

Transcript of RELIEF podcast with Johnny Figueroa and Robert Sorge

RELIEF: Hello everyone. My name is Stephani Sutherland. I'm with relief.news, and today we're going to be talking about diet and inflammation and chronic pain. My guests today are Johnny Figueroa, who's an assistant professor at Loma Linda University in southern California and also Robert Sorge, who's an assistant professor at the University of Alabama at Birmingham. Thank you both for joining me today.

Johnny Figueroa: Thank you.

Robert Sorge: Thank you, Stephani.

RELIEF: Great, so what we're going to talk about today is how can diet possibly influence chronic pain, and can our diet, in fact, be used as a complementary treatment or as part of a chronic pain treatment plan? So I recently, last month in May, attended the annual meeting of the American Pain Society, where Dr. Sorge and Dr. Figueroa presented their research in a session of research presentations called "Molecules to Man: Diet as Treatment for Chronic Pain," which, Rob, you organized. So I'd like you to start out, just by introducing us a little bit to the field of studying diet and chronic pain, how is that branch of pain research developed? Are there many people looking at it, and what's the link? Maybe you can tell us a little bit about how diet influences inflammation, and why that's important for pain.

Robert Sorge: Sure. So, in terms of it being a new area, it's certainly not a new area. People have been looking at this for years; in fact, there [have been] clinical trials since the 80s, looking at ketogenic diets and Mediterranean diets changing pain sensitivity in humans. But those sort of things don't get a whole lot of press, because of course, as you know, there are new fad diets that come out just about every week, and so they tend to get lost in the shuffle. In terms of pre-clinical stuff, Susan Masino and Dave Ruskin at Trinity College, they've been looking at ketogenic diets for neuropathic pain for about ten years, so it's not new, but it's certainly not a big thing. In terms of inflammation, we know that a lot of the foods that we eat cause the sort of inflammatory response—carbohydrates, saturated fats, omega-6 polyunsaturated fatty acids, that Johnny, I'm sure, is going to talk more about. All of these things trigger the inflammatory response and lead to inflammation. And so in terms of people looking at immunity and immunology, people have been looking at diets for a long time, but has that transferred into pain, not so much. And so that's really what I was hoping to do is bring a spotlight into this new realm of treatments for pain.

RELIEF: Great, thank you. Okay, Johnny, now, I'd like you to, as Rob mentioned, talk a little bit more specifically, and I know Rob mentioned carbohydrates as one of the potentially inflammatory things in our own standard American diet, as we'll talk about; but also saturated fats. So can you give us the lay of the land when it comes to saturated fats: What are they? What do they do in our body, and why do we need them? And where do we get them?

Johnny Figueroa: So from a chemical standpoint, to give us the biochemistry of saturated fats, although they are required for our proper metabolism, they are fatty acids that have a lot of hydrogen and carbons usually. And what happens with these fats, when they're metabolized, [is that] they produce a lot of bioactive lipids and fatty acids that are pro-inflammatory. So that's one of the major consequences of consuming these saturated fats. In terms of what foods or food groups contain these saturated fats, they are very rich indeed—butter, cheese, and also these saturated fats, again, contain a lot of hydrogen, and this saturation contributes to that pro-inflammatory environment.

RELIEF: So all that delicious stuff that we're not really supposed to eat, like red meat, butter, fried foods. What about unsaturated fats?

Johnny Figueroa: So unsaturated fats in this case, and there have been a lot of studies showing that these unsaturated fats can contribute to an anti-inflammatory [response], we have the omega-3s, and I know that a lot of people have heard about omega-3 fatty acids. And we also have the omega-6 fatty acids. Again, both of them are really critical and important, not only for brain development, but also for brain function. But the ratio of those fatty acids can create havoc in terms of inflammation, so if you have a lot of these omega-6 fatty acids, that again, are contained in meat and friend foods—soybean oil is rich in these omega-6 fatty acids—then you will have a more pro-inflammatory environment, versus consuming omega-3 fatty acids that are totally unsaturated fatty acids that contribute to brain stability, brain metabolism, proper development, and those are contained more in fish oils, walnuts and other seeds.

RELIEF: Okay, so omega-6 and omega-3 are both unsaturated fats, but really omega-3 is the one that we're aiming for. And too much omega-6 can tip the balance towards inflammation, where we want to keep the balance more tipped towards omega-3, which is rich in fish oils and nuts and things like that, right?

Johnny Figueroa: That's right.

