

When the villain becomes your friend: The strange tale of muscle lactate

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In a paper published this week in *The Journal of Physiology*, Frank de Paoli and colleagues, working at the University of Aarhus in Denmark, add to the growing literature leading to a more complete understanding of the physiological role of lactic acid production in muscle.

In the late 19th century, fermentation chemists realized that juice left to ferment without adequate oxygen resulted in acid products. Then, in the early 20th century, when physiologists stimulated isolated frog muscles to contract until exhaustion, they found that the tissues had accumulated high amounts of lactic acid. Since then, the idea that lactic acid accumulation causes muscle fatigue has persisted. But did early scientists fail to address the various issues adequately and interpret the results appropriately? Did they fail to ask the essential question "Why does nature make lactic acid?", and did they in effect put one and one together and make them a minus?"

De Paoli and colleagues looked at the effects of lactic acid and adrenaline on the processes that signal contractions in skeletal muscles. Using rat muscles, the study examined the combined effect of potassium ions, lactic acid and adrenaline on the electrical signalling system that serves to forward the activating signals from the brain to the muscle fibres where contraction takes place. They showed that in combination, lactic acid and adrenalin serve to help working muscles ward off the effects of potassium ions which leak from the inside to the outside of working muscle cells and negatively effect the signaling process by which muscles contract. In this, the latest of a series of reports from the

Aarhus group, in combination with reports from other scientists in Scandinavia, the UK, US and Canada, long-standing ideas about the role of lactic acid in muscle are being overturned.

So, why do muscles contract" Usually, muscles contract because the central and peripheral nervous system signals them to do so. Why do the muscles make lactic acid" Lactic acid is the result of the glycolytic energy production system. It is an energy source to be used in muscle cells of origin, or adjacent fibres (cells), or fibres in the heart and cells in the brain. Lactic acid is also the material that the liver prefers to make glucose (sugar) for the blood when exercise is prolonged. Lactic acid production in muscle is stimulated in part by circulating adrenalin. Now, from de Paoli and colleagues we learn that adrenalin and lactic acid also help protect against the electrolyte imbalance across muscle membranes brought on by the loss of potassium.

Why does potassium have such a negative effect? In the study, when potassium ions outside the muscle fibres were increased to levels seen during intense exercise, the ability of the signalling system to forward electrical signals was profoundly reduced and the muscle became paralysed. If, however, lactic acid and adrenaline were added in combination, the function of the signalling system was largely recovered and the contractile response of the muscles restored. It was further shown that the positive effect of lactic acid was specifically related to an acidification of the interior of the muscle cells, which is one of the hallmarks of intense exercise.

The muscle lactic acid story, however, is still incomplete. It may even be found that lactate production is adaptive because its presence signals the activation of genes responsible for controlling muscle function. So, it seems that there is wisdom in the way that the body functions, a retrospective realisation that seems obvious, and which for lactic acid is supported by a century of strides even after a few false steps.

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