Neuroinflammation & What To Do About It? Transcript

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Introduction and Background

– Welcome to another episode of reversing inflammation, summit body and mind longevity medicine and in this episode, I'm very pleased to have Austin Perlmutter, he's a board certified in internal medicine and he's a internationally recognized expert in environmental influences on mental and brain health.

He's also the co author of a New York Times, bestselling book, Brainwash. Welcome to our program. Austin is so nice to have you here. – I'm thrilled to be here.

– Thank you. Thank you. Let's get the conversation started by telling us a little bit about your background and what got you into this field. – Sure, well, so many things, right. I guess the important background background is that my grandfather was a neurosurgeon and my dad is a neurologist, so there's always been kind of a slant towards paying attention to the biology of the brain and where things go wrong. Um I needed to have my own journey to get me to the point where I felt like this was important for me and something that I wanted to learn more about. And that journey was in essence going into internal medicine. Um So internal medicine as, as most people may be familiar is more general medicine and then you can sub specialize many internal medicine Doctors work in the hospital admitting people and caring for them.

There are many of them are in primary care, looking after a wide variety of ailments and again some sub specialized cardiology pulmonologist, gastroenterology, but for me, during my internal medicine training and in med school as well, there was a very clear signal that I got and it was an increasingly clear signal as I neared the end of my training and that was that despite every amazing modern medicine and therapeutic that we had, that the things that were driving the majority of diseases were not being adequately addressed in the clinic.

And this probably isn't, you know, breakthrough information for people listening to this program. But for me who had expected that coming out with this arsenal of antihypertensive medications, heart failure medications, diabetes medications that would be capable of reversing disease and realizing that that was just not the case. It was a big deal.

So this led to a number of patient visits where I had this really significant revelation that the best I was doing in most of these cases was slowing the rate of decline, meaning you're going along, you're getting worse and that slope can be a little bit less steep, but really not addressing the reasons why people were on that downhill slope in the first place. And what became really clear to me is that at the core of the majority of our modern day top killers and contributors to disability is how our brains work and why is that? It's because our our brains are the principal driver of our decision making.

Aging, Longevity, and Immune Health

So you want to talk about the value of exercising eating healthy food well in order to care enough to do those things to be motivated to do those things. Your brain has to be set up in the right way.

You want to talk about mental health, mental health issues are brain issues, and what I recognize is that we really do have access to some powerful resources as it relates to prevention of brain problems and even treatment of brain problems.

And so for the last years my mission has been to understand the biological basis for what I call stuckness. And that stuckness, this is what happens in our bodies and especially in our brains, that programs us towards these destructive patterns and helping to understand how lifestyle modification everything from decision neuroscience, understanding how we make choices and how we can improve that to the foods that we eat and how they're incorporated into our brain cell membranes and change our brain structure and function can be leveraged to improve people's quality of life and decision making and cognition through the brain.

And so that led me on a whole a number of different kind of pursuits in the last few years writing books, doing research, educating, it's been incredibly fulfilling.

But the bottom line is I'm thrilled to be here to have the opportunity to deliver some of this information to people who maybe haven't heard about the power they have to prevent brain diseases, to prevent a number of other diseases through lifestyle modification.

– I appreciate your use of the word stuckness because it's it's something that actually I write about in terms of how our early childhood the lessons of early childhood, which I referred to as primitive gestalt patterns actually freeze our ability to adapt to the environment of our childhood. So we're really talking on the same page, let's let's take your interest and your work and kind of look at aging and longevity. What's your perspective on aging and longevity?

– Well, it's it's a great question. So, as evidenced by this summer that even existing people are desperate to know what they can do to live longer healthier lives.

And what we've seen in the United States for the last few years is that people are actually dying earlier. What we've also seen is that the last decades of people's lives tend to be pretty low quality as it relates to their health.

So that's a real problem because it means that first of all, we're not living maybe as long as we could be. I think that's pretty true. And second of all, the quality of those years, our health span is not as good as it could be.

So then you can say, well, why is this the case? And what science has been pretty clear on is that the top causes of disease of death of disability. These are things that relate to the quality of our decisions.

