Introducing Episode Seven: Aging of the Brain

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- Welcome to the Lifespan Podcast, where we discuss the science of aging and how to be healthier at any stage of life.
0:09
Hi, I'm David Sinclair. I'm a professor at Harvard Medical School in the Department of Genetics,
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and I'm co-director of the Paul F. Glenn Center for Biology of Aging Research. This podcast is about why we age, and efforts,
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and things you can do in your daily life to slow, stop, and even reverse the aging process.
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In the last episode, we talked about the skin, the largest organ in the body. We talked about how to stay looking young
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and feeling good about yourself. But today we're talking about perhaps the most important organ in the body,
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and that's the brain. I'm joined today, and on all episodes so far, at least,
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by my- - Wait, so far, at least? - Yeah, well, we'll see how you're doing today. - Wait, do you know something that I don't? - No, just, I'm enjoying this.
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It's going really well. Matt and I have been together for years. We wrote the book "Lifespan," and he's also my lovely co-host of this podcast series.
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- Hey. - Welcome, Matthew. - I'm really terrified now. Like we're coming up on episode eight, and I'm not going to be here for season two.
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- Well, we're going to do a season two, no doubt. And I would not do this without you by my side.
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- Ah, can, Rob, can we make sure that that part of,
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like that I will not do this without you by my side, we really want to make sure that that gets broadcast.
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- Though I've been known to change my mind. - [laughs] So so far in this series,
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we've spoken about how aging impacts our bodies. And even though very clearly,
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there's really actually no separation between our bodies and our minds, these are integrated systems,
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but we've sort of up until this point, not talked a lot or much at all about the brain.
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And the reason for this is because nobody at all wants to stay healthy in their body if they're not also healthy in their mind.

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- Absolutely. And we live in a world where modern medicine, as we call it, has been very good at keeping most parts of the body healthy,
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the heart, so cardiovascular disease, cholesterol drugs, heart drugs.
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- Increasingly over the years, we've gotten better and better and better. - Right, we're living longer, but we're not living better, because the brain is still aging and getting these diseases.
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Alzheimer's and other types of dementia are becoming more prevalent because we're living longer, but not whole body,
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not holistically slowing down the aging process. - In fact, so currently, about 6.2 million Americans
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who are over the age of 65 are living with Alzheimer's. That's just one of several forms of dementia.
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But because we're living longer, that number could grow more than twofold to 13.8 by 2060
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if we don't come up with some medical interventions that can prevent or reverse Alzheimer's disease.
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- And there's very little, there's a recent drug that was approved, but it barely works. It makes a minor difference. So we have to make a breakthrough.
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And what we're going to talk about today is a totally new approach to treating dementia, and that is boosting the body's defenses
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against not just Alzheimer's, but against aging itself. And it's my belief in my labs,
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evidence that if you reverse the age of the human brain, Alzheimer's and other diseases of the brain will go away,
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and you'll even get your lost memories back again. But also, it's not just about Alzheimer is today.
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We're talking about other things that happen in the brain. We're talking about molecular changes that make cells forget what type of cell they are.
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So nerve cells become more like skin cells. And there's another process that's important during aging that we'll touch upon,
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and particularly about its reversibility, and that's loss of blood flow. - And this is really important because a lot of people,
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if you just say Alzheimer's, dementia, people think that's far away. They're going to fix that before I get to that point.
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But all of us, virtually all of us go through some amount of cognitive decline
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in our middle years. And so this isn't just about preventing these things that are way downstream. This is about making our mental,

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our intellectual lives better right now. - Well, the biological clock is ticking all the time. We're not talking about a female's biological clock.
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If you've listened to previous episodes, you know we're talking about what's called the epigenetic or Horvath clock,
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and this is ticking from conception. So even when you're 20, 30, 40, and onward,
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that clock is ticking away. And what you do in your 20s and 30s will impact how healthy you are in your 70s, 80s, and 90s.
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So it's never too early to listen to this podcast and do the kind of things that we're talking about
4:28
to slow down that clock. - Before we can get to that, we got to thank our sponsors. - Absolutely, because this podcast
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goes out for free thanks to them. So first up, Athletic Greens. Athletic Greens is an all-in-one daily greens drink

Thanking the Sponsors

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that supports better health and peak performance. It's developed from a complex blend of 75 vitamins,
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minerals, and whole food sourced ingredients. It's filled with adaptogens for recovery, probiotics,
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prebiotics, and digestive enzymes for gut health. There's also vitamin C and zinc citrate for immune support.
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I've been drinking Athletic Greens for a number of years now as a way to cover all my nutritional bases.
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I'm often traveling, and sometimes my diet isn't the best. So by drinking Athletic Greens, I know I'm getting the vitamins and minerals
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that I need to stay healthy. So if you'd like to try Athletic Greens, you should go to athleticgreens.com/sinclair,
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and you can claim a special offer. They're giving five free travel packs plus a year supply of vitamin D3 for immune support,
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and vitamin K2, which keeps the calcium out of your arteries and puts it in your bones. Again, go to athleticgreens.com/sinclair
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to claim this special offer. Today's podcast is also brought to us by InsideTracker.
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InsideTracker is a personalized nutrition platform that analyzes data from your blood and DNA
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to help you better understand your body and reach your health goals. I've been using InsideTracker for over a decade,
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and I'm the chair of their advisory board. The reason I've long used InsideTracker is because they provide the best blood
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and DNA analysis that I'm aware of. They make it easy to get your blood drawn. You can either go to a clinic
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or have someone come to your house and have it done there like I do. InsideTracker then presents your blood analysis in an easy way to understand.
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There are graphs, and then they give guide and lifestyle recommendations that'll improve your blood by a markers.
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Another feature that InsideTracker has is their inner age test, which I helped develop. The test shows you what your biological age is,
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how it compares to your chronological age, and what you can do to improve it. So if you'd like to try InsideTracker,
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you can visit them at insidetracker.com/sinclair to get 25% off any of their InsideTracker plans.
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Use the code Sinclair, my last name at the checkout. Today's podcast is also brought to us by Levels.
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Levels is an app that syncs with a continuous glucose monitor that they provide. And it interprets your glucose data for you.
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I've been so impressed using Levels that I recently joined the company as an advisor. By monitoring your blood glucose levels,
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the app allows you to see what different foods do to impact you. I've had lots of fun running tests on my own
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seeing how different foods impact my blood sugar levels. For example, I've learned that white rice really spikes my blood sugar,
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whereas potatoes don't. As we'll discuss on today's podcast, having stable blood glucose is very important,
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not only for daily mental and physical energy, but also for long-term health. If you would like to try Levels,
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you can skip 150,000 people on a wait list, and you can join today by going to levels.link/sinclair.
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That's levels.link/sinclair. - Anyone who's been following along knows that we have presented a case over the last few episodes

