Food, brain health, and the rise of chronic disease

Eating certain foods is something that we can do to help to improve our health. Why are people so sick? Why is it that were seeing such high rates of especially chronic and these largely preventable conditions?

One of the big variables of course is food. If we want to actually be able to use food as medicine, we need to understand how food acts on the exact same pathways as pharmaceuticals.

how food can be reliably used as a way to bias key pathways that can help us to live longer, healthier lives. Even though the science continued to progress, these are big issues.

We don't want to lose the magic of what nature provides. A message I would put out for everybody as of right now is that the best studied way Hello, everyone.

I'm Dr. David Perlmutter. Welcome again to The Empowering Neurologist. What are polyphenols? We're hearing so much about why we need to have a diet that's rich in poly phenols.

and he has really become one of the leading authorities on this topic. We're going to explore what polyphenols are all about and his research in this area that is actually really very, very exciting, what we can do to increase poly phenols in our food and why that needs to happen in terms of our health outcome.

I'm very as you can imagine excited about this interview today, so let's jump right in. Dr. Austin Perlmutter, welcome to the Empower Neurologist. Thanks so much for having me back.

You are a repeat offender on the empowering neurologist, which is great. And I think the reason, you know, always have new information to share with us.

I said in the introduction, we're going to be looking at food, food in brain, and then we are going do a deep dive into polyphenols, as well as your really exciting 2024 research that looked at the effect of poly phenols on aging, and we'll call it like it is, but let's start off by talking about your interest and why you became interested in the role of food as it relates to brain health.

So if we look at brain-health issues around the world and see mental health issues being what they are, hundreds of millions of people struggling from mental- health-issues, now we have dementia, roughly 60 million people estimated to hit about 150 million in coming decades, These are big issues, and I think as listeners to your podcast know, well, they're the most important issues.

If your brain health isn't good, nothing else matters. And so then the question is, what can we do about it? And certainly there are a range of options, I'm not anti-pharmaceutical in the right setting, but here's the thing.

When we look at the variables that predict brainhealth over decades, food is at top of the list. It's food, exercise, sleep. And as we look at how food is capable of influencing our brain health, we don't get to opt in or out of eating food.

We have to eat food, so the question then becomes, are certain dietary patterns and certain foods more likely to support good brain-health, not just in the long run in terms of decreasing risk for conditions like Alzheimer's, but even in optimizing brainhealth on a given day?

And as it turns out, certain foods absolutely have these correlations. So various dietary studies have shown that people who adopt certain diets may have up to a 50% lower chance of developing dementia compared to the people, who eat more of a standard American or a Western pattern diet.

And so the reason that I've been so fascinated with this research, is number one, there's so much to leverage. If we can just get people to eat a slightly healthier diet in terms of preventing and optimizing brain health issues, but beyond this, we're starting to understand how certain nutrients, certain molecules within our food may have an outsized potential in helping to mitigate certain brain-health conditions.

And that's really where getting into these plant-based nutrients is so fascinating because as we'll discuss, there are some studies now showing that people who eat more of these very specific plant nutrients may themselves be at a dramatically lower chance for developing brain health issues.

And beyond this, now what we're seeing is some study showing even acutely an intervention with these nutrients can augment, can boost certain aspects of brain function.

So it's very exciting stuff. So when people think about their food, they're thinking macronutrients, fat, protein, carbs. That's the big discussion today.

What's a ratio of these types of foods? How much protein should I get per gram body weight and all that? That is the discussion. There is secondarily some discussion about so-called micronutrians, vitamins and minerals.

You were speaking at a recent conference about the so-called dark matter in food and how influential that is. Let's double-click on the dark-matter idea, because I'm not sure that's a term you developed, but it really, I think, says a lot that there's lot going on in the background that most people don't appreciate.

Well, one of the themes that I've been talking about now for a bit is this incredible hubris that humans have in general in terms of our belief that we understand nature.

And I think food is probably the best example. So we as modern day humans, have this belief, that, we, understand what is in our food, because we've, been able to compartmentalize and lock down the key macronutrients.

We can say this has this many grams of fat, this, many, grams, of carbs, and this may grams a protein. Therefore, And it's really only in the last 100 or so years that we started to say, oh, turns out there's more to it.

There are vitamins that actually need, there are minerals that are actually needed. So we'd say well, this food is a good food because it has enough calories to keep us alive, enough macronutrients to where we're getting fats, carbs and proteins and then some vitamins and minerals.

Honestly, even though the science continued to progress, I feel like the public understanding of food really stopped because what we did was we carved out the actual nutrient profile in a real food, and then we started to retrospectively, or I guess after the fact, we had started Take some whole grains, you strip away all the fiber, strip all of the plant nutrients, bleach it, refine it and make a loaf of white bread.

That loaf is mostly refined carbohydrates. Now we understand, probably not the best thing for your overall health. But we recognized decades ago, researchers recognized, hey, because we've done all of this stripping out of nutrients, we probably need to add some things back in.

So then we fortify these foods. We throw in some B vitamins. If you look at, for example, cereal that you buy on the store shelf, you'll see that it's been fortified with nutrients because the idea is we understand food so well and nutrition so while that even though we have destroyed the actual architecture of the food itself, We're able to toss in some vitamins and minerals.

