Can You Really Reverse Alzheimer’s? Here's What Works Transcript

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Summit Introduction and Guest Welcome

Hello and welcome to a very special interview for the Reversing Alzheimer's Summit. I am your summit co-host, Doctor Kristine Burke. Over the last decade, I helped many patients reverse their cognitive decline, and that is why I have co-founded True Neuro, a brain health software company, to help patients and practitioners be extraordinarily successful in this work.

In this summit, I'm bringing you interviews with thought leaders who can help you understand the pillars of brain health and the root causes of cognitive decline, because I want you to learn what you need to know to prevent and reverse cognitive decline and Alzheimer's disease for yourself and your loved ones.

I am extremely honored today to introduce you to one of my teachers and a leading voice in brain health, Doctor David Perlmutter. Doctor Perlmutter is a bestselling author, speaker, and researcher, a renowned neurologist, a five time New York Times bestselling author, and a thought leader in the field of brain health and functional medicine.

With decades of clinical experience, Doctor Perlmutter has dedicated his career to uncovering how lifestyle choices and environmental factors impact our brain health and our overall well-being.

His groundbreaking books, including Green Brain and Brain Maker, which I have on my shelf, have transformed the way we think about the connection between our diet, our microbiome, and the health of our brains.

Through his pioneering work and bestselling books. Doctor Perlmutter has empowered millions of people to take charge of their cognitive health and reduce their risk of neurodegenerative diseases.

Today, he joins us to share his expert insights and practical strategies for protecting and restoring brain health. Please join me in giving a warm welcome to Doctor David Perlmutter.

Well, Doctor Burke, thank you for having me. Absolutely. I would love to start our discussion with what you and I were talking about earlier today, how the misunderstanding of the cause of this disease has led us down the wrong paths for treatment.

Well, let's begin with just how disease is sort of looked upon in modern Western world. And that is really through one lens. If we can figure out what's causing a disease through the notion of what's called monotherapy, then we can develop a single drug and that single drug can be a homerun and will solve the problem.

And I definitely want to make sure that your audience does. I put solve the problem in quotes because certainly it does not. And so the idea of creating, let's say, monotherapy for Alzheimer's disease would be great if in fact, there was one cause of Alzheimer's.

But there isn't this whole notion that beta amyloid is the cause of Alzheimer's is preposterous. I think the research that went into that development of the so-called amyloid hypothesis was highly flawed.

Why Alzheimer's Is Multifactorial

And we know that there are certainly plenty of people who have lots of amyloid in their brains and are cognitively quite intact, and others who are fully diagnosed with Alzheimer's, who have none or very little of that sticky protein, beta amyloid, to begin with.

You know, the idea that we could create a monotherapy creates a paradigm that sets the stage for a blockbuster drug and also makes the deliverance of health care very easy.

You say you have X and I have a prescription to fix it. You say you have high blood pressure. Here's your nervous. You say you have diabetes. Here's your metformin.

You have Alzheimer's. Here's a drug. We don't exist in that world. I think, as Doctor Bateson has made very clear for many years that Alzheimer's is multifactorial.

And I think that primarily the biggest issue that underlies what's going on in the brains of Alzheimer's and other Alzheimer's related dementias is really in the area of what we call immuno metabolism.

It deals with the effects of our profoundly dysregulated metabolism these days on the immune system, hence the term immuno metabolism. And in the brain, we're talking about a specific population of cells called the micro glial cells, that are involved in determining whether the brain is going to be functional and persistent in allowing us to enjoy life or not. So I think what I've just said sets the stage for our further conversation, that metabolism is really key here.

And the good news is that we, in our day to day lifestyle choices, can really determine how effective and healthy our metabolism really is. And that influences directly the immune function of the brain, which plays a central role in the development of things like Alzheimer's or not.

Yeah, there's really a really interesting connection between what happens when our metabolism goes awry and then the whole the entire inflammatory cascade.

That's a part of this process. And I know you're a strong advocate for the ketogenic diet and blood sugar control in promoting brain health. Can you maybe explain to the viewers how this diet impacts the brain, why it might be particularly beneficial for those at risk for Alzheimer's or other neurodegenerative conditions?

Sure. Well, you know, the ketogenic diet is certainly popular. People talk about it for weight loss, along with various other things that have become popular today for weight loss, including the use of certain types of drugs that we call GLP one agonists.

