EDITORIAL

Exercise and its Troubles

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Rising from the couch to go jogging in the fields requires profound changes in various bodily functions. "The wisdom of the body"[1] appears to guarantee that these changes be just right, within physiological limits, to perform the task at hand. Some changes are quite straightforward. Apart from activating and coordinating the motor system to get going, energy resources must be mobilized, oxygen supplied, carbon dioxide removed. This requires increases in ventilation, blood pressure, heart rate and the redistribution of blood flow to the working muscles and brain. There are other changes, however, which are less obvious. These issues are concisely reviewed by Decherchi and Dousset[2] in this issue.

Cardiovascular and respiratory adaptations to exercise have been proposed to be effected by three, not mutually exclusive, types of mechanism[2]: (i) The central motor commands provide a corollary signal to the brainstem cardio-vascular and respiratory centres. (ii) The cardio-vascular and respiratory centres are activated directly or indirectly by humoral substances released by the working muscles. (iii) The cardio-vascular and respiratory centres are activated by nervous signals originating in the working muscles.

It is the third class of mechanisms with which Decherchi and Dousset[2] are mainly concerned. The required signals are carried by small-diameter nerve fibers of groups III (Aδ) and IV (C), which may be activated by mechanical and chemical stimuli in the working muscle. These fibers distribute signals to the brainstem[3] and thus influence the cardio-vascular and respiratory systems, contributing to this part of body wisdom. In addition, however, they project to the spinal cord,[4] where they exert less conspicuous actions on the motor system via a number of reflex mechanisms. Here, they influence the activities of many different types of neurons, including skeleto-motoneurons innervating skeletal muscle fibers, γ-motoneurons innervating muscle spindles, various sorts of interneurons, and preganglionic sympathetic neurons. The effects exerted are complex and not well-understood. Of great interest are those involved in adaptations to muscle fatigue and pain.

Part and parcel of body wisdom may be *muscle wisdom* (Decherchi and Dousset's[2] *sagesse musculaire*).[5,6] The term refers to a particular experimental paradigm and phenomenon. During prolonged fatiguing maximal voluntary muscle contractions under isometric conditions, human motor units start firing at a high rate that subsequently adapts to lower rates over several tens of seconds. This discharge adaptation has been hypothesized to adjust the discharge intervals to the lengthening motor unit contractions during progressing fatigue and thus to optimize force output. Several different, albeit interacting, mechanisms, comprised under the rubric of *central fatigue*, might contribute to this adjustment: intrinsic motoneuron properties; diminishing descending motor commands; changes in recurrent inhibition via Renshaw cells, presynaptic inhibition, and 'autogenic inhibition' from Golgi tendon organs; diminishing facilitation from muscle spindle afferents; and inhibition of skeleto-motoneurons from group III-IV muscle afferents that are increasingly excited by metabolites released by the fatiguing muscle fibers.[5,6] As rightly pointed out by Decherchi and Dousset,[2] these interacting mechanisms are much more complex than simple reflex inhibition of skeleto-motoneurons by group III-IV afferents. In fact, these afferents may also excite γ-motoneurons,[7] which should, in turn, alter muscle-spindle discharge and thereby skeleto-motoneuron discharge. Furthermore, group III-IV afferents may excite preganglionic sympathetic neurons[8] which, in turn, influence the discharge patterns of muscle spindles.[9] Such effects would, however, be modulated by changes in presynaptic inhibition of large-diameter muscle afferents.[10,11] As well, autogenic inhibition[12] and recurrent inhibition[13] may be altered by activity of group III-IV afferents.

These partial effects appear like bits and pieces of a mosaic whose grand design still escapes our view. The reasons are manifold. The effects have been observed in different species, using different paradigms, experimental constraints and methods. They may vary along with variations in paradigmatic constraints. Indeed, there are almost certainly many *task-dependent wisdoms*, each adapted to its particular circumstances.[14] For example, the mechanisms involved in counteracting fatigue are most probably different in sub-maximal and rhythmic contractions. There is no unique mosaic, but a manifold. Thus, Decherchi and Dousset's[2] demand to more precisely elucidate the central effects of group III-IV muscle afferents is well-taken, albeit not easy to realize in view of different paradigms to be studied and the technical difficulties in trying to do so.

Wisdom is good but fallible. As stressed by Decherchi and Dousset, the role of group III-IVmuscle afferents in adapting the body to the conditions of exercise may be deficient in patients suffering from chronic respiratory insufficiency and in humans living at high altitude, leading to malfunction and pronounced, early-onset fatigue. There are other such conditions. For instance, in the rare mitochondrial myopathies, the associated lactacidosis should strongly excite group III-IV muscle afferents.[6] Another example, although deliberately not treated by Decherchi and Dousset[2], is provided by the nociceptive functions of group III-IV muscle afferents, which – beneficial as they may be under some conditions – can also go astray.[15] After all, muscle fatigue and pain are relatives, the first often fathering the second. *Chronic occupational muscle pain* has been hypothesized to result from derailed functions involving group III-IV muscle afferents.[7,16] The basic idea is simple: production of muscle metabolites → increase in activity of group III-IV afferents → increase in activity of γ-motoneurons → increase in activity of muscle spindle afferents → increase in skeleto-motoneuron activity → increase in muscle activity → increase in production of metabolites, and so forth. This vicious circle might be complemented by other mechanisms mentioned above in the

context of central fatigue: actions of group III-IV afferents on (i) the sympathetic outflow and thence on muscle spindle activity, (ii) recurrent, autogenic and presynaptic inhibition, etc. The evoked changes in reflex operation could be perpetuated by plastic changes at sensory receptor level (peripheral sensitization) and CNS level (central sensitization).[17,18] This general scheme may indicate a possible route from sustained muscle fatigue to pain. Yet again we do not know much about how the many mechanisms interact, which should be sharp enough a stimulus to chase us from the couch and get going with further research.

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