Ex-differentiation as a Driver of Aging

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that aging is largely a result of X differentiation of cells.
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Let's touch on that really quickly, 'cause that's going to be an important point drawing through this episode as well.
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- You won't read a lot of this in textbooks. This is new science. - You won't even read the word X differentiation. This is something we-
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- That comes out of our work, yeah. And this podcast, you heard it here first. The idea, the new idea of aging is
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that it's not just random stuff going wrong. Is that there's actually a program that begins at birth.
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What happens during birth and prior to that is that cells gain an identity.
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We start as a stem cell that's fertilized, and these cells different identities. Brain cells, skin cells, liver cells,
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everything that makes our body up, the many thousands of different types, tens of thousands actually are given
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their cell type specificity by turning on different genes out of the same genome,
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so almost- - Through epigenetic signalers. - It's called epigenetic. The epigenome is the regulator of the genome.
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And the epigenome is not as easy to describe as the genome. The genome is just a chemical with four letters,
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four chemicals that is the instructions, but then there's a computer that reads that software called the epigenome.
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Or we also use the analogy, the reader of the compact disc, that old device we used to fit like 20 songs on it,
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was really exciting. But what we can now do instead of 20 songs, there's 20,000 genes, but the reader is the epigenome.
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And over time, by that analogy, aging is due to scratches on the CD, and you cannot read the right songs at the right time.
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And a brain cell over time starts to play the music of a liver cell or a skin cell and doesn't function as well.
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And we get diseases of aging, including Alzheimer's as a result. - In the last episode, we said that skin,
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it appears that skin ages faster than most other systems in our body. And we can use these clocks also,

The Brain Ages Slowly

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and have used these clocks to measure aging in the brain. And when we measure aging in the brain, we find something really interesting.
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- That the brain ages slower than the rest of the body. - Like significantly slower. Your brain is biologic,
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very good chance that your brain is biologically younger than you are. - Well, thank goodness, 'cause it's the most important organ.
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Without a functioning brain, we're really quite useless. - So one of these studies was led,
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actually a couple of these studies was led by your friend and sometimes collaborator Steve Horvath. - All right, before I get into Steve Horvath's work
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on the cerebellum, important stuff, let's talk about how that clock is actually measured. 'Cause that'll be important later
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for when we talk about diet. Steve measures the methylation on the DNA. It's a chemical called a methyl
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that the cells add to the DNA and it sticks there, it doesn't wash away, and it makes sure cells have their identity
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and play the right genes for the rest of your life. The problem is with aging, that changes, and you can measure that.
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In my lab, we can do it for about a dollar. And then the readout tells you, okay, that brain,
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even though the person is 40 years old, actually is 50. - But you could look at the liver and you could see that the liver is actually 55,
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and you could look at the skin and say, oh, the liver's actually 62 in equivalent numbers.
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Horvath and his associates looked at tissue samples from 112-year-old woman.
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And they measured the clock in all these different parts of her body. And the regions of the brain were all much,
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much less methylated than her other organs. So that was the first study. And then they've done other studies just a few years later.
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They did a study that showed across a lot of samples,
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predicted age is lower in the brain than really anywhere else in the body.
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Sometimes like a quarter of the age of other parts of the body. - Well, there's a practical and an evolutionary explanation for those.
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The practical one is that our brain is protected. There's a blood-brain barrier. It doesn't get hit by UV light like our skin does. - We have these big thick skulls.
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- We're basically lollipops on a stick. But our brain needs to be protected from these toxins that are in the environment,
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and of course anything that leads to brain aging. But of course, our brains will still age.
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DNA breaks, we've talked about. Broken chromosomes accelerate that clock. And this happens naturally even to cells that don't divide,
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including neurons, the nerve cells in our brain. - One thing to note is that a cellular turnover is relatively low in the brain.
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So even though these cells, even if they're not dividing, they still do age.
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That process of slow cellular turnover could explain some of the reasons why the brain doesn't X differentiate
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as fast as other regions in the body. - Yeah, that's probably right. Unlike the liver, you can cut a piece out, it grows back,
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the brain doesn't easily do that. There's a little neurogenesis, as we call it, but mostly those nerve cells are
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going to there for your whole life. And so they have these super protective mechanisms, these adversity systems
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that keep the brain younger for longer, but they're not perfect, of course. We do have an aging brain,
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but there are ways to turn on those defenses greater than they naturally would be activated.
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- And so all of this is the good news. The good news is, in general, our brains age more slowly than the rest of our bodies.
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The bad news, as we said at the beginning of the show, is that we are living longer. That's actually good news too,
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but it's got a bad news component because our bodies are now outliving, in some cases, our brain.
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The average onset of dementia is 80 years old. And in most advanced nations now,
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the average lifespan is more than 80 years old. And so what that really means is
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that more and more of us are living with dementia at the ends of our lives and other cognitive impairments.

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That's a terrible fate. That's something that we should all be working to prevent.
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- Well, that's why I work on aging and not Alzheimer's disease or cancer, specifically.
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As we've said in earlier episodes, by working on aging, we can keep the whole body young,
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including the brain, which is really what we want to do if we want to have maximal gains in longevity and health
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and mental capacity right up to the end. - And again, there's not, because you work on the whole body,
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you're not working on the whole body when people become old. We're talking about the whole body across the span of a human life.
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And there are advantages to that too, because everybody suffers some cognitive decline.
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This is a little terrifying. The volume of the brain after the age of 40 reduces about 5% per decade.
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And that's got cognitive implications for all of us as we enter what's used to be called our middle years.
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- Well, yeah, I'm 52. I can already feel it happening, but I'm doing certain things in my lifestyle. We're going to tell people about some of those things
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you can do to slow that process down and even reverse it later in life. - So a lot of people might think, well, okay,

Cognitive Function and Plasticity

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it does make a lot of evolutionary sense that the brain starts to have struggles at 30, 40, 50,
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but for one thing, for a long period of our history, people didn't actually last that long in general.
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- Right, most males would die from predation or war or starvation in their 40s and 50s.
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Some people did make it to their 80s. But for most of our history, we didn't need our brains as an 80-year-old, same for women.
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- Well, and we didn't need a really super sophisticated executive functioning to survive even when we were in our 30s and 50s,
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well, 30s, 40s, and 50s. If you made it that far, your life was going to be pretty much the same
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on Monday as it was on Sunday. And it was going to be pretty much the same on Sunday as it was two Sundays before
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and two months before and two years before, and even like 200 years before. - Right, as we talked about in the last episode,