So talking about the quality of our day to day choices as being principal drivers of how long we live and the quality of those years. And there's a number of different ways you can kind of slice into aging. There are a number of different pathways that are involved. Um I'm sure, you know, you'll have experts talking about many of those, the ones that I have been kind of principally involved with, or I guess the specific one that I've been spending my time on is the connection between the immune system and how we age. Uh there are tons of studies, tons of research now showing that as our immune system ages, it correlates with our overall body's aging and that the aging of our immune system may actually increase the rate at which we develop diseases and even die earlier.

Inflammation, Brain Health, and Decision Making

And why that's important is of all the systems in our body. The immune system is one which turns over incredibly rapidly. So you're making millions of new immune cells every minute.

There's an incredible opportunity to kind of reset and reprogram your immune system for the better. So that you are reducing your risk of developing these things that increase your risk of dying early, of having a worse overall health span.

So we've kind of gone from very wide to very narrow here, We're talking about people are dying earlier than they need to. They're having a lower quality of their life experience than they need to.

There's a number of things that contribute to that. One of those things is issues with the immune system specifically elevation and inflammation and other uh aging related immune problems and that's something that we can act on to go all the way back up to the top of that and act on how long we live and the quality of those years.

– So I'm interested in how you uh like to think about influencing the immune system function, but you also talk about neuro inflammation. So let's see if we fit this into the conversation as as well, Austin. – For sure. You know, there's there's a lot here that we've already covered in the first few minutes and I want to make sure that we make this actionable.

Many people have heard about inflammation and I think we have to break this down a little bit so that we can

understand some of these higher level concepts.

So inflammation is in essence defined as kind of damage to swelling, heat, um pain of tissue, that's the way people usually think about it, and that's that's true. But as it relates to risk for dying early as it relates to risk for basically the majority of our chronic diseases, what we're talking about is chronic inflammation and what that is, is a sustained imbalance in the immune system. And to say this again, inflammation, chronic inflammation is actually a sustained imbalance in the immune system.

So if you're really looking to improve your inflammation, you're actually looking to improve your immune balance. That's the pathway that you need to activate.

That relates to risk for again most diseases, but why I care about it so much is that we now understand that the immune state of our brains specifically the inflammatory state of our brains correlates with our decision making with our cognitive state.

So meaning risk for developing Alzheimer's and other dementias quality of our thinking in a given day and our mood. So that's really important because what we're saying here is the inflammation in our brains may increase our risk for developing age related diseases like dementia. It may increase our risk for developing things like depression, which is a big deal at any age and where I get really excited is influencing brain inflammation may actually improve the quality of our cognition of our decisions right now. So yes, working on that is a good strategy if you want to reduce your risk for age related conditions like Alzheimer's disease, but also working on your brain inflammation or neuro inflammation may be a good strategy to improve your decisions so that you're doing better at work.

So you're more available in your relationships. So you're more motivated to make lifestyle changes. So this is really a key kind of facet of what we can do as far as understanding how we develop problems and understanding how we can act on them. – And I like how you connected the mental with the physical inflammation with our mood and our and our cognitive processes.

Because what I find is that we can create this snowball running downhill where inflammation impacts our thinking process. So we don't think as well creating poor decisions which create more inflammation and then it just bounces back and forth.

Can you address how we interrupt that pattern and reverse it in which we're getting, it's snowballing down in the right direction. – And you're absolutely right. This is one of the more concerning aspects of this, where you're in essence creating a feed forward cycle that snowball rolling downhill where your bad decisions lead to more inflammation, inflammation leads to worse decisions. And before you know it, all, the aspects of what should be healthy behavior are moving towards destructive behaviors that promote inflammation. So this is really a big issue.

So what can we do about this?

Social Stress and Environmental Inputs

How do you break that cycle as it relates to inflammation? Specifically in the brain? And I think there are two things to look at. So what can we do to help break the cycle of neuro inflammation?

The first is to understand that the brain's inflammatory state is largely a reflection of environmental inputs. So, meaning, what happens around us, what we take in has a big role to play in our overall immune state and may influence our brain's immune state.

So what are those inputs? What are those variables? Well, certainly it's what we put in our mouths. So, the food that we eat, we know plays a large role in our overall health and it appears to significantly influence our immune system and we'll go into this in a bit more detail in a moment, but just to make this connection, why would the food you eat influence your brain?