And now all of a sudden, that food is good for us again.

What polyphenols are and why they matter

But coming back to the hubris piece of it, now what we understand based on research that was published in the New England Journal of Medicine and other leading journals is that, food contains over 100,000 different

molecules.

That's again, the so-called dark matter of nutrition. It is an incredible universe of data that we're just scratching the surface of. Why that matters so much is, Coming back to the central conversation, why are people so sick?

Why is it that we're seeing such high rates of especially chronic and these largely preventable conditions? One of the big variables of course is food, and it's easy to default to simply saying people are eating too many calories, people are eating not enough fruits and vegetables and people just need to make sure that they are, eating less of the junk food and more of actual food.

And yes, that's true, but the why, right? So the, why is in part because there are these incredible groups of these nutrients found really only in minimally processed food, some of which can have an outsize effect specifically on brain health.

So that the dark matter of it. glossed over first. Yeah, I mean, from a from marketing perspective, or I guess purely from bulk production perspective.

That's just not the goal. So kind of post World War Two, the gold was to mass produce foods that were readily available for people make sure everyone has enough calories.

And you can see in the United States what that led to was the growth of monocultures, right? We want enough corn and we want We want to ensure that there is enough calories for the population.

That wasn't necessarily the wrong decision in terms of optimizing towards a variable. Yes, it's important that we have enough calorie, but we've lost things in the process.

And the other piece of this is it is not just about optimizing toward other variables. It just wasn t known. We've only more recently started to understand how to analyze food to be able to what is in it.

And a good kind of corollary to this is think about the microbiome, right? So even when I was in elementary school, which you know very well, not so long ago, The sign in the bathroom was telling us about germs.

Germs are bad, bacteria are back. I'd never learned in those days, hey, you know, You really need to be paying attention to what antibiotics might do to your microbiome because there are good bugs in your gut.

It's the exact same parallel. it's just a blanket statement of we understand what's good and bad. And beyond that, nothing else really is that valuable.

Sure, there's a little bit maybe of additional value you could get from back in the day, maybe eating some kefir or having some sauerkraut. But it wasn't until recently that we started to understand that there were specific microbes that could have an outsized effect within our gut.

And I want to bring that up, too, because one of the things that You know, we think about these probiotic foods. It turns out that all foods have some sort of a combination of microbes that live on them.

So if you buy an apple in the farmer's market, you don't think of an Apple as a fermented food because it's not. But if were to eat that apple that comes from, Farmer Joe's farm down the road versus some other guy's far, which has been shipped over from across the country, there are different bacteria on that Apple.

And it turns that those bacteria also colonize the gut and can have So really what all of this is that we're talking about is just reopening a little bit our spectrum of input and asking these questions about, is there something we've missed along the way that nature provides that when we bring back can provide health benefits to people?

It really gets back to what our friend Dr. Jeffrey Bland has been talking about for decades, and that's the idea that food is information. I think we're going to certainly go deeper into how these foods influence us through epigenetic

mechanisms.

But let's talk about that if we can. These molecules that you're referring to, many of which are polyphenols but there are others, what are the pathways by which they work?

How do they influence us physiologically and what's the play in terms of our health? So let us back up for just a second before we jump into what poly phenols are.

What I started by saying is that there are over 100,000 different molecules in our food. And some of these we're just starting to discover, and some these may have a major effect on our health.

Polyphenols are one group of molecules. They're secondary metabolites made by plants, which means plants don't absolutely need them to survive, but they use them kind of tweak survival pathways.

So polyphenol are so named based on their chemical structure. There's 8,00 plus that we know about. And they are molecules that are made by plants to allow a plant to optimize for resilience.

So plants make polyphenols to defend themselves against UV radiation. Plants also make Polyphenol to create communication pathways with microbes in the soil.

plants Make poly phenols. To defend against various pests. so they're found in plants. What's really interesting is if you look at the history of how we have understand these polyphenols, they've actually been popularized in the last couple of decades specifically because they're associated with longevity pathways.

And so resveratrol, good example, peaked and now it's a little bit less popular. But one of the things that was understood about this polyfenolic is that it may act on pathways related to sirtuins.

These are key NAD-dependent longevity pathway. You don't have to go down that kind of tangent too much but these are actually molecules that have been studied in conjunction with some of the most hardcore longevity science because what they seem to do is activate some these specifically longevity pathways now taking a step back That's just one of the things that they seem to do.

So polyphenols appear to act on the immune system. They change the microbiome. The influence metabolism. And maybe most interesting for the purposes of this conversation, they influence how our DNA is used, so-called epigenetics.

I also want to ensure that we don't go too technical on this because the reality is that the best studied diets in the world, especially for brain health, so for example the Mediterranean pattern diet, the mind patterned diet.

If you look at the research on those diets, one of the things that researchers consistently say is these are diets that are rich in polyphenols and it's actually one the reasons why these some of the best diets for overall health.

And so individual foods, some are the top foods people think about for brain health, whether that's something like green tea or coffee or dark chocolate, or even you know, this potential benefit of red wine, it's because of polyphenols that are found in those foods.

So they've kind of been there below the surface and Honestly, just slightly below the surface of the public understanding, most people have that base level of, oh, these are valuable, but the reason they've heard of them is because they're antioxidants.

