



Conscious Life presents

Hormones and Mental Health

Guest: Dr David Perlmutter

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[00:00:09] Meagen Gibson

Welcome, everybody. I'm Meagen Gibson, your conference co-host. Today I'm speaking with Dr David Perlmutter, a board-certified neurologist and six-times New York Times bestselling author. He serves on the board of directors and is a fellow of the American College of Nutrition and currently serves as the director of neuroscience research at Bryan Therapeutics.

His New York Times best selling book, *Drop Acid*, focusing on the pivotal role of uric acid in metabolic diseases, is out now. Dr David Perlmutter, thank you so much for being with us today.

Dr David Perlmutter

Meagen, I'm delighted to spend time with you.

Meagen Gibson

You have extensively discussed the gut-brain connection. How do hormones play a role in this connection? And what are some of the key hormonal factors that can impact mental health?

Dr David Perlmutter

I guess we could write a book about that. I think your intro says that I do a lot of work relating the gut to the brain. I think then the question is, how do hormones, and I presume you're talking about sex hormones, interact in this whole system. But there is one hormone that I think is really fundamentally important as it relates to the so-called gut-brain/brain-gut axis, and that is the hormone cortisol.

Cortisol we talk about as being a stress hormone. It's secreted when we are preparing our bodies for fight-or-flight, if we find ourselves in a situation of threat, that we prepare ourselves by shuttling blood to our muscles and away from the digestive system, et cetera, so we can be better in touch with our abilities to protect ourselves.

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But chronically, when we are experiencing higher levels of cortisol, because we are chronically experiencing low grade stress, it doesn't have to be being chased by the lion, but just the low grade stress of our daily lives, of the comparisons that we make of ourselves to others on social media, the threatening nature of the evening news, pretty much the challenges of our modern world lower levels of cortisol are expressed, but they're still higher than is healthy. Higher than what we would consider to be a normal baseline.

Now, to get back to the original topic, how does that threaten this connection between them, the gut, and the brain? Why might that pose a threat to our brain health? It does so because cortisol itself does a couple of things that aren't good.

First, it changes the array and the functionality of the organisms that live within the gut. Normally, we have an array of organisms, a wide diversity of organisms, that do various good things for us. They make various chemicals like vitamins and neurotransmitters. They are also involved in the maintenance of the gut lining. Cortisol threatens both of those, so that the products made by our gut bacteria, including the neurotransmitters that are involved in things like mood, things like serotonin, et cetera, are disrupted, and that can set the stage for changes in mood.

The other thing is very important, because it's not just mood related and brain related, but really body related. And that is the changes in the gut lining permeability. We have this gut lining, this gut barrier, if you will, that works to keep things out of the systemic circulation and in the gut where they belong, things like toxins and bacterial components and a variety of chemicals that find their way into the gut.

When that barrier is compromised, as can happen when the hormone cortisol is elevated, those harmful components can get into the bloodstream, and even before they get in the bloodstream, they can get into the immune system that lines the gut and increase, for example, inflammation. Inflammation is a bad thing in this regard, not that it's always a bad thing. It is not. But higher levels of inflammation are associated with things like depression, anxiety, Alzheimer's, Parkinson's, and multiple sclerosis, for that matter, as well as cardiovascular disease, diabetes, obesity, and even various forms of cancer.

So in this way, the hormone cortisol, when chronically low-grade elevated, can really threaten our health in the long run. Again, higher levels of cortisol in the acute situation are probably life saving. That's a good mechanism. But when we constantly are exposed to stress, it leads to basically a chemical situation that sets us up for some pretty unfriendly experiences in life, like mood disorders, depression, anxiety, and even cognitive failure like we see in Alzheimer's disease.

Meagen Gibson

Absolutely. You talked about chronic stress and cortisol on... Specifically cortisol and the effects that it has. But it also has, and you alluded to this a little bit, but I want you to go into it even further, the way that the other hormones in our system are both produced, released, absorbed, understood by our bodies and especially in the gut. If cortisol is creating havoc, what are the other kind of hormonal systems and then downline mental health effects that are going to happen?

