INTERVIEW TRANSCRIPT

DISCUSSIONS WITH WORLD-LEADING EXPERTS

What the Science Says About Food & Migraine

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Introduction (00:04): Food can feel like both a friend and a foe for people with migraine. Over the years, we've heard countless opinions about what to eat, what to avoid, and which supplements might help. But what does the science actually say? To help us separate fact from fiction and discover realistic ways to use diet as part of migraine management, we're joined by associate professor Margaret Slavin, a registered dietitian and researcher who has studied the relationship between nutrition and migraine. Dr. Slavin, welcome back to the Migraine World Summit.

Dr. Slavin (00:36): My pleasure. Thanks for having me.

Carl Cincinnato (00:39): Why do you think food and migraine generates so much confusion and contradictory advice?

Dr. Slavin (00:45): I think because the evidence is heterogeneous, meaning there's lots of different study designs, lots of different types of foods and nutrients being studied. We look at studies of the whole diet versus supplements, isolated and individual nutrients, and it's a lot of information to try to parse and then layer that on top of the complexity of migraine, which folks here are probably familiar with. It's a difficult thing to study and distill down information into actionable things that we can do within our lives.

Dr. Slavin (01:32): So, if I could give an example of why it's so hard to study diet and why we don't have more consistent evidence, I like to talk about randomized controlled trials, which is considered the gold standard of how we investigate treatments. And it allows us to recruit a group of participants, randomly assign them to receive either the intervention or the control condition, and then at the end of the study, if we see a difference between groups, we can say it was due to that difference in the intervention. And this works very well for drugs and pharmaceuticals because it's easy to blind people to the pill that they're taking or an injection or whatever it might be.

Dr. Slavin (02:21): And it works to some extent with diet studies, but there are a lot of challenges to that design that are difficult to implement in diet studies. So, if we want to study, for example, a high-fiber diet, then the intervention diet is relatively easy and straightforward. We can design a diet that contains high levels of fiber. The question becomes, what is the meaningful comparison in the control group?

Dr. Slavin (02:54): And if we change the foods that contain fiber, we're inherently probably changing other components of the food. The fiber tends to occur in high-carbohydrate foods or vegetables, and so if we add those foods to the diet, what would be a meaningful comparison in the control group that allows us to really isolate the effect of the fiber and not all of these other changes that happen when we design that control diet?

Dr. Slavin (03:23): So, even if we're providing everyone their foods, there's still that comparison that different research teams in different places will make different decisions about what that meaningful control is. And it can be really challenging to design that control diet condition. Add on top of that, it can be difficult to blind people. They know if they're consuming a diet with fish in it, they probably know. And so there's a certain amount of blinding that can't be done with diet studies.

Dr. Slavin (03:57): And even when it can be done, it's labor intensive. If we're doing one of these really thorough diets for 12 weeks or longer, providing most of their foods for a really controlled condition, that takes a lot of time on the part of the research team. The participant as well, even just getting the food and consuming it, can be taxing for that period of time. So, it's hard to do, it takes a long time, it's expensive, and so we don't have nearly as many of those randomized controlled trials as I would like, and I think a lot of people would like to have, as well.

Dr. Slavin (04:35): Then sometimes we'll take a reductionist approach and we'll look at maybe an isolated nutrient in a dietary supplement we want to understand — if it's magnesium or riboflavin or any of these nutrients — that if we can just increase the intake of that through a supplement, provide a placebo and study that. And that's a meaningful type of research as well, but in terms of the nutrition space, we know the B vitamins are interdependent for their metabolism. Magnesium works with vitamin D and so many other things. And so it really isolates one nutrient and doesn't necessarily account for the broader spectrum of nutritional status that could influence nutrient metabolism.

Carl Cincinnato (05:23): That's interesting. And that's something that hasn't been spoken about a whole lot, is that you can shoot up your doses — double or triple your doses of magnesium — but you do need other minerals and vitamins to process that effectively. And so just doing that high dose of magnesium in isolation may give you false results.

Carl Cincinnato (05:43): And if you're doing that as an individual with migraine to combat migraine, it may be actually worth pairing that with other supplements and minerals or with other dietary things that you know will support the absorption and the effective use of that magnesium.

Dr. Slavin (06:00): And I'll mention one thing about magnesium. So, you mentioned taking a high dose of magnesium. We know magnesium and calcium and some other minerals compete for absorption in the digestive tract. So, if we increase a dose of one and are not getting necessarily enough of another, it can throw things out of balance, too.

Carl Cincinnato (06:22): Yeah, and so don't take them at the same time either because are they're kind of canceling each other out?

Dr. Slavin (06:29): To some extent we can saturate the transporters in the intestines that absorb the nutrients from the intestine into circulation in the body. So, there is a maximum capacity for some of the nutrients of what we can absorb at any one time.

Carl Cincinnato (06:48): So, we know the research into diets and migraine is very difficult, to say the least. How has the research evolved in recent years? Are we getting better evidence overall?