Perhaps more familiar term would be ozempic and these are all ways of targeting metabolism. And to get a little bit into the weeds, specifically as it relates to Alzheimer's targeting the metabolism of the brain's immune cells.

So we are quickly right back to this notion of immuno metabolism. Ketogenic diet and GLP one agonist drugs favor mitochondrial function, allowing those energy producing organelles within the neurons but also within the immune cells in the brain, called the micro glial cells allow these immune cells to function more appropriately and to be nurturing, as opposed to being threatening the micro glial cells within the brain, making up about 10% of the cells of the brain.

The really important players of the brain's innate immune system can exist in a multitude of configurations. But for our discussion, we'll just choose two.

Friend and foe. Friend being called M2 and foe being called M1. And it turns out that these micro glial cells can shift back and forth between being friend, nurturing our brain cells, causing us to grow new brain cells, nurturing our synapses, repairing the blood brain barrier or foe.

And, one configuration where they threaten synapses, they actually digest away synapses. They threaten the growth of new brain cells.

Ketogenic Diet, GLP-1s, and Brain Metabolism

They destroy the blood brain barrier influenced by their metabolism, in other words, influenced by their mitochondrial health and function, which is strongly influenced by our dietary choices, like a ketogenic diet, also influenced by the use of GLP one agonist drugs, there are receptors for GLP one on the surface of these immune cells, but more indirectly, we know that drugs like Ozempic semaglutide have a very, very low ability to make their

way into the brain.

But it doesn't matter, because what influences the brain is systemic levels of things that threaten brain cell metabolism and microglial metabolism, like systemic insulin resistance and systemic inflammation.

So that's why we favor things that nurture mitochondrial function, like ketogenic diet, because it favors metabolism and it favors appropriate function of the brain's immune cells, which play a key and central role in determining whether the brain will be fit or the brain will succumb to Alzheimer's.

And I think two, maybe it's important for people to understand that because of the type, transporters that move glucose or sugar from the blood into the brain, the brain doesn't have an ability to modulate the amount of, of glucose that comes in.

And so that whether you have a nice normal amount of glucose in your blood or you have an elevated amount of blood that directly impacts the the way the brain receives that and receives that message in terms of how it turns on or off certain parts of the metabolism.

That's right. And there, you know, there are a lot of interesting factors that play into what you just said, including the functionality, for example, of insulin.

We're all aware that as we live a less salubrious lifestyle, our blood sugars go up and more insulin is required. Ultimately, insulin becomes less functional.

Everyone's familiar with that, but I think to look at insulin functionality through another lens for a moment would be really important. And that is that for insulin to do its job, we have to have adequate amounts of a gas present called nitric oxide.

Who knew that this nitric oxide is really important for a number of things related to brain health, including blood supply, delivering blood to the brain, but also this functionality of insulin that is required in many important parts of the brain to deliver that life supportive glucose, such that the mitochondria can do their work and as such, keep the microglia in a supportive role as opposed to a threatening role.

So it helps us understand then, a variety of relationships to Alzheimer's. For example, we know that poor dental health, periodontal disease is related, to increased risk for Alzheimer's disease.

And a lot of research has focused on the presence of a particular bacterium called poor from honest gingival. But I want to take a step back and just try to connect some dots here to overall health of the oral microbiome and the function of insulin.

Now, that may seem like a long way away, but bear with me for just a moment. It turns out that the bacteria living within the mouth play an important role in converting dietary, to giving us the raw materials in terms of nitrogen to allow our bodies to make nitric oxide.

What I just alluded to as being very important for insulin function and for delivery of blood throughout the body. So this is yet another indication that we've got to maintain good oral health because of the conversion of dietary nitrate and nitrite and the conversion of that into the form that can be used for the body, then to make nitric oxide to allow insulin to do its job, to allow microglia cells to undergo good metabolism and to keep our brain healthy.

So there are a lot of interesting connections that through the lens of immuno metabolism, begin to make sense. So that's how we can understand oral health and Alzheimer's risk.

What about the relationship between obesity and Alzheimer's risk? We know that people who are obese or even overweight in midlife have an increased risk for Alzheimer's.