And what I want to talk about today is it's not about the antioxidant effect. It's about these far deeper pathways that can lead to long-term benefits to overall health and then especially to brain health.

Hey everyone, we're gonna get right back to the podcast, but I have an important message for you. If you're caring for somebody with Alzheimer's, any other form of dementia or even what we call mild cognitive impairment, or

maybe you've received one of these diagnoses yourself, Or if you are focused on preventing cognitive decline, I want to speak directly to you for just a moment about some serious research that's going on looking what we call 40 Hertz light and sound simulation.

We've been actually talking about that on the program. Here's the challenge. Not all 40 hertz light devices are the same. Most use what's called stroboscopic light, and that is the type of light that flashes, then you can see the flashing.

And that can cause nausea, it can cost headaches. And if you can't tolerate that, you won't use it. So there is a company called Optosudix. They've solved this problem with a patented technology that still gives you the 40 Hertz light flashing, but through light that looks and feels quite normal.

Epigenetics and how food influences gene expression

It's the device I actually have on my desk when I'm working. And that's why this company sees a 94% adherence rate and significant improvements across various metrics, including mood, energy, focus, sleep, and memory.

And the light is called the EV light, EVY. You can use it as I do when you're working on your computer, when your reading, watching TV, eating breakfast, whatever.

It becomes really part of your day, not just another burden, it's kind of passive in the background. So I recommend giving it a try for 90 days. And if you and your family don't see value in it, then you can return the device for a full refund.

They cover the shipping both ways. This is a device that really is risk free in terms of getting involved with 40 Hertz stimulation. Important information.

Let's get right back to our podcast. Well, you mentioned something a moment ago that people in my generation continue to be somewhat amazed by, and that is that something in our food, in this case we're talking about polyphenols and other molecules, can influence the expression of my DNA life code.

I mean, DNA was locked up and it was a one-way street from DNA to basically transcription, protein formation, and that was inviolate. And now you guys of your generation just sort of throw this around like, oh yeah, we know food can modify epigenetically the expression of DNA.

that takes a lot for somebody of my generation to really embrace. Because the doctrine of this one-way pathway and the inviolate nature of our DNA was deeply inculcated into our psyches.

So yeah, it's great that I'm living at a time when we can see these incredible changes. Let's just say one thing on that front, because I think it is easy to lose the significance of what you just said within the context of the larger conversation.

If we're thinking about the nature versus nurture piece, that's what I grew up learning. You have these two variables, you have your genes and then you your environment.

And the combination of those two things determines what happens as it relates to your health. What epigenetics does is it bridges the gap, because what it says is that your life experiences can change the degree, not just a binary does the gene get activated and turn into a protein, but the degrees to which that happens, the dimmer switch.

That's absolutely fascinating, maybe the most important conditions that we worry about for most people, these chronic diseases, it turns out that epigenetics may play a significant role in driving those processes.

So, you know, not to jump too far into Alzheimer's here for a moment, but we think about these various genotypes that are associated with higher risk.

Now we're starting to understand that at least in part, epagenetics made determine the degree to which those various gene types are expressed. And what's fascinating about this is, It really makes a lot of sense if you were designing a mechanism in a human that was most likely to succeed given the fact that environmental pressures would obviously be different decade over decade whether it's the weather or scarcity of food you would start with your belief that This is a good set of basic rules, right?

So that's your genetic code. We only have around 20,000 genes, not that many. But you start with the idea of, hey, these are the basics that we're going to build.

So a human is going look basically this way, it's going be around this height, going have two eyes. And then what you would need to consider is why is it that humans only have 20,000 genes, whereas other animals, even incredibly small and seemingly simple animals have so many more genes?

It's because what humans have is the incredible potential to change the way they behave and the ways their health goes as a reflection of environmental input.

That's the whole concept of neuroplasticity. It's this incredible advantage. So the way I look at it is we started out with this genetic code, but then we built in all these mechanisms whereby we could fine tune and tweak the ways that those genes were expressed based on whatever was most relevant in our environment.

And so it's one of the things I believe that's allowed humans to be able to differentiate and do so well across so many different parts of planet. Other species tend to niche down.

They say, you know, I can only handle these temperatures. I could only handled these foods. Humans have been able generalize in a way that is absolutely unprecedented.

And it is because we are capable of taking this environmental data and changing our physiology, changing various pathways in way hopefully that benefits us.

But the inverse of this and the real issue is, When we look at what so much of the modern world has done in terms of signals that it is sending to our genes and our epigenome, it's actually the exact opposite.

So if we're programming epigeneetics with a certain set of patterns that increases our risk for diseases because we are eating the wrong foods, we aren't sedentary, not getting enough sleep, watching too much stressful media, that's exactly what we want to try to mitigate.

So it is really such an incredible opportunity because here what were talking about is that bucket that we've historically said is untouchable, which is the genetic code, turns out to be modifiable, but we need to take that with a whole lot of consideration because, you know, just like neuroplasticity, the rewiring of the brain, this isn't an opt-in, opt out scenario.

What we can do, however, is determine what inputs we wanna feed our epigenome. Well, an analogy that comes to mind is the idea that you have a symphony orchestra playing a beautiful symphony, but there might be one section that's too loud or too soft.

