during incremental exercise to exhaustion? One explanation could be that under these conditions sensory feedback is suppressed, blocked or simply counteracted by a stronger central command. Overall, these studies suggest that the central command during all-out testing may easily overcome sensory feedback signalling peripheral fatigue to the extreme of even increasing the accumulation of end products of the anaerobic metabolism beyond the limits normally reached during the same exercise conditions in normoxia.

During an all-out test the subject aims at developing the maximal power output from the start to the end of the exercise and presumably sensory feedback is not critical to modulate motor output. During open-loop tasks in which the exercise intensity is maintained constant, sensory feedback is not needed to regulate motor output, as shown by Kjaer *et al.* (1999). These authors demonstrated that blocking sensory feedback with epidural anaesthesia during a constant intensity exercise to exhaustion (open-loop) has no repercussion on endurance time or on the accumulation of muscle metabolites at exhaustion. Moreover, if anything, epidural anaesthesia resulted in an enhancement of the rate of perceived exertion due to a small reduction of muscle strength. According to the findings of Amann *et al.* (2006) epidural anaesthesia should impede the regulation of fatigue accumulation during time trials.

Niels Secher and colleagues have shown that for a given metabolic rate central command is increased and so is the rate of perceived exertion when the exercise is performed after partial curarization. In the latter case fatigue cannot be explained by metabolic factors alone. Curarization experiments are compatible with the existence of some feed-forward neural mechanism that triggers signals contributing to the perception of fatigue

DOI: 10.1113/jphysiol.2006.116087

depending on the magnitude of central command.

In summary, in this issue of *The Journal of Physiology* Amann *et al.* (2006) show that the rate of fatigue accumulation is a sensed variable useful to regulate central command during endurance events. Future studies should clarify how the signal is generated and sensed, what factors may modulate it and how it is integrated with other sensory and descending nervous signals.

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