Introduction and Guest Background

Hi, everyone. Welcome. Welcome to the Reversing Type 2 Diabetes Summit. I'm your host, Dr. Beverly Yates, ND. For this episode. It's my distinct honor and privilege to interview Dr.

Austin Perlmutter. He's a wonderful expert. He is the kind of doctor that we all wish we had. One of his areas of focus has been around immunology and in boosting the immune system, having the body work for you rather than against you.

And also with brain health. Today he's going to talk to us about brain metabolism and how it intersects with blood sugar and blood sugar dysregulation.

But before we dive into that, Dr. Austin Perlmutter would you please introduce yourself to our audience? I would be happy to. And Beverly, thank you so much for having me.

This is such an important topic, and I'm honored to be here and participating in the conversation. So a little bit about my background. I trained as a conventional M. D., I did my medical training in Miami, and then I did my internal medicine residency in Portland, Oregon.

Beautiful Portland, Oregon, at OHSU. But I think I realized early on, because I had access to resources through family members, my father is a relatively well-known functional neurologist that there was more to the equation than just prescribing medications to try to slow the rate of decline of people's diseases.

And that seemed so intuitive for all of you out there listening. You probably said, of course there's more to it. And yet that's really not the way that conventional medicine looks at health.

So as I was realizing there's more to this puzzle that I wanted to be involved with prevention of disease and not just maintenance of people's chronic disease management, I needed to look elsewhere and I had the opportunity to work on a number of different projects with some really amazing people.

One of those was a book called Brainwash, which I wrote with my father, and we were privileged to have that become the New York Times bestselling book.

We've had it published in around 20 countries around the world. But beyond that, I've been able to do research with others and I guess just independently trying to look at what are the mechanisms that are driving people to be so unhealthy today and what can we do beyond just telling people to exercise and eat healthier, that is actually going to work.

So that has led me to trying to understand the brain, trying to understand how the brain becomes influenced by our lifestyles and what we can do to empower ourselves and the people around us to change our brains.

And in doing so, take back control over our lives and over our health. That for most people today unfortunately, has been kind of taken out of our hands as put into a place where chronic preventable diseases are the norm.

So I think like you, Beverly, I think we can do a whole lot better. And that's why I'm excited to be here. That's so great to know. Thank you. Austin.

I couldn't agree with you more. I think we've come to normalized illness and we've got to turn this around because it's not sustainable for the health of humanity for our current generation or for the kids and all the people who come into the future. Right?

So we look at this big picture and we think about the impacts of blood sugar and the health of our brains and our energy systems. Please share with us how it is that our brains are powered.

Like we all know they have energy. Where does it come from and how does all that work? Right. Well, I guess it's first of all, important to to understand that as much as we tend to ignore this, our brains are part of our bodies.

And because of this, our thoughts, our actions, our mental health are part of our brains and therefore part of our bodies. So it's not like your thoughts and your mental health are powered by some sort of magical energy.

It's the same energy production that occurs throughout the rest of your body. It's the same ATP that you need in your brain to be able to power yourself to think clearly and potentially even to feel good about your day, that you needed your muscles to keep them moving, that you need to keep your liver metabolizing.

So why are that so important is because the brain is kind of uniquely dependent on a ton of energy. If you think about it by weight, the brain is roughly 2% by weight of our body, but it requires about 20% of our energetic and resources, and it means it's actually using up over 20% of the glucose that we consume in our meals to keep it running.

How the Brain Uses Energy

So that I think alone is a statistic that should force all of us to pay attention to how do we get the brain consistent, high quality energy. But the other thing, Beverly, that I learned recently that I think changes the whole calculus is that the brain doesn't have all that much empty stored space where we're using our brains to work on memory.

It's to process data. And so unlike, for example, our muscles and unlike, for example, our fat cells, we don't have big energy stores in our brains. There's no room for extra glycogen, there's no room for kind of fat storage.

So it means that our brains need that energy to be kind of produced and available on demand. So unlike other parts of our body, it's thought this is one of the reasons why our brains are sensitive to changes that happen with fluctuating blood sugar levels.

So all of these reasons speak directly to the point of this conversation, which is if we're looking at blood sugar issues in the world today or in the United States and you say statistically how many people have blood sugar issues and then remembering that blood sugar is so vital to healthy brain function, how many people are at risk of having brain issues because of that?

And these are statistics that I'm sure not the first time people are hearing these, but I think they're important to say we're at one in ten Americans with Type 2 diabetes.

It's pretty much the majority being Type 2 diabetes. And the statistic that we all need to pay attention to is that one in three Americans have pre diabetes and that 80% of these people are not aware that they have this.

So when you layer all this together and you say, hey, we I think care about making sure our brains work, well, I would argue it's the most important thing.

You want to enjoy your day. You want to think clearly. You want to show up for your grandkids, for your spouse, for your other partners, for your friends, for yourself.

You need your brain to work well. Then you need to power your brain with fuel. And if you're saying, well, that fuel is only as good as our blood sugar regulation and one in three Americans at least have pre-diabetes, those numbers are actually increasing, unfortunately.

Then basically everybody needs to be paying attention to this message, which is how does it blood sugar in your basically the rest of your body connect with your brain health?

And what can you do today to help enhance the quality of the energy that gets to your brain? That makes total sense. Your brain is central in your function every day.

And I think sometimes because some of these processes, often they're silent, people may not understand how much chronic issues with blood sugar completely undermined their brain health.

They might have more information, frankly, about connections with heart disease, other things around inflammation. But probably not the brain. I just think we can't say this enough.