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getting gray, losing your hair was signs of wisdom and you got respect. And presumably, you didn't need to be that quick witted.
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You had a lot of wisdom and experience that would compensate. But we live in a world now where every year, you have to be learning something new,
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and jobs are turning over. And it all started in the 1700s. Now we find ourselves at the point
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where it's really difficult, even for young people, to keep up with this change. - And this is what we call a plastic environment,
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an ever changing environment. And that has implications in terms of how our brains develop,
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and the plasticity that we need to respond to these changes over time.
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- Yeah, I watched my grandmother, who passed away, and we wrote about in "Lifespan." She was a mentor to me. Actually the reason that I do this research.
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She told me to make the world a better place. So she has a very dear spot in my heart.
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What I saw happen to her as she got older was she just shut down. She didn't care about life,
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but she also didn't care about change. And so she didn't worry about computers. She didn't bother learning how to use that.
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She didn't bother learning how to play a compact disc. And the last 20 years of her life weren't that great.
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Nowadays, you cannot be an older person and ignore technology, or you'll be isolated. You can't talk to your grandkids.
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This COVID-19 and the pandemic. - Yeah, imagine what, and this did happen to a lot of people,
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but this is a really terrible thing. If you were not able or willing to adopt new changes to your environment,
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you were not going to be able to talk to people during the shutdowns, during the pandemic. - Yeah, I was just at the Apple store getting
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a new phone just a couple of days ago. And I was there, there was a lot of young people, but then in Cayman, an older person,
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she was probably 85, the way she looked, and the way she wasn't walking that well. But she went up, and I reckon 20 years ago,
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it would be rare to see someone in a computer shop of that age. Now she went up and said, "Hey, I know about the new operating system.
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I need to get a new iPhone. And by the way, my iPad needs an update as well." I was shocked, and I remembered my grandma-
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- Can I link this to my smart walker? - Yeah, exactly. And I find also in our generation,
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so you're on your 40s, I'm in my 50s, we cannot slow down either. We can't say, all right, I'm just going to deal
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with my compact disc or record collection. We have to be, use Spotify to talk to our kids, we share files, social media.
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If you need dates, you need to figure out that. Jobs, the job market's changing totally.
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We used to have one or two jobs in our lives. Now we might have three jobs, we're mobile, we work remotely, and it's turning over all the time.
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That requires a brain that is highly, highly adaptable. - And so what we want to talk about now is

Three Longevity Pathways: mTOR, AMPK, and Sirtuins

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this idea of keeping our brains and bodies aging at about the same rate so that we don't suffer physical decline,
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and we don't suffer cognitive decline through the, as much of the entirety of our lifespan as possible.
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And that's really, as we've had all of these advances in keeping our bodies younger and healthier,
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it's really about keeping the brain younger and healthier too. That comes down to some of the same things
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that we've been talking about throughout this podcast, these three longevity pathways.
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- Yeah, so those who've been with us will know that there are three main buckets of longevity factors
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that respond to adversity. And these have evolved to sense the environment when times are tough.
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We call them adversity mimetics that turn on these three things. So the buckets are mTOR, which respond to low amounts of amino acids,
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particularly leucine, isoleucine, valine. There's the AMPK pathway. AMPK senses low energy, low glucose levels,
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and makes more energy, more mitochondria, boost NAD. And that's important for the third group, which are the sirtuins that require NAD
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and can be activated by certain chemicals. Importantly, they all work together.
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We'll talk about later that sirtuins can activate AMPK. AMPK can activate sirtuins and mTOR.

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What they do downstream is complicated. We're not going to get into that except relevant to the brain, but they protect the body.
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They turn up metabolism, they burn fat, they repair DNA, they clear out senescent cells,
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they lower inflammation among many other things. - Can we dive a little into mTOR? We're going to talk mostly about sirtuins,
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but there's a real key role that mTOR plays in autophagy. - Well it does.
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They all play a role in autophagy, but mTOR is the most potent one. mTOR responds to insulin signaling and fasting.
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And in response, it mobilizes proteins to be recycled and made into new proteins when you're hungry.
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And that's called autophagy, the garbage collection and trash recycling system of the cell. And that's particularly important for the brain.
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'Cause as we get older, there are these misfolded proteins. In the eye, they're called lipofuscin, and then in Alzheimer's,
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they're plaques and tangles of proteins. And to get rid of those, you need really deep cleansing. It's called chaperone-mediated autophagy.
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And mTOR is a really great way, not activating, but downregulating mTOR, turns on those recycling pathways really effectively.
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We're not going to talk so much about that, though we are going to talk a little bit about changing our diet to ensure
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that all three of these pathways are working in the way that will promote brain health. - And even though we're really mostly going to be focusing
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today on the sirtuin pathways, you could be assured that the lifestyle advice
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that comes along with this, it works for all three of these pathways. - It does, 'cause they're talking to each other.
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The reason we're going to focus on the sirtuins is in part 'cause I've been working on them in my lab, but also because they become central to brain health.
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And so we'll cover both. And also what's important about the sirtuins as opposed to these other two buckets is
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that the sirtuins respond to whole variety of environmental pseudo-stresses.
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We call them adversity mimetics. We're going to talk about food, talk about exercise and supplements that you can take

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that should activate these three pathways quite effectively. And we think based on animal studies as well,
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and human studies, should slow down brain aging and even potentially reverse it. - And there's several types of sirtuins,
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but one in particular, there's a couple that are important to brain aging. One in particular is called SIRT1.
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- Right, so there are seven of these genes in every cell in our body. The brain makes a lot of SIRT6 and SIRT1.
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And over time, the levels of both go down with aging, as well as the fuel that those enzymes need called NAD.
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But we'll focus on SIRT1 mostly because that's what seems to be the most important for controlling brain aging.
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- Let's talk about the role of sirtuins when it comes to aging in the brain.
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- Well, remember this clock is ticking away because the loops and the bundles of the DNA are getting messed up.
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The bundles become loops, the loops are becoming bundles. We've linked the sirtuins to that process.
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What happens when a cell is overstressed, overbroke, and overdamaged is that the sirtuins have two jobs.
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They have to create these bundles of DNA and make sure the cell has its identity, so the genes are read like a proper compact disc
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or a software in a computer. But when chromosomes break or you crush a cell,
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there's a panic attack. And the sirtuins rush away to help with that stress and repair the broken DNA.
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But then they have to find their way back to where they came from and reestablish that structure of the epigenome.
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And they do a pretty good job. 99.9% of all of those structures go back to how they were. But that .1% never goes back, and over time accumulates.
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And these are the scratches that cause aging. - And in order to mitigate that,
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what we want to do is upregulate the sirtuins. And we can do that through NAD boosters.
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- Right, well, in the mouse in 2008, we published that just upregulating SIRT1 gene
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in the nerve cells of a mouse's brain were sufficient to slow aging and prevent those loops and bundles from changing.
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And that was the first evidence you could slow down a mouse's brain age. But you can't modify our brains genetically just yet,
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so we need to find safe ways you could take a chemical, a pill hopefully, rather than an injection,
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that will increase SIRT1's activity. The ones we know of are resveratrol and NAD boosters.
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We'll talk about those in a second. And then they give the benefit of a good diet and exercise.
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And in combination, even better. - Well, let's talk about those things first.
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Let's talk about diet and exercise, 'cause that's got to be the foundation on which we build all this other stuff.

