Why your brain tires when exercising

March 4 2013

A marathon runner approaches the finishing line, but suddenly the sweaty athlete collapses to the ground. Everyone probably assumes that this is because he has expended all energy in his muscles. What few people know is that it might also be a braking mechanism in the brain which swings into effect and makes us too tired to continue. What may be occurring is what is referred to as 'central fatigue'.

"Our discovery is helping to shed light on the paradox which has long been the subject of discussion by researchers. We have always known that the neurotransmitter serotonin is released when you exercise, and indeed, it helps us to keep going. However, the answer to what role the substance plays in relation to the fact that we also feel so exhausted we have to stop has been eluding us for years. We can now see it is actually a surplus of serotonin that triggers a braking mechanism in the brain. In other words, serotonin functions as an accelerator but also as a brake when the strain becomes excessive," says Associate Professor Jean-François Perrier from the Department of Neuroscience and Pharmacology, who has spearheaded the new research.

Help in the battle against doping

Jean-François Perrier hopes that mapping the mechanism that prompts central fatigue will be useful in several ways. Central fatigue is a phenomenon which has been known for about 80 years; it is a sort of tiredness which, instead of affecting the muscles, hits the brain and nervous system. By conducting scientific experiments, it is possible to observe and measure that the brain sends insufficient signals to the

muscles to keep going, which in turn means that we are unable to keep performing. This makes the mechanism behind central fatigue an interesting area in the battle against doping, and it is for this reason that Anti Doping Danmark has also helped fund the group's research.

"In combating the use of doping, it is crucial to identify which methods athletes can use to prevent central fatigue and thereby continue to perform beyond what is naturally possible. And the best way of doing so is to understand the underlying mechanism," says Jean-François Perrier.

Developing better drugs

The brain communicates with our muscles using so-called motoneurons (see fact box). In several diseases, motoneurons are hyperactive. This is true, for example, of people suffering from spasticity and cerebral palsy, who are unable to control their movements. Jean-François Perrier therefore hopes that, in the long term, this new knowledge can also be used to help develop drugs against these symptoms and to find out more about the effects of antidepressants.

"This new discovery brings us a step closer to finding ways of controlling serotonin. In other words, whether it will have an activating effect or trigger central fatigue. It is all about selectively activating the receptors which serotonin attaches to," explains Jean-François Perrier.

"For selective serotonin re-uptake inhibitor (SSRI) drugs which are used as antidepressants, we can possibly help explain why those who take the drugs often feel more tired and also become slightly clumsier than other people. What we now know can help us develop better drugs," concludes Jean-François Perrier.

More information: 'Serotonin spillover onto the axon initial segment of motoneurons induces central fatigue by inhibiting action potential

initiation'. *PNAS*, 2013. DOI:10.1073/pnas.201216150