Dr. Slavin (06:58): We're getting more, certainly. I think there's been an explosion in the past couple of years to the point where it's hard to keep up with all of it, which I started this over a decade ago. So, in some ways, it's really exciting to see that kind of very dramatic increase in researchers all over the world publishing interesting and relevant research. In the past year or two, I think some of the study designs have gotten more heterogeneous, more varying rather than more similar, and so that is not something I would want to see, but maybe people will find other designs that work better for understanding this relationship between diet and migraine.

Dr. Slavin (07:54): For the first time, I'm excited to see some longitudinal population research done in the Danish Birth Cohort study published recently — a birth cohort where they had nutritional information about the mom, and they followed up when the offspring were 20 years old, looking at risk of headache and frequent headache.

Dr. Slavin (08:20): And so they were able to draw some conclusions about nutritional intake of mom during pregnancy and headache outcomes, as well as in the kids themselves earlier in their life when they were adolescents versus their risk of migraine when they're 20. So, that, I think, is a really good advancement for us to be moving in the direction of longitudinal dietary intake and migraine studies.

Dr. Slavin (08:52): And the reason I say that is because that's where a lot of our nutrition research — things we take for granted now, things that we understand — that dietary fiber and especially soluble fiber reduces risk of cardiovascular disease. Diets high in fruits and vegetables reduce risk of

cardiovascular disease. A lot of those initial observations came from population-level studies where we observed dietary intake in people and risk of developing heart disease over time.

Dr. Slavin (09:23): And we just haven't had that type of research in migraine to use to target. If we see this in a population study, then we can use it to design a randomized controlled trial that's very targeted at a specific hypothesis to see if it holds under much more controlled conditions.

Carl Cincinnato (09:46): Let's talk about a couple of different diets. And perhaps we could start with the ketogenic diet since it comes up often in the migraine community. What does the evidence show so far and who might it be most suitable for?

Dr. Slavin (09:58): So, the ketogenic diet, first, for anyone who doesn't know, is a pattern of eating that is very, very low in carbohydrates, moderate in protein, and high in fat to make up for the energy needs. And what it does in the body in keeping carbohydrate content very low, it almost mimics a fasting state where the body does not have access to the high levels of glucose to power what would otherwise normally be used for energy metabolism in the body.

Dr. Slavin (10:41): And so, instead the body metabolizes fats to this alternate source of energy that cells in the body can use instead of glucose. And there are some tissues like the brain, which use primarily glucose for energy. And so when that supply is gone, the brain during a ketogenic diet switches to this alternate fuel source of the ketones. And so the evidence for migraine is there are, at this point, a few clinical trials using different forms of the ketogenic diet.

Dr. Slavin (11:16): Some are very low-calorie ketogenic diets, some kind of the more classic version that was developed in the 1930s for epilepsy. Then there's a less restrictive version called the modified Atkins diet. And so, several different studies — small to moderate size — have shown some benefit to consuming a ketogenic diet for migraine outcomes and especially migraine frequency. There is not a clear distinction in the evidence as to which form of the ketogenic diet is better than the others.

Dr. Slavin (11:57): So, the other question of who is likely to benefit from the ketogenic diet would be typically people who have probably a little more of severe migraine or migraine is impacting their life more so. Because the diet, you might imagine, is a very big shift for a lot of people compared to how we typically eat, especially in Western society. Carbohydrates make up the bulk of our energy intake for a lot of people. And so to cut it down is a dramatic change.

Dr. Slavin (12:32): And it does take time and effort to figure that out, how to fit it into your life, and how to eat these foods and still eat things that hopefully make you happy. So, I would expect people who have a little more severe symptoms might be more motivated to make those changes.

Carl Cincinnato (12:52): It's a really tough diet to follow. I tried it twice, and I would say of all the diets I've tried, it was by far the most difficult to sustain because of the high fat content. And it's not like it's all the fun fats like french fries and burgers and so forth. It's healthy fats that you're supposed to be eating that are good for the brain and get you into a state of ketosis.

Carl Cincinnato (13:18): But you mentioned that there's modified versions that you could apply. Does that make it a little bit more sustainable or easier for someone to follow?

Dr. Slavin (13:27): Yes. So, they can still produce ketosis, meaning you're still shifting that metabolism, but it's not as extreme. There's one that I haven't seen studied in migraine — and I really would like to — that uses medium-chain triglycerides, which is a workaround. So, medium-chain triglyceride is basically a shorter version of dietary fats, where dietary fats are kind of a longer chain of carbons. Medium-chain is shorter. They get absorbed in a different route.

Dr. Slavin (14:05): They get metabolized in a slightly different route. And for the ketogenic diet, if you're using medium-chain triglycerides, folks can still achieve ketosis with a little more carbohydrate. And so it lets it be a little more liberalized, as we say in the nutrition world. You can get a little more carbohydrates that way. But again, I haven't seen that studied in migraine, unfortunately.