[00:05:53] Dr David Perlmutter

That's a really good question, I think what you touched upon is really very important, because as we look at hormones within an individual, we look at some of the important... Well, not that they're more or less important, but things that people are familiar with, let's say estrogen, specifically estradiol or E2, progesterone, testosterone, et cetera. What you mentioned is actually very important that we have to look at not just how these are produced, the sequence in which they are produced, the enzymes that regulate their production at various points along the way, how our lifestyles impact the functionality of those enzymes. That then is translated into the functionality of these hormones. And even take it as far as recognizing that various nuances of our genetics can even influence the levels of these hormones and even their metabolism.

Not to mention... Why do people say not to mention then they mention what they're not to mention?

I think it's really relevant for the time in which we live, the effect of various chemicals in our environment in terms of intercepting or blocking the way that these hormones do their job, and even the levels of those hormones that are available within our bodies.

For example, we know that aged-matched men, meaning if you looked at a man 40 years ago who was, let's say, 50 years old, and a man today who's 50 years old, that overall testosterone levels have plummeted by 50%. Now, we haven't changed genetically in that short period of time, obviously. What has happened is we've been exposed to a series of chemicals in our environment, manmade chemicals, like forever chemicals, the PFAS, the phthalates, et cetera, that are profound endocrine disruptors, that have severe effects upon the production and the metabolism of various hormones within our bodies.

There are chemicals that we are now exposed to on a daily basis that inhibit testosterone, specifically, causing what I just described, as well as those that tend to mimic estrogen or inhibit estrogen. The fact that we are seeing an incredible array of clinical conditions that are really a manifestation of the disruption of the levels and functionality of hormones within our bodies is not a surprise.

For example, the most common cause of infertility in women in America is a situation called PCOS, or Polycystic Ovarian Syndrome, such that estradiol becomes less available and functional in these women and become really oversaturated with testosterone, which is not typical for women in childbearing years.

This manifests, as mentioned, as infertility, often but not always, the presence of multiple cysts demonstrated on ultrasound in the ovaries, facial hair, masculinization of the facial appearance, pigmentation of the body in various areas, increased back acne, et cetera. We're also seeing higher levels of infertility or decreased ability of men, for example, to appropriately sire babies. They have much lower testosterone levels, lower sperm counts, and lower sperm motility.

Fecundity is something that is being threatened on the counts of both men and women. Normally, when we talk about infertility, it's a woman's issue. The reality is that the male side of this equation is taking a huge hit based upon these PFAS that are so ubiquitous in our world today that line our paper cups at the coffee store, that are seen even in various types of clothing that people tend to

wear. We're really exposed to these PFAS very aggressively. There is a move to limit their production and therefore their use.

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One study that I wrote about maybe about a month ago, talked about, when you look at fast food, how pervasive the PFA elevation is in fast food. Various fast food outlets were sampled in this blog that I wrote, and it's really quite stunning the levels of these chemicals to which people are exposed, especially younger people whose bodies depend upon these hormones, not just for the upcoming possibility of becoming a parent, but even for the normal functioning of their brains, in terms of cognition and even the balance and regulation of mood.

Meagen Gibson

Absolutely. As many people may have heard, and is well documented, we have worse mental health in our youth than we have ever had in history. A lot of that has to do with media and cell phones and things like that, but also we're able to absorb our food system, our food culture and diet, and all the things that go into that.

Now that we're talking about food, it's a great time for us to talk about nutrition and maintaining hormonal balance. I'm hearing you talk about PFAS and all the things that are against us. What is in our control? What do we have that we can have influence over that will help us maintain hormonal balance as much as possible when all these things are stacked against us, out of our control.

Dr David Perlmutter

The world does tend to stack against us in this regard with the pervasiveness of these chemicals. Almost assuredly, you and I have levels of these chemicals in our bloodstreams. Blood samples taken from the Inuit show these chemicals in their blood. It's a global issue, and you can't fully run away from it, these chemicals are everywhere.

I think that some things are common sense, that you don't want to be heating food in plastic, for example. You don't want to be using those cups that I described. The chemicals are found in types of soaps, in dishwashing machines, the stuff you put in your dishwasher. They're everywhere.

