Case Study:

Assessing mitochondrial health with functional testing

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Kirsty Cullen - [00:00:15]

Welcome to the Fatigue Super Conference, I'm Kirsty Cullen, CEO at the Optimum Health Clinic, and today I'm joined by Juliana Bernardes, a member of our nutrition team here at the clinic.

Hi Juliana.

Juliana Bernardes

Hi Kirsty.

Kirsty Cullen

So today, we're going to discuss one of the functional tests that we might use in the clinic in order to gain both a general overview of energy production but also metabolic balance within the body.

Firstly, Juliana, it's important to discuss, isn't it, that there are some challenges to testing within the fatigue community?

Juliana Bernardes

Yes, absolutely. So some people with ME and CFS, they can have a mild form of ME and they might be able to go to school, they might be able to go to work while reducing some other activities. But there is a large percentage that have a moderate to severe form of ME and CFS, and they might not be able to go to school or to work or even to a GP practice.

Some clients experienced even severe ME and CFS. So they have to stay in bed, they have to stay at home and they can actually be dependent on help for all their daily care.

So having a test that can be done at home, a test that is very easy to do, it's a huge help. And with the functional tests that we use in the clinic, the test kits are sent to the client's home through a courier. The samples are very easy to collect. We'll talk more about that in just a moment. The saliva or stool. And then again, a courier is arranged to pick up the samples from the client's home and take it to the test.

So our tests are easily achievable for our clients when they are at home with a chronic fatigue picture. And...

Kirsty Cullen

So you mentioned there, Juliana, what we're collecting, in essence. So we're not always collecting serum. What are some of the other elements that we might collect for functional testing?

Juliana Bernardes - [00:02:14]

So a lot of the functional tests that we use, they require just a urine sample or a pinprick or a saliva or stool. And they don't really require, we do use tests that require blood to be drawn, but we have a vast array of tests that are very easy to collect in the comfort of the client's home and send it back to the lab for the results to be analyzed.

Kirsty Cullen

Superb. So for the purposes of today, we're going to discuss the organic acid test. Can you just explain for those who don't know what organic acids actually are?

Juliana Bernardes

Sure. So, talking about the test in general and then going into what the organic acids really are, the organic acid test provides us with some key nutritional biomarkers. So it uses, like we mentioned, one of the samples that it uses urine for that one, and it's the first void urine in the morning. So it's very non-invasive. It's very client friendly and it assesses the functional needs for antioxidants, for B vitamins and minerals, digestive capacity, fatty acids, detoxification capacity.

We're going to talk about some mitochondrial function, which is, of course, this is of great interest. And we'll talk more about that in a moment. So it really allows us to have a very good understanding of different metabolic processes.

So, what are the organic acids? So the organic acids are metabolic intermediates. They are produced in the body. So we have a lot of enzyme pathways, a lot of cycles for energy production, detoxification, neurotransmitters production. And there's a lot of metabolic reactions happening in the body that are producing these compounds called organic acids.

So when we find, for example, a significant accumulation of organic acid in the urine or low levels of a particular organic acid, that can signal a metabolic inhibition or a block of a certain pathway in the body. And we're going to talk about some of these pathways and reactions in a minute. And this metabolic block can be caused by a nutrient efficiency, it can be caused by a toxin buildup, for example. And we have an array of nutritional therapy interventions that we can use to address that. So in a nutshell, that's what it is.

Kirsty Cullen

So let's start by looking at how we might use organic acid testing to consider energy production. Juliana can you tell us a little bit about what this test would offer in that situation?

Juliana Bernardes

Of course. I think the very important, so energy production is the production of ATP. So that's the energy currency that our body has inside the mitochondria, which are these little powerhouses inside the cell that is going to be burning fuel for energy. And of course, that's of great interest for our clients with ME and CFS.

Now, it's important to mention that with the organic acids, what we're looking at, we're looking at co-factors. So we're looking at the materials that the mitochondria need to function, so we're looking at specific vitamins and minerals and other nutrients that the mitochondria needs to function properly and produce ATP.

What we're not looking at, with the test, is the actual structure of the mitochondria. We are not really looking at the mitochondrial functioning per say, but we are looking at, from a nutritional therapy perspective, what are the nutrients that the mitochondria needs to be able to produce this energy. And then, of course, we can understand and target nutritional protocols, supplements and these kind of things.

Kirsty Cullen - [00:06:11]

And as a perfect illustration of this, almost, Juliana, you'll walk us through the first graphic, which looks incredibly complex but is actually extremely useful clinically, isn't it?