So what are the links specifically between blood sugar dysregulation and brain issues? Well, Beverly, you're so spot on, which is we've we've kind of made some connections over the last few decades that link blood sugar issues with other diseases.

And I think this is a more general issue as it relates to the brain. So, for example, if you see people out jogging, they might say they're doing that to improve their cardiovascular health.

I think that's probably if they're going to say this is the reason I do it from a health perspective as well. I'm jogging because running is good for my cardiovascular health.

But how many of those people are out there saying I'm jogging because it is good for my metabolic health? And how many of those people are out there saying I'm jogging because it's good for my brain health?

And yet we know that physical exercise is one of the most powerful, if not the most powerful things that we can do to improve our metabolic health, reduce our risk for and even reverse aspects of diabetes.

And it can help to lower our chances of developing conditions like Alzheimer's disease, as well as potentially have been a preventive effect and a therapeutic effect on depression.

But let's talk more specifically about the connection between blood sugar levels and risk for brain conditions. So there are some very clear data from the research.

For example, pre-diabetes and diabetes are risk factors for all cause dementia, including Alzheimer's, dementia and vascular dementia. That right there needs to be broadcast pre-diabetes and diabetes issues with blood sugar regulation.

Our risk factors for the development of Alzheimer's dementia. Right now, as we sit here, as we talk, there are no solid therapeutic modalities from a pharmaceutical perspective for Alzheimer's disease.

All of the drugs that are out there are not designed to significantly impact and do not significantly impact the kind of progression. They might slow it a little bit, but nothing's really getting to the root cause mechanism.

Even the amyloid drugs, we're not necessarily seeing the level of improvement we would expect to see. So right now, our best bet for Alzheimer's is preventive strategies of which exercise and metabolic regulation and food.

Basically, things that connect to blood sugar seem to be the strongest data set. So again, to recap prediabetes, diabetes, risk factors for Alzheimer's dementia as well as Alzheimer's dementia.

But moving one step forward, which is one step back, I guess you could say, which is really where so many of us need to be focusing our attention is it's not just once you get diabetes that matters just like it's not just when you get Alzheimer's that we need to care about this.

And the precursor or the well established precursor to Alzheimer's dementia is mild cognitive impairment. So if you think about this in the spectrum of a person who is really not able to remember anything about what's happening around them, somebody with advanced dementia walked that back about a decade and you might see a person who is having trouble remembering where they put things is having trouble remembering names.

It's getting a little bit more lost, but isn't necessarily needing some sort of advanced care and certainly hasn't gotten a overt diagnosis of dementia.

And so what the research shows here is that this mild cognitive impairment, which is again a precursor to full blown dementia, that risk for mild cognitive impairment increases alongside the severity of diabetes.

So what we're talking about here is almost a dose response kind of graph where the worse your blood sugar management, the higher your risk of developing this precursor issue to dementia, to Alzheimer's disease and the last thing I'll mention here, and maybe something we can jump into in a little bit more detail is I've been thinking about this a lot, which is we tend to maybe say things are very clear when they're not quite as clear.

Blood Sugar Dysregulation and Brain Risk

We say things are not clear when they are clear, but is there a kind of very clear dose response mechanism between blood sugar regulation and brain function so we can jump into what it means to be hangry?

Right. People are a lot of people are often talking about hangry. We'll see the Snickers commercial. You're not you when you're hungry. There is a connection there between the food we eat and how we feel.

But I don't think it's exactly the way that it's portrayed. What I do think is the case is that if you work in a hospital, you work as especially in an ICU and you were just say, what happens to a person when their blood sugar level crashes?

What happens to a person when their blood sugar level goes really, really high? And so here we're not talking about maybe just the little ups and downs that happen during the day, but rather if your blood sugar plummets or if your blood sugar is in the hundreds.

Right. So much higher than it perhaps should be with regular regulation. What is your brain health going to do? And it is absolutely the case that if a person's blood sugar is 40 30, they're going to behaving some brain issues.

That's not debated, that is well-established medicine. On the flip side, people coming in with diabetic ketoacidosis or a condition that occurs more often in type 2 diabetics, which is basically it's hyper osmosis or hyperglycemic state will regularly have brain issues, confusion.

There's also a number of other brain states that come along with it. So the point I'm making here is we know in the bigger picture, blood sugar, regulation issues, diabetes, pre-diabetes, these things correlate with risks for brain health conditions.

We can talk about mental health as well, but dementia is, I think, a really important place to start. And sure, this could just be an association, meaning it just so happens that people who have blood sugar issues also have a higher risk for brain issues.

Maybe that's because they eat an unhealthy diet. They don't exercise. But when you look at this additional data which says what happens if you take an otherwise healthy person and crash their blood sugar or spike it up really high and you absolutely see changes in their brain function, then we start to say, well, maybe there's some causal mechanistic work at play here that tells us this is more important than just a casual association.

And instead maybe one of the core mechanisms that links what we do with our lifestyles, with our risk for brain health issues. That's totally making sense.

So what I'm hearing you say right now, Austin, is that if the brain is subjected to a whipsaw, right, the rollercoaster, the peaks of high blood sugar, the tops of the glycemic issue, and then the bottoms as well, low blood sugar, hypoglycemia, they're at risk.

And so the more time people spend outside of what considered a healthy blood sugar range, the more risk they

may experience. And this could show up in various aspects of brain health, whether it's mild cognitive impairment or perhaps risks for various kinds of dementia.

Is that right? That's true. I think let's jump into that for a second, because if we're considering how a person actually gets in touch with their blood sugar levels, for most people, there's kind of two ways this would happen.

One is what's called a fasting blood sugar level typical lab that you'll get with your doctor. The other one is a screening test called Hemoglobin A1C and A1C test is kind of the shorthand for it.