Well, the majority of your immune system is located in your gut. We're talking 70 plus percent of your immune cells in your gut. So those immune systems or those immune cells in your gut are going to influence your whole body and your whole body's immune system. So you get inflammation in the gut, that's not necessarily going to stay localized. Food that you take in, influences the immune cells in your gut. Those immune cells and signals influence your entire body, including your brain, but also the vagus nerve which runs throughout kind of the body. But especially from the brain to the gut and backwards again, is picking up data from your food and converting that data into signals that may influence your brain's immune state. So just let's put that aside for a moment.

But food is a significant way in which we influence our overall immune state and may influence our brain's immune state. So making the right choices there.

But the other bucket that I think is largely missed as it relates to what we can do in a given day to reduce our risk for brain inflammation is to pay attention to what comes in through our eyes and through our ears. What do I mean by that?

One of the strongest connections between inflammation and our environment relates to stress, high levels of sustained stress correlate with higher levels of inflammation.

And it's thought that this is also the case, as it relates to the neuro inflammation, inflammation in the brain stress can come from a variety of sources, but when we're talking about a psychological stress, it's more of how we interpret our environment than it is something objective in our environment.

For many of us, not across the board, there are certain people who, you know, can't necessarily escape from psychological stress, but for many of us we get to make decisions as to how much of that to take in.

So now layer into this story The fact that the average American adult is spending upwards of 11 hours a day in front of their screens. That is a direct conduit between the media coming through your screens and the state of your brain stress, and that stress is a direct conduit into your brain's inflammatory state.

So what is the quality of that media that we're taking in? Well, it differs depending on what we consume. But I will just say, even though I do think it's important to remain informed that excess exposure to news is probably one of the biggest contributors to chronic stress.

Actually. It turns out, it is when you pull American adults that's seen as a big contributor, so, to kind of expand back into the big picture here. The point being, if we want to positively influence our brain's immune state, if we want to do things that may help lower inflammation in our brains, we have to pay attention to what we're taking it.

And that means paying attention to what we consume through our mouth and what we consume through our eyes and ears and really dialing in the quality of those inputs across the board.

– Yes, I that is such an important point that you're making here, and when you talk about environmental influences and you're talking about media, but I would say that uh social influences in general play an important role in this process, wouldn't you? – Well, I think it's uh it's undeniable and some of the best research on kind of quality of life which comes from the Harvard study of adult development would indicate that our social connections are the strongest predictor of long term happiness meaning when we have them, we're happy when we don't we are less happy and it's not a 1 to 1 right? There are some people who don't need as much interaction with other people, but for the average person that's really important and you can kind of get into some of the mechanisms there.

So uh at a very basic level, having people that you can confide in uh seems to correlate with lower risk for depression. Um but we also know mechanistic lee that having people who are close to us that we care about maybe an anti stress intervention, That oxytocin, which is a molecule that tends to be produced in certain kind of interpersonal interactions may have an anti inflammatory effect and may have other effects on our brain function, which are linked to better mood to better long term outcomes.

So social connection is it's a double edged sword. I think we have to be clear there. Um but it is a major variable.

And I think just generally speaking, you know, forget about the research for a moment and think about the people in your life who seem fulfilled, who seem to wake up with vigor.

It's rare for me to see those people who are not closely linked into a social web. Um whether you're looking at Robin Dunbar's number 150 people or facebook followers of 6000 people, I don't think that's the important thing I think what I've seen is people who have close relationships with other people that they feel they can trust that they can learn from, that they can enjoy their life with.

That seems to be so important in protecting our overall health and protecting our brain health? – Yeah, I agree. I think that is so important.

Rewiring the Brain Through Sleep

I like to ask people to ask themselves, are the people they're in contact with, are they caring, support of people or people who could be critical and judgmental because if you're with people who are critical and judgmental that can create stress as opposed to creating a calmness in you. Right?

– Well, so let's stay on that for a second. I'm just going to throw out this concept, which is social contagion. And there's this idea that's kind of a movement from psychology into biochemistry, which is uh to look at how certain things may be contagious in ways that are not necessarily like an infectious disease.

Right? So from an logical perspective, we can talk about a virus being contagious, but now we're recognizing that other things are contagious. So we could talk about obesity. There seems to be a correlation there where people may have this contagious aspect of people in certain circles carrying more body weight. But let's go back to your specific example, which is, you know, you're going to take on, let's say some of the stress of the people around you. So if inflammation correlates with worst patterns of decision making, then in theory being around people who have higher levels of inflammation would mean being around people who maybe are making more impulsive choices.