Chemicals are found in things that are scented. Get into an uber and you look under the rear view mirror and there's that Christmas tree hanging, and you can smell that stuff, and you're going to smell from that stuff. And it's affecting the hormone functionality in your body that affects the function of your brain, it affects your mood.

You can't request an uber without scent, but you can choose not to do that in your car. You can choose to wash your clothes, not using some of the very popular brands that are heavily scented.

There's a move these days to using white vinegar in the washing machine to wash your clothes. Apparently it works pretty well, I'm getting ready to actually try that. There are apps that can be used, one is [Think Dirty](#), and it isn't what the name connotes. It actually is a way of scanning the various products. I was actually doing it last night, scanning the barcodes on the various products.

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These products are then ranked in terms of their threat to you in terms of what they're made of, because frankly, no one is able to fully understand all the chemical names of the things that go into these products that are listed. But who's going to be able to have the wherewithal to deconstruct all of these ingredients and figure out what's threatening and what isn't? Well, the app does that, and there are actually several of them out there, and I would encourage people to do that.

I think eating food that's organic is a good idea, by and large, if that's available to you. Certainly water, bottled water that is in glass is the way to go. Not plastic. Plastic bottles, as you probably know, not only contain microplastics that you then ingest, but are covered with things like Bisphenol A, that is an endocrine disruptor that we don't want to be ingesting. Certainly we don't want to be cooking in anything like that as well, because that liberates these chemicals and is much more readily available for absorption.

Now, on the other side of this equation, I think there's some very good tests available for people. If we want to narrow down our assessment and look just at hormones, there are wonderful tests out there to look at saliva and urine and blood, to get a sense as to where hormones are in an individual's body, both male and female. I think that is... I mean, we're already testing hormones at your annual blood work. We test your thyroid function. We're indirectly testing pancreatic function, insulin, by looking at your blood sugar.

So in a very real sense, we are already testing hormones. I think it's reasonable to add things like progesterone, E1, E2, testosterone, both free and total testosterone, to blood panels each year and see where a person is, now that we recognize how fundamentally important adequate levels of these hormones are. Even beyond that, getting a sense as to their functionality, meaning that a particular level of a hormone in one person may not do the same as it does in another person based upon his or her genetics.

Unfortunately, these days we're able to look at someone's genetics and determine who might need a little bit more of this or that hormone. What male might need a little bit more testosterone, for example. Not just based upon the level, but based upon how the testosterone receptors are working. We can get an inference of that based upon looking at a genetic profile.

There's a lot to do, and it's a lot more nuanced and complicated than simply a 15 minute evaluation with a doctor who might look at your blood work and say, "Here's what you need", or "You're doing really well, be on your way."

I will tell you that as it relates to one particular hormone, we've come a long way in terms of entering the mainstream, and having mainstream medicine look at the levels of this hormone and then make adjustments. And that hormone is called vitamin D. "Oh, I thought it was a vitamin". Well, vitamin D really acts throughout the body as a hormone.

It is derived from cholesterol, just like estrogen and testosterone and progesterone are. It has multiple receptors throughout the body, throughout every part of the body, including the brain. In really every way we should be considering vitamin D as a hormone. I know that raises eyebrows, et cetera, but that's just maybe how I see it. But I think a lot of other people are embracing that notion.

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Back to our topic. Yes, this is the type of assessment that we should all have, and I think we now have creative ways of increasing hormone levels as needed, and it's really not that difficult to do anymore.

Meagen Gibson

It's interesting because one of the contributors, I can't remember which one off the top of my head now, that we've interviewed for this conference, was just talking about how we test some hormones and, as you were implying, it would be so useful to test them over a person's lifetime, because even normal hormone levels are only normal to that population that was tested to set the norm. Not for me as an individual with my genetics, and my history, and my body composition, and where I live, and the culture that I'm a part of, all of these things are going to contribute to what my blood work and what my hormones and what my health is going to look like.

By testing over time, we might be able to reveal when things are out of whack, not just when they're at normal levels for these people that I'm not related to that don't share my genetics.

Dr David Perlmutter

Normal means average. Let's look at something as simple as blood sugar. Typically, you're told your blood sugar is 100, you're "In the normal range". I don't want to be mean, for me, we can do better. We should be looking at what's the optimal range, and specifically, what's the optimal range for you, for each individual?