The fasting blood sugar is a snapshot in time. It is what is your blood sugar at the level that it was drawn that morning of the doctor's appointment, if it was actually a fasting blood sugar.

I know people sometimes don't know exactly what that means as far as what is it, what is their real fasting blood sugar. But the other piece of this, and I would say when I was seeing patients more consistently, it would be the A1 C that we would look at.

This is a screening test that looks at basically how much glucose has been added to your hemoglobin molecules. So hemoglobin red blood cells, these kind of live for about three months.

The red blood cells have a life span of about three months. So measuring the kind of amount of exposure to high blood sugar through these red blood cells gives you a sense of what were the average blood sugar levels over the last three months.

And generally speaking, we know that at a higher agency, first of all, his diagnostic for both prediabetes and diabetes, but also has its own correlations with risk for a number of other conditions And the overt manifestations that we know very well.

Or the case in diabetes is cardiovascular issues. Microvascular other issues. So kidney problems are very common, higher risk for infections and amputations, very common, higher risk for heart disease or stroke.

Obviously, stroke is a brain related condition issues. So vascular issues in the eye are very common. So all of this is well known. What we know about is that a average higher blood sugar.

So what we were talking about here in the upper hundreds to hundreds, that there is a strong correlation with risk for disease. But what you're alluding to here, which I think is so important to understand around the brain, is that it may not just be whether the blood sugar is high, and rather it's a question of how consistently is our brain getting access to the amount of glucose it needs to allow it to function appropriately.

Because coming back to what we've already established, the brain doesn't have a whole lot of reserve of blood sugar, which means it really needs to have access to consistent levels of blood sugar from the blood stream.

So if the blood stream levels are going up and down exactly as you described, whipsaw, there's concern that this may actually be a independent issue. Even if and this is so important, your agency is completely normal.

You could have half the time too low, half the time too high, and all of the time going way up and down and it would still read normal, which is really interesting to think about.

So even though the hemoglobin A1 C is in theory a snapshot of what happens over a three month window, it's still only a slice and it doesn't tell you any real time data as to what's happening in any given day.

So let me take this just one step further. This all seems mechanistically to be a concern, but there was a paper that was published by Yale researchers recently, and it suggested that when blood sugar levels whipsaw, that that variability is connected with oxidative stress and inflammation.

And so having highly variable blood sugar levels is thought to have a negative impact on our bodies and on our

brains by basically increasing risk for oxidative stress and inflammation.

And these are pretty well-established to be true of the mechanistic processes by which our cells and importantly our brains get damaged, increasing our risk for a number of conditions dementia, depression and other mental health conditions.

So the point you make is a really good one and it's all the more reason to start paying attention to what is happening in your body at a level greater than what you can get from just a simple point in time once every couple of years.

Exactly. Thank you for doing a great job of walking us through and peeling back the layers here. I think that the information people get around their fasting morning blood sugar numbers and their A1 C is part of the puzzle.

It's not the whole story. And thanks for the detail around why if you get a pat on the back around your agency and still might not be telling you what you really need to know, you know, if you're on that blood sugar whipsaw, that roller coaster that's not good.

HANGRY should not be the new normal delivery. All right. Cool. Cool. So what are the pathways by which blood sugar issues, poor glycemic regulation or just a variable blood sugar response is right?

How can they do damage to our brains? Yeah, well, this is a really interesting question as well. I think when we talk about the brain, it's important to understand that even though it is part of and absolutely connected to what is happening in the bloodstream in the rest of the body, there are some interesting, unique aspects of how the brain gets access to data from the bloodstream from the body.

Best example of this would be we now understand there is a gut brain connection, and so data in the gut is able to change what happens in the brain, not because, you know, necessarily the molecules in the gut directly get into the brain, which can be the case.

But because there are a number of pathways, for example, the vagus nerve, the immune system by which data can be translated from the gut into signals that the brain can respond here.

So while we've talked here about the glucose part of this, I think that it's not just the actual access to the fuel in the brain is a reflection of what's in the bloodstream.

That's important to talk about. So it is probably the case that what's happening is a lot of things in the rest of the body as a response to the metabolic dysfunction that then leads to issues with the brain.

So let me give you an example. One of the kind of core mechanisms that is well established in diabetes is in type 2 diabetes. You build up a resistance to the molecule insulin and in a homeostatic state or in a state of non diabetes, you would release insulin in response to higher blood sugar levels.

That would happen after a meal. That insulin facilitates the removal of glucose from your bloodstream and pulls it into cells as people become more and more diabetic.

Blood Sugar Variability, A1C, and Brain Damage

It's thought that the cells themselves become resistant to insulin, meaning they the insulin's there knocking on the door saying, hey, we're here, we've got the glucose, you ready?

And the person behind the door in the stall says, No, no, we're good for now and we don't need the extra fuel. And also, I'm not listening to your signal.

So the combination of these two things leads to high levels of glucose and high levels of insulin in the bloodstream. So what's interesting about this is could insulin resistance develop within the brain?

And there are now researchers, Suzanne Lamont is one of those researchers we had a chance to talk to a couple of years ago who have proposed that Alzheimer's disease actually represents type three diabetes in that there are shared mechanisms between diabetes and Alzheimer's disease that relates to insulin resistance.

Insulin, we don't know how much is produced. It's possible that a little bit is produced within the brain, but it's almost certain that the vast majority of it is produced outside the brain and needs to get into the brain to do its task.

Now, here's the thing that most people don't know. We think about insulin as key to regulating blood sugar levels, maybe regulating fat deposition. It's another role.