Juliana Bernardes

Yeah, I mean, look, we're not really expecting a client to understand this graph, but what it does for us as clinicians is that it gives us an opportunity to look at the various stages of energy production. And I mean, obviously, that looks complicated, but we are able to pinpoint a few of these markers as indicative that there are some breakdowns in energy production.

So, like I mentioned, there are various co-factors that can alter mitochondrial enzymes, such as nutrients and vitamin deficiencies and toxins and these enzymes they catalyze, they make the energy cycle possible.

So when we look at the graph here, we can see that we have the fats and the carbohydrates and we have the proteins there. But we don't really use protein for energy except in extreme circumstances. So we're focusing on the carbohydrates and the fats. So, we can see here that we need to transform both carbohydrates and fats into the Acetyl-CoA to enter the citric cycle, which is basically the energy cycle.

So for us to transform carbohydrates into Acetyl-CoA, we need, as we can see here on the green, magnesium so we can see that this client here, for example, that has low levels of the organic acid intermediate pyruvic acid might be deficient in magnesium.

And again, to get the pyruvic acid into the Acetyl-CoA, there's some other vitamins and minerals. So in this case, the B1, the B2, the B3, the magnesium. And we can also see some impairment here in the fats metabolism. So both carbohydrates and fats need to be transformed into the Acetyl-CoA. So the fats again, we're needing more magnesium and more carnitine and we can see that this client here could do with some support with the metabolism of these micronutrients.

Now going further, when we see the Acetyl-CoA going into the Krebs cycle, we can see here every checkpoint, every box here that we can see around this cycle is an organic acid. So we can see that, for example, the citric acid to become the cis-Aconitic acid. We need iron, we need glutathione. And every checkpoint we can see here, the potential deficiencies of nutrients. We're also talking about coenzyme Q10 and we're also talking about alpha-lipoic acid, lots of different nutrients that are absolutely essential for the cycle to turn.

Kirsty Cullen

Superb. And within that, there are also some of those little red circles which tell us about some of the toxins that might also block that cycle in addition to those essential nutrients.

Juliana Bernardes

Absolutely, yeah. So toxic exposures, so things like mercury that we can find, for example, in fish, aluminum, that is really widespread, arsenic, lead, all of those can interfere with mitochondrial function. So, again, that's very useful information for us to know how to target our protocols and to see what might be stopping that cycle from turning efficiently.

Kirsty Cullen

And it's important to say, isn't it, that the nutrient deficiencies we're seeing here within this graphic as relative to energy production are also relevant elsewhere in other functional systems too.

Juliana Bernardes - [00:09:45]

Absolutely. So as we were talking about the energy cycle, we discussed importance, for example, of magnesium. So magnesium is important for the carbohydrates and fat to become that active nutrient to go inside, or active compound I should say, to go inside the citric cycle.

But magnesium is, as we've seen important for energy production, but it has 300 other roles in the body. Magnesium is a mineral that's involved in so many different reactions. It's super important for adrenal function, it's very important for muscle health, it's an electrolytes. So whenever we start uncovering deficiencies, we can understand the impact of a potential deficiency in many different other body systems.

And we could say that as well, for example, for the B vitamins that we mentioned here, very important for energy production. But as we will chat in a minute, you will see that vitamins are also involved in many other metabolic processes, such as methylation that we'll talk about.

So what I think is very interesting and useful about this test is that it is assessing different pathways. It is looking at different metabolic pathways. So we cannot only ascertain if there is a potential deficiency, but also the extent of the deficiency when we are looking at all the different pathways and where else these minerals and vitamins can be used. So I think that's very useful.

Kirsty Cullen

Indeed it is. And within the citric acid cycle there you mentioned glutathione, shall we talk a little more about what glutathione is? Why it's such a helpful marker? And what it tells us in the context of detoxification capacity?

Juliana Bernardes

Absolutely. So these urinary markers, so if we look at the graph here, at the image, what we can see here are some markers that can reflect exposure to environmental toxins or we can look at, that could mean upregulation of the detoxification pathways in response to these exposures.

And so when these markers are elevated, we're going to be thinking about toxic load and we're thinking about detoxification. We're thinking about antioxidants.

Now, the marker that we can see here, the pyroglutamic acid in particular and we can see on this image is quite raised, it's a functional marker of glutathione. And why is glutathione so important? Glutathione is often referred as the master antioxidant because it can be found in nearly every cell in the body at the same concentration as some of the most important nutrients for energy and cellular function.

And it is important because it prevents or slows down cell damage in the body that can be caused by free radicals and free radicals can attack DNA, proteins. In a nutshell, free radicals are part of our metabolic processes. So we produce free radicals in our bodies. But a poor diet, chemicals, pesticides, contaminated water or pollution in general can create excessive numbers of these free radicals. And these free radicals are unstable molecules that can go creating damage inside our cells.