Um but what's also seen is that inflammation may correlate with things like ability to relate to other people. Uh So what you're finding is that inflammation um, seems to have people withdraw from social interactions.

So there's all these ways in which what you're seeing as far as how people behave is actually a reflection of these exact things. We're talking about, what's going on in the brain, what's their inflammatory status in their body.

So, again, you're looking at things from a more macro perspective, as far as though that person is feeling this way, that person is talking to me about this thing. What you're seeing is a manifestation of their brains in Union State. And there's really fascinating research showing that if you take healthy participants or volunteers and you inject them with a molecule called LPS, which is a piece of a bacteria that reliably increases inflammation in the body, that they will feel a desire to withdraw from other people.

They will feel the desire to not participate, you know, in social activities. Uh, they will feel depressed. So thinking about this and thinking about the correlation between inflammation in our bodies and the food that we eat, and thinking about how our modern society in the United States and increasingly, in the kind of Western exportation of our diet and our lifestyle is promoting inflammation. Could there be a correlation there between how people's mental health around the world appears to be declining?

Could there be a correlation there between loneliness and people feeling socially withdrawn and their diet? I mean, I think there there is at least we should talk about it, because what we're talking about here is that with the mass exportation of unhealthy food patterns, the Western diet or the standard American diet around the world, what we may be doing is not just decreasing people's metabolic health, what we may be doing is not just decreasing people's lifespan, but we may be getting to these fundamental mechanisms of how we interact with other people and how we feel and in doing so, having a much, much bigger effect on the health of our planet than we think by something as simple as eating more sugar or eating less fiber, eating less variety of nutrients. So it's a really big deal.

– This is a great connection that you are that you are talking about right now. I know parents would always reflect on how when the kids have sugar, they're bouncing off the walls.

But you're taking it another step here. You're talking in a in a broader sense about how this can influence what goes on in our society in fact. – That's right. And I understand that this may be a little heavy for for some people, but one of the revelations that I had is that when you start to understand neuroscience a little bit more uh the biochemistry of what happens at the neuron at the synapse, you can begin to appreciate that the way that we feel and experience life and interact with other people is a reflection of these molecules, these tiny little molecules and receptors, the structure of our neurons, the connections between our neurons and that that is constantly in flux.

So we talked earlier about this idea of starkness and I do want to qualify that by saying it's really important to understand that your body and specifically your brain is always changing. So you've got billions of neurons, you have trillions of connections between those neurons and those connections in particular are always changing. And the example I give people is, if you know something right now that you didn't know yesterday, how is that possible? It's because you have changed the function structure of your brain in a way that you've encoded new memories.

So this is always happening and it can happen for the better where you are actively changing your brain function to improve your quality of life or can happen for the worse.

And I think that's really key. So certainly we can get stuck in uh self perpetuating patterns where we make unhealthy choices that strengthens the connections and those neurons makes it more likely that we make an unhealthy choice the next day.

That happens a lot. And that's actually what we see a lot, as far as people saying, I don't understand every day, I eat the same junk foods or I want to exercise, but I just can't get off the couch and go to the gym. We've solidified these patterns in our brains that make it really hard to, to pull ourselves out.

That happens through the same mechanism of changing out of those neurons and the way that they connect with each other. But that's still an open door to go the opposite direction. And so a lot of my education has been in helping people to understand simple tools they can use to rewire their brains and it gets to a lot of the things that we've already discussed. – So on that note, Austin, can you give our audience some strategies so that those changes that happen in us moment to moment, day to day can be directed in the healthy direction.

– I would love to do that and let me start with what I believe is the lowest hanging fruit and then we'll talk about some other ones. So what I think people should understand is that the quickest way for most people to make these changes to their brains that are going to enable them to make more and better changes is going to be paying attention to your sleep.

Why do I say this? I cannot tell you how many times I educated patients on the value of eating healthy food or the value of exercise both of which we know strongly correlate with improvements in overall and brain health, moving your body fundamental, eating real food as opposed to process food, fundamental, but not always fun. Not always enjoyable.

There's a reason why junk food is so popular and it's not because it tastes really bad. It's because it tastes really good, It activates our reward centers.