I would submit that in general, an optimal range of blood sugar, for example, should be far lower than 100. I think upper 80s would be reasonable, but then the question would be, how does that person function at that level? What if it were lower? What if it were higher? What are the other markers of that blood sugar that we want to look at? Like glycation of proteins, for example, fructosamine, various things we can look at to determine what is that blood sugar actually doing in that individual, and what would be the best level for that person? That is called personalized medicine.

And into that equation, we actually do include genetics. In my situation, for example, I know that I have what are called polymorphisms, changes or variances or nuances in my vitamin D receptor, such that when you tell me that a good level of vitamin D would be 50 based upon looking at 1000 people, that's interesting but do those people have that vitamin D receptor nuance? Who knows? For me, I have it, and therefore, I know I need a very significantly higher level of vitamin D such that I'm able to stimulate the receptor and therefore have better responsiveness of that vitamin D receptor, doing all the great things that it does.

Similarly, I have other changes in my genetics that indicate I need a higher level of B vitamins that are actually modified in such a way called methylated. These are good things to know about people.

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I think that, getting back to the hormone story, when we, as a neurologist, understand that not adequate functionality of things like estrogen or estradiols in particular, and testosterone, for example, not having adequate function of these hormones isn't good for the brain.

You had mentioned at your age an individual, and I think where you were going was, we expect a decline in our hormones over time. That's true, and it does happen, but as it relates to women, there is kind of a marked transition that happens called menopause, where suddenly the rug gets pulled out from under your feet in terms of estrogen and specifically estradiol. We now understand that this estradiol plays a really important role in body metabolism, specifically by allowing nitric oxide to work.

Why that's important is, nitric oxide's function is both blood supply to the body and meaning the brain. That's part of the body, last time I checked. And also how insulin works. We need good functionality of estradiol to let nitric oxide work such that insulin will work. When you don't have adequate insulin functionality and you don't have adequate blood supply, one part of the body really suffers, and it's called the brain.

As such, we now begin to get an understanding that we may really have an idea as to why Alzheimer's patients are twice as often women than they are men, because women suddenly go through this crash as it relates to estradiol that has a metabolic consequence.

We're now understanding that the primary mechanism of Alzheimer's isn't really this accumulation of this so-called sticky protein, beta amyloid, but it's actually a metabolic issue that the brain is not metabolizing glucose appropriately. Because insulin, first of all, isn't getting there, because blood supply is compromised. And second, because insulin is not optimized because nitric oxide is not doing its job, because estrogen isn't available to push it along.

Interestingly, if I could continue this, that the function, then, of nitric oxide after it's been manufactured, because there's enough estradiol around or not, once it's manufactured, because we had adequate amounts of E2 or we didn't, then the actual function of that nitric oxide depends on testosterone. Generally, testosterone levels are lower by a factor of eight in women and continue to decline through aging and certainly after menopause. So women get a double hit as it relates to brain metabolism related to this nitric oxide story.

Similarly with men, the declining function with age of testosterone, coupled with the overall global decline in testosterone, regardless of our age, really sets us up for metabolic issues related to the body and certainly related to the brain.

Meagen Gibson

All of that impacts, in subtle ways, if we're not aware of it and not working actively against it, our ability, brain fog, and our ability to want to contribute to the world and work longer or be fit longer, get into the gym and keep ourselves mobile and healthy and strong and keep our bones strong. It impacts our ability to make good decisions about our health and longevity as well.

[00:24:28] Dr David Perlmutter

It's fascinating that you say that we wrote a book about this exact topic, that estrogen, or estradiol in particular, is really quite necessary for adequate function, along with testosterone, I might add, of what is called the prefrontal cortex. We could characterize the prefrontal cortex, or the area of the brain behind your forehead, as being pretty much the adult in the room in terms of decision making, that the prefrontal cortex exerts what we call top down control over more primitive parts of the brain, in the realm of decision making, one area in particular called the amygdala.

We really need to have adequate estrogen levels, functional estrogen levels, to keep that prefrontal cortex from letting the amygdala make the decisions, which would be, "I want to stay up later. I want to eat garbage food. I don't care about other people. I don't care about what happens tomorrow. I just want to do this right now".