Well, that's understandable through the lens of immuno metabolism, because when we are significantly overweight

or obese, several things happen. We compromise this function further, as we just talked about, of insulin, and we create higher levels of inflammation in the body.

Those chemical mediators of inflammation called cytokines make their way into the brain. And guess what? They help shift those micro glial cells away from being friend to being foe.

So just the presence of obesity through the notion of immuno metabolism ultimately leads to things like digestion of our brain synapses, so that cells can't communicate with each other, a reduction of the growth of new brain cells and the destabilization of the blood brain barrier.

And let me expand just a moment.

Insulin, Nitric Oxide, and Oral Health

The just how important this immuno metabolism concept is, because fundamentally, when we get our arms around the fact that it's metabolism that's regulating the brain's immunity and that the immune function of these micro glial cells is really fundamental across all neurodegenerative conditions, it really makes us understand that we're in charge, we're in charge of our metabolism based on our lifestyle choices.

And as such, we're in charge of the brain's immune function. And as such, we are determining we're the architects of our brains destiny. So whether we look at blood sugar and insulin functionality or obesity or hypertension or any number of factors that play into even those three levers, we realize that, you know, this idea of living until we have a problem and then hoping that there's a cure is one way of looking at it.

But I think more and more people are realizing that it's really up to each and every one of us, you know, to me, to architect our health, destiny and, you know, that's what having tools to improve our metabolism is all about.

And, and really the most important tools for metabolic health are lifestyle choices like exercise, sleep, diet, stress mitigation, etc.. Absolutely. And I think, you know, earlier you were talking about the GDP one agonist.

And I think, you know, one thing that people often forget is that these are naturally occurring peptides in a healthy metabolism. We're already making these.

And that's that's how it's supposed to work. It isn't that we all suddenly have a deficiency in these peptides. It's that the choices that we've made that have led through the immuno modulation that you've just talked about, have led to a change in the way our metabolism function alters that production, just like it alters the production of many other cytokines or cell signaling messages, messengers that we have.

That's right. And when we see studies published as one recently was, that demonstrates, for example, a 70% risk reduction for the development of Alzheimer's over a three year period of time in diabetics who are using semaglutide or ozempic in comparison to other drugs.

Some of them GLP ones, but other sulfonylurea type drugs, metformin or even insulin. The. The most dramatic comparison was in comparison to those receiving insulin.

Wonder why I bring up these studies? Not because, I am necessarily in favor of people jumping on taken ozempic because it's good for your brain. It's not what I'm saying.

I mean, when I write about them and blog about them, etc. and then I get accused of being on the payroll by the pharmaceutical payroll. I'm not I doing this because it further exemplifies the central role of metabolism in brain health and disease.

Here is a class of drugs that aggressively and positively affects cellular metabolism, including metabolism, systemically and to some degree in the brain.

And it is simply a case in point to, again, further support the notion that when metabolism is in the right place, the brain is happy. So again, Doctor Perlmutter is not saying on this summit right now, zip it for one and all, you'll have a great brain.

But I am saying that because of the data coming out with respect to GLP one agonists, in terms of Alzheimer's, in terms of Parkinson's, that it's an indication that metabolism is important.

That's all. And therefore, let's look at what we should be choosing to do with respect to our lifestyle choices, to enhance our metabolism in terms of day to day activities.

Yeah. Having that normal communication of normal metabolism is key to brain health. You know, one of the other things that you were interviewed about recently that is also on the inflammation side was the two studies, that suggested that the shingles vaccine may help to slow the development of dementia.

I think it's interesting on the other side, like, what are the other routes that can lead to this final common denominator of inflammation and the change, the changes in the way the microglia respond?

I think that is kind of a segue then to the whole notion of infectious agents and their possible relationship to the development of Alzheimer's disease.

I mean, we've known for quite some time that infection with herpes simplex virus type one has been demonstrated to Co localize with activated microglia around beta amyloid in the brain.

Obesity, Inflammation, and Microglial Polarization

In the brain, a work originally done by Doctor Ruth Itsuki in England. And subsequently we've seen similar findings related to chlamydia, pneumonia. But I think now there are a variety of other types of infections, including Epstein-Barr virus, cytomegalovirus, SARS-CoV-2 virus for a modest gingival as a bacterium, and even for certain types of fungal infections that have been found to be associated with increased risk.