It makes us uh enjoy that meal even if it isn't good for us. You know, take a, I don't know uh pick your poison a granola bar made of pure kale and ham seeds. And then compare that to uh Krispy Kreme doughnut. One of those things is going to be palatable to most people and the other one is going to be palatable to a very small percentage of people.

So the point I'm making here is if you're looking at ways to improve your overall health, it's not just about finding things that work in the science, it's about things that work for you. And that's why we have to look at things that both work as far as their mechanisms and the research and are enjoyable.

People do things they enjoy. They don't do things, especially in a sustainable fashion that they don't enjoy. So sleep. This all gets me to sleep. When people get a good night of sleep, they are significantly more likely to choose healthier and less calories the next day. That's it.

Right. That's enough. If you're looking at a way to eat healthier, pay attention to your sleep, that takes us outside of this scenario that most people find themselves in, which is I learned all this good stuff about what to eat for a healthy body for healthy brain to live longer. And then I get to the restaurant, it's just so hard, you know, not to eat the rolls, not to have the soda, not to have the dessert, I know what I need to do, but I can't do it.

And that's the scenario most people find themselves in. It's not a lack of information, it's a lack of follow through. So what you need to do is not wait until the moment of choice to make a healthier choice.

You need to program your brain from a probability perspective to make it more likely that tomorrow you make a healthier choice sleep does that? People who get more sleep tend to make better choices around food the next day.

Similarly, people who get more sleep have been shown to have a decreased activation of a part of the brain called the amygdala involved in fear processing.

Why is that important if you want to move through life in a way that allows you to make healthy choices to feel good to be reflective, it requires you to engage a part of your brain called the prefrontal cortex and it requires you to have good connection between that prefrontal cortex and the amygdala, the fear, and also just emotional response and decision making hub that speaks to the prefrontal cortex. People who don't get enough sleep seem to have a decrease in that communication and increase in activation of the amygdala.

So mechanistic lee what we see is uh you know, there's changes in how the brain functions based on missing out on a night of sleep and from the more pragmatic perspective there are changes in how people act and feel the next day when they don't get that good night of sleep.

So I had to recommend for people if you're going to do one thing today, it's improve the quality of your sleep and I can give a whole bunch of suggestions on how to do that if you like. But I would start there.

Um, and then the other things I wanted to address our neural plasticity and habits, but we don't have to go there yet. – Yeah. So yeah, let's take a moment. Um, by the way, one of the things, I as you just recommended, one of the things I like to suggest to people that I'm working with is doing planning about your what you're going to do tomorrow or the next day.

Because when you try and make a decision in the moment, you're more likely to make an emotionally based decision. Whereas if you plan and then program you're more likely to make a more rational cognitive choice.

But uh, and you know, sleep is very important with regard to this. So, yeah, why don't you give our our viewers our listeners a few suggestions to improve their sleep? Because that's one of the symptoms that pops up the most in my work. And I'm sure in your work as well.

– So there's I think a starting point here, which is some people will know that they don't sleep well. You know, if you're burning the candle at both ends and you're getting three hours of sleep at night.

You're probably not out there saying it was great. I feel rested. Um, but about a third of American adults consistently get less and 76 hours of sleep, which is really not enough.

There is still this question of how do I know if I'm getting good sleep and I think there's several ways to slice it. So on one end of the spectrum is a wearable.

Your whoop your aura. Not everybody has access to that. Not everybody I think needs access to that. On the other end of the spectrum is the subjective feeling. So you wake up feeling rested, Are you drowsy during the day? Are

you needing to take naps?

Um Then there's also some additional data you could get if you have a partner. Um They could tell you if you snore. Do you stop breathing in the night?

These are signs that you may not be getting quality sleep even if you feel okay. But I really look at those first ones, which is, do I feel rested. Do I feel sleepy during the day or my energy levels relatively stable?

Am I needing to take naps? These are indicators that you may not be getting good quality sleep.

Microglia and Brain Inflammation

And even though there's a pretty big range of what people will say, person needs, generally speaking, we're talking between 7 to 9 hours or maybe 7 to 8 if you want a slightly tighter window of quality sleep each night and I say quality there because some people get in bed and they toss and turn and they're awake half the night and they might have spent nine hours in bed, but they wake up the next day with only a couple hours of good sleep.

So that would be, I would say a starting point is to ask yourself subjectively have you done unless you have access to something like a wearable, which again, I'm not recommending people will rush out and buy.