But in the brain, insulin turns out to be involved with neuroplasticity. It is a kind of a anabolic growth factor, which we know, but in the brain it's a neurotrophic.

And that means that insulin is a signal for neurons to both grow new neurons and to make connections between neurons. So why does that matter? Well, if we're starting to get insulin resistance and that resistance gets to the brain and our brain has a relatively low access to the insulin it needs, because it just maybe saying, oh, we don't need so much of you, the receptors don't get as sensitive to it.

You could be missing out on the signals that you need to create connections between neurons and create new neurons, both of which are essential mechanisms in the prevention of conditions like Alzheimer's.

And it turns out maybe key mechanisms in mental health conditions. So mechanism one, I guess I would say here is the interplay between higher blood sugar levels and insulin resistance that may translate into brain problems.

There are a couple of other ones that we could get into, and some of these are a little bit more technical. I think inflammation is an important one to discuss so we can jump into that one.

There's also more of a mitochondrial issue, a metabolic issue, and so a couple of different pathways by which this may develop, but we can go to whatever you think would be most helpful next.

I think the inflammation one is particularly interesting because it speaks to mental health and Alzheimer's disease. Okay. I think talking about both of those.

So why don't we start out with inflammation these and then with mitochondria, because we've had some of the speakers talk a little bit about inflammation from a completely different angle and about mitochondria, but again from a completely different angle.

We want to give people as much as we can a 360 view while we're here. Great. So let's jump into the connection between inflammation and blood sugar metabolism and brain health outcomes.

Most people have heard about inflammation. They generally think about it in a kind of negative connotation, which is inflammation is bad. And I really wanted to make sure that we dispelled this myth that information is bad without inflammation, we'd probably, each of us die within 24 hours because inflammation is is it's not good or bad.

It is just an essential part of our immune system. It's like saying T cells are bad or B cells are bad. You need those. They're essential. Can they create problems with autoimmunity?

Of course they can. It doesn't necessarily mean that we should label them as good or bad, and inflammation is just like that. Inflammation is a natural process in our body, in which our body responds to a perceived threat.

It creates a kind of symphony of different molecules, activates a whole bunch of different blood cells, and in the best of scenarios, addresses the threat and removes it in the worst of scenarios.

It doesn't address the threat and continues to kind of feed on itself, creating this low level smoldering inflammation that is strongly associated with risk for basically every chronic disease as well as dying early as well as disability.

So all the things we don't want, and that's the version of inflammation most people are talking about when they're just kind of broad brush, painting it with a negative lens.

It is just important to recognize the goal is never to shut off inflammation. It's simply to have it respond to what is necessary and then go back to a more quiescent state.

So with that said, how does inflammation map on to, we'll say first metabolic health and then we'll go to the brain. It's depending on who you listen to, depending on the study you read.

There is either a directional relationship between metabolic health and increase inflammation, meaning worse metabolic health increases inflammation or inflammation increases or decreases metabolic wellness.

I'm going to go ahead and say yes and yes. It seems like both of these things are happening. And so there's some pathways that we could talk about by which these things seem to occur.

But the bottom line is people with metabolic dysfunction tend to have higher levels of inflammation. People with higher levels of inflammation have a higher risk for metabolic dysfunction.

And so if you are a person with poor metabolic health, there is not a slight chance that you will have some degree of smoldering, low level inflammation.

And maybe one of the best ways to demonstrate how solid that connection is is talking about fat cells. And before I get into this, I'm just going to say I think the way that we have talked about fat and obesity kind of sucks.

It's tend to be blaming people for having extra weight, calling people that I don't think that's helpful in the least. But what I do think is helpful is saying that just like every other part of your body, you can have cells that are healthy or unhealthy and that cells themselves are basically their repositories of energy.

And and this important thing, they do a number of other things within our body. They produce a number of chemicals that send signals throughout the body and to the brain.

So these are called adipose kind of fat cell molecules that transfer signals depending on how the state is deposited, depending on where it is deposited, those signals from the bad cell can be healthy or unhealthy.

And when they're unhealthy, they tend to be inflammatory signals. So if a fat cell is kind of packed full of fat in the wrong spot, and in this case, it's usually when we've overwhelmed all the other fat storage places where we have we filled up all of our muscles and other places.

Well, I should say we filled up our typical fat stores with energy. So now we're putting the fat places that shouldn't be. So we're putting the fat in our muscles. We're putting the fat in our liver.

We're putting the fat around our organs. That's the fat that tends to be more inflammatory. And that is a reflection of a number of things. But it is kind of the emblematic signal of metabolic dysfunction.

So when we're getting into these scenarios where the fat cells are being put in the wrong spaces, where they're getting the wrong signals and therefore are producing unhealthy signals, this is strongly associated with inflammation.

And it's thought that this may be one of the reasons why there are connections with higher BMI, which is a very imperfect measurement of these fat cells, but specifically fat cells that are around organs.

We call these visceral fat production and risk for brain health issues. It's the inflammation produced by those fat cells that seems to increase our risk for brain health issues.

So here we've said metabolic health connected to inflammation. One mechanism is through the production of

inflammatory molecules that come from fat cells that are overloaded because there wasn't anywhere else to put them.

And also because sometimes there's a correlation between our dietary choices and how that fat gets deposited. So I know it's a little bit technical, but that's kind of one of the major pathways.

The other question, though, is how does inflammation then influence the brain? And if we want to bring this full circle, how does the brain then influence our metabolic choices?

Right. Because our brain, depending on how it's being structure, is going to tell us, am I going to reach for the unhealthy food? Am I going to go exercise?

I'm going to sit on the couch and watch TV for the next 4 hours. So inflammation in the brain is really where I spent a lot of my time the last two years, where I published research.