Carl Cincinnato (14:33): What about exogenous ketone supplementation with BHB [beta-hydroxybutyrate]? Can you break that question down into plain language and then respond?

Dr. Slavin (14:42): I'll try. So, exogenous ketones is something that's under investigation instead of, or in the hopes that, it might allow us to achieve the benefits to migraine that we see with the ketogenic diet without having to do the very restrictive eating pattern that it takes to put the body into ketosis. And so beta-hydroxybutyrate is one of the ketones that is produced in the body during that state of ketosis.

Dr. Slavin (15:20): So, some folks have been doing some research to investigate if we give that orally as a supplement, would that enable people to reap the benefits of having ketones in their bloodstream? And there is some early research to indicate that it looks like at least some people might benefit from this. The one trial I'm familiar with looked at a group of 40 or so people, and when they looked at the group as a whole, there wasn't a statistical difference.

Dr. Slavin (15:57): But when they looked at certain metabolic markers, they were able to identify a couple things in people's blood panels that might help to predict who might be more responsive to the ketones — to those exogenous ketones. So, it's still early in a lot of ways, but promising, especially given the history of the ketogenic diet with migraine and the evidence built up there.

Carl Cincinnato (16:27): Let's shift now to the omega-3/omega-6 pattern. There's exciting research on diets that are high in omega-3 and low in omega-6 fats. What did those studies show and how might someone translate that into their actual eating habits?

Dr. Slavin (16:42): There are two large, good, well-designed studies investigating a diet that controls the ratio of omega-3 fats to omega-6 fats. One of the studies was in people with chronic daily headache, another in people with migraine. Both of them showed reductions in headache or migraine on the diet that is high in omega-3 and low in omega-6 fatty acids. And so what does that mean? How does that translate to those of us making decisions of what to have for dinner?

Dr. Slavin (17:19): So omega-6 fats are the ones that we tend to encounter more in the food supply. So, vegetable oils — corn oil, soybean oil, sunflower oil, safflower oil — are a lot of the common ones that have relatively high proportions of omega-6 in them. So, they're not only in those oils and when we cook with them, but in a lot of processed foods. Those types of oils tend to be what is used in processed foods, especially soybean oil.

Dr. Slavin (17:52): And so a diet that is low in omega-6 is not only avoiding those oils, but also often avoiding processed foods because of their content. Omega-3 — I want to be very specific — the diet patterns that were studied in these two trials used omega-3 in fish especially. So, that refers to these longer-chain omega-3 fats. And this is in contrast to — there are omega-3s found in plant-based sources like walnuts — that's a slightly not as long of a chain chemically, and so that is not as active in the body.

Dr. Slavin (18:37): So, it is an important distinction that these studies used fish for those EPA [eicosapentaenoic acid] and DHA [docosahexaenoic acid], these long-chain omega-3s. And so their diets increased fish intake, decreased those other oils, and then instead used things like olive oil and macadamia nut oil, which is a monounsaturated fat, which is neither omega-3 nor omega-6, to fill in the gap of fats in the diet.

Carl Cincinnato (19:05): Is coconut oil alongside olive oil OK to use as well?

Dr. Slavin (19:09): Coconut oil is more of a saturated fat. So, in the omega-3/omega-6 distinction, it would fit that pattern in that it's not as prominent in omega-6, but it does tend to have a higher amount of saturated fat — which can have other concerns, especially risk for cardiovascular disease. And so it is generally not recommended on the same level as olive oil. But recognizing that there are times when olive oil isn't the right choice for a recipe, in that case, then it could be a substitute.

Carl Cincinnato (20:06): An easy way to think about it is processed foods, typically higher in vegetable oils and higher in omega-6s — reducing those. The research so far suggests that that's quite good for migraine. And if we can eat some fatty fish, that's going to elevate our omega-3s, and that's also going to be a real positive. And it seems like that diet, that sort of approach — and we'll talk about a couple of other diets — but that approach out of all the other diets seems like it has the most merit. Would you say that's a fair summary?

Dr. Slavin (20:38): Yes, I would say that has the most elegant research done to support it. Going back to what I said earlier about randomized controlled trials, their design for the omega-3/omega-6 studies was excellent.

Carl Cincinnato (20:57): So, talking about the next diet, we are also hearing more about low-glycemic diets and stable blood sugar levels for migraine. What's the rationale here and how can people apply that principle day to day?

Dr. Slavin (21:11): So, when it comes to low-glycemic diets, the rationale is tied into the overall understanding of migraine pathophysiology and characteristics of people with migraine. And so there's this prevailing understanding that maintenance of homeostasis — or keeping steady habits, steady lifestyle — seems to be beneficial for people with migraine. So, sleeping consistently, staying hydrated consistently, exercising consistently, and so forth.