So if you're concerned that you're not getting quality sleep. And to be honest, I would say all of us should be concerned about that because of the significance of brain function and sleep, meaning people who don't get quality sleep seem to be at an increased risk of developing depression.

And Alzheimer's is an overall worst cognition, worse overall health, cardiovascular disease, cancer. You want to pay attention to your sleep. So now you've established you care about it either because you know that there's something telling you you didn't get good quality sleep or because I convinced you you need to care independent of that, what can you do to improve that quality of your sleep?

So there are some simple steps that I think most, if not everyone should be able to take. And there are some that I think a certain subset of people would really benefit from let's start with the basics when you're thinking about sleep, you really want to make sure just like you've already said that you're not trying to make it happen on the spot, it's not like you run your day, you run your race and then 9 30 PM you turn off your phone, you turn off the tv, you get into bed and you're going to fall asleep.

That's not how the human body works. Our bodies. Our brains are accustomed to a time that is very different than when we live now, meaning we're accustomed to be paying attention to the light that comes in from the sun hits our eyes. We are also incredibly sensitive to the light that comes in through our screens. We're accustomed to us a version of ourselves that isn't, you know, drinking four cups of coffee each day.

That's not the environment that our ancestors grew up and they weren't uh you know, tens of thousands of years ago, they weren't waking up and having their triple shot espresso before they started their day of hunting or gathering.

That's just not how it works. So we're kind of adding in these additional elements that are throwing some things off. So I always tell people you really need to start your sleep routine midday. And that means paying attention to what chemicals you're putting into your body that are going to throw off your sleep.

Most people don't know that caffeine has a half life of six hours. So that means if you have a cup of coffee at 12 o'clock in the afternoon, there's still half of that caffeine hanging around in your system at six p.m.

And there's still a quarter of it hanging around your system at midnight. So I would tell people if you're not already doing this seriously consider stopping your caffeine and take at two p.m. There are some people who are fast metabolizes of caffeine who can handle it later. There are some people who are slow metabolizes caffeine, who may need to increase that to noon or even 10 a.m.

But I think as a starting point, understanding that if you're taking in coffee late in the afternoon or any caffeinated drink that's gonna throw off your sleep quality and just similar on that subject, alcohol is a significant disrupter of sleep quality so that extra nightcap or whatever might feel like it's making you sleepy but your sleep quality will actually be declining because of that.

So that's one a couple of other quick tips. One is to lower the temperature of your room. Research shows that when the temperature of the room is lower, it actually promotes better sleep. Somewhere between 60 and 67 degrees is most researchers would recommend finding what works for you there.

But trying to find ways to cool off the room seems like an important step. I'll give one more here, which is consistency of sleep. So a study published in 2018 showed that adults who had more fragmented sleep, meaning they didn't go to sleep at the same time.

They woke up at different times had a number of negative health outcomes. Uh, we all kind of know intrinsically that for kids, consistency is really important, turns out that's key for adults too. So I think getting to bed at a similar time, at least five days of the week and waking up at a similar time, at least five days of the week is really important for keeping our brains in a pattern of feeling sleepy at a certain time and being able to wake up and having high energy at a certain time. The last thing I'll just say because you can talk about sleep for a while is especially if you carry extra weight, especially if you snore, especially if you feel sleepy during the day or your spouse or partner tells you that you stop breathing in the night. Seriously consider talking to your medical provider about getting a sleep study. Sleep apnea is an increasingly large threat, meaning that many more people are experiencing this than they used to and it is incredibly damaging to our overall immune cardio metabolic health.

So that's one of the most straightforward things you can do is ask your practitioner if you need to be screened for sleep apnea, especially if you have some of those risk factors I described, because there is, there are good things we can do to manage that and it's one of the things that most strongly relates with a lot of these health outcomes that I've already described. – And we are spending a significant amount of time on it.

But that's because of its significance in our lives. So it's really appropriate. You had wanted to touch on neurotransmitters, but I also, perhaps in the same conversation, you've talked about micro glial cells.

Maybe you can explain what they are and their significance totally. – Well, for a long time and still for many people, there's been this idea that the immune system is outside the brain and then we have this impermeable blood brain barrier that keeps everything out and then there's no immunity in the brain.

Um, this is this is very much not the case for a long time. Researchers, scientists have known that the brain has its own immune system and there's a special cell that lives only in the brain. It's kind of a specialized immune cell.