Plant-based Diets and B-vitamins

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- Well, absolutely. We've talked previously about the Mediterranean diet. And one of the reasons is that it's very clear
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in over a dozen studies that a Mediterranean-type diet protects the brain from aging,
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and can even reverse aspects of aging in the elderly with mild cognitive impairments.
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- Yeah, there's a study earlier this year from a really large international research group. It was led by Tommaso Boldrini.
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It showed higher adherence to a healthy diet, in this case, the Mediterranean diet, is associated with less amyloid beta,
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less tau, larger gray matter volume. If some of these words are sounding familiar, it's because they're all associated
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with Alzheimer's disease. - And there was a second study that I found fascinating. This one was by Anastasio et al., 2017.
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And it was over 1,000, actually close to 2000 people. And there was a 10% reduction in dementia risk
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for people on the Mediterranean diet. And- - There's actually a 10% risk reduction
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for each Mediterranean diet score, which means the more Mediterranean your diet,
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the better you were doing. - Right, and so that includes olive oil in the diet, red wine, and not a lot of red meat.
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- Yeah, and not surprisingly, this is a research team from Greece. They really like the Mediterranean diet
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for obvious reasons. - Yeah, what I want to get into later, and hopefully we will is,
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what is it in that diet chemically that can help the brain? - Well, I don't know that we need to wait too long to get into that.
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Let's talk about that. What is it in that diet chemically that can help the brain? - Well, there are a number of things.
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I would put them into a few different buckets. There are vitamin that can be deficient,
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that we need to talk about the clock later. But first up, there's red wine, which has polyphenols.
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Resveratrol is one of those. And my lab has been working on resveratrol for many years. And that directly activates SIRT1.
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It makes the enzyme, it's like Pac-Man, and it's controlling genes and it works faster.
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So resveratrol from red wine has clearly been shown to be beneficial, and also prevents cancer
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and not just has metabolic and brain-enhancing effects. The other component of Mediterranean diet
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that works on SIRT1 is olive oil. And [indistinct] recently showed that if you add oleic acid,
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which is a major component of olive oil, it's also found in avocados and other good foods like that, can also directly activate the enzyme
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by sticking to it and making this Pac-Man, I don't know if everyone knows what a Pac-Man is, this little puppet creature on an electronic game,
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chomp faster. And there's probably other molecules. We talked previously in another episode about xenohormetic molecules.
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Plants make these molecules to survive stress, and when we eat them, we get the benefits of that stress, because we worry,
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our bodies worry that our food supply might run out. - One of the, and that's sort of the overarching nature of a plant-based diet,
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whether it's Mediterranean diet or some other diet, is that it is mimicking adversity.
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Your body's got to work a little harder to get everything that it needs, that's sending the signals that maybe times aren't so great
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and we need to activate these longevity pathways. - Well, that's the difference between a Mediterranean diet,
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and a high fat carnivorous diet, and a typical Western diet. They're full with calories,
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full with a whole bunch of stuff that tells the body times are good. It's a bounty. No need to protect ourselves.
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Let's just burn the candle at both ends and forget about life later. And that's not what you want.
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What you want to do is to have the perception of adversity. And the Mediterranean diet, as well as in Japan,
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what's called the Okinawan diet, which has low levels of protein and mostly plant-based,
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those two trick the body into thinking that the food supply sucks and could run out any minute.
27:09
- And these diets aren't perfect, right? Let's talk about some of the things that you need to make sure that you're getting enough of
27:16
if you are eating this plant-based diet. - Right, well, one of the first things to worry about
27:21
if you're just focusing on plants only is a deficiency in folic acid.
27:26
This is vitamin B12. Low- - This is the supplementation that they give to pregnant women, 'cause they're often low in folic acid.
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- Yeah, and there's a good reason why, which I'll get to in a second. There are other B vitamins that are also important to make sure that you have enough of,
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vitamin B6 and B3. We've talked about B3 as early component that's building up that NAD for the sirtuins.
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So B vitamins, especially if you're on a plant-based diet, but for everybody, don't be deficient in these.
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Why? Because the B vitamins are the ones that make sure you have the methyls
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that are added and subtracted from the DNA, that controls the DNA methylation clock. If you have low levels of B12,
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it's known that you have deficiency in the ability to methylate DNA, and that will mess up your epigenome,
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and very likely accelerate the clock in a way that causes aging. And there are a lot of studies that have shown
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that deficiencies in B12 accelerate a variety of diseases, heart disease is the major one,
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but also dementia in the brain. And the main reason I think what's going on is that aging is being accelerated
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when you don't have enough of these B vitamins. - And the result of low B vitamins is an elevated level of homocysteines.

Homocysteine, Plaque, and Vasculature

28:34
- Well, that's a markers, yeah, exactly. So often your doctor, but not all the time, measures homocysteine levels
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because it's been shown to go up as a predictor of heart disease and dementia.
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And high levels are particularly dangerous. Most doctors would want you to have less
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than 10 micromoles per liter. Some people go as high as 100. If you're that high,
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you're certainly going to die in the next few years of cardiovascular events. So you try to keep the homocysteine levels down.
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And the best way to do that is to make sure B12 levels are optimal, not too high, 'cause that can also cause problems.
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Again, you have to measure it. I use InsideTracker to measure my B vitamins. But also you want to avoid too much alcohol,
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definitely don't smoke. Your menopause will also affect your homocysteine levels. Certain types of cancer will.
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And aging itself leads to increases in homocysteine. - And this all materializes as plaque.
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- Well it does, but homocysteine itself, I don't think is the problem. It's that the methylation pattern on the DNA is getting messed up.
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The sirtuins can't cope. SIRT1's not good at going back to where it came from. And your body will get older.
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And when your body is older, it has more inflammation, can't get rid of plaque, builds up calcium in the arteries instead of being in your bones,
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and that we call diseases, but that's actually aging going on. - I think a lot of people think about elevated homocysteines
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in terms of what's going on in their blood vessels throughout their body. But we're having a conversation here about our brains.
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It's important there as well, maybe even more so. - Well, yeah, it's known that high homocysteine levels,
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which is a version of an amino acid, do correlate with increased susceptibility to dementia.
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And the reason probably is that we have vasculature in our brain, and that these are very small vessels
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that are needed to bring oxygen and take away toxins, and they clog up really quickly. And with high homocysteine levels as an indicator,
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we're getting plaque also building up. And not only that, the endothelial cells that are like the lining of the blood vessels,
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they literally are, but they need to remain flexible, like rubber bands, they become defective, they age, and they become stiff.
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And then they start to accumulate this cholesterol, and then you get occlusions. And that can ultimately end in a stroke.
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But even before that, those occlusions are limiting the amount of oxygen your brain gets,
30:46
leading to of course losing your ability to remember things, even at my age, but ultimately what's called vascular dementia.
30:53
- There's a pretty simple way to monitor that accumulation.
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- Yeah, you just look in your eye. Well, you don't look in your eye. - It's really it hard. I actually tried earlier. - Yeah, a doctor, an ophthalmologist,
31:05
or even an optician will look in there and have a look at the back of the eye, the retina, and they can see very clearly.
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And they'll take photographs. They can show you of whether you've got a perfect blood vessel lining, these blood vessels sit on top of the nerves,
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which is a bad design, but that's how we are designed. They will see those blood vessels.
31:23
And if they're occluded, that's a really, really bad sign. We've actually known for many decades that if you see one of these occlusions and a lot of plaque,
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you basically are going to suffer from a heart attack and die pretty soon. - Yeah, you have like a,
31:36
it's like a 15% chance of death within a year. And then it goes up from there in really scary measure.
31:43
- Exactly. In 1959, Dr. Robert Hollenhorst found that these plaques, these little occlusions that he could see
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in the back of the eye with his lens predicted survival. It got really bad, in fact, what's now known,
31:57
if you see these, you got a 50-50 chance of being alive seven years later, and that's really scary.
32:02
- That's really scary. So obviously, staying ahead of this, not letting that accumulate at all is preferential,
32:10