The woodwinds, the strings, whatever it may be. And that the job of the conductor, I think, is to regulate the volume of expression of each individual part so that ultimately there's beautiful music.

And I would say to our viewers, if you want to learn more about this specific topic, a podcast I recently did with a Dr. Sarah Marzi from the Marzzi Neuroscience Institute in England, talking about lifestyle and regulating epigenetic control over our gene expression and how that relates specifically to neurodegenerative diseases.

Austin, you were talking the idea that we shouldn't really focus on the antioxidant activity of polyphenols that there's a lot more going on. Well, what's going?

If we wanted to call polyphenols antioxidants, the reason we would do that is because their chemical structure allows them to be antioxidants in a cell model.

They are able to quench oxidative radicals, and so they are technically antioxidants. But then some interesting questions. One is, when you give humans high doses of antioxidants does it dramatically enhance their health?

If the whole problem, which some people might believe, is that life is just a series of developing more oxidative stress and that leads to every disease under the sun, then we would assume that just being capable of taking a high dose of an antioxidant would fix everything.

But that's not what happens. When you give humans high doses of antioxidants, their health doesn't dramatically improve, and in some instances, it actually worsens.

So that is not quite the case. Beyond this, when we look at what actually happens in humans, either in an interventional trial or an observational trial, they consume higher doses than polyphenols, the mechanisms don't necessarily fit with just a pure antioxidant effect.

As one example, We now know that when you consume polyphenols, the majority of them can't be digested, they can be brought into our bodies because they're kind of bound to various other molecules, so they pass into the large intestine undigested.

Now, you could say, well, it sounds like we don't do anything with these molecules because clearly we're not able to absorb them.

Why polyphenols work beyond antioxidants

But what turns out to be the case is that the gut microbiome can use these polyphenols. So, it can actually metabolize these Polyphenol and convert them into new molecules, which may be more effective for us.

We might be able to absorb them and they might more be effective than the original molecule. Beyond this, research shows that certain poly phenols can influence the makeup of the Gut Microbiome.

So, as much as it might be nice to say, well, they're antioxidants, again, there may be driving effects by what they do to the microbiome in our gut. So very interesting stuff there.

Beyond this, when we look at what the do in the body, what we're starting to see is that they are influencing various metabolic and immune pathways. A study that we can talk about here in a moment, which we actually published a couple years back, showed that giving people a decent dose of polyphenols from a plant called Himalayan Tartary Buckwheat was associated with dramatic changes across almost 900 different epigenetic sites.

And these were not necessarily associated with antioxidant status. They were linked to things like longevity pathways, the immune system, brain pathways.

What I find really interesting is when you start with observational data. Looking at certain patterns of polyphenol intake in the top journal, I guess you could qualify this, but neurology.

When you look at observable data on people who consume highest total amounts of certain poly phenols, you see that rates of developing Alzheimer's disease based on some studies are about 50% lower.

So then we'd say, look, if it's just an antioxidant effect, then why not just give them high doses of various vitamins? And again, we just haven't seen anything even remotely as advantageous when those types of studies have been executed.

One other study I want to highlight here before we kind of move forward is If you think about what's most interesting around brain health for, I would say, the average person, but hopefully for your audience, right?

It's preventing Alzheimer's disease. It is optimizing brain function. One of the things that is kind of more specific to it is to try to prevent the shrinkage of right, the memory centers of the brain.

I know your audience is obviously very familiar with this. Shrinkage of hippocampi are kind of one of hallmark features of Alzheimer's and correlates with the loss of memory, all the things that we don't want.

There was a study that was done looking at people, specifically there were people in a nuclear power plant, so they had some degree of control over that population.

but they gave them an intervention, which was 18 months of a high polyphenol diet. So, one group did a control diet, and one did high-polyphenols diet which is the Mediterranean diet and then one groups did boosted poly phenol diets.

Mediterranean diets plus some additional poly-phenyls, so they're getting roughly 1200 or so milligrams of additional Poly-Phenols a day. What they showed is, using imaging, so MRI at the end of this study, is that the people who were consuming this highest polyphenol amount showed the slowest rate of brain shrinkage, specifically in the hippocampus.

So it seemed as though consuming the poly phenols actually mitigates some of the age-related shrinkages within the brain. And I don't know of really any other study that you can look at that shows that a dietary intervention is capable of something like this.

So, then you talk about, well, what are the mechanisms within the brain? Again, it's immune. It's metabolic. Uh, It could be epigenetic. There's some good data.

Dr. William Lee likes to talk this, that polyphenols can influence vascular health, which is obviously advantageous to the, given that the is incredibly dependent on vascular supply for both oxygen as well as for glucose, as far as other molecules.

But the bottom line here seems to be, consumption of higher levels of these molecules, especially as part of a diet similar to a Mediterranean pattern diet, seems to be associated with better overall brain outcomes through a variety of different pathways.

Well, so that's an interventional trial that you mentioned. You actually conducted an Interventional Trial using this Himalayan Tartary Buckwheat that that, you talked about.

And tell us about that study, because I think the results that your demonstrated are really quite astounding. Tell us Yeah, so my bias is always going to be look at food first, right?