It's called the micro glial cell. This is an immune cell that patrols the brain, looking for threats. So if you get a bacteria in the brain, this is the cell that says found you going to take you out?

If you have damage in the brain. So if you suffer a concussion or something, they might get activated to help clean up or respond to that damage. Why is this so important?

So, micro glial cells may be kind of the portal by which inflammation in the body gets converted into inflammation in the brain. This is really important because it means that these micro glial cells are actually critical as far as brokering that connection between your overall state and your brain state and what's fundamental to understand about micro glial cells is that they have these different, what we call phenotype but really different states of function at a very simplified level.

Micro glial cell can have, let's say three states of function. One is a resting state, it's not really resting, it's not really a fair thing to say. But these are micro glial cells that are spending their time patrolling and looking for data for threats and the way they do this is actually fascinating.

Neuroplasticity, BDNF, and Psychedelics

They have all these networks of interconnecting micro glial cells where they in essence span the entirety of your brain and are constantly reaching out, looking to see is there a signal that something is going wrong when these micro glial cells detect that signal and that signal might be inflammation or basically a piece of a damaged cell they respond by changing the way they look and changing the way they function.

They kind of evolve into the next stage in their function and that can turn them into a pro inflammatory type where they're actually increasing levels of inflammation which sometimes it's necessary or more of an anti inflammation cleanup version of themselves.

So research across the board as it relates to neurodegenerative conditions. So, thinking of Alzheimer's Parkinson's Lewy body a whole lot of different brain states as well as research in depression and other mental health states.

I've shown that micro glial cell activation may be a significant contributor to perpetuation of those states. So I called them kind of signal amplifiers in that if you have inflammation in your body and the micro glial cell gets a taste of that, it says okay we're doing the inflammation game and it might actually increase the inflammation and sustain that inflammation in the brain. Even if you never had an immune cell from you know, your bloodstream getting into the brain. And that's been really a fundamental misunderstanding I think. Which is that you need to have immune cells from your bloodstream break through the blood brain barrier to cause its inflammation.

It may be the case that these microbial cells can do it on their own. So the long story short here is that your brain has an immune system that your brain's immune cells are called micro glia. And there are things that we may be able to do to help keep those micro glial cells on our team.

So they're not running rampant causing damage and contributing to things like cognitive decline and mood issues. – Do they also cause damage to the cells?

– It's it's a good question. Yes. So um micro glial cells when left unchecked in this more pro inflammatory state are thought to contribute to damage to neurons and other cells.

I do think it's important to understand that the inflammatory state of anything is actually, it's a defense mechanism. It's very helpful and necessary, right? So if you had a bacterium that gets into your brain, you want that microbial cell to go and create inflammation, Bring in the cavalry and destroy that bacteria. So you don't get an infection in your brain.

That's really important. But it's not that over time that we can get to a place where we just have a chronic level of inflammation in our brains, much like what we might see in our bodies and that this is correlated with risk for disease.

So here, you get to a point where either because of diet or because you're not giving your body other things it needs, or because maybe you have an A.

P. B. For genetic type, but there is an increased risk for these micro glial cells to be activated. And that's really the concern. So, we're in all of these conversations talking about really what happens over months and years more than we're talking about, what happens in the context of a short term issue.

– And I would assume that all of the strategies that we've been talking about are consistent with how you maintain good brain health as well. – That's right.

I mean, it tends to be the case that what's good for your body is good for your brain, who would have thought and it tends to also be the case that there are a lot of communication channels between your gut and your brain and even your fat cells in your brain and your muscles and your brain. All of these things are speaking to each other.

So what you do for your body tends to translate into things that you do for your brain and that's good news, because it means for most of us it's the simple things that matter most as it relates to all of the health outcomes we care about.

– So, one of my last couple of questions here is can you uh tell us a little bit about how you see neural plasticity playing a role here in inflammation and longevity. – Totally. I think that so neural plasticity is the technical term for something we've already described, which is that your brain is always changing moment to moment, day to day and that can be in a good direction or a bad direction.

It's just the idea that your brain is always changing as a reflection of what's coming into your body. What research shows is that issues with neuro plasticity are linked to a variety of mental health and cognitive health conditions.

So, where I focus my attention is primarily an understanding how neural plasticity maps onto depression and hear what's been very interesting is kind of these bidirectional pathways and by bidirectional, I mean they both influence each other.