even to catching it early. - Right, and think of this. Your eyes are a window into your brain. In fact, your eyes are your brain.
32:16
They're extensions of those nerves with balls at the end- - I know, that's creepy. You told me that before, and I got creeped out. - Yeah, when you look at someone in the eye, you're actually looking at their brain.
32:23
Pretty cool. But what's great about is you can see into your brain. And that's what we're talking about here is getting an indicator of how much occlusion,
32:30
plaque there is building up inside your skull. - Let's talk also about fatty acids

Fatty Acids

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and the importance of really making sure that you're getting the right and the right kinds of fatty acids. Particularly if you are on a plant-based diet
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and you're concerned about brain health, which we all should be. - Right, even with a normal diet,
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you often don't get enough of these omega three fatty acids, which are the types that we don't make ourselves.
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If you're only meat and you don't eat fish, you eat animals besides fish, you're not getting a lot of them.
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And they're the building blocks of the brain, so we need a lot of them. And they've been shown in a number of studies to help with many different things,
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from wound healing, and of course, depression. Now, what are the sources? Well, if you eat fish, you're probably in good shape.
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You've got salmon and mackerel, krill, sardines. These are good sources of omega-3s.
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- And these are giving us the DHAs and the EPAs. 'Cause there's three different kinds of these, right? - Well, there are lots, but the three main ones
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that people talk about are EPA and DHA. The EPA is the more important one.
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You want to get at least a gram of that. Sometimes people say, get 1.6 grams of this ratio of EPA to DHA,
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and women about 1.3 grams. And that's been shown to greatly improve memory and counteract depression.
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Now, if you're a plant-based person, you can't obviously get as much, you have to focus on other types of food
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that have what's called alpha-linolenic acid or ALA, which is converted slowly, not efficiently.
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About 10% of it gets converted by the body into the two types we just mentioned that are important,
34:02
the DHA, and importantly, the EPA. Focus then on flaxseed, walnuts, chia seeds.
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That's where you get your ALA. Linseed oil is where it was first discovered, ALA, linolenic acid.
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I use that to polish certain things, keep wood looking good, cricket bats, you put it on there. But you can also, you can consume a little bit.
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There's a lot of it in there as well. And there's one other thing I want to mention that isn't in that list of three,
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which is a monounsaturated fatty acid called oleic acid, which is really important.
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And I mentioned it earlier. It's a component of olive oil and avocados. And I have that included in my supplement every night,
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along with these other components. - As a recent convert to seaweed salads, I would be remiss not to note that you can actually get,
34:46
it's one of the few plant sources you can get DHA and EPA from is from seaweed. - Is that right? - It is right.
34:52
- Well, I don't know if you get enough of it. I think it's really a good thing to consider. And talk to your doctor about it,
34:58
to take at least a gram of these omega-3 fatty acids every day. - So we know we should be consuming these omega-3s, but why?
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What are they doing on ourselves? - So it turns out these omega-3s actually form a structural component of the brain.
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They insert along with other fats in the brain. So fat is actually good for the brain. A lot of our brain is made up of these fats.
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The reason is that the nerves aren't naked. Much like an electrical wire, you don't have them lying around your house naked.
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They're actually wrapped with insulation tape or insulating material. And that's what these fats do.
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And these are membranes that wrap around, it's called the myelin sheath. And these fats, actually, some of them are omega-3s.
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And the more omega-3s you have in your diet, the more you'll have in those membranes. And that protects from inflammation and damage,
35:43
and helps the nerves function and repair if they get damaged. - We have to eat for brain health because what we eat,

Physical Activity

35:49
what we consume helps make up the parts of our brain that keep our brain healthy. We also have to exercise for brain health.
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We can't neglect that part. And we can't think that exercise just affects us from here down, it doesn't. - Well, that's actually known in dozens of studies.
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It's been shown that if you do aerobic exercise or even just walk, that'll improve your chances of having a better memory and cognition as you get older.
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The reason we think that is, is that there's two reasons. One is better blood flow, and also better neuronal activity
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and slowing aging of those cells. That involves the sirtuins, this third protective survival pathway.
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That can be activated, of course, by the food, and also by exercise. - We've seen this in a number
36:29
of both human and animal studies. - Well, that's right. There are a number of studies that we could talk about. The one that stood out for me in our research was
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the one that involved 160 sedentary, sitting down, non-exercising adults that were told for six months
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to do extra aerobic exercise, to do some aerobic exercise. - Yeah, they were actually, they were led through this process,
36:48
'cause you can't just tell humans to do anything. They're just not going to do it. - They had a cattle prod and they're pushed onto a treadmill.
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Something like that? - I don't think it's that highly regulated, but they do make sure they actually do the exercises.
36:59
- So Blumenthal and his colleagues found, what was it, 2019, that this greatly improved executive function.
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- Executive function. - Yeah. - That's the function that's like co-equal to the judicial and legislative function?
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- It's kind of like that, but kind of different, which is, so you know a lot of kids don't have executive function. They can't focus.
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They can't do tasks right. That's what executive function is. Concentration, focus, do some tasks. - And so just a little bit of exercise,
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six months of exercise improved for these people, they're all over the age of 55, improved dramatically their ability to do these things.
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- Well, they did. And I think that that's one of the main reasons for exercising. You might want to do it not to just because you feel better,
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but you will think better too. - It's hard to take people who have Alzheimer's, Parkinson's disease,
37:46
other cognitive problems through things like that, because it's just, at a certain point,
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you lose the ability to get them to respond to you. But there's also lots of evidence in mice for this. There's a study this year out of Brazil that showed
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that exercise had a really significant effect on mouse models of Alzheimer's and Parkinson's.
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- Right, so it's not just aging that exercise works on. What you're saying, and what's in the literature is that diseases of aging,
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and also including Parkinson's, which is age-related, are benefited as well. There's another study.
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It doesn't have to include aerobic exercise. There's one where there's strength exercise. So if you don't like running, pick up some weights,
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because what's been found in this study, this is 2013, Perera and colleagues found that in an elderly cohort,
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they had 451 people, just 10 weeks of strength training increased the level of factors that grow new brain cells, new nerves.
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This marker is called BDNF, or brain-derived neurotrophic factor. And we use that as a way of indicating
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the youthfulness of the brain and regrowth of new nerve cells. - And the takeaway here is that at a time in many people's lives
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when they're becoming less active, it's actually more important than ever before to become more active and to stay active.
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- Before it's too late. It's very hard to get a very elderly grandparent or parent to get on a treadmill or lift weights.
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So what we want to do for ourselves and for our parents and grandparents is to get them moving early on before it's too late.
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- Even if we're eating well, even if we're exercising, presumably, our ancestors did these things too.