RELIEF: Great. Okay, let's talk about the research that you presented at the American Pain Society meeting. First, let's start with some of the research that you've done over the last few years, which you started out doing as a postdoctoral fellow with Marino De Leon. Maybe you could tell us about what you found investigating the effects of diet, and how we can protect against pain in animals, in rodents, who have had an experimental spinal cord injury, which is a model for spinal cord injury pain in humans. Maybe you could tell us a little bit about that.

Johnny Figueroa: So in one of the original investigations that we decided to undertake, we fed rats for their adolescent period with different diets. Our idea was that if you consume a healthy diet, and you have an injury that creates pain or pain-like behavior in rats, the idea was that we will see some sort of protection in the rats that were fed a healthy diet.

So we did that experiment. We fed the animals during their adolescence with this healthy

diet and not so healthy diet, and we performed experimental spinal cord injuries on them. And then we evaluated the recovery and also their pain-like behaviors. And what we found, which was really surprising, is that the rats that were eating the healthier diet, they didn't only recover faster, but they didn't show strong signs of pain-like behaviors, as we evaluated. So those were the original investigations that led our group to actually investigate what specifically are the mechanisms and the bioactive lipids coming from these omega-3 fatty acids that can confer some protection [because of their] anti-inflammatory properties. And we recently published a study showing that these metabolites that come from these omega-3 fatty acids can have a very, very robust effect in terms of protecting from pain.

RELIEF: Okay. And, so again, when you said they had a healthier diet, you were supplementing with omega-3 fatty acids, is that right? So they had some fish oil or something like we would take [in] a supplement ourselves?

Johnny Figueroa: So in our study, we were using ratios of omega-3 to omega-6 fatty acids. The control diet basically was 7.5 omega-6 versus one omega-3. That's the ratio or the proportion we had of omega-6 to omega-3. In this experimental diet, which was omega-6 fatty acids, we had a ratio [of] almost 3.75 or 4 molecules of omega-3 fatty acids versus one of omega-6. So the differences in those ratios that we see is actually contributing to this pro-inflammatory environment after the injury.

RELIEF: Okay, great. So, again, it's that balance of omega-3 and omega-6.

Johnny Figueroa: That's right.

RELIEF: Great. So Dr. Figueroa is looking at supplementing the diet with that beneficial fatty acid, but what about the harmful effects of the diet that we are typically eating everyday as Americans. Some of us are more healthy than others, but let's face it, we're eating saturated fats, and we're eating a lot of carbohydrates, and in fact, carbohydrates, Dr. Sorge believes, is along with the saturated fats, a big problem in our diet. And he's looked at feeding animals a diet that's more typical of the American unhealthy diet. So maybe you could tell us, Rob, a little bit about that, and what you found when you fed animals that SAD Standard American Diet?

Robert Sorge: Right, so we were concerned that a lot of the work that was being done, looking at these bad diets [that] were really just high-fat diets. And we've been told for years that everything we eat is supposed to be low fat, and we're supposed to get lots of breads and cereals. And as we know now, that may not necessarily be the best thing for our health, because when you have carbohydrates, you get the spike in insulin, and [those] repeated spikes in insulin, and all the sugar in our diet, leads to things like metabolic disease and type 2 diabetes, and it also triggers an immune response, and that immune response can lead to inflammation. And so if you [take] a correlational look at things, if you look over years, Americans have been following that food pyramid where you increase your breads and cereals. And we've also seen a dramatic increase in obesity and type 2 diabetes that tracks right onto that. And so we were concerned that some of

these diets that were primarily just high fat might not actually be what Americans are eating. And so we created a diet that is almost equivalent or almost exact on the nutritional value that Americans are getting. And so we focused on things like carbohydrates from white flour and sugar. We increased the omega-6 fatty acid levels to a human-relevant level. And we added trans fats also at the human-relevant level. And so we thought this is probably more typical of an American diet than these high fats.

RELIEF: And all that, again, delicious junk food that we're eating.

Robert Sorge: Yes, all the good things aren't good for you. So when we fed this to animals, basically the animals got fat. And it's not necessarily that they gained more weight, and that was the interesting thing. Some of these animals really didn't gain any more weight than the controls, but when we looked and we imaged their bodies, more of their body was fat. And so it had changed the makeup of their bodies. So more of their body was actually fat tissue, and so they were actually very unhealthy and had this pro-inflammatory state, even though they really didn't look any bigger than any of the other animals.