That's where I've tried to bring attention to the mechanisms because we still exist in a world in which we think about the brain as separate from the body.

The mind is separate from the brain and all these things that are myths that don't make any sense to me, but I think make sense when you don't think clearly about what's going on here.

If you think about what the brain is, you have, as I said before, about 2% of around, let's say, a couple pounds worth of your body.

Inflammation, Mood, and Brain Health

This is going to be a network of billions of neurons and other cells, trillions of connections between these neurons that are powered by the glucose as well as to some extent, ketones and other energy sources that come from our diet.

But this isn't some sort of a magic process here. It is going to be constantly influenced by what happens in our bodies. What are the signals from our bodies that tell our brains, Here's what's going on and here's how you should behave differently while inflammation turns out to be a major one.

So this helps to explain why inflammation is a well-established risk factor for development of depression, that higher levels of inflammation seem to induce feelings of depression.

And the example that I always give because it's one I personally experience and it's very clearly stated in science, is how is your mood when you get sick, when you come down with an illness?

For me, I don't feel great. I don't feel as motivated, I don't feel as interested, I don't feel as happy. And this is exactly what the science is showing us, is that if you increase inflammation in a healthy person by giving them an injection of what is basically a piece of a bacterium, they feel depressed.

So it's fascinating stuff. You can create feelings of depression by increasing inflammation. And all of this is just saying this is one example of how we know that inflammation influences brain health.

This was a major topic of brainwashed. The book that we wrote. The bottom line here is to understand what happens in the body influences the brain. Inflammation in the body appears to influence the brain, and one of the drivers of this inflammation appears to be metabolic dysfunction.

So I know a very long winded explanation of some of these topics, but I think it's important to understand how all of these things come together. Otherwise we're missing the bigger picture.

I agree it's important to unpack these things and to give people a robust, thorough answer and not just the

superficial two or three sentences. And then they're like, Well, wait, because, you know, you've hit on a lot of the pieces that are often missing so that people can understand that inflammation is not necessarily the enemy.

There are normal processes in the body that invoke inflammation. Like if you cut your finger, you absolutely want it to knit up. And inflammation is how that happens. Right?

So with this in mind and we think about the role with that, I'm glad you talked about moods and how people feel because again, people are often blamed for their problems and depression can be a prominent part of the health journey when someone has pre-diabetes or Type 2 diabetes, really any blood sugar dysregulation, they can go with metabolic syndrome, polycystic ovarian syndrome, etc..

Will you please share this something you had talked about before? Before we move on to our next question, your thoughts about mitochondrial function, because the mitochondria, the powerhouses of the cell, they are the organelles.

So if you share with us about mitochondria while we're here, that'd be great. I mean, I think it's it's in you can't really separate metabolic health from mitochondria because if you think about how nutrients in our food are actually converted into energy, I mean, the majority of it is happening at least the high efficiency parts of it are happening within the mitochondria.

So these are the kind of primordial bacterial cells that came into our ancient cells and basically came onboard as designated energy production factories.

They turn out to do a lot more. For example, they create steroid hormones, they're involved with cell health. But for the purposes of the metabolic health discussion, you can't have that metabolic health without good mitochondrial health.

And so there are a number of kind of pathways by which researchers have identified mitochondria might be getting damaged by our modern day diets, our modern day metabolically unhealthy lifestyles.

Maybe the easiest one to understand and I'm not necessarily saying this is the only one, nor is it necessarily the absolute most correct one. But if you just think about the mitochondria or mitochondria and if it's tasked with basically converting fuel into energy and it has an absolute excess of fuel where it's just constantly being inundated with calories, food.

So you're eating all day long, you're eating very high calorie foods and potentially you're eating foods that are by themselves. Not great as far as how cleanly the mitochondria can process them.

Then on the back end of this thing, the mitochondria are going to have a build up of kind of the waste products of metabolism. And on the front end they're going to have a buildup of kind of energy that can't be adequately burned because they're just overloaded.

So one of the important things to know about mitochondria is that this is where oxidative energy production occurs. So the electron transport chain, oxidative phosphorylation, this is the way that we're able to convert a molecule glucose into a bunch of ATP.

It's the most effective way to convert basically fuel into a high number of ATP. But in the process it creates oxidative stress and this process seems to be exacerbated when mitochondria are overloaded.

Oxidative stress by itself may be a driver of metabolic functions that you might get a feedforward cycle, but oxidative stress, which is basically the buildup of certain tiny molecules that can in essence rust your cells more rapidly, is a mechanism by which we think many diseases are worse.

And so the bottom line to all of this is that if you're trying to understand metabolism, which is the idea of taking energy from basically outside the body, because we don't know how to do photosynthesis as far as I know, and

converting it into basically building blocks for cells, data for cells, and also fuel, then you have to have these mitochondria healthy.

Last thing I'll say about this, which is again, something that when I learned it, I was thinking to myself, this is absolutely incredible. When we think about the brain I mentioned somewhere in the neighborhood of, let's say, 80 billion neurons, somewhere in the neighborhood of, you know, each of those neurons might have a thousand synapses, which means you're in the neighborhood of a billion trillions of synapses.

It turns out that an individual neuron can have thousands, potentially many more mitochondria. So if you think about how many opportunities there are for something to go wrong, when you look at mitochondrial health and brain health, it is the number I looked at.

I think it was a quadrillion. So it's a whole lot of zeros to try to understand how many mitochondria you have in your brain. And to that end, how important it is that they're working well.

So there's been a lot of research now focused on what are the interventions that improve mitochondrial health. The ranges from everything from intermittent fasting to ketosis to other strategies that kind of give the mitochondria a break and let them clean themselves up, potentially form new mitochondria and get rid of the old defective ones.

