

Wetenschap voor Patiënten (Science to patients)

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Webinar 46: The metabolism and the muscles

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Why does acid accumulate in the muscles?

So our experiments performed with MRI scans where we've asked people with ME to exercise while we were measuring the accumulation of acid in their muscles, suggest that patients with ME have about 20 times more acid in their muscles than we would expect them to have. The findings from our experiments with patients with ME are very similar to those from patients with fatigue associated chronic diseases. In terms of why this might happen, in our experiments we've been able to show that the degree to which the acid accumulates seems to associate with the presence and severity of autonomic dysfunction. So we think in some way, the autonomic nervous system is regulating or modulating this accumulation of acid.

We know that the autonomic nervous system controls some of the transporters that are on the cell surfaces of muscle cells. So it may be that these transporters are not working as efficiently to remove acid from the cells as they really ought. Or it may equally be that the blood flow run off from the muscles as they exercise, which we know is modulated by the autonomic nervous system, perhaps again is meaning that the acid is not washed away from the muscles as they exercise. It's difficult to know why the transmitters don't work properly. It may be that there's some process that damages these transmitters or it may be that there's some problem in the metabolic chain that leads up to the development of acid within the cells. Our experiments performed with the muscle cells in the lab, suggest that there may be deficiencies of certain proteins or kinases within the metabolic pathway which could potentially be modulated by medication.

How to handle acid accumulation in the muscles?

In terms of handling acid accumulation in the muscles, that raises some very interesting questions. I frequently get asked: 'Will exercise influence the amount of acid that I accumulate in my muscles?' When we've done our experiments, both in the MRI scanner and in the laboratory with the muscle cells, it becomes clear that there are at least two different types of muscle abnormality, something that we call phenotypes.

When we've looked at these different phenotypes, it's clear that perhaps one of those phenotypes would improve with exercise and perhaps the second one would not improve with exercise. So as a result we would propose further experiments are needed to look at how the different types of muscle abnormality respond to exercise therapies such as graded exercise therapy. Because our finding of two different phenotypes of muscle abnormality,

might explain why some people feel they get better with exercise while some people feel that they don't or describe themselves as feeling worse with exercise.

How are the muscle cells influenced by ME and what are the consequences?

We've done experiments where we've taken muscle biopsies from patients with ME and we've grown those muscle cells in the laboratory into what we call muscle tubules. When we've done that, our impression is that the muscle cells don't grow as well as in patients who don't have ME. And when we've done experiments in the laboratory using something called nanosensors which are tiny little technological materials that go across the cell wall of patients' muscle cells. These nanosensors will fluoresce at different pH's so we're able to exercise muscle cells in the laboratory while we look at how they accumulate acid real time.

So when we do those experiments, we can then begin to put things into the experimental kit so that we can look at influencing how the acid is accumulated. And the experiments that we've done already suggests that this acid accumulation that we've reproduced in the laboratory is reversible. Which means that there is the potential with further experiments, that we can begin to tease out particular drugs that could be used in clinical trials to reverse these muscle abnormalities.

How is the autonomic nervous system influenced by ME and what does this cause?

So in patients with ME we know that about nearly 90% of patients will describe symptoms of autonomic dysfunction. And when we perform tests, objective tests looking at how the autonomic nervous system works, we'll find lots of abnormalities in the autonomic nervous system when we objectively test. We're not sure yet why these abnormalities are so common in people with ME. Our current experiments are looking at individuals, about 80 patients with ME, seeing whether or not we can begin to understand where the abnormalities lie. We wonder whether it might be problems of the brain centres that control the autonomic nervous system, so they are areas in the brain stem, whether or not it might be an abnormality of the hypothalamic pituitary axis, so how hormones are produced and the impact that they might have on the vascular system. Or alternatively it could be that the autonomic nervous system is having difficulties regulating the cardiovascular system and that the symptoms of autonomic dysfunction arise as a consequence of that.