I sound right now like a five year old, and those are not good decision parameters or decision guideposts. Those are guideposts that really allow for worse decision making that are really obviously not going to be good for our health and good for our cognitive health.

To keep that prefrontal cortex function on par, doing its job as the gatekeeper, as the adult in the room, it really is, to some degree, a significant degree, dependent upon adequate amounts of functional estrogen and testosterone. A lot of my work deals with preserving the brain and even enhancing the brain. We focus a lot on one particular lifestyle choice called exercise, and how research shows that we can increase the growth of new brain cells with physical exercise.

Physical exercise ultimately amplifies the creation in the body of a trophic chemical, or hormone called brain derived neurotrophic factor, that strengthens neurons, it strengthens synapses, and it actually leads to what we call neurogenesis, the growth of new brain cells. Well, it turns out that BDNF, to do its job and do those wonderful things for us and preserve our cognitive function. BDNF is dependent upon adequate functionality of estrogen.

My hope is that the viewers of our time together begin to get the idea that hormones are more important than just having a period, getting pregnant, having good sex drive, et cetera. That hormones, we've pigeonholed them by calling them sex hormones, but they have pervasive effects throughout the body that affect every organ system you can imagine.

Meagen Gibson

Yeah, that's exactly it. You said something I want to come back to, which is the functionality of estrogen. We talk so much about levels, and somebody set me straight last week, I didn't know that men had estrogen. I was like, "Oh, shoot, sorry". So men have estrogen as well, to a certain level.

Dr David Perlmutter

Why did you say that?

Meagen Gibson

I was just wrong, I don't have a problem admitting that I was just ignorant about something.

[00:27:52] Dr David Perlmutter

That's a wonderful point. Because, again, estrogen is the female hormone and testosterone is the male hormone. Once we lock into that, we tend to become very myopic. Insulin, same thing. What does insulin do? Well, it helps the body lower and control blood sugar. End of story. Well, it's not quite the end of the story. Insulin is a trophic hormone in the brain. Insulin is necessary for the growth of new neurons. If you were in a laboratory and you have neurons in a petri dish and you want to grow them, you add insulin.

We tend to lock these ideas to the names. Progesterone, meaning 'for gestation', what you need to have if there's going to be a fertilized egg and you're going to grow a fetus out of it, you need progesterone. Of course, progesterone levels do go up, but why would I have then progesterone in my body and estrogen in my body if these are purely female hormones? They are not.

Meagen Gibson

Absolutely, and that's why I love this conversation.

Dr David Perlmutter

Why do you have testosterone? Because your brain is desperate for it, your bones are desperate for it, your libido is desperate for it, and your muscles are desperate for it as well. We lock into these ideas based upon the names because it's convenient. We had to learn it for the test. But then we characterize these things and those characterizations stay with us, and we need to break those barriers down.

Meagen Gibson

Talking about the functionality, or functional estrogen, it's not just a matter of checking our levels, but making sure that they're actually doing the jobs intended and things like stress contributing to the ability for estrogen to do what it's there for, and to help with the absorption of chemicals and neurotransmitters and all the things in our brain. If you wanted to say one word as a last bit so that I don't go over your time here...

Dr David Perlmutter

Have we really already done the whole thing? I was just clearing my throat, getting ready for the interview!

Meagen Gibson

I'm just getting started. I'm not going to make you stop, don't worry! I'll take you as long as I can get you. Let's talk about lowering stress, lowering cortisol, because I think, if I'm not mistaken, that part of your *Brain Wash* book was about, how do we take control of our stress and what's coming in? Like we did with diet, for stress and cortisol, how can we... People often forget, again, when we're talking about these marketing of hormones, cortisol is always seen as the stress hormone, when you wouldn't wake up without it, right?

[00:30:38] Dr David Perlmutter

I'm not sure you wouldn't wake up, but there is an upside to cortisol. We talked about the response that you might need, the sympathetic response to protect yourself. But even from a brain perspective, it turns out that low levels, but a spike in cortisol, but at a lower level, is really important. It's necessary for memories. The actual memory triage center called the hippocampus is really dependent upon cortisol in order to do its job. It's a question really of degree, though. What much higher levels do, is compromise in the brain. Higher levels of cortisol directly compromise this growth of neurons. Neurogenesis is down regulated. The growth of new neurons is depressed with high levels of cortisol.