So glutathione is our, the master antioxidant, it's one of our great protections against the cellular damage. And that's incredibly important in the context of ME and CFS. And that is because the mitochondria that we're talking about, which is where that cycle happens and we produce energy, has its DNA kind of swimming inside itself. It's called a cytosol. And so its DNA is not protected by a membrane. It's very prone to oxidative damage. And a mitochondria that has been damaged, of course, is not going to be working very well, is not going to be producing energy as well as it could.

So keeping our oxidative damage and our toxic load in check is incredibly important for the whole body, but for the mitochondria and energy production in particular.

So seeing the elevations in the pyroglutamic acid and the other markers can reflect potentially a lack

of protein which is necessary. It can reflect other cofactors such as magnesium. So, again, it can really help us to refine and know what to put in place in a protocol.

Kirsty Cullen - [00:14:27]

So what's wonderful about this test is, as well as showing us markers for toxins and detoxification, we also have a marker here that tells us a little bit about the level of oxidative damage. Juliana, do you just want to talk us through an example of that?

Juliana Bernardes

Yes. So the markers in this test, in this particular section that we can see here, it can indicate problems in two key areas, so antioxidant capacity and in oxidative damage. So like we discussed, oxidative stress is relevant to an entire host of clinical conditions. So it reflects the need to support antioxidant capacity through dietary changes, also supplemental options alongside reducing free radical exposure.

So we can see from this example here that this particular client has a pretty good antioxidant capacity and not a lot of oxidative damage.

Kirsty Cullen

So let's switch focus, because another area that organic acids testing can consider for us is methylation. And methylation is a topic and probably another session in its own right. But at least we can summarize it a little bit today and look at how this test might help us in terms of assessment.

Juliana Bernardes

So the topic of methylation is getting a fair share of attention lately, and I think it's rightly so. Methylation is actually quite simple, but it's definitely essential. It's a biochemical process that happens constantly everywhere in our body.

And it basically involves, and there's a little bit of biochemistry, but it basically involves adding a methyl group onto other chemical compounds, which then allows the body to do most of its processes. So when optimum methylation is happening in the body it has a significant positive impact on many biochemical reactions that regulates the activity of our cardiovascular system, neurological health, reproductive health, detoxification systems. So it's involved in hormone metabolism, gene expression, neurotransmitter production, which are the feel good chemicals that we have in our brain and of course, cellular energy.

So energy production, the health of our thyroid, our adrenal glands, our nervous system, the function of all of these systems are dependent on methylation and a good supply of folate, which is vitamin B9 and vitamin B12, are important to get the methylation cycle going.

So we can see here on this example that we have for the methylation markers, we have two markers there. So we have the FIGlu, which is functional marker for B9, for folate, and we have the methylmalonic acid we called MMA, which is a function of marker for B12.

Now, FIGlu, when we say that FIGlu and methylmalonic acid are functional markers, I think it's really important to mention that what I see very often in clinic, are clients who have normal blood levels of B12 and folate, but when we run an organic acid test we find functional deficiencies.

And what do I mean by a functional deficiency? Or when I say that these are functional markers? We are looking at cellular, we're looking at deficiencies at cellular level. What is running in our blood it's not necessarily being absorbed or going where it needs to go. So the organic acid can really ascertain are the chemical processes that should be running, running? And if not, what's going on? So it's very common for me to see normal serum levels of these vitamins, but to find potential functional deficiencies there.

So the folate is interesting, the FIGlu. It's a marker not just of the folate. And we can see that this client has a significant deficiency, it's actually on a supplement recommendation of 1200 micrograms of folate, which is something I would never ordinarily do in clinic without a test result to supplement such a high level.

But what is interesting about the FIGlu, it can also reflect vitamin B12 status, because in the methylation cycle and again a little bit of biochemistry, we need to recycle folate and we require B12 to do that, it's a step in the methylation cycle.

Now, the B12, like I mentioned, the MMA is a functional marker of the B12, and it is considered a much more sensitive index of B12 compared to serum, like I mentioned.

And I think what's really important to mention as well is that of course, folate and B12 are not just part of the methylation cycle. They are also very important for red blood cells and the red blood cells are going to be transporting oxygen to all parts of our body. And the lack of these vitamins, fatigue, tiredness, all of these things can be aggravated or further compromised. So for energy production these nutrients are extremely important.

Kirsty Cullen - [00:19:51]

Great stuff, so let's talk about how we might use organic acid testing as an assessment for dietary intake, particularly with reference to proteins and amino acids.