Dr. Slavin (21:52): And so within that is a theory of if we keep blood glucose levels consistent — we don't get these extremes of high blood glucose after a meal with lots of carbs and simple sugars, and we don't get the extremes of low blood glucose from crashing after eating something like that. And so it maintains this metabolic stability — maintains a consistent energy supply to the brain with these consistent blood glucose levels.

Dr. Slavin (22:27): And the rationale is that that will lead to less triggering of migraine attacks. The low-glycemic diet, what it looks like in practice, is choosing foods that have more complex carbohydrates. And what I mean by that is foods that still have carbohydrates — we're not trying to avoid them with a low-glycemic diet — but choosing ones that are higher in fiber, higher in starch, and have less sugar, less simple sugar, in the food.

Dr. Slavin (23:07): And when something is defined as being low glycemic or high glycemic, there's a process that we can do to monitor response to blood glucose. We would feed someone a food of a known amount of carbohydrate in that food, and then we would monitor their blood glucose for the couple hours after they eat it.

Dr. Slavin (23:30): Basically how high it spikes tells us if it's a high-glycemic food — if their blood glucose spikes really high, really fast — or it would be a low-glycemic food if it takes a while for that food to be digested. The carbohydrates take some time to be absorbed into the bloodstream. And so it's this more gentle increase in blood glucose — increase and decrease back to baseline. And so the low-glycemic diet is trying to piece together all the foods that are more low glycemic and avoiding some that are high glycemic or high GI [glycemic index].

Carl Cincinnato (24:06): So, one example of that might be a banana that's low GI versus a bar of chocolate, which might be high GI?

Dr. Slavin (24:14): I am often surprised by what is low GI and what is high GI. I have to look at the table sometimes to confirm. And the reason I hesitate — a bar of chocolate is also higher in fat. And so fat is something that slows down digestion in the stomach, slows down release from the stomach into the small intestine. And so that — I would have to look it up to be perfectly honest, which is high GI and which is lower in that category.

Dr. Slavin (24:49): Maybe an example that would help would be if you wanted to have a sandwich and you wanted some slices of bread — and you could choose something like a white bread made with refined wheat. Sometimes there's even some sugar in there to make it taste better. And so that I would expect to be digested pretty quickly. It's got low fiber.

Dr. Slavin (25:17): And so that I would expect to be digested quickly and hit the bloodstream faster in the form of glucose than if you took a nice whole-grain piece of bread that maybe even has some nuts and seeds in it, which slows down digestion. And even what's there in the form of carbohydrates takes a while to digest. And so it sits in the stomach longer, and then when it releases, it takes a longer time, lower spike in blood glucose.

Carl Cincinnato (25:47): Do you think it's worthwhile to try to reduce and potentially eliminate sugar from our diet?

Dr. Slavin (25:52): I think a lot of us could reduce sugar in our diets and improve health outcomes as a result of that. There's a good bit of evidence on a population level, at least here in the U.S., that we consume more than the recommended amounts. I don't think it's necessarily feasible to completely eliminate sugar. We can try to cut down added sugar as low as possible … so from sources of added sugar and table sugar.

Dr. Slavin (26:27): But that also includes things like honey, maple syrup, even jams and jellies that have sugar in them. And so we can try to cut back on that. It is certainly not necessary for a healthy diet for those to be present. But to completely avoid it may make for a challenging eating pattern in a way that may make it hard to eat in society.

Carl Cincinnato (26:59): What about gluten? What are your thoughts on gluten?

Dr. Slavin (27:05): Gluten — certainly there are some people with celiac disease, and there's a higher incidence of celiac disease with migraine — and so certainly for them, absolutely eliminating gluten intake would be the treatment for that. And some people when they do that, if they have migraine and celiac disease, some people see a benefit to their migraines, but not all, when they cut out gluten. For others, it's less clear.

Dr. Slavin (27:35): I think what is clear is that there are some people who are sensitive to gluten. So, it's not an allergy, but there's some sensitivity — whether through GI [gastrointestinal symptoms] or even more diffuse symptoms throughout the body — when they eat gluten that they have sensitivity. It's a challenge to diagnose and to identify. And so, unfortunately, I don't have better practical guidance at this point.

Carl Cincinnato (28:04): One of the things I've noticed is a significant difference after I switched to whole-grain bread and rice and whole-grain pasta. And I come from an Italian family, so a big bowl of pasta at lunch, and then I would be just wiped — kind of in a carb coma in the afternoon — processing and digesting. Why do you think that might be the case that I've noticed that difference? Is that due to the GI aspect or the lower GI of the whole-grain bread and rice?

Dr. Slavin (28:35): Could be. That could be part of it. So, it could be, again, that you're introducing a more stable supply of glucose coming in from your digestive tract, getting into your system. What people may not realize is after eating a big bowl of pasta, which contains carbohydrates in the form of starch — and that starch is basically just a big, long molecule composed of glucose molecules linked one to another, end on end.