This was demonstrated many, many years ago in the really seminal work of Dr Robert Sapolsky, who was able to demonstrate in stressed monkeys, chronically stressed monkeys, subordinate monkeys that were dominated or threatened constantly, looking at their brains, and they had a profound dropout of cells in the hippocampus. Really very evident, but again, low level, necessary higher level than sort of the opposite effect. As it relates to the production of cortisol, we can get back to sex hormones as well.

We know, for example, that to calm ourselves, we need to have activation in the brain of certain receptors called the GABA receptors. They're involved in allowing us to have a calmness, and serenity, and just really regulating mood. The functionality of the GABA receptor is in fact, dependent to some degree upon adequate stimulation by progesterone. So interestingly then, in individuals with anxiety, who might have higher cortisol levels as a downstream manifestation, it may be that the upstream issue has to do with availability of progesterone.

That's the kind of thing that will reveal itself when you look. You're never going to know unless you look, and you do the laboratory studies to look at these hormones. When you're able to tweak these hormone levels based, not just upon what we consider to be normal, but getting back to our point earlier about what is normal for that individual, based upon the clinical presentation. If a person, for example, were to have anxiety, one approach is to dumb them down with an anxiolytic medication, out the office door you go. Another might be to ask why those GABA receptors are not helping calm that person down?

We know that GABA receptors require progesterone. And now, as a matter of fact, I noticed that the progesterone level on the blood test or saliva test is not really where it needs to be. Let's try to actually fix the problem instead of covering it up with an anxiolytic medication, which really is treating the smoke and not the fire.

Meagen Gibson

Absolutely. That experience can be so frustrating for people dealing with mental health issues, and anxiety included. I was going to talk about my friend, but we'll just say it's me.

Seven years ago, I went to the doctor and I was like, "I'm doing everything right. I'm exercising six days a week. I meditate. I have a mindfulness and a gratitude journal. I have a stable income and a good family, and everything is fine, and yet my brain is on fire and I can't sleep. And all these things are going on". And all that's offered to you as the first offer out the door in most scenarios, with a general practitioner, even an obstetrician and gynecologist, is exactly what you're talking about. Let's just tamp down that feeling.

[00:34:38]

That's how I ended up in this job. I got curious. I was like, it can't be that simple. Thank you. It provides a certain level of relief to give me the ability to get curious and do a deeper dive and find smart people like yourself to help me out. But most people just want to feel better and don't have the bandwidth to get curious and make their entire living about finding out what the deeper cause of the fire could be.

Dr David Perlmutter

Exactly. I don't want to fully derogate the notion of treating symptoms. It's very reasonable to consider allowing a person to have a better quality of life while you're doing the work. To give somebody an anxiolytic medication, hey, if that's what they need in the short term, to help feel better and be functional, while we're dealing with the underlying problem, or first while we're trying to figure it out, by all means.

If a person's getting zero sleep at night and we don't know why, I think it's not unreasonable to give somebody a medication to help them sleep. But we need to find out what's going on with your thyroid, or your progesterone level, or whatever it may be that's keeping you from getting an adequate night's sleep. Once we solve that problem, we can take away the crutch. You give somebody a crutch when they got a broken leg, and pretty soon that heals and you don't need the crutch anymore. That's the metaphoric use of the term crutch.

I'm glad that projected you into this deep exploration, and then we had time together today. Awesome.

Meagen Gibson

Yeah, absolutely. Just to go with your analogy there, it's like we give somebody the crutch and then their foot heals, but now they've got armpit problems because they've used the crutch. There's downline effects to using anything too long without trying to investigate. Lots of people need medication for life, I'm not at all disparaging that. They are life saving medications in all respects of medicine and in many people's lives.