Juliana Bernardes

I think this test is a fantastic overview of protein intake, and I think in our society nowadays, we have become carbotarians, isn't it? We just got used to special breakfast foods and toast for breakfast with jam and marmalade or cereals or bread in general, sandwiches, takeaways and it's very common for me to see lack of protein in clinical practice.

And protein has so many crucial functions in the body. So protein, the amino acids, which are the building blocks of proteins, so proteins are this combination of different amino acids, they are the precursors of our antibodies for our robust immune system, the precursors of our enzymes. So for us to be able to digest our food well, they are the precursors of our neurotransmitters. So again, the feel good chemicals in the brain for our sleep.

So regulating sleep is so important. And we can see from the tests and I'll show you that in just a moment, that we have amino acids that are the precursors of serotonin, which is one of the feel good neurotransmitters, which then becomes melatonin, which helps us to sleep and stay asleep.

So there are so many important roles of protein in the body. And I think it's always a conversation that I have with my clients. Let's include more protein, it's important for blood sugar regulation. Whenever we're thinking about energy, when we're thinking about fatigue and having more energy, regulating blood sugars is absolutely crucial. When we're starting our day with a cereal or bread and some jam we're spiking our blood sugar levels only for us to have a trough very soon after. And we enter what we call the blood sugar rollercoaster.

So the mid-morning crashes or if you're having a spike just before going to bed and you have a trough when you are asleep, disrupted sleep. And having protein with each meal helps to balance that. So that's something that I'm always talking to my clients.

So what this test shows us is the breakdown of the essential amino acids and the non essential amino acids. So the essential amino acids are the ones that we cannot make ourselves. These are the ones that we have to source from our foods. And we can see from this test here that we have, from the essential amino acids, you know, the isoleucine is below detectable levels and the other ones are really borderline. We can see here raised taurine, and I'll talk about that in just a second.

And we have the non essential amino acids as part of this test as well, which is basically amino acids that we can produce ourselves. But in order to make them, we rely on the essentials. So we need to have a pool of amino acids so we can make the non essential amino acids.

And we can see from this test that everything is so borderline, so alanine is already in the red, glutamine is in the amber. I would argue that there is a protein deficiency here with this result and it goes hand in hand with the clinical signs and symptoms of that particular client.

Now, what's really interesting here is the interpretation of the test. Of course, we are doing an interpretation at a glance and we're just talking about the possibilities here. But there are many caveats and things that we need to consider. So for taurine you might think that the client is having a lot of taurine, isn't it? There's too much being excreted in the urine, so therefore there's a lot of nutritional intake. Well, actually, when we have high levels of taurine in the urine, we call that taurine wasting.

And there are other markers in the test that can help us have an idea of why this is happening. But basically, this client here is wasting a lot of taurine rather than retaining it. And taurine is important for magnesium and for calcium to enter the cells.

So it's not just about having magnesium or supplementing magnesium, can it enter the cell and do its job? It's the same for calcium. Taurine is also important for bioproduction so it's going to have a direct role in digestion and this client was struggling to digest fats.

So it really helps us to target supplementation and to know, how is the protein intake? And to design our intervention perhaps with protein powders and of course, nutritional strategies that we can put in place.

Kirsty Cullen - [00:24:50]

And also having assessed the amino acid levels, we can then consider how well the client is actually accessing and absorbing protein within the same test, can't we?

Juliana Bernardes

Yes. So we have some incredible markers here for protein digestion, protein absorption and again, clients with digestive issues, gut issues that can bring a lot of light into what might be going on, it goes really well hand in hand with a stool test, but in its own right, it can give us some really interesting information.

So the diet related peptides, they indicate protein maldigestion. It's important to mention that is limited for animal protein. So for our vegan vegetarian clients, that marker would always be very low. But for the meat eaters, we can see, so the example here, we can see some raised carnosine. And the raised carnosine indicates a need of digestive support. It indicates in particular the need for zinc, the need for digestive enzymes, the need for hydrochloric acid.

So hydrochloric acid is what we have in our stomach. It's the first, it's the beginning of protein digestion. And it's so common to see clients without robust levels of hydrochloric acid and therefore are not digesting the protein very well.

So yeah, the zinc, the digestive enzymes, the hydrochloric acid we can see here, a borderline low anserine and anserine can be indicative of low protein intake, which it's definitely what was the case with this client. It also can be seen in vegan and vegetarian clients. So it can really help us target a nutritional support for the clients based on those results.

Kirsty Cullen

Juliana, thank you so much for giving us a whistle stop tour of organic acids. I'm sure we could talk for another couple of hours on this test, because that's the level of information that it offers. But it's been

a really useful example of how some of those markers might be used clinically. So thank you for joining us today.

Juliana Bernardes - [00:27:01]

It's a pleasure. Thank you so much for having me.