I think it's really tempting to go to saying let's take a quercetin supplement or high dose vitamin C as opposed to eating some onions which are high in quersetin or trying to consume more citrus food for vitamin c.

What we are trying to do is trying understand how is it exactly that when we say food is medicine that that works. And so we've been using a plant called Himalayan Tartary Buckwheat and just for quick background here for people who aren't aware.

So Tardary buckwheats is a type of buck wheat. There are multiple types of Buck Wheat. Common Buck wheat is the most common type that you're going to find in the store.

What makes Tarnary is that it's a very intense version of this plant. Tardary buckwheat historically has grown in some of the most inhospitable conditions on the planet.

The way that its capable of doing that is because it produces just an insane concentration of these polyphenols, specifically one called rutin. Rutin kind of interconverts with quercetin, which is one that people might be more familiar with.

But tardary buckwheat can have almost 2 to 500 times more rootin than common buck wheat based on some of the analyses that we've looked at. So it's very, very concentrated in certain polyphenols.

We have known that people have consumed this plant for millennia. It's been used medicinally for thousands of years as well. we have been curious about the phytonutrient content or the poly phenol content of this plan because several recent studies have shown that when you replace wheat with tartary buckwheat, it improves metabolic parameters, immune parameters and weight loss.

It also improves fatigue parameters. We wanted to see what is it about this plant and the nutrients in it that could influence human health. The first pilot trial that you're describing, which we published in Frontiers of Nutrition in 2024, we were looking at a concentrate of key phytonutrients or polyphenols from Tardary Buckwheat in healthy people to see what it did to epigenetics.

So we used an epi genetic chip that looked at almost a million different sites on the gene at the start and at What we found was, I guess I should say, we didn't go in with the expectation that we were going to find necessarily anything all that remarkable because it's really hard to change health within a 90-day period with just a dietary influence that you'll be able to see in statistically significant ways.

What we found was almost 900 epigenetic sites that were changed with a p-value of.001 or less, so highly statistically significant. And then when we looked at it in more detail, what we find is a couple of things.

One is for a population of people who are aging more rapidly, we saw based on a certain aging clock, these are how you use epigeneetics to kind of determine longevity pathways, that they had a 47% slowing in their rate of aging from the start to the end of the study.

But what was even more interesting to me is we were able to isolate certain pathways that had a dramatic change from the start to the end of the study.

So, one was called ceramide kinase. Another was the COP9 signals home. These are things that probably nobody has heard about before, but what makes them so interesting is that they're key governing pathways linked to immune system and to metabolism as well as to longevity.

We also found changes as related to things like glial cells and neuronal development in the brain. So there were a whole lot of incredible findings that we found.

And this was, again, this is a pilot study.

Himalayan Tartary Buckwheat research and aging

We were just trying to see, are we capable of seeing changes in healthy humans using the polyphenols from Tardary buckwheat over a relatively short amount of time, which is 90 days?

And what's really exciting about this is what we're doing now, which is this incredibly large, randomized, double-blinded controlled trial, placebo-controlled trial with a food here.

So Himalayan Tartary Buckwheat, we were using a sprout powder on specifically cognition. This is, from my understanding, the largest study that has ever been conducted on an individual food for cognition, it's ongoing right now.

Stay tuned, I can't wait to talk more about that as the results come out. So how many people did you recruit for this and how long is it going to be? So this newest trial is 850 people, 425 per arm, for 4.25 placebo, four 25 active.

We've completed at this point a distal pendulum when people listen to this. So completed enrollment, we expect to have the results about middle of the year.

And so then we'll be looking for publication. But what makes me so excited about this study is, you know, We think about this idea of food is medicine.

A lot of people, whether in the government or in academic institutions or the general public, a lot people love this belief that eating certain foods is something that we can do to help to improve our health.

And then the question is, how does that happen, and why does it happen? And generally, it becomes a default where we say, well, foods can influence our health because, again, they're antioxidants.

They have vitamins and minerals. And maybe they have an anti-inflammatory or a metabolic benefit. But it's not good enough, right? If we want to actually be able to use food as medicine, we need to understand how food acts on the exact same pathways as pharmaceuticals.

How food can be reliably used as a way to bias key pathways that can help us to live longer, healthier lives. And as it relates especially to brain health, you know, we know that eating the right type of diet is probably one of the best things that a person can do or is one the things a people can to decrease their chances of developing dementia.

But we have to go one step beyond simply saying, well, you should eat a Mediterranean pattern diet or a mind patterned diet and say, we know that food is capable of exerting these effects because food contains molecules that can preferentially bias these pathways.

I know this is complicated stuff, but this the bridge. This is the gap that exists right now between modern pharmaceutical medicine and what people would talk about that you're picking out some healthy foods in your grocery store because of course you want to eat some colorful fruits and vegetables.

For close to 40 years, I have found myself in examining rooms watching a family struggle through the loss of a loved one, not because that loved on aged, but because, that love one had lost his or her cognitive function.

And, you know, basically I think we were all told that there was nothing that could be done. In fact, they even parroted that narrative for quite some time.

But ultimately, I found myself in a place of not being able to accept that. I'm Dr. David Perlmutter. And Brain Defenders is my new book, clearly the book that I have spent my entire career building.