Dr. Slavin (29:03): And so the digestion process is just breaking down that starch and releasing those individual glucose molecules. When that happens after a big bowl of pasta, you get that higher GI response, you get faster blood glucose levels. The insulin response that your pancreas then puts out to try to get glucose levels down, take the glucose out of the blood into the tissues.

Dr. Slavin (29:32): The insulin is necessary, but with a big glucose spike, you also get a big hit of insulin, and that can cause blood glucose levels to drop quickly as well. And so that crash feeling or that really tired feeling could be related to that, for sure, in the short term after that. The other thing I'll mention is about whole grains themselves. Whole grains have a lot of extra vitamins and minerals in them as compared to their refined grain version.

Dr. Slavin (30:13): So brown rice has more magnesium, more B vitamins, and certainly more fiber than white rice. And so it's also possible that if — especially if these positive benefits appear over time — it could be from that more nutrient-dense profile helping you feel better over that longer period of time as well.

Carl Cincinnato (30:39): What about dairy?

Dr. Slavin (30:40): Dairy — I don't have a lot of evidence to draw on for migraine specifically in terms of studies. I know more generally, there have been a number of studies looking at dairy and broad inflammation in the body. And the more recent research seems to show that it does not produce inflammation in the way that prior work had shown. So, I think that is fine to incorporate into a healthy eating pattern for people with migraine.

Carl Cincinnato (31:18): What's your opinion about whole-food, plant-based diets?

Dr. Slavin (31:23): So, whole-food, plant-based diets — when I think of that, I think of eating a lot of vegetables, fruits, beans, nuts, and seeds. And whole food would mean whole grains. And so there's broad evidence in the nutrition sphere that that can be a very healthy way of eating. It's in accordance with a lot of the recommendations and eating patterns that we see to broadly promote health, like the Mediterranean diet — I would put in that category — which also would include some fish and olive oil and some meat and some cheese, but not excessive amounts.

Dr. Slavin (32:11): And so broadly speaking, yes, I do think it can be a very healthy way of eating for people. And when I say healthy, I mean in the ability to reduce risk of multiple chronic diseases — cardiovascular disease, diabetes, overweight, and obesity, and things like that.

Carl Cincinnato (32:32): The average person with migraine doesn't necessarily have the perfect diet. None of us do all the time. But does that mean we need to take supplements? And what's your view?

Dr. Slavin (32:48): So first, I would say there is no such thing as a perfect diet. And I think we can let ourselves off the hook a little and stop trying to do perfect. But there are many different ways to get to a healthy diet that take different shapes for different people. In terms of do we need to take supplements, it depends person to person.

Carl Cincinnato (33:17): I've read somewhere that 50% of women with migraine are deficient in magnesium.

Dr. Slavin (33:21): Yes, we do see very high rates of magnesium deficiency in the population, especially in the U.S. and in Western styles of eating, where we're not eating high amounts of whole grains, beans, nuts and seeds, and leafy greens. So, in that case, taking a magnesium supplement is one way to try to make up for some shortfall in that nutrient. But that doesn't mean it's the only option. There are dietary factors that people could attempt to change their diet.

Dr. Slavin (33:56): And if that's not for them, supplements are an option in that case, yes. There are some blood tests for magnesium that, especially if you're working with a healthcare provider, you could ask to have your serum magnesium levels checked. They are not a perfect indicator of magnesium status. And there's some disagreement over what should be considered a deficient level in magnesium serum levels. So, even if you can get access to that test, it's not a perfect indicator.

Dr. Slavin (34:34): The evidence for magnesium supplementation for migraine actually does not take into account background magnesium status. So, there have been a number of clinical trials that investigated magnesium supplements for migraine. They used the forms that I've seen most in the research — magnesium oxide and magnesium citrate — which are forms that are available for people to purchase. And they were in doses of about — there were six different studies — but the most common was 600 milligrams of magnesium per day.

Dr. Slavin (35:14): And the trials did not measure background magnesium status. So, they took magnesium supplements and still showed benefit across multiple studies of magnesium supplementation reducing migraine frequency especially.

Carl Cincinnato (35:34): Without knowing whether the individual participant was deficient in magnesium in the first place or not.

Dr. Slavin (35:39): Correct. But as you say, the magnesium status of the population is not ideal. And so it's very likely that they had people who were magnesium deficient in their study, and this may have corrected the deficiency.

Carl Cincinnato (35:58): So, magnesium is only one supplement. There are others as well. I mean, we've spoken a little bit about fiber. There are other supplements, minerals, or vitamins that we should be aware of that are crucial to migraine, like vitamin D is coming up a lot these days.

Carl Cincinnato (36:14): What are the things that should be on our radar as someone with migraine that perhaps are wondering whether a deficiency in something or supplementation might be potentially super helpful in managing my migraine condition?