Grasshoppers disease. And I think that when we again look at the immune cells in the brain and recognize that the micro glial cells can bind those infectious agents, that we begin to understand what may be going on here, that activation of pathways and activation of what is called the NLRB inflammasome in other words, a series of cascades within that micro glial cell culminates in down regulating mitochondrial activity.

In other words, metabolism, and causes that micro glial cells to start doing bad things in the brain. So all of these inroads and even things like, for example, BRCA and, and, and syphilis act similarly in the brain that all of these inroads through their effects on what we call micro glial polarization, meaning shifting the microglia away from being trend to being pho really becomes like a funnel.

Then for us to understand what the relationship is between these infectious agents and the production of downstream consequences in the brain that ultimately succumbs to Alzheimer's and it.

All right, let's get let's get back to your question. Therefore, the idea of reducing viral infection, be it through a vaccine, as to, you know, as you were mentioning with respect to shingles vaccination or even the use of antiviral medications, I think is something that we should be thinking about.

There has been, a talk for quite some time getting back to the work of Doctor Ruth. Attack of keeping people, especially the ApoE4 group, away from higher risk for herpes simplex type one infection.

We know that being ApoE e4 heterozygous or homozygous and having higher levels of herpes simplex virus type one antibodies, as one might see in people who get cold sores.

That combination is particularly related to increased risk for Alzheimer's. So they're playing upon each other, and it's no surprise because ApoE e4, one of the things that it does is it sets the stage to activate those microglial cells.

When you add HSV one infection to that, it makes a situation even worse, as we have seen, for example, in the combination of diabetes with ApoE e4 and obesity with ApoE e4.

Yeah, that ApoE4 just accelerates your inflammatory response in a sense. And so everything becomes amplified. Every exposure becomes amplified in that group whether they have one copy and then worse if they have two copies.

So when I'm hearing from you in a sense, is that the more we investigate the things that turn on or off that polarization of the microglia, then the better understanding we will have of the true root causes of Alzheimer's and other neurodegenerative conditions.

That's right. It explains an awful lot. It explains why we see elevation of beta amyloid, for example, in some people who have Alzheimer's, but not all because these microglial cells are really happy to digest away beta amyloid that might become present when they're in their M2.

Good constructive supported phenotype. They lose that ability when they're in the M1 phenotype, such that then a beta amyloid can accumulate and the accumulation of beta amyloid within the brain increases the production of these inflammatory mediators called cytokines, which does what it further polarizes.

Those micro glia away from being our friend to being foe. So it does tend to explain a quite a bit. I mean, we've seen we've known for quite some time that markers for activated or polarized or M1 microglia are higher in postmortem analysis of brain tissue.

Now, there's autopsy specimens of brain tissue in looking at the Alzheimer's brain in comparison to the non afflicted individual. And even more exciting is the fact that in living people now we can image activated microglia using a tracer called well it's a that would bind to something called TSB.

So a transporter protein located on the surface of microglia cells. So the activation of TSB is a marker of microglial activation. So you can image micro glial activation in living people.

And you see activation of microglia in depression and schizophrenia, Parkinson's even macular degeneration, retinitis pigmentosa and certainly Alzheimer's disease as well, and autism.

So it really allows us to characterize activation of microglia as being a really central focus for what's going on, to make a good brain go bad across various types of pathologies.

Infections, ApoE4, and Dementia Risk

Now, is that something that's going to be clinically available, or is that only available in the research setting? Right now? You can't get a bio scan of your brain right now.

But, you know, one of the things that, as we've talked about, shifts microglia from being friend to being foe is changes in brain metabolism, specifically how the brain utilizes glucose.

And that type of scan is available. It's called a, Flora deoxy glucose, Pet scan. And that is a scan that not only indicates decreased brain metabolism as relates to glucose setting the stage for microglial activation, but predicts Alzheimer's as much as two decades ahead of time.

So what happens long before you forget the Wi-Fi code in your grandchildren's names, is that there are changes in your brain's metabolism brought on by your lifestyle, and this can be imaged now using these glucose Pet scans, if you will, that mark and charge brain metabolism.

Yes, it's a research tool, but it is something that's available. And beyond that, I'm aware of research now that's looking at modification of MRI scan availability to actually mark brain metabolism.