Dr David Perlmutter

I'll never forget, I was having breakfast in the Florida keys with somebody with whom I was going to go fishing. We were actually, dare I say, we were at a certain type of restaurant that didn't serve great food, though you could get eggs. I watched the breakfast that this individual consumed, and I said... It was the waffle, I think it was. On top of that was syrup, maple syrup. It wasn't maple syrup. Let's be clear. These restaurants don't serve maple... Anyway, whether it was or wasn't. I said, "I thought you're diabetic?" And he said, "Oh, no worry, I take Metformin. I take a drug", "Okay..."

The Metformin is a wonderful drug, but that's treating the smoke. Metformin doesn't treat the diabetes. There is no treatment that we have today in the drug world to treat diabetes. None. We don't have a drug to treat high blood pressure. None. We can control the symptoms of diabetes by

using drugs like Metformin and Sulfonylureas, et cetera, to lower the blood sugar, and drugs to lower blood pressure. But to target the underlying problem, that's a bit of a stretch.

[00:38:01]

Having said that, I think I need to modify that now in the world of these GLP-1 agonists that really do target insulin functionality, so maybe we've transitioned to a newer time. Not that I'm, right now, advocating that, but it's certainly something to keep your eye on.

Meagen Gibson

We're getting into territory we didn't plan on here, but let's go with it, it'll be fun for the people. With the GLP-1s, the thing that's been so fascinating for me about that, especially from the mental health perspective, has been the anecdotal stories that we're getting from people about the voice in their head finally going silent, that they had been battling. The noise they didn't even know, that they had been battling against for 30, 40 years. That was just telling them to eat more or trying to fill the urge, or get the dopamine, and it's just quiet. I felt so much compassion for that.

Dr David Perlmutter

A lot in my career has been really focused on non-drug approaches to this or that. This is causing many of us in integrative functional medicine to take a step back and realize that this is one that's really got potential to help a lot of people for whom that voice could not be silenced. Let's call it like it is. I think there's going to be an even bigger application, beyond weight loss and blood sugar control of these GLP-1 agonist drugs.

Like any drug, there are risks, the potential for complications that are being described. But I think overall, this is a pretty intriguing time for us to finally see the development, utilization of a drug that utilizes an existing pathway, stimulating this glucagon-like... Using a glucagon-like agonist to stimulate this receptor and really play into a normal physiology by attacking it this way, or utilizing it in this way.

One study back in 2016 looked at a relatively small number of people, I think it was 18, followed them over eight months. These were existing Alzheimer's patients treated with a GLP-1 agonist that's no longer on the market because it caused pancreatitis, but this demonstrated pretty dramatic changes in their brain metabolism, some improvement in cognitive function, not dramatic. But recognizing that Alzheimer's is a metabolic issue of the brain, pretty outstanding.

There are several ongoing studies right now using these drugs to treat Alzheimer's, the results of which I obviously do not yet know, so I can't be an advocate. But I think, to be fair, as an integrative type of healthcare practitioner... Integrative is not alternative. Alternative medicine means one or the alternative, which is the other.

Integrative means a big open toolbox, and you bring in as many ideas as you possibly can and assess their risk benefit ratio. Are they risky, and how does that compare to the potential benefit? So it's going to be interesting to see how this plays out. A lot of the stories are pretty amazing, like you just described.

[00:41:25] Meagen Gibson

Absolutely, it's an exciting time. There's a lot of things that are stacked against us, as we already said, but it's also a really exciting time in development, and knowledge, and all the things that we're learning about the brain and all the ways that pharmaceuticals are developing. We've got a lot of really smart people on the job, like yourself. How can people learn more about you and your work?

Dr David Perlmutter

I think the best thing would be to go to my website, which is, oddly enough, www.DrPerlmutter.com. I post on [Instagram](#) just about every day, and I do a lot of Instagram Lives. [X, formerly Twitter](#) I post there as well. I don't do TikTok quite yet, but who knows, maybe eventually. But the best place would be my website.

My books, I think, are very helpful for people trying to understand metabolism. My most recent book is called *Drop Acid*, and that deals with this uric acid issue that we talked about being related to metabolic issues in the body, and this does relate back to our hormone discussion in terms of metabolism.

Meagen Gibson

Fantastic. Thank you so much for being with us today.

Dr David Perlmutter

Sure. Thank you for having me, Meagen.