Dr. Slavin (36:28): Yeah. So magnesium is one, definitely. Riboflavin, also known as vitamin B2, is another. And then I'll add CoQ10 (coenzyme Q10) to that list. And so those are the three that I think we've seen multiple studies, to different degrees, supporting the use of those supplements in prevention of migraine attacks prospectively. So, after people take the supplement for three months, seeing reductions in the frequency of their migraines.

Dr. Slavin (37:09): You mentioned vitamin D. This one is a little newer to the field, so, it hasn't received the same kind of critical review from the migraine research community in the same way magnesium, riboflavin, and CoQ10 have all been reviewed by different clinical practice guidelines. And they've survived that gauntlet to still be mentioned. Vitamin D is newer and hasn't gone through the same critical review process since the evidence is more recent. But I will say, when I review it, I do think it's very promising. And so some level of vitamin D supplementation — I expect we may see some recommendations on that moving forward.

Carl Cincinnato (37:55): And it seems to play a role in a whole bunch of other health components as well, right?

Dr. Slavin (38:01): Yes, many different health conditions. Same with magnesium especially.

Carl Cincinnato (38:07): Yeah, it's involved in like 300 bodily processes — some crazy high number. But the thing with magnesium is if you take too much of it, it can cause your gut to be upset and you have to go to the bathroom. And so there's different formats as well that are more bioavailable or easily digested, like there's a chelated form of magnesium.

Carl Cincinnato (38:31): And the type I take is diglycinate — magnesium diglycinate — which is a chelated form, which seems to agree with me, which is not the citrate or the oxide that you mentioned earlier. Can you comment on that?

Dr. Slavin (38:44): Yeah, sure. Again, strictly, the evidence for magnesium supplementation in migraine is mostly using magnesium oxide or magnesium citrate as forms. But you're absolutely right that there are gastrointestinal side effects of taking magnesium. I want to mention first that those side effects — if people take a magnesium supplement and have loose stools — it is not a major cause for concern in most cases.

Dr. Slavin (39:21): It's usually a passing event that once that magnesium supplement is out of the system, you'll go back to better regularity. The other thing is that generally there is some kind of acclimation process that can happen. And so people can start off with a lower dose — maybe 200 milligrams a day — and then work their way up as symptoms subside a little bit, work their way up to maybe to 400 and then if they can tolerate 600. So, that's one option.

Dr. Slavin (39:53): With the specific forms of magnesium, magnesium oxide we know is not well absorbed in the intestinal tract. And so it's actually kind of surprising in some ways that it was effective for migraine, which I think is an intriguing question for science someday. But yeah, so magnesium citrate is more bioavailable than magnesium oxide. Magnesium glycinate is in that category as well of being a little more bioavailable. But I find some people respond differently to different forms.

Dr. Slavin (40:32): And so when I give recommendations, I generally recommend citrate or glycinate, partly because they're more bioavailable and people tend to tolerate them better. And in terms of affordability as well, the citrate tends to be kind of a happy medium of cost and symptoms.

Carl Cincinnato (41:00): And when taking supplements, is it a good idea to talk to a healthcare professional about what you're taking or at least tell your doctor or speak to the pharmacist? Because some of these are not suitable if you're thinking about getting pregnant or if you're breastfeeding. Is that right?

Dr. Slavin (41:16): Yeah. I always recommend people be having conversations with your doctor or your healthcare provider, whoever that is, about the supplements that you're taking. Supplements can interfere with medications, and [people who have] certain diseases and conditions should not be taking certain supplements. And so it's hard to give blanket advice, and that care really should be personalized to your specific health needs and conditions.

Carl Cincinnato (41:43): So, this one might sound a little bit left field, so go with me on this. But creatine — do you suggest creatine for any of your patients? This is something I've just discovered as a parent, who's not getting a whole lot of sleep with newborn babies, to alleviate the brain fog that accompanies sleep deprivation and migraine. And I found it really helpful, at least initially. I mean, I could still be in the honeymoon placebo period, but it seems to have some evidence to support that.

Dr. Slavin (42:16): Well, first of all, congratulations. And I'm also happy that the creatine seems to be helping. Creatine is a supplement that is taken with this underlying hypothesis of helping with stabilizing energy metabolism in the brain. There seems to be, in people with migraine, there's a

hypothesis that there's dysregulation of energy metabolism in the brain. And so creatine is an alternate source of energy, alternate to ATP [adenosine triphosphate], like cellular energy.

Dr. Slavin (43:00): And so having this additional creatine from supplements, the theory is that that could help to stabilize energy metabolism and consistent energy supply in the brain. The evidence for migraine and creatine — I haven't seen it. What I can say is that there's evidence to show that taking creatine supplements can increase levels of creatine in the brain. There is some there that is produced naturally, but we can increase levels through supplementation. The question is whether that actually translates to outcomes like migraine or brain fog, a symptom of it. I haven't seen the data for that.