And as non-invasively as you can be, I mean, a Pet scan is a bit invasive. You're giving a radioactive tracer. And yet if MRI can be utilized as I think it will be when software becomes more widely available to image brain metabolism, not only will that be useful to determine who's at risk and who's not at risk, but also, more importantly, to follow how effective an interventional program is in terms of improving brain metabolism.

And that's the home run. That's where it's at. Yeah, that really is the home run. There's so many new tools that are coming out the the brain biomarkers that we have access to now for earlier detection of some of the pathological changes that are occurring in the brain and this that you're, that you're speaking about.

And then the ability to start, you know, in the future. Not ready now, but measuring the actual mitochondrial function. All of these things are going to give us so much understanding about where the system is failing, so that the the clinicians can then help intervene.

I agree, and and what's very exciting is, so many of these things are now being coming available without a prescription. And at a doctor having to be involved.

It's so empowering that people can look at neuro filament light or whatever it may be. Forms of phosphorylated tau available without a prescription and even ways of measuring in real time biometrics like blood sugar with a continuous glucose monitor to measure your sleep quality using a tracker of one sort or another.

It's very, very exciting that people are becoming empowered with these tools, and I've always wondered, why not? I mean, you're allowed to buy a bathroom scale and know how much you weigh.

Why shouldn't you know your blood sugar? Why shouldn't you know your cognitive performance and be allowed to take a cognitive test online? You are. And to know the, levels of things like the brain scan report, where you're able to look at these unique proteins and determine where you are on the scale of risk, on the continuum of brain degeneration or not.

And then to be given tools to intervene that are non-pharmaceutical, by and large, is pretty, it's it's very exciting. It is really exciting. And I think two, we're at a time where it's, you know, maybe a decade ago, it would have been terrifying to have these tools that tell us that the process is coming.

Right. And the light at the end of the tunnel looks like a train coming your way. But now we have so many tools and so much more understanding about the drivers of brain degeneration.

And much of that is in the control of the patient through their lifestyle choices. Yes. And, you know, many, many years ago, when we first were able to get genomic data on our patients and we knew that ApoE e4 that we talked about earlier was a risk factor for Alzheimer's, it was called the Alzheimer's gene.

That was really aggressive and I thought ill suited for the clinic, that's for sure. You know, the empowering part of that is people say, well, gosh, nobody wants to know if they carry that gene.

I think that's exactly wrong. I think people really want to know what their risk is. And, you know, as it relates to, because they can make changes after, let's say, ApoE4.

How wrong was the idea that, you know, this was an Alzheimer's gene and sort of charted your destiny? Nothing could be further from the truth. We can absolutely offset pretty much all of the risk imparted by ApoE4 now.

And so the idea that people had learned it, that they were appealing for positive and felt that they were destined to Alzheimer's was so wrong, as we know now.

I mean, there are ApoE e4 four homozygous patients who've gone through, for example, Doctor Breton's protocol who have shown improvement in cognitive function and that absolutely rewrites the book in terms of the the general teaching on Alzheimer's and what is an individual's destiny.

Yeah, it really does. And it informs the patient that they have a bigger job to do. They need to be vigilant to all of these things that we've talked about in their metabolism and their dietary and lifestyle choices and their inflammatory exposures.

All of those things are really what confer their risk.

Brain Imaging, Biomarkers, and Early Detection

The gene is just their vulnerability. It's true. By and large, I mean more than 95% chance that Alzheimer's, in an individual is not caused by genes, it's caused by other variables.

The good news is, if it's not genetic, it's environmental, i.e. it's a it's a variable over which we can exercise strong control, like diet, like exercise or lack thereof, and quality of sleep and stress, toxins, exposures, many things that, you know, we've got to be able to get out there and tell people about because the common messaging is live your life come what may, and we'll fix it when you get a problem that's not working as it relates to Alzheimer's.

Never did before that amyloid targeted drugs that are not working. We were told to use cholinesterase inhibiting drugs like aricept donepezil, because it was found that the brains of the Alzheimer's patients were low in acetylcholine.

If we can raise acetylcholine, problem solved. And these drugs were developed to do just that. Well, and it turns out that when you look at large meta analyzes, evaluation of the efficacy of these studies in terms of how people proceed down the continuum of cognitive function, those taking the cholinesterase inhibitor drugs actually decline cognitively more rapidly than those who did not take the drug for Alzheimer's disease.