Metformin

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If they hadn't, we wouldn't be here. They faced these sorts of adversities all throughout their lives.
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And that's what we're trying to mimic through our diets and our exercise.

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It still might not be enough, because we do live these lives of incredible comfort, and we eat a lot of food.
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And so we might need a little additional help
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when it comes to keeping our brains healthy. This is where supplementation comes in. And one of the supplements we want to talk about is metformin.
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A lot of people are going to say, oh wait, that's an AMPK activator. You guys said you were talking about SIRT. But we're actually kind of talking about both.
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- Well, yeah, there's crosstalk between these various defenses. The AMPK pathway talks to the NAD sirtuin pathway.
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When you take metformin, and you get this mitochondrial hormesis, mitohormesis, that will raise NAD levels.
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It'll stimulate the production of the enzyme that turns NMN, a precursor of NAD, into NAD itself and raise NAD levels,
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and get the sirtuins active as well in the brain. - Okay, and we know that metformin is good for brain health from a variety of studies.
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One we want to start with today is this fish study, which I did not know that they did cognitive studies on fish.
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- Fish are actually used quite often in labs. And most of them live about two years, as long as a mouse, which doesn't make them that much more advantageous,
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but there are short-lived fish. There's one called Nothobranchius furzeri that lives only a few months.
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There's one, in this study, they used redtail notho, which is guentheri, Nothobranchius guentheri,
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and it comes from Zambia. It lives a bit longer. Its environment isn't as harsh as the other one.
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And over that year, what it does is it breeds very quickly. It lays eggs that become encased in a shell.
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The fish then dies, and those eggs will survive until the rains come again. But it's a great model for aging,
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because it goes through its lifecycle super quickly, but it's built of the same stuff that mice and we are.
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- And how do you tell that a fish is having cognitive impairment or cognitive success?
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- So it sounds crazy measuring memory in a fish, but they do have good memories. You can test it in a variety of ways.
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You can put food and a light, and see if they remember that the light is where the food is. They come to the light if they have a good memory.
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You can put them through mazes, like a mouse, they swim through if they've got a good memory, and they know where the food is at the other end.
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And the third one is where you test their fear conditioning. It's reaction and memory of fear.
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And you shine a red light in the tank, and then you get a stir like you would a cocktail, and swizzle it around, and they,
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sure, if they remember that, next time they see the light, they should run away, or swim away, I should say.
41:57
And so what they did was, in this study was they found that by treating these fish with metformin, put a little bit of metformin in their food,
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those fish were able to remember those tasks much better as they got older. - And so the Ted lasso quote
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about being a goldfish and immediately forgetting things, that's not true? - No, fish have a really good memory actually,
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and they have brains that are quite similar to mammals. - So when you give these fish the metformin,
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what's happening cellularly? - Molecularly, what's happening is that the metformin molecule gets
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inside the cell and into the mitochondria where there's what's called the electron transport chain. This is a series of bundles of proteins, five in all,
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that pass electrons between them like a hot potato, and generate chemical energy. Metformin disrupts that first step,
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and in doing so releases free radicals. Superoxide anion is one that goes off and damages parts of the cell.
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And we call this damage mitohormesis, which is a little bit of damage makes actually the cells stronger.
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One of the main things that happens is that the cells react and say, oh my goodness, we don't have enough energy, make more mitochondria, more battery packs,
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more energy for the body. That's always a good thing with aging and health and longevity. The other thing that happens is that this signal sends
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a protein called GLUT4 to the outside of the cell in the membrane to suck more sugar out of the blood stream,
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and having lower blood sugar protects the body from this caramelization process that also causes many diseases,
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including dementia, by clogging up the arteries. - High blood sugar is not good for brain activity.
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- No, it's not good for any tissue. What happens is this glucose that's in your bloodstream, if it gets too high,
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it actually binds to proteins, about 10%, five to 10% can be covered in this glucose molecule.
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That's bad for their function. It's often hard to remove, and it leads to dysfunction particularly of the cardiovascular system.
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- We're not just seeing improvement in cognitive function with metformin and fish.
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There's been studies on mice. There's been studies on rats. There's been studies on humans. - Yeah, there's a bunch.
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Our researchers did a great job, and they're all fairly recent, 2014 to 2019.
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The one that I want to bring up is Koenig and colleagues in 2017, a really good study.
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It's randomized, placebo-controlled crossover. That's what you always look for. Metformin improved, again, this executive functioning,
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the ability to focus, by treating 20 non-diabetic normal subjects.
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And they had mild dementia when they started, and they improved, which means that dementia is
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somewhat reversible with this drug. It also means that if you're starting to lose focus in your job, daily activities,
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either taking Metformin may help, or just keeping your glucose level steady, which is what a lot of us do,
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and we measure that daily with monitors on our arms. That is also a way to stay focused.
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- And that's a small, really well controlled study. There's also a really big, less well controlled study,
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but nonetheless really impressive study from 2019. It took a really huge cohort of diabetic patients,
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tens of thousands of them. Dementia incidence for the metformin users, 55% lower.
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- So actually, it was preventing the onset of dementia by what, 55%? - Right. - That's a massive number.
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When we talk about these numbers, often it's a five to 10% decrease in disease. 55% is a massive number
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that we should definitely pay attention to. - There's been some suggestion that metformin,
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in addition to acting on AMPK, and then the chain of custody moves its way down

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and AMPK acts upon NAD, metformin actually might impact NAD directly as well.
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- Yeah, so that study was super interesting from a few years ago that metformin could directly interact with, bind to the enzyme,
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and make that Muppet, that Pac-Man creature go faster, in the same way that resveratrol has been shown to.
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But that was only done in one study. And of course, in all science, we need to reproduce it, and we're still waiting on those results.
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In my lab, we've tried it. We haven't had perfect results yet, but we're still trying. - In the meantime,
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there are more direct ways to impact NAD levels. And that's through NAD boosters.