Carl Cincinnato (43:45): Yeah, it's just interesting. I kind of knew about creatine back in my college days when athletes were taking it in the gym to bulk up, like the gym bros and gym junkies are doing it, are taking it. But I didn't realize that it had this cognitive benefit, particularly in the setting of sleep deprivation. But you're right, I haven't seen any evidence either.

Carl Cincinnato (44:09): And I've looked for creatine with migraine, but certainly sleep deprivation and brain fog that's associated with sleep deprivation, which for me overlaps a lot with migraine. I seem to have — this is an N-of-1, it's just my experience — but there seems to be a benefit there, which I'm kind of excited about and telling everyone. Because it's cheap as well. Creatine has been around forever. It's one of the cheapest supplements that I take out of all the things I take for migraine.

Dr. Slavin (44:41): Yeah, and so then the question is what's the safety profile? And so everything in medical care and nutritional care, we're constantly balancing what's the risk and what's the benefit, and does that stack up in favor of doing any particular treatment or nutritional intervention in my case.

Dr. Slavin (45:06): And so creatine — you mentioned sports nutrition — does have a reasonable history of people using creatine as a supplement for a different reason, for more athletic performance and especially those fast-twitch muscles in athletic performance. And so there's some safety profile there that we can extrapolate a little bit, but I'll wait to see more on migraine before I'll make recommendations.

Carl Cincinnato (45:37): It's a good point to say, no matter what you're taking, it's so easy today to just go online, order in your magnesiums, they get delivered, you never go to the pharmacy, you never go to your doctor. And then all of a sudden, you're taking five or six of these supplements. And then sometimes there's ingredients across multiple of those things that you're not realizing are there.

Carl Cincinnato (45:56): Like, for example B6, which recently got some media coverage about really high levels of B6 that can be in all these products seemingly innocently, which can accumulate and cause problems in the body if it's not monitored. So, it is a good idea to be talking to the healthcare professional about the stuff you're buying over the counter or ordering online.

Dr. Slavin (46:18): Absolutely.

Carl Cincinnato (46:20): One other ingredient — NAD+ [nicotinamide adenine dinucleotide] — can you tell us what that is and whether we should be paying attention to it?

Dr. Slavin (46:28): NAD+ has come on the scene, also people mentioning it as a supplement as well. It is in line with some of these other hypotheses of what dietary factors might help with migraine. It's in line with that hypothesis of that energy deficit that might exist in the brain of people with migraine and finding ways to support metabolism to provide a consistent energy source to our brains. So NAD+ is another one of those molecules that is involved in the energy metabolism pathway.

Dr. Slavin (47:12): And so NAD+ as a supplement is attempting to remedy some of that energy deficit in the brain. But, like so many other things, it's got this mechanistic rationale of how it might work, but very little to support that it actually does. So, we need more research on that one, for sure.

Carl Cincinnato (47:37): Still very early days — OK. So, there are so many diets and supplements, it can feel overwhelming. If someone wanted to start improving their diet for migraine, what are some of the first one or two steps that you'd suggest?

Dr. Slavin (47:50): So, if someone wants to improve their diet for migraine, I think one of the important first steps is to accept that there is no perfect diet for migraine and let that go from the start. And I think you can set yourself up for success with the understanding that there are things we can do that probably will help you feel better. Some of it may be migraine, some of it may be other things — like how your gut feels.

Dr. Slavin (48:23): So, not expecting perfection in either the foods we eat or in the outcomes. I don't think diet can cure migraine, and I don't think we should be thinking that way. But we can think about how diet can improve how we feel in terms of migraine and more broadly. With that understanding, I would say then the next thing I would recommend is to do some sort of assessment of what you are eating.

Dr. Slavin (49:00): And this can be even just keeping a food diary for a couple days — write down what you eat. A lot of people with migraine do that already. You could also use an app. Some of the apps will give you a nutritional printout — if you type in what you eat, they'll give you a report of what nutrients it might contain. And so just — and it doesn't have to be a really strict assessment, but just taking stock of "how *do* I eat?"

Dr. Slavin (49:30): And then comparing that against something — maybe if one of the eating patterns we've talked about is appealing. So, things like the Mediterranean diet, a low-glycemic diet, trying to increase omega-3s — deciding if any of that makes sense for you. And then trying to find small things — maybe one thing at a time, not changing everything at a time — but looking and saying, "You know, I haven't eaten any fish in the past week. That's my goal for this week. I'm going to try to eat fish twice this week to increase my omega-3 intake from food."

Dr. Slavin (50:15): Try to make progress and work towards that. Identify places in your day — grocery store, restaurants — where you might be able to do that. And that's my recommendation, to focus on a small thing, one thing at a time. And then to support that, I would encourage you to try to build out a support system — friends, family, coworkers, people you eat with. I think a lot of people are shy when sharing dietary changes. Not everyone, but some people are maybe a little embarrassed that, "I'm doing this."