It's officially launched and it's available for order right now. And I truly believe that this is the most important work that I've ever done. Inside what you will find are the hidden threats that are working against your brain right now, and also the exact science-backed actions that you can take to protect your memory, to your cognitive function, your clarity.

your independence, your ability to interact with other people. Starting today, not someday, but actually starting today. For those of you who want to be all in, I'm excited to announce that we now have the Brain Defenders Immersion Course, which is a guided path to put the very work that was described in the book Brain defenders into action.

Step by step so that protecting your brain isn't something that you just read about. It's something you actually participate in. Something that actually do.

Your brain's future is actually being decided right now by the choices that you are making today. So order Brain Defenders and join the Immersion Course today and you can get all this information by visiting my website which is drperlmutter.com.

That's drPERLMUTTER. COM to learn more about both the immersion course and the book. I wrote this book for you and for everyone you love. Let's defend your brain together and defend the brains of everyone.

You love as well. Remember the time to defend. Your brain is right now. Where are people getting most of their

polyphenols in the normal standard diet?

Well, the number one source, as I think you know, of polyphenols in the American diet is coffee. I'm a huge fan of coffee as you really well, but we're not drinking coffee for the poly phenols.

We're drinking Other top sources, of course, would be tea. I mentioned chocolate. They're widely distributed kind of across the spectrum of plant-based foods.

And there's actually some interesting research being done by a guy named Stefan Van Vliet, who's at Utah State, showing that in animal products, there is actually polyphenol metabolites.

So you can get some poly phenols from eating meat, but those poly-phenyl metabolite differ depending on what the animal consumed. If you have a grass-fed cow, that grass-fed cow is going to have different polyphenol metabolites in its body than a feedlot cow.

And so what makes them so unique, I think, is that poly phenols are this data signaling mechanism across ecosystems. So they go from soil to plant to animal to human, and they can transfer into resilience signals if they're consumed in the right kind of context.

One of the examples I'll give you here just in terms of how much they change is we've been engaged in this sprouting process with this Targery Buckwheat to see what happens when you take a seed and sprout it.

Give it about four days of sproting and what it does is it boosts the polyphenols by about three-fold just over a couple of days because what you're basically doing is activating these key pathways including epigenetic pathways within the plant to interconvert these molecules into a different set of information, because what a plant that is growing needs versus what seed that it is trying to protect and kind of guard against the environment needs, totally different.

So just like if you were going to eat A plant that had been grown organically versus a plant having been growing more conventionally. Those plants create different sets of signals and different polyphenols because of what they're trying to basically exert on their environment or what their good environment is exerting around them.

At some point this conversation transcends from just being, you know, this is what's good for me, for my personal health, to saying this an interconnected web, right?

And polyphenols are just one of the languages discussed by the soil microbes, the plants, animals, and humans. You know, I've had on the podcast a couple of times, Dr.

Steven Gundry, and your grandfather would have said, oh, that guy's a character. And I agree, he's character and I enjoy talking to him. Anyway, at his last appearance, He was really making a point that in many ways, polyphenols act towards our health because they are somewhat pro-oxidant.

So that's, a bit conjectural. What does that actually mean? And what's the evidence? Yeah, so one of the things that's been proposed is that polyphenols are actually hormetic stressors, meaning that when we consume poly phenols and poly-phenol-rich foods, they do exert a low-level stress on our physiology.

And because of this concept of hormesis, which is a that low level stress can actually be advantageous, that in the aggregate, this leads to a value to our health.

You know, Dr. Gundry has a lot of perspectives on plant nutrients in particular and their potential downsides as it relates to things like lectins. What I would say is some of these things are true mechanistically, but at a population level are relatively unhelpful.

And some these are things true at mechanistic and at population levels are incredibly useful. So, right now, We could debate exactly how polyphenols work.

Is it because they have this hormetic effect that leads to a little bit of an oxidant stress or a bit a positive stress at a cellular level? Is is because the regulate the immune system and help to dampen inflammation?

is it is they help you improve vascular tone? We don't know for sure. And it may be that different polyphenols have different effects depending on how they're consumed.

What are the other molecules they are consumed with? What part of the body they in? One of things that's fascinating around epigenetics is we see that epi genetics changes depending upon the tissue.

So epigentic aging could tell you something about what's happening in the liver versus what is happening the brain. It could be the same poly phenol has a different effect on different tissues.

We don't know exactly. That's what we are trying to learn. Yeah, I think his argument was, again, getting back to the notion of a hormetic stress on mitochondria in particular and ultimately leading to more functional mitochondrial, enhancing autophagy, and enhancing mitochondriobiogenesis.

But let's go back for just a moment and talk about one of the, i think, pathways I'm sure that you'd like to talk, about the nRF2 pathway. And I'll let you explain what it all does, what the downstream activation pathways are from activating nRF2.

Where to get polyphenols in everyday foods

But primarily, we know that polyphenols activate the nrf2 pathway, but we also know it is quite responsive as a regulator to increase oxidative stress in the body.

I mean, that's what it seems to do. And that, you know, the polyphenols activate this pathway as well. So in that regard, if poly phenols are pro-oxidant, it might, That might be one of the mechanisms by which NRF2 is dissociated from the key protein and then does all the cool things that it does.