Something else that's interesting about mitochondria is they're constantly undergoing fusion and fusion, which sounds like nuclear reactions, but it's actually just the breaking apart of one mitochondria into two or two mitochondria coming together and fuzing into one.

Fascinating stuff. The bottom line is that every vote that you take from a lifestyle perspective, whether it's food or exercise or even sleep, is impacting your mitochondrial health.

And that's probably one of the major mechanisms by which metabolic dysfunction occurs. Absolutely. Yeah. You know, I'm thinking of some of my earlier research and information and learnings about mitochondria and their importance, let's say with cardiovascular function, with congestive heart failure, etc., certainly with diabetes.

And when it comes to any of brain health concerns or trying to, you know, mitigate damage to the brain or simply protected muscles, athletes, whatever it may be, whatever state we are in life, the energy functions, the mitochondria and metabolism are always intimately, you know, tied together.

So thanks for sharing that with us because I think it's important that people understand and again, these aren't the most, you know, direct or common conversations for the general public.

And I'm well aware that probably about 20% of our audience is our fellow colleagues or other health professionals. So I'm glad that you explained that.

Okay, so now that we've gone through these topics and pathways, what are the best ways to restore and to protect healthy brain metabolism? Yeah. You ever get into a topic that depending on who you ask, people are going to have different perspectives.

And I think that it is absolutely the case that today we have a polarization in people's perspectives on anything that's going to touch on diet, right?

So everyone's got their best diet. I'm going to try to be a centrist here and try to stick to what I know as far as what the research would indicate are the effective strategies that relate to metabolic wellness and specifically to brain metabolic health.

I will say at the start, most of the research around interventional trials, meaning where they've taken humans and they've done something to them pre and post measured things around the brain and brain metabolism is very limited, meaning we just don't have much data.

There. We have a whole lot more data around peripheral metabolic health. So Type 2 diabetes, for example, and what we can do to reverse aspects of Type 2 diabetes.

So some of what I'll say I guess is generalize to the brain from what we know happens in the body. But there are a couple of data points for the brain that I definitely want to bring up.

So the first thing I'll say is, as much as it tends to be over complicated, I think that majority of our health lifestyle is going to be the major driver.

And so while I'm certainly somebody who has prescribed insulin, well, I'm certainly in favor of, you know, looking at medications like was empiric and metformin and all these other interventions.

I think that as we look at what's happening in the world today, those can't be the solution that we look for. Because to basically assume that the only scenario that works is that we wait for people to be so sick they require pharmaceuticals is kind of giving up on the most important part of this, right?

Mitochondria and Cellular Energy

How do we live healthy lives that don't require us to, you know, get through the end of the race with the diagnosis before we start taking things seriously?

So what do I know as far as lifestyle modification for metabolic health? It's it's really the basics. As much as I would love to say that there's some incredible hack, it's certainly exercise.

I think that cannot be overstated. Physical activity is absolutely vital to preserving metabolic wellness and the reason I say that is because what happens to our bodies when we exercise is so much more than just burning up some extra glucose.

So in the context of mobilizing, let's say your muscle groups, your leg muscle groups with resistance training, you're actually translocated more glute receptors to the periphery of the cells, which allows you to pull more glucose out of your bloodstream and into your muscles.

These mechanisms are really stunning. There's another important mechanism, which means that in the context of exercise, you produce muscle specific molecules that can go out.

They're called mayo kinds and actually have an anti-inflammatory effect and potentially increase insulin sensitivity throughout the body and potentially in the brain.

So mechanistically, I think it's absolutely vital. I think if a person is looking at how they can improve their metabolic physical activity turns out to be so much more than just trying to lose weight because actually it isn't a very effective weight loss intervention when done on its own.

But there's one study that's been done recently, which is an interventional study looking at humans and whether exercise could improve brain metabolic sensitivity and what they found is in this study they had people exercise for a couple of months and they looked at what happened when they gave them intranasal insulin, which is an interesting thing.

But yeah, just bear with me here for a moment. So we know that insulin has this really important role in the brain. We also know that as people develop metabolic dysfunction, they can become more resistant to insulin.

The insulin, the bloodstream has a harder time getting to the brain. So one thing that you can do is basically give somebody insulin into the nose to see what happens in the brain.

And so in this recent study, they were basically looking at what happens when people exercise. They Gibbon's insulin. And what they shown is that people had different brain responses to this insulin after they've exercised.

So basically indicating that there was a improvement. And in a reversal of that, I guess, metabolic dysfunction in the context of physical activity. So again, we don't have all that much data specific to brain metabolism, but that's one of the few studies, and I think it's certainly something we should be paying attention to, especially because we know peripherally it's really helpful and we know that people who exercise have much lower rates of certain brain related conditions.

Exercise is a a huge benefit for prevention of Alzheimer's disease. It's actually been shown to improve aspects of neuroplasticity and cognition in people with existing brain dysfunction.

So it's super important. I will say, though, one last thought on this. People all have their ideas as far as what the best exercise looks like. And if you are somebody who doesn't move your body often as a doctor, as a person, I want to make sure that I tell you my goal is not for you to get out and run a5k today.

My goal is just for you to find something that you enjoy and that you can move your body and literally stretching, Pilates, walking, all of that stuff is amazing if you're not somebody who's doing that to start with.

So I don't want to get stuck in this framework of saying, you know, it's got to be 150 minutes a week, otherwise it doesn't matter. I think that's that's nonsense.

So just moving the body that seems to be really important for improving metabolic dysfunction by way of improving insulin resistance, by way of improving glucose uptake, by way of making you metabolically healthier.