Dr. Slavin (51:11): But what I find is when we reach out for support, a lot of people are very happy to help. And what I mean by help is working with family at your house and saying, "Hey, I want to eat more fish. If I incorporate that into a meal, would you try it?" If fish just shows up on the table, it might be a surprise. But if people hear, "I think this really might help me feel better," we can often get more support. So, accepting that it won't be perfect, making small changes until they're sustainable, and trying to enlist help of our friends and loved ones to help support us in making those changes.

Carl Cincinnato (51:44): I love that tip about recruiting friends and family to help. It would make things so much easier if someone is going through the same dietary changes with you at home when their meals are cooked. What does a balanced, sustainable, migraine-friendly plate look like for most people?

Dr. Slavin (52:05): For most people, I would say a balanced, migraine-friendly plate doesn't have to look all that different than what I would recommend for health promotion and disease prevention for a

lot of people — with the exception if somebody has food triggers that they really, really have a strong connection, when they eat this food, they always get an attack. Of course, don't eat that.

Dr. Slavin (52:37): But in the absence of strong reasons to avoid foods, I think it can be a similar plate as for the general public who's looking to promote health and avoid heart disease and so forth. So, the plate that I would envision would be a lot of vegetables and fruits, whole grain, and some sort of protein. And that could be beans, nuts, seeds — those would be my picks for the predominant protein sources.

Dr. Slavin (53:18): Sometimes some meat, or maybe a little bit of meat to flavor a dish, could be a way of going about it. But definitely, I like to promote the consumption of the vegetables, the fruits, whole grains, and other things fill in the rest.

Carl Cincinnato (53:37): That's really helpful. I get the sense listening to you that I'm eating too much meat. Maybe it's a cultural thing, but is meat something that we should probably eat sparingly, in your opinion?

Dr. Slavin (53:49): Meat, according to various research, something like the Mediterranean diet — which promotes these other plant-based protein sources — does include meat, but it is more sparing. And the Mediterranean diet has a lot of evidence to support its chronic disease prevention efficacy. I would say meat can be part of a healthy diet. We tend to — if I look more to the model of MyPlate in the U.S., which is part of our dietary guidelines — meat can be that. It's a quarter of the plate in that model that is protein, and meat fits in that category.

Dr. Slavin (54:35): But really the guidance would be looking for a variety of protein sources — so not just meat every day, but beans one day, meat the next, and so forth. And when choosing meat, looking for leaner cuts and watching portion sizes, like we should with anything.

Carl Cincinnato (55:06): Do you tend to encourage eating more chicken versus meat overall?

Dr. Slavin (55:10): Well, it depends on dietary needs. Red meat is a good source of iron. And so if someone is deficient in iron, then maybe in their case red meat should be something that should be higher up on their list of priorities versus chicken, which is a lower source of iron. So, when I think of the difference between whether or not to recommend chicken or red meat, my mind goes to a couple things.

Dr. Slavin (55:44): One would be the iron content. Red meat has a higher iron content, so if that's deficient in someone's eating pattern, then we can take that into account. The other thing I think about is saturated fat content, which can vary in different cuts of meat. Choosing a lean cut of meat is what I would typically recommend to keep saturated fat down. In chicken, the white meat is leaner and has less of the fat content. And in cuts of beef, top round is a cut here in the U.S. that tends to be leaner, or choosing ground beef, if that's what's being used, with a lower fat content.

Carl Cincinnato (56:34): Many people have tried multiple diets without much lasting success. What would you say to someone who's discouraged or feels like their efforts haven't made a difference?

Dr. Slavin (56:47): I'm sorry, first, and I would recognize that they've put in a lot of work to try different diets. I think that I would encourage them that they may not have seen success in migraine outcomes, but a lot of these eating patterns that I promote also have other health benefits. Something like increasing omega-3 content is good for long-term cardiovascular health, also. A low-glycemic diet is good for metabolic health and blood glucose levels.

Dr. Slavin (57:33): So, the efforts they're making to follow one of these diets — or multiple diets — probably are also increasing the nutritional quality of their overall diet, which is impacting their risk

for these other conditions, many of which commonly co-occur with migraine. And so, it may not be as evident, but hopefully there are some other benefits that they're accruing from the different dietary strategies they've taken.

Dr. Slavin (58:07): And then the other thing I would say is some of these diets can take — a lot of the studies use a three-month minimum before they start to assess an effect. And that's a long time to try a diet before feeling better. So, just encouraging — if they haven't given it that time — that yes, there are these other benefits, and maybe a little more time might help.

Carl Cincinnato (58:34): Dr. Slavin, it's been a fantastic interview. I'm certainly going to make a few gentle changes to my eating habits. I won't call it a diet; I'll call it eating habits, so it's not something temporary. And you've given me some great tips, and I think a lot of people have gotten some great tips out of this. So, thank you so much for joining us again on the Migraine World Summit.

Dr. Slavin (58:54): Thank you for having me.