RELIEF: Interesting. So let's touch on that for a minute. You said that one of the things with the repeated insulin, which comes from eating sugar and white flour, in particular, [is that] it causes an immune response. And you've been talking about inflammation. And now you're talking about more fat tissue in the body. Can you talk a little bit about the link between [these]—I know that fat cells themselves can release signaling molecules. Talk a little bit more about what that mean[s] when it's pro-inflammatory—inflammation at the cellular level—and how does that influence pain?

Robert Sorge: Sure. So generally when we think of pain, we think of inflammation. This is due to immune cells releasing signals—cytokines—that are triggering and sensitizing nerve cells and signaling a greater pain response. So when we have an increase in adipose tissue, fat tissue, these cells do release chemicals, like leptin, which is a satiety signal, but leptin also causes an immune response and activates these immune cells, [and] gets them working and releasing these pro-inflammatory or increasing-pain signals. When we have an increase of fat tissue, that fat tissue also recruits T cells and macrophages into that tissue, activates those cells, and again, you get this cycle of increasing immune activation. And so when you look at our animals or individuals in the population in general, obese individuals, in the absence of any pain, tend to have higher levels of these circulating cytokines, things like interleukin 6 [IL-6] and IL-beta, TNF-alpha. They tend to be in a low-grade inflammatory state. And so we think it's that state which is leading to these health conditions that are coming later.

Johnny Figueroa: If I might add, in terms of the molecular mechanism Dr. Sorge mentioned, once those cytokines are released into the bloodstream and get to either the spinal cord or supraspinal levels in the brain or even the peripheral nerves, those cytokines hyperactivate neurons that are implicated in the pain pathways. So that's one of the mechanisms, and at least our studies show that depending on the type of diet that you're providing, you will see more or less activation of those neurons that transmit that

pain signal. So that's one of the potential mechanisms that might lead to this nociception and pain in our model.

RELIEF: Wow. So the diet is really having a pretty profound effect specifically on all those cells that are important for pain transmission and pain sensation. So, Rob, maybe go back then and tell us a little bit, what did you find when you fed rats the Standard American Diet that you created?

Robert Sorge: Well, like I said, they had a lot more body fat. We saw a dramatic increase in systemic inflammation, so these cytokines in the blood, so they're in this low-grade inflammatory state. And when we looked in their spinal cords, just as Johnny was saying, we see an increase in—we were looking at immune cells—and there was almost a doubling or tripling of the number of immune cells that are activated in their spinal cord. And, as Johnny said, the more of these cells that are there, the more they're going to influence the activity of those neurons and give this hypersensitive pain signal.

RELIEF: Interesting. And then the rats, after they have an injury, rats fed that diet took longer to recover, didn't they?

Robert Sorge: Yes, they did. We've shown the same sort of thing in mice as well. It basically is doubling their recovery time. So all of the animals get the same injury, but they do recover. Normal rats recovered in about three weeks, and these other rats took almost seven weeks to recover. So it is dramatically changing how their body is reacting to an injury. And this is again something that we see in humans. So obese individuals tend to take longer to recover from surgery or from injuries, and we think this is due to chronic immune system activation.

RELIEF: Great. And then, Johnny, you've done some research as well, now in your own lab, feeding rats a western diet as well, so more of an unhealthy diet. And maybe you can tell us about the effect on their baseline pain sensitivity? And you've done some really interesting work using a new behavioral test with the rodents; a lot of what we do in research, what researchers do, is to evoke pain with something painful. But a lot of researchers are now trying to get at the question of, is an animal in pain to begin with, if we don't have to poke them or hurt them. So maybe you could tell us a little bit about the work that you've done and what you've found?

Johnny Figueroa: Thank you, Stephani. So one of the things that we are looking at in my lab now is the effect of [the] type of high-fat diet consumption during adolescence, in terms of the nerve development of the pain mechanisms or the pain circuitry, as we call it. So areas that are implicated with pain, in the brain, like the amygdala, the periaqueductal gray, and sensory cortex, and also in the spinal cord, how [are] these neurons wired once these animals are fed with these high fat diets? And again, one of the main sources that we use in our diets are saturated fats, which I mentioned are harder to metabolize in our system, and they have these pro-inflammatory properties. They can actually activate directly [that] same cytokine release and also the inflammatory cells.