Wow. You know, that directly violates the notion of premium. Not no, sir. Above all, do no harm. And so we live and learn. And I think the lesson here is that when we as clinicians, are being fed advertisements to tell us how we should treat patients, we need to take a deep breath, and take a step back, because, you know, certainly as it relates to Alzheimer's, there's nothing meaningful available to us.

As you and I have this conversation right now. Yeah, it's really important. Well, maybe we could wrap up with some practical steps for prevention. You've mentioned quite a few over the course of our conversation, but for viewers who may feel overwhelmed by what they need to do to try to prevent Alzheimer's, what would you say are the first three actionable steps that they could take today to start protecting their brain health?

Well, I will answer that question, but first, I would like to say to all the viewers that if you live in be age 85, and that's the most rapidly growing segment of our population, your risk for this disease is at least doubled.

I mean, at least going to be 50%, meaning that if you live to be age 85, your risk of having Alzheimer's is a flip of a coin. That, you know, this is a disease affecting now some 7 million Americans.

And those numbers are only going to get significantly greater as we move forward in time. The number one risk factor for Alzheimer's is a metric over which we have no control.

And that is our age. Okay, we get it. But the other factors we do have control over, and that's the empowerment part of why we're together today. So to answer the question, the top three, I would say, exercise, exercise.

And the third would be exercise. And it's so important, I think, that, you know, we've seen literature lately suggesting that you can get exercise two days a week and still lower your risk for a variety.

I think it was 60 different, disease states. I think people should exercise every day and should alternate between resistance training and aerobic training.

Muscles are an, endocrine gland.

Practical Prevention Strategies and Closing Remarks

They are secreting chemicals that are really good for the brain and really good for immuno metabolism, good for metabolism, therefore good for immuno metabolism.

So exercise is really very important. Number two I know the top three were excellent. But number two would be a diet that controls your blood sugar. So that may be Mediterranean.

That may be ketogenic, that may be eating foods that start with a particular letter or end with a vowel. I don't care, I just want to be sure that the diets people are gravitating to are diets that control their blood sugar.

How do you know? You know, by doing things like wearing a continuous glucose monitor, following your A1 c and most importantly, following your fasting insulin level.

That should be between, let's say, two and five. Keep it really low because your blood sugar may actually be normal, but the insulin is telling you where you are as it relates to insulin resistance.

That will ultimately lead to a situation where the blood sugar is not normal anymore. So number one and number two, exercise and a diet that's good for your blood sugar.

What is number three. Not sure. I'm really not sure what I would put third on the list. I think paying attention to, organisms in and on your body is important, i.e the microbiome, in your gut microbiome in your mouth.

Really very important because it plays a role in inflammation. We could be talking about getting obesity and blood sugar control and, amount of inflammatory chemicals in our bodies.

So I think I to have a tough time coming up with number three, because there are a lot of things out there. But I think if people can learn what to eat and can exercise every day, it's going to go a long way to actually preventing this global pandemic of Alzheimer's and dementia type diseases that we are seeing now.

That's wonderful. Well, Doctor Perlmutter, this has been really an amazing discussion, and I so appreciate that you're providing this really important information with everyone on the summit today.

I know that you have already written at least six books, and I hear maybe one more on the way. So people have a lot of access to learn from you. So where can people find out more about your work and, and access all of that great information that you've created it?

Well, my website is, oddly enough drperlmutter.com, Doctor perlmutter.com and Instagram I think is David Perlmutter. Facebook I think is David Perlmutter.

And my new book is called Brain Wars that focuses, oddly enough, on the war between, the M1 and M2 microglia. That'll be my 16th book. There have been there have been a few over the years.

I appreciate the opportunity to spend time with you and to get in formation. On the aging. In the fourth century BCE, the Yellow Emperor said that prevention is the ultimate principle of wisdom.

To cure a disease after it has manifests is like digging a well when one feels thirsty or forging weapons when the war has already begun. So we really have to emphasize prevention, and the tools are very straightforward.

It's all about keeping our metabolism in check. Thank you so much for joining us today. Thank you for having me. It was a pleasure. My pleasure as well.