Yeah, I think that is interesting. So there are kind of a couple of key pathways at the level of the cell that polyphenols seem to influence. NRF2 being one, they seem potentially suppress the inflammasome.

They seem act on mTOR and AP kinase. And again, mostly this is mechanistic at a cellular level, right? So if you're looking at NRf2 expression, you are probably going to be looking a cell level study as opposed to a human study.

And I think this is really a great opportunity to highlight one of the key pieces of what we're trying to do with this research, which is it is amazing to get excited about individual pathways.

So I'm sure I could say polyphenols augment autophagy because they have this positive effect through antioxidant pathways, NRF2, mTOR, et cetera. And so if you consume poly phenols, you'll remove old or dying cells You will clean up the cells that are not efficient.

We don't know if that happens in humans. What we do know happens is that at scale, when people consume diets higher in polyphenols, they have better health.

They have a better brain health in particular. And what we're starting to see through some of these interventional data points is, that when we consume poly phenols or poly-phenol interventions, it seems to beneficially augment cognition in a short amount of time.

over the course of minutes, potentially, after an intervention. And then in kind of a middle-range amount of time, it seems to be protective against certain aspects of brain dysfunction.

So, coming back to this study I mentioned before, this green med direct plus study, the 18-month study showing a slowing of the brain atrophy. If you really drill down to the level of this cell, you can go down any of pathways you want to.

You can CREB cycle, mitochondrial oxidation, MTOR AMP kinase, and there's data for all of those. We've been a little bit more focused, again, trying to move away from this purely antioxidant pathway towards the immunometabolic component.

And so I know we've spoken about this a bit before, but where polyphenols have kind of emerged as exciting in the research in just the last decade or so is through the longevity pathways associated with molecules, or I should say associated channels, like the AMP kinase mTOR kind bifurcation.

Again, we've moved away from just resveratrol being the golden child of this, but why this is exciting is if you look at the longevity research right now, what you'll see is that we're talking about molecules called cenotherapeutics.

So these are molecules that target aging at a level of the cell. and some of these are purely pharmaceutical, so some these potent molecules, some are chemotherapeutics, but polyphenols like quercetin as an example, or luteolin, phycetin, what I want to just describe here is Yes, antioxidant, yes, nrf2, Yes.

Inflammosome. Yes mTOR and AMP kinase. yes metabolic and immune pathways. Otherwise, that's really interesting for the people who want to know the specifics.

What I think we need to focus on right now is for a person listening to this podcast, right, who has been told this thing, which is that it's all about calories in versus calories out.

Next level in, it is about your macronutrients. You need to get enough protein. Don't eat that many carbs. The next level is it about getting enough magnesium, making sure you get your B vitamins.

We don't want to lose the magic of what nature provides. And nature isn't providing a very specific dose of polyphenols so that you can get a specific activation of NRF2.

What it trying to do is give you a set of signals so that your body can best respond to the environment around you. And I think to that point, you know, one of the takeaways I want to make sure people leave with is to say as you're going out and making dietary choices today, Consider diversifying the amount of polyphenol-rich foods.

Our friend Deanna Minnick talks about this often, but the rainbow, the idea of consuming a range of colors in the fruits and the vegetables that you consume is an amazing way to make sure not only that your getting more poly phenols, that that's you're getting a good range poly-phenols so that yourselves are being exposed to a whole set of signals that can help to promote health.

Colors in foods, tastes in food, especially bitter tastes and foods are signals that they are rich in polyphenols. This is why coffee is bitter, dark chocolate is better.

And our goal is to move away from a culture in which we've said bland and sweet are kind of the major signals we want to pursue and readdress this fact that we have co-evolved with these molecules and with plants to be able to internalize those signals to promote health.

So poly phenols are a great instance of that. Would it be fair to say that the new recommended dietary guidelines for America are going to shift the recommendation more towards a diet that has higher levels of polyphenols?

I'd say yes and no. So there are aspects of the New Dietary Guidelines that I'm in favor of. I think the most significant of those is they've done a great job with the marketing campaign around food, around eating more real whole food.

and I'm a huge proponent of this. But moving to some of their recommendations, which is a reintroduction of higher levels of saturated fat containing products, moving steak to the top left corner, I don't think that Americans suffer from a lack of eating red meat.

I do not actually think increasing the amount of standardized red meats consumed by an average American is

going to be a value add for their health. One of the things that's been rightfully criticized is that one of best sources of plant-based protein and also many polyphenols as well as fiber legumes, right?

So why are we not prioritizing those given that they're an excellent source of so many of things we're looking for? Yeah, there are plenty of additional things to discuss around the dietary guidelines.

But what I really do like around, you know, the premise of it is let's make a big deal about Americans or really anybody not only eating more real minimally processed foods, but can we actually do something to increase the chances that they have access to them?

And I think that the kind of cop out with a lot of this is to say, well, we, the government, or we as doctors have told you that these are the types of foods that you should be eating because they're healthy, but then we've set up a system where purchasing those foods and maintaining access to them is harder by the day.

So I that's obviously a little bit more of a political conversation, But I am in favor of the idea of advocating for and making more accessible high polyphenol foods.

We're going to get right back to the podcast, but I do have an important message. You know, for decades we've been told that our genes are basically our destiny as it relates to health and that everything's locked in place, predicting even our future brain health.