NAD Boosters

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There's been lots of animal research on this. It elevates cognitive functioning. It promotes recovery after brain injury, all good stuff.
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- Yeah, why would you want to supplement NAD in the first place? Well, it's known, just like the rest of the body that in the brain,
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NAD levels go down for a couple of main reasons. One is that we don't make as much that NAMPT enzyme
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that's activated by metformin and exercise, goes down, so you don't make as much. But also it was shown by Jeffrey Milbrandt
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at Washington University in a couple of high profile papers just in the last few years that there's an enzyme
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that gets turned on in nerve cells when they're damaged called SARM1. And it depletes the cell rapidly of NAD.
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So what you've got is a decrease in the production of NAD, also with an increase in the degradation of NAD.
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So supplementation we think is important, to not just get the youthful levels back, but go beyond that, to mimic exercise,
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mimicking a perfect diet, especially for the elderly who cannot always do those things. - And we've got a long history now of research
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going back almost 20 years of NAD supplementation on brain health. There was a study in 2004
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that showed treatment with NADH slowed Alzheimer's. And a lot of people hear about NAD+.

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NADH might be a little unfamiliar. - NADH is basically NAD with a hydrogen atom attached to it.
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NAD+ has a positive charge like the end of a battery. And then if you stick the hydrogen onto the vitamin B3 part of the NAD,
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then that's going to be called NADH. And that's important in a cell, 'cause that's the other major function of NAD.
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One is to turn on the sirtuins and DNA repair and all that good stuff. But it also is known as a hydrogen carrier molecule
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that takes hydrogens and moves it from one place to another. - So why would NADH work if NAD+ is what's the standard?
47:55
- Well, what I think is going on here is that, so NAD activates sirtuins in a test tube and in the cell.
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NADH actually has the opposite effect, so you don't want high levels. So what's probably happening is that NADH gets into the bloodstream,
48:07
gets degraded into its various components, vitamin B3, there's a phosphate, there's a part of DNA called a nucleotide, the A letter,
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and they get reassembled back into NAD+. You're just giving the components in a concentrated form by taking NADH.
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- Another more recent result, a combination of NR, which is another kind of NAD booster
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that we talked about a few episodes back, and pterostilbene slowed down the progression of ALS.
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- So NR is different from NMN. Let's go through that again. When you want to make NAD,
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what the cell does is it takes vitamin B3, or niacin, or nicotinamide, turns it into NR.
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So the nicotinamide gets now a sugar, ribose. And then to make NMN, it puts a phosphate,
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which is phosphorus and oxygen. And then it combines that together to form NAD. So those are the various steps.
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Now, what NR is, it's a couple of steps back from NAD. And so when you take NR,
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it's made into NMN, made into NAD. But it's been shown in humans by taking large doses,
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about a gram of NR, you'll make NMN, and you'll make higher levels of NAD,
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which is shown to be important in this study in ALS patients. Those ALS patients actually benefited greatly
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from this supplementation. The other component I forgot to mention is pterostilbene. And the pterostilbene part of it is resveratrol.
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It's resveratrol with three methyl chemicals on it. It's essentially a way of delivering in a pill form resveratrol plus an NAD booster.
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- This was a pretty short-term study. It showed immediate returns for ALS patients
49:44
when they took this combination of NR and pterostilbene. But Lenny Guarente, who's running the study out of his lab at MIT,
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your former mentor there, we chatted with him this morning. He said, actually, they're now looking at a year long study
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so that they can see if these results continue on for a longer term for patients who are dealing
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with a really, really debilitating disease. - For which there is no cure, or even effective treatment.
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So this would be a big deal. And most of these trials fail in the first stage, phase one.
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They're in phase two, so they made it further than most, but of course, it's a very difficult disease, ALS,
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Stephen Hawking, it's just a terrible, debilitating disease, very hard to treat, but fingers crossed for this one.
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Hopefully those patients will continue to do better. - Can we talk a little bit about this idea of increasing blood flow,

Increasing Blood Flow

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and what NAD boosters do for blood flow? One of the studies that you were involved in
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showed vascular improvements in mice
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that were put on these boosters. But vascular flow isn't just important in our bodies.
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It's, well, frankly, it's more important in our brains, right? - Right, we forget about our brain
50:59
needing blood flow and oxygenation, 'cause we don't really see it. It's not part of our daily thoughts.
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But it's just as important, if not more important than the rest of the body. We found not only does NMN and SIRT1 activity
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maintain the youthfulness and ability to grow new blood vessels in the mouse as muscle,
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but we collaborated with Zoltan Ungvari at the University of Oklahoma to show that mice,
51:24

even in their brains, benefit from NMN by building new blood vessels. And those elderly mice not just had better blood flow,
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but could think and remember things better. - And we think that's because of the improvement in vascular tissue.
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- Well, almost undoubtedly, that's what was going on in those mice, because we could block the effect. We could actually downregulate the SIRT1 specifically
51:46
in those endothelial cells that line blood vessels, and then the benefit of NMN went away. - And this turns mice with older brains
51:53
into mice with younger brains? - That's essentially what happens when mice and people get their ability to learn again,
52:00
that's reversing an aspect of aging. - So before we move off of the topic of sirtuins in the brain,
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it's not just blood vessel that are being affected. It's not just the cerebellum. There are other parts of the brain
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that are also really well impacted by SIRT. - There are a few things I want to mention about SIRT1
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before we leave this topic. One is that overexpression, turning up SIRT1 in all of the nerve cells
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in the brain extends a mouse's lifespan and protects them against these diseases that we induce in them,
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ALS, Huntington's, and Alzheimer's disease. The other thing is, there are a couple of regions that are of note.
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One is the hippocampus, which secretes hormones into the bloodstream, and that can actually reduce blood glucose levels
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by talking to the liver. The other area of the brain is the hippocampus. This is the part of the brain that consolidates memory.
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And it was found in old mice, if we activated that part of the brain with resveratrol, or activated SIRT1 by putting in more copies
52:55
of that gene and turning it on, those mice had better memory even in old age. So really what this says is that SIRT1 plays
53:01
an amazingly important role in delaying aging, preventing diseases of aging in a mouse,
53:07
and potentially even in a human. We'll see how those trials continue. But let's talk a little bit about sleep,
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'cause the hypothalamus controls the circadian rhythm, day and night rhythms of the body.
53:18
- Yeah, let's talk about sleep, because quite frankly, if you don't sleep,