So what we did in our model, once we fed the animals, was [that we] adapted the mechanical conflict avoidance system, and that way, the affective component of pain. So it's not that we are poking the animal and seeing or observing a response, but we are evaluating how the animals cope with a stressful situation and also pain-like situations. If you can imagine the device that we normally use to evaluate this behavior, imagine basically two different boxes, [one has] very bright lights, and [the other is] a dark box. So there's a light box, a dark box, and the animal has to decide to cross to the dark side. Usually rats prefer to be in the dark. They hate being in the light.

So we'll use that aversive conditioning for the animals, to train them to cross to the dark side. Now, once they are trained, what we do is that we put a probe, which contains a lot of types of nails. They look like probes and nails that create a little bit of pain in the animal, so the animal now has a decision to make. They have to decide whether they're going to cross from the light to the dark and expose themselves to this probe that can create pain. So [in] that way, we have found that animals that are fed with our high-fat diets are really sensitive; I mean, they exhibit anxiety-like behavior, but they are also really sensitive in terms of their hyperalgesia, in this case, mechanical hyperalgesia. And those are some of the findings that we've been putting together in the last few years.

RELIEF: Great. So the animals—they want to cross from the bright chamber, where they don't want to be, over to the dark, where they feel safer. But once they're trained to do that, these little, painful needle-like spikes come out of the floor, and they have to decide whether to stay in this unhappy situation or withstand the pain. And so the animals fed the western diet choose to endure the stress rather than brave the pain.

Johnny Figueroa: Yes, that's exactly what happens.

RELIEF: Well, that's really profound. And then you said also that it's actually changing the way—and these are not rats or animals that have been injured or had spinal cord injury or any sort of injection like that. These are just raised on the diet, right, and they're more prone to anxiety and pain sensitivity. And, as you mentioned, even their brain wiring looks different, just from the diet, so that's pretty amazing. Wow. So let's bring it back to Dr. Sorge. We've shown in these animal models that diet really does have a profound influence on not only how the animals seem to sense pain and how they act, how their brain is wired, the chemicals in their bodies and their spinal cord—it's a pretty profound effect. Rob, maybe you can tell us a little bit about the Anti-Inflammatory Diet, the AID, and what can we do—let's not have all doom and gloom. Is there anything we can do to protect ourselves with anti-inflammatory foods? So maybe talk a little bit about the work you did, both in animals and in humans, looking at anti-inflammatory protective measures, and maybe we'll have some light at the end of the tunnel.

Robert Sorge: Sure, I think I can do that. So for animals, we wanted to create a diet that did have a number of anti-inflammatory foods. So we know that there are certain things that are good for us, and certainly Johnny has very good data showing that omega-3s are good. So we added some oils that were rich in omega-3s. We also added ginseng. We added curcumin, sulforaphane, which is the active ingredient in broccoli, resveratrol,

which is in grapes, so if you're drinking wine, you're getting some resveratrol. And EGCG, which is basically like a green tea extract. So, of course, you've heard that green tea is good for you.

RELIEF: Yeah, we've heard of all those things in the media, that those are all anti-inflammatory, good things, so you just basically rounded those all up and added them to the diet?

Robert Sorge: Yes. So we wanted to look for things that we knew, from a scientific perspective, had direct effects on inflammatory pathways. And so we took those, and we've tried to add them in a human-relevant amount. So a lot of times when people are testing these supplements, they give them to animals in these massive amounts; some of the resveratrol work is something like ten gallons of grapes a day. Well, we're probably not going to do that. So we tried to do it—so our green tea extract is the equivalent of about six cups a day. The resveratrol is equivalent to about a cup of grapes a day. So it's something that you could do.

RELIEF: These are doable, right?

Robert Sorge: Yes, you may not do it every day, but certainly it's something that you could do as a supplement or something like that. And so, we had our animals that were fed this American diet, and at the time of injury—so the day that they got injured—we switched them to this anti-inflammatory diet, so to mimic [that] something happened, and this is one of the treatments. And what we found is that they recovered in about a third the amount of time that the other animals recovered, so it dramatically sped up their recovery. It decreased their inflammation. Some of these animals were showing signs of pre-diabetes, and it reversed that as well in as little as two weeks. And so this looked great.

We were very encouraged with this, and so we thought, well, what could we do to translate this into people? And so, we took a bunch of older adults with knee osteoarthritis pain, and we randomly assigned them to either eat what they're normally eating, [go] on a calorie-reduced diet—so your typical diet where you're cutting calories—or [go on] what we were considering our anti-inflammatory diet, which is really just a low-carbohydrate diet. So it was similar to an Atkins or ketogenic diet, but really, they just needed to cut down on the carbs. And they were on this diet for 12 weeks.