But let's be clear, your DNA isn't a verdict, it's a roadmap. And I'm talking to you today about 3×4 genetics. I actually described them in the new book, Brain Defenders.

And this is a committee that helps you understand your genetics, what you've inherited, and I think more importantly, how your daily choices can influence how those genes are actually expressed.

In other words, you can control your own genetic expression. That matters for your health and it really matters to your brain health. including things like memory and mood and cognitive resilience.

You may carry genetic markers associated with cognitive decline, like as we've talked about APOE4, but possession doesn't equal expression.

Practical takeaways for a polyphenol-rich diet

Your lifestyle, your nutrition and metabolic health, all the things that we talk about here on the podcast, can powerfully influence which genes are turned on, and which stay quiet.

The 3×4 genetics test looks at how your genes impact brain function at a cellular level and, which then through the 3X4 health journey, in which they provide you, guides you through a clear and a science-backed program focused on inflammation, methylation, oxidation, oxidative stress, things that we routinely discuss here on the podcast that are the key drivers of basically what makes a good brain go bad.

And we have spoken with the team at 3X4 Genetics and they were able to get a special offer for our podcast community. So head on over to 3x4genetics.com 4 slash drpearlmutter and get that special off and start really your personalized brain health journey today.

Let's get your genes working for you and let's go back to the podcast. Tell us what's the hidden ingredient in coffee that people should know about. Coffee is wonderful for a number of reasons.

It's one of my favorite beverages. Partially it's because of the caffeine, but the thing that people need to understand is that coffee is an incredibly rich source in brain active polyphenols.

These are plant nutrients that may have a numbers of beneficial effects on everything from dementia prevention to stroke risk. And it is one the reasons why I drink a cup of coffee every day.

How do we know right off the bat if our olive oil is rich in poly phenols or not? When you drink an olive oil, what you want to be looking for is how does it taste, and specifically, does is have a little bit of a bite?

When we consume an extra virgin olive that's rich in polyphenols, you actually want that to have an aftertaste, specifically that bite, that freshness that tells you there's something very interesting going on in this food.

Most olive oils can be a little bit more on the fence, and as many people know, about half of the olive oil in the United States can cut with inferior olive.

As you're looking for that olive that is rich in polyphenols, it should taste bright, peppery, very plant-forward. If you are not getting those notes, you should consider finding a different source.

Milk chocolate, dark chocolate. What's best? So a recent study actually found that when they compared a polyphenol-rich chocolate versus a low-polyphenols chocolate there were some associations with improved cognition in the group that consumed the higher poly phenol rich chocolate in comparison to the lower poly-phenyl chocolate Why would we even talk about polypenols?

Where polyfenols are a very interesting set of molecules that are about four to five times more concentrated in dark-chocolate compared to milk chocolate So I would say, if you're going to be consuming chocolate, shoot for about 70% or higher cocoa content, and that'll ensure that you are getting the right types of polyphenols that want.

Dr. Asim Perlmutter, this has been a revelation, I think, for our viewers to learn that there's so much going on in their food. You characterize it as dark matter, but there is so many focus on how much protein I should be eating each day.

I'm going boost my protein with a supplement. I think you're getting us away from the idea of supplementing and the ideas of really eating foods that are rich in a variety of chemicals well beyond polyphenols.

What's it going to take, do you think, to get this messaging out so people can begin to reframe the we should stop scientizing our food and really just settle back and eat whole foods?

A message I would put out for everybody as of right now is that despite the fact that we have this hundreds of billions of dollar each year going into longevity, wellness, and the longevity industry plus wellness is now a multi-trillion dollar valuation.

The best studied way to live a long and healthy life specifically around brain health has nothing to do with supplementation. And it certainly has to nothing do any sort of fancy gadget.

It's specifically to the basics well. And as it relates to food, one of the things that we lose as we start moving towards more supplements, more customized and kind of broken down food is the nutrients that have been provided by nature.

So the places around the world where people tend to live the longest, have the lowest rates of dementia, tend be healthiest, are the place where the people eat a regular diet that is made of a diversity of primarily plant-based foods exercise with regularity, engage in communication with friends and family, something that many people now might struggle with.

And as we look specifically at what we should be doing around food, I am 100% invested in trying to understand exactly why it is that certain foods can be so beneficial to our health and especially our brain health.

But you need to understand that right now, your best chance at preventing dementia is going to be on your plate. It's going be in the steps you take around each day, exercising the connections you make with each person in your life, the sleep quality that you get.

And so I would incredibly highly advocate for a person to say, what steps can I take to create a more balanced diet

and including more polyphenols? Polyphenol-rich plant-based foods is an amazing way to take advantage of all the research we've been discussing today.

Wow, Austin, thank you. Thank you for sharing your wisdom. It always is very enlightening for me and how proud could I be? I appreciate your time. Thanks so much for having me.

functionality. But as we learned today from Dr. Austin Perlmutter, to actually change our gene expression through what's called epigenetic modulation.

Changing how our genes express something that's relatively new, but you know it's been going on an awful long time as long as humans have been eating these polyphenols.

That's exciting. Thank you for joining us today here on The Empowered Neurologist. I'm Dr David Perlemuter and we will be back soon. Bye for now.