Sleep

53:23
you're in a lot of trouble. And you're going to age faster. There's lots of research on this.
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- Yeah, even at the molecular level, we understand that SIRT1 and NAD play a fundamental role in controlling your wake-sleep cycle.
53:35
SIRT1 and NAD are going up in the morning, coming down later in the day, getting your body ready for sleep, and in doing so,
53:42
what they do is they turn on a particular gene called BMAL, which is part of the clock, not the Horvath clock, but the daily clock,
53:48
the circadian rhythm clock. And those genes tell the liver to calm down,
53:53
it tells the brain to calm down, and in the morning, tells everything to wake up again. And so what is really important to understand is
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if you start to lose the function of SIRT1 and have low NAD levels, you're probably not going to sleep well,
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but also, you're going to age prematurely. - And the big problem here is
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that sleep efficiency actually declines with age. So we got to work harder at sleep as we get older,
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just like we have to work harder at exercise as we get older to promote brain health. - Yeah, another way of saying it is that as you get older,
54:23
you lose your ability to sleep. And if you don't sleep well, you'll lose your ability to fight aging. And it's just a feed forward disaster.
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So you've got to intervene. You can intervene with the kind of things we talk about here, which is eating well, exercising,
54:36
and intervening with the kind of things that you can take perhaps as a supplement. But now, let's talk about what do we do
54:42
to make sure we sleep well, and we have the right rhythm. And one of the key things that I use is NMN.
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NMN is going to raise NAD levels in the morning. I take a gram of it then. But I also, when I travel, I use it to reset my body.
54:57
And I definitely feel that I can avoid jet lag if I do that. - There's some other supplements that a lot of people take.
55:03
Magnesium? - That's good for sleep. L-theanine is another one that people try. I've used it, seems to help me.
55:10

But essentially, you just want to calm down at night. Don't do your emails too late. Relax your brain. - And then I think a little counterintuitive,
55:17
one of the best things that you can do for sleep at night is actually not something you do before you go to sleep.
55:23
It's something you do right away when you wake up. - You mean go outside? Get some light? - Well, you got to get light. You got to reset your circadian rhythms.
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And the best way to do that is put yourself in a situation where your body knows it's daytime.
55:35
- Well, you can. But here in Boston where I live, there's not a lot of light in winter. So I actually have some blue light
55:41
that I can shine in my eyes to get my cortisol levels up, synthetic way, not naturally. But whatever you do,
55:47
try to get some light early in the morning, 'cause that always gives you an energy boost and helps you reset your circadian rhythms
55:52
if they're not perfectly in sync. - And like the other things we've talked about today,
55:58
there's lots and lots of research. We're not just making this up. Sleep is important, we know this.
56:03
- Well, yeah, even in flies. Flies sleep. It's a little known fact. But before we get to the humans, I want to, this is a really cute study.
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It was a study that was in 2020 in fruit flies. They found that if you deprive flies from sleep, they have a lot of oxidative stress in their gut,
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and they also have a short lifespan, which by the way, could be rescued by treating them with an NAD booster.
56:23
- Which is also a way that we've seen that you can rescue human subjects from sleep deprivation.
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But even just one night of sleep deprivation, a lot of people say, oh, you know, I'll catch up tomorrow.
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I'll catch up the next day, whatever. Maybe I didn't sleep well tonight, but I can sleep well the rest of the week. One night of sleep deprivation increases
56:43
amyloid beta production by 5%.
56:48
That's, you don't want to miss with amyloid beta, right? - No, that will accumulate in your brain.
56:53
It's very hard to get rid of. And I was also shocked to read that it's not just the brain that ages if you don't sleep.
57:00
We already know that if you restrict rats from sleep, they get diabetes within two weeks.
57:06

In humans, looking at a million people, this study's from 2010, Capucho et al. What they found was
57:11
that in people that had very little sleep, the risk of dying was 30% higher
57:16
than those that got a natural, normal night's sleep. - And the thing is, our brains are getting so much adversity right now.
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We talk about a little bit of adversity being good, but we evolved to have a pretty low,
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constant low level of adversity popping up now and then. And right now in terms of the insults
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and injuries that we're taking in in terms of stresses, daily stresses, everything changing,
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our brains are being besieged all the time, we need sleep to reset.
57:45
- It's just too much. There's too much to remember. There's too much to cope with, too much anxiety. We just are living through a pandemic.
57:52
This is really stressful times. And just lack of sleep makes it worse. And physically, we will regret it decades later.
57:59
- The overall message today is we got to keep our brains healthy. And we have to work to keep our brains healthy.

Overall Message: Keep your Brain Healthy

58:07
We can't just expect that they're going to do what they've always done throughout our evolutionary history, which is to last longer than we have.
58:15
We've figured out many of the tricks that are going to keep us alive for longer holistically,
58:21
but we got to keep our brains healthy for at least one day longer than the rest of us last.
58:28
- It's super important that we look after our brains. It's not just about ourselves. It's about our families.
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Many families have had to take care of parents and grandparents that have dementia. This is not pleasant for anybody.
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And we have a responsibility to society, and particularly our family members, to stay healthy for longer,
58:44
particularly keeping our brains younger for longer. - In our next episode, we're going to be talking about a lot of the things

Next Week’s Episode and the Future of Medicine

58:52
that we sort of hinted at throughout the series so far

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in terms of what's coming next. Maybe what's coming next in a few years, maybe what's coming next in 10 years.
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And what if we can keep ourselves from aging too quickly over the next couple of decades,
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might be a quarter century away and sort of waiting for us there if we get there healthy.
59:16
- Well, it's a super exciting time. The reason we're doing this podcast now is to bring the audience, the world along with us,
59:23
and to experience these changes essentially in real time as they're being made. And the kind of results that are in the lab
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and increasingly going to customers, consumers, and eventually to patients in hospitals and at home
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with medicines will be directed towards lengthening lifespan, not just by one or two years, but by decades.
59:41
And I can see that coming. We're going to talk about some of these things that'll include wearables, monitors,
59:46
and even age reversal technologies that get that Horvath DNA methylation clock to go back, not just a couple of years, but potentially by decades.
59:54
- One of the things that I noticed, and we've talked about this a lot, you and I,
1:00:00
many of the things that we talked about in the book, that we said, these are a little ways down the line.
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It's only been three years since the book, two years since the book was published, and a lot of those things are coming to fruition
1:00:12
a lot faster than we had even thought. And so these things that maybe in the next episode,
1:00:18
we're going to say, ah, these are kind of far down the line, who knows, they could be here next Tuesday.
1:00:23
- Right, it's blowing my mind how quickly things are changing. I didn't realize the discovery of reprogramming in the eye,
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which was in the book, and we published very recently, has taken the world by storm.
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There's billions of dollars being poured into this. So it's very hard to predict how this is going to look just a few years from now.
1:00:41
Plus the wearables, these things are changing, and coming to the public all the time. The other thing that's happened thanks to the pandemic is
1:00:48
that home remedies and home testing has taken off. So there are things we can now do at home
1:00:54

that were beyond even the imagination when we wrote the book. - Yes, fundamentally changing
1:00:59
what healthcare is going to look like in this next part of the 21st century. - Well, it's exciting. A lot of our health
1:01:05
and our wellness is in our own hands now. we have the tools, we'll have the knowledge to greatly lengthen our lifespan,
1:01:11
of those of our parents, our grandparents, and our kids. And that's in part what we're going to talk about in the next episode of "Lifespan."
1:01:18
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