We measured their functional pain and daily pain, and one of the big effects here is that when we asked them to do things that would cause pain in their knee—one of those things was repeatedly getting up and down from a chair—after the 12 weeks on this anti-inflammatory, low-carb diet, these subjects showed almost no pain with that functional task, which was very encouraging. The people that were on the low-fat or the calorie-reduced diet showed just as much pain after 12 weeks as they did at the beginning. And what was really cool is that both groups lost the same amount of weight, so it wasn't a difference due to less pressure on the knee—this was actually due to the actual diet itself.

RELIEF: So what's inside, not just the sheer weight of the body?

Robert Sorge: Right. And the knee is definitely a weight-bearing joint, and as you lose weight, you're going to reduce some of that pressure. But in this case, both groups lost the same amount of weight, but only one group showed a change in the functional pain.

RELIEF: Great. Well, thank you so much for describing that research, and both of you for describing that research. I'd like to come back and speak with both of you and wrap it up and bring it back to patients and what people can do in their daily life. How can we take these results that you both have found, and others working in the field [have found], and what's the message that we can [give]—how can we interpret this? And a lot of this work is still in animals, and is moving into humans? Maybe you can give us the outlook—what is the outlook for the research moving into human clinical trials, and then, what do you think people can do, just in their daily lives? Maybe we'll start with you, Johnny.

Johnny Figueroa: In terms of translating the findings—and I think Rob and I have very similar results in terms of our rat models—I think balance is a key. It's really unlikely that you will have a healthy diet 24/7, all the time, so I think that in terms of translating some of these findings, it's going to be really critical to establish a healthy diet, and to sustain a balance in terms of those components that we know are healthier or anti-inflammatory versus the ones that we already know create this chaos, in terms of inflammation. So I think balance is the key.

[There are] other findings that we've been putting together, in terms of these special diets such as [what] Professor Sorge has and omega-3 fatty acids. I think that in terms of the new technologies that are arising, genomics and metabolomics, we are now [looking at what] are the specific components of these dietary interventions that are critical to sustain recovery or promote recovery and also to ameliorate pain. So with that in mind, one of the things that I think the field is moving forward to is finding those critical components and actually preparing them for different therapies or interventions, with specific components of the diet. So I think, at least on my side, those are critical components to translate the findings—[a] balanced diet and also finding out specifically [what] are the nutrients and specifically the molecules that are implicated in these responses.

RELIEF: Right, so if we can get down to the nitty-gritty, like what are the actual molecules working at the cellular level—then we could maybe skip the whole diet and go right to those targeted molecules?

Johnny Figueroa: For people who are actually suffering from pain, I think that would be a really good intervention. [For] diets in our rodent models, usually we see that [happen] fast, but in humans, diet effects usually take a little bit longer to take effect.

RELIEF: Also, I would point out, it's harder to get humans to stick to a diet than it is to get rodents when you're feeding them. They don't have much choice. Humans are tougher, right? And Dr. Sorge, maybe you could wrap up for us, and again, just what do

you see as future directions in terms of translating to a complementary pain treatment, and what people can do today?

Robert Sorge: I'll just echo a lot of what Johnny said. It comes down to the general lifestyle change, and if enough people get on board with the [recognition that] our general diet just isn't good—that certain things do have to change. I think that will have a big impact, but again, just like you're saying, Stephani, it's hard to get people to stick to a diet, unless there is a direct reason, and so one of the things that we're hoping to start looking at is not just pain, but some of the peripheral things that diet can help as well—things like cardiovascular disease and cholesterol, and all of those things that can also be improved with diet. So as much as, in general, we want a pill that's going to just reduce our pain, diet has all of these other benefits as well. And so not only can it reduce your pain and inflammation, but [also] decrease your risk for a whole host of other things. And so I think that this is going to progress in two basic streams, where there's going to be people [who] are really trying to get these lifestyle changes accepted, and there's going to be people who are looking at the specific molecular substrates of the diet, and how we can block that. Of course, if people could eat whatever they want and block the bad part of it, that would be fantastic, but in the long run a lifestyle change is probably the best thing.

Johnny Figueroa: Right. I totally agree with that.

RELIEF: Great. Well, Robert Sorge from the University of Alabama and Johnny Figueroa from Loma Linda University, I want to thank you both so much for being my guests today at relief.news, talking about diet and inflammation and pain. Thank you both.

Robert Sorge: Thank you very much.

Johnny Figueroa: Thank you, Stephani, for having us.