So that's one happy to go into. Any strategies around there if you'd like. But the other big one is obviously diet, and this is like I said, things get very controversial, so I guess I'll jump into this in whatever way is most helpful for you as I'll let you drive that conversation.

Yeah, interesting in today's world how complicated we made the entire notion of nourishing ourselves, right? People have whole wars about nutrition and how to eat, and I agree with you, but your points about exercise, I've always felt that the best exercise is the one that you will actually do that wins. You know, people have pain.

They have all kinds of things that sometimes make it complicated. Maybe going out for a walk or a run or a jog may not be safe where they live. Maybe the weather's terrible, know be too hot or too cold.

There's all kinds of constraining factors, right? Maybe their home space isn't really large enough to do other things. It might be more complicated, etc.

I just think we we just got to get back to the basics as quickly as we possibly can. And when it comes to nutrition, yeah, again, people have to find what nutrition works for them.

I've personally found there's no such thing as one size fits all nutrition, you know, and 30 plus years of clinical practice. I've gotten away from giving people a list of Thou shall eat this and thou shalt not eat that.

Because from a blood sugar point of view, never mind that other things like their mood, whether or not it agrees with their belly, you know, they have a lot of gas and flatulence, bloating.

Everybody doesn't react the same to food. We can certainly watch that with blood sugar reactions. So it's okay. What are your thoughts about CGM continuous glucose monitors?

Because as you can imagine, throughout our Type 2 diabetes reversal site here, we've been talking on and off about the use of continuous glucose monitors, CGM to really help people get actionable insights into what their blood sugar is doing.

So I'd love to get your thoughts. Well, let me let me kind of describe the two, I think opposing perspectives. So on the one hand, the opponents of CGM monitoring would say this was a technology that was developed for people with diabetes.

It hasn't been proven effective in people who do not have diabetes. It creates additional concerns, data that isn't helpful and people don't know what to do about it.

And also it may not be as reliable as people think it is. So these are always an additional cost, I should say, reasons why people would be opposed to people using CGM who don't have diabetes.

Now, on the flip side, there are people who would say, let's look at the rates of prediabetes, metabolic dysfunction. As I said before, we're talking about maybe 100 million people in the United States with undiagnosed prediabetes in addition to those who already have diabetes.

So we're not talking about a small fraction of people. We also know that probably about 10% or less of people are metabolically healthy. So I think if you want to make the case that, oh well, it's only helpful for people who have a preexisting issue, well, most of us have a preexisting issue.

And I think that's a tough pill to swallow. But it's true.

Restoring Brain Metabolism with Lifestyle and CGM

And one of I think the most helpful reasons why I've enjoyed CGM is if you don't do this, you're kind of relying on a health care system that is set up to wait until things get so wrong that you have a diagnosis before it does anything.

And that fundamentally just doesn't make sense to me as the strategy, right? So if you're comfortable to say, I'm going to wait until I have a diagnosis, until I have a nice disease, you have to also be comfortable working within a system that is not designed to actually get rid of said disease, which is why most people over the age of 50 have at least one chronic disease diagnosis and or on at least one medication because we've set things up for that being the norm.

So I think if the goal is to be preventive in a real way, then you have to have data that comes in before you have a diagnosable disease. And CGM is, from what I can tell, one of the best ways to get real time insight into what your blood sugar is doing.

The other thing that I really enjoyed about CGM or have been enjoying, I've used them multiple times is you can learn what is unique to you and how fascinating to know that for me, for example, if I ate some brown rice, my blood sugar went up pretty high.

Even though it's brown rice, which is supposed to be super healthy, whole grain, all the extra fiber. But when I ate the brown rice with a piece of salmon didn't really go up that much.

So these are insights. So you think, Oh, well, I didn't necessarily know that. And it's not necessarily the case for everyone else. When I'm with family members or with my partner and we eat the exact same meal, we have different blood sugar responses and even beyond the food, let's say, I mean, we're all going to eat food.

That is, we're not really going to argue that point. So we're going to eat our meal. But then what comes next? That's actually really interesting and it's only something that you can really learn if you're using CGM.

So you eat your meal, you realize that your blood sugar is going up more than you expected. And again, the naysayers would say, well, maybe that's a normal excursion, but we're now learning that the ups and downs may not be all that helpful.

So maybe you say, well, my blood sugar is going up way more and staying up higher than I would like. Maybe now this is an opportunity to go for a walk or meditate.

We know that stress has a major role to play in blood sugar regulation. I can see in real time what that does to my blood sugar. And I think even beyond the question of what does that do for my overall health, it is super empowering to have the biofeedback and know that my actions, my lifestyle actions have an immediate and a

powerful effect on what's happening with my blood sugar.

So where I come down to on this is I think dreams are a really powerful tool. I think there are instances in which they're not great, so certain people may respond to them in a way that increases kind of neuroticism around what you eat and exercise, and that's not a healthy thing.

I think that in an optimal scenario, people are doing this with assistance. I think that's really important. You know, I think about even sleep tech, right?

So or earrings and other sleep tech wear or genetic testing that is readily available to the public where it's all of a sudden you're getting this data that you don't know what to do with.

It can be really stressful. So I think it's really important to have it set up as a scenario where if you're getting information that concerns you or that you don't understand, there's somebody around to help you walk through that and understand, Hey, this is or isn't actually a concerning thing.

This is what we'd expect to see. And maybe the most important part of the whole thing is if you get a CGM, that's your first time that you've ever actually learned about your blood sugar.

How do you know when you need to actually see a practitioner for that? And how does a practitioner know how to interpret the CGM? And those last two things aren't quite dialed in yet.

So something that I know many people are working on, but big picture wise, with those caveats, I'm in favor of learning more about our bodies and I think CGM is going amazingly great.

I agree. I agree. I do think we had the forefront of making this more understood, both for the general public and for our colleagues as health professionals and medical experts.

And I think over the next 5 to 10 years, we'll really start to close those gaps as we just kind of in a way crowdsource some of this and find out what are the best practices in particular for those who already have the problem around blood sugar, something diagnosed as well as those who may have a strong family history and who are worried. And they're like, I want to dodge this.

I do not want this outcome for me. How do I make it different and find out if I'm starting to lose blood sugar control, especially on the windows around, let's say, menopause for women and and reports where men's testosterone levels really start to vary.

It's kind of like we have the bookends of life, you know, in 15 years and puberty in middle school, we get that rise and change in our sexual reproductive hormones.

Then as we exit that window of active, you know, fertility hormones can shift whether or not we do any bioidentical hormone replacement therapy. Still our sensitivity to insulin and other things that shifting to right now might be a great time to have a CGM and catch it.

Like you're saying, before we have the problem, which is a different mindset because that's not what gets rewarded right now. Right. Well, let me just say one more thing to that, because something that I didn't necessarily address, but I think is important is, you know, really I was talking about what is the utility of CGM in a person who is either pre-diabetic or just a I guess, what we call a metabolically healthy person.

But if you think about what it does for diabetes, so it's already being used in diabetes. That's where it got it started. But I do think there's still so much more that can be gleaned from it once we have higher level algorithms.

So what I mean by that is so I've had patients come in with download the CGM data and it's just kind of it's overwhelming. And so you have to you have to parse out trends, right?

You say, well, looks like you're having high blood sugars in the morning or it looks like you're getting low blood sugar is at 2 a.m.. So this is really helpful because obviously one of the goals is not to have very low blood sugars for most people with diabetes that is that's really the scary thing because low blood sugar from a brain perspective is incredibly dangerous.

A little bit higher in the hundreds. Maybe you're not as concerned until gets much higher than that, but low blood sugars can be deadly. So CGM can start telling you about where are things getting too low and help you to mitigate that.

But beyond where I'm really excited is CGM is when coupled with higher level algorithms, can start telling you insights about what does or doesn't work with your body.

And you know, so much of your diabetes management, at least in primary care, is just trying to cover blood sugar levels with doses of insulin, right? So you have your long acting insulin, you have your mealtime insulin and you can get fancier and you can get a pump that you can get all these different ways to try to keep things a little bit more steady state.

But I think what is most often ignored is this idea that each person has an individual response to different types of food. And the goal, I feel maybe not the primary goal, but eventually the goal would be to say, Why is it that you're needing all this different insulin for different types of foods?

And to the point I guess, of the summit is are there things we can do to reduce your insulin dependance, even if it's just reducing the amount of insulin that you need potentially to get you off of insulin altogether?

And in order to do that, you can't just be saying, well, the goal is just to make sure that whatever you eat, we're covering you with insulin. That's the first stage risk mitigation approach.

And I think CGM gives you some of that opportunity, right? You can start to say, well, it's not just that the massive bowl of frosted honey nut oat clusters in the morning is increasing.

Your your blood sugar is so high that we need to give you some more mealtime insulin. It's actually the question of saying, well, maybe that in and of itself is one of the reasons why you're having such poorly controlled diabetes.

mechanistically not just that the blood sugar is going up high and we have to chase it, but rather saying there's that high level of basically crazy glucose, sugar rush is creating damage to your insulin, it's creating damage to your inflammation.

And that by saying we want to actually not just cover that meal with more insulin, but change that meal so you don't need as much insulin. So we're not unnecessarily creating an insulin resistance that seems important to you.

And CGM allows for that level of understanding. So my hope here is pretty soon we'll start getting these algorithms that will be able to tell us based on your CGM data, here's what we could recommend as far as a diet and lifestyle modification plan to help reverse the course get you off of the amount of insulin you need, start potentially taking away some of these other medications.

What's super interesting is that we've seen that several groups, the United States, have now been able to demonstrate that by dietary intervention, by lifestyle intervention, you can do just that.

I think that's incredible. Removing insulin from a person's protocols, getting a person to a place of going from being a diabetic to not being a diabetic are things that are happening now and are just so exciting as far as giving hope to and just empowering people to know that there is more that can be done than just constantly chasing blood sugar with insulin.

Absolutely. In the case of Type 2 diabetes, this is, you know, a reasonable approach. And I'm excited about that progress because I really feel like that will be a large part of how people heal so often.

Thank you so much for being here with us at the summit. All of your insights, your gems, your tips, and not only your point of view, but your willingness to explain behind the scenes, giving people a real sense of what goes on behind the curtain so they can understand, you know, okay, where am I relative to this what did I actually know about this before?

What did I just learn? And then, you know, like I've been saying throughout our summit time, friends, as you listen to these wonderful experts like Dr.

Austin Perlmutter, please share this time with everyone that you know who cares about their health or who has this problem or is looking to prevent it, because we're talking about millions of people around the world who are concerned or who are part of this right now.

All right. If people would like to connect with you often, where can they find you? Easy to spot would be my website. AustinPerlmutter.com. The I sent out a newsletter probably about once a week, just filled with all the tips and thoughts I have primarily around brain health, but certainly around metabolic health.

And some of the other topics you brought up today. All right, great. Thank you so much for being here with us. And, you know, we look forward to all of the things that you're up to now and other things in the future.

I hope people connect up with you. Take good care. Appreciate it. Thanks for having me.