Uh so between inflammation and neural plasticity is a great example of that. What research has shown pretty consistently is that inflammation as well as high levels of stress in the brain appear to dampen healthy neural plasticity.

So they may actually make it harder for us to rewire our brains for the better. Uh there's a number of ways in which this may happen. One of the examples that I like to give is that both chronic stress and inflammation, decreased levels of a molecule called brain drive neurotrophic factor, or BDNF. BDNF sometimes thought of as a micro glial for our brain cells is key to both creating new brain connections and even growing new brain cells, BDNF levels tend to be lower in conditions like Alzheimer's and depression if you measure them in the spinal fluid, if you measure them in the bloodstream.

And it's actually thought that some of our drugs that we use for various conditions may work in part by increasing BDNF and increasing neural plasticity.

So, I'll go over this again, inflammation may damage healthy neural plasticity by lowering levels of BDNF interventions for conditions like depression are thought to work in part by increasing neural plasticity through increase in BDNF and I'll just throw out for interest here S. S. R. I. S have been shown to increase BDNF levels, as have things like psychedelics. So this may be one of the ways in which we're understanding these molecules that seem very different, you know, surface level, as far as what they're doing, may all kind of contribute to some of the benefits to brain structure function and mood. – You jumped the gun there with me because that was going to be my next question. What you thought in terms of psychedelics, whether they enhance neural plasticity? – Well, I'll make my car statement on the matter, which is that I am incredibly frustrated with the current state of mental health in the United States especially, which is that despite access to everything that we thought is supposed to make us happy and healthy people are pretty miserable and the pandemic has certainly contributed to this. But we are seeing record levels of depression and that's especially the case in unfortunately our youngest demographic.

So, Children and adolescents that's for prevalence, rates of depression seem to especially have been increasing. We also see similar rates with anxiety and general stress. Um, so with that said I asked myself, well, what is the best the standard of care, as far as how to manage this?

And like it is the case with most medical conditions are structure of our society and health care system is really only set up to manage mental health issues when they become so bad that they can be diagnosed and treated with conventional therapeutics and or psychotherapy.

So, in this context, I am incredibly bullish on learning about new modalities that may help us to improve mental health and psychedelics fall squarely in that category.

My bias is that we have um, over concerned ourselves with the downside potential of psychedelics and missed out on some of the upside potential for a range of factors.

And we're starting to move back in the other direction and maybe have flipped in some ways where some people are saying that they are the cure for everything.

But the question would be uh you know how do psychedelics work? That's the question that I'm really fascinated by. Because it's one thing to just say well you take it, everything gets better. I think it's necessary for us to understand more of what happens when a person uses psychedelics to gain larger acceptance in the scientific community that these aren't just molecules that lead to a trip a hallucination.

And that's the primary mechanism just like we were talking about before. If you see somebody and they're feeling low and they're acting in a certain way.

What you're really seeing is their underlying neurochemistry and neurobiology manifesting in their thoughts and their actions. And similarly when you think about psychedelics, yes if you were to take a couple of grams of psilocybin you would have a very intense psychedelic experience that is a reflection of what's happening in your brain at the level of the synapse. So with all that as a preamble, what do we know about how psychedelics work? The primary mechanism of action for classic or classical psychedelics. And that would be things like LSD and psilocybin and D. M. T uh Mescal in would be that they bind to a specific serotonin receptor called the two A receptor.

But what we now understand is that the two A receptor itself may activate neural plasticity. And another way that psychedelics may work and this is especially the case for ketamine is by way of activating neural plasticity through glutamate channels.

So I know that's getting very technical. Let me give a couple of details to help kind of round this out. There have been a number of studies conducted in the last few years to look at what happens when people are given psychedelics as it relates to their BDNF levels.

And what we've seen, at least in these preliminary studies that LSD I ayahuasca, psilocybin and ketamine are linked to elevations and BDNF levels. So that isn't to say that we've sealed the deal. The connection is secure, but it is to say that there's more at play than just the trip experience, that what we're seeing, there is a manifestation of these chemicals pathways in the brain and coming back to the initial idea here, if the premise is that so many if not most of us today are experiencing some degree of stuck nous were locked into patterns of thought and feeling and action that we don't want any more.

But we can't get out of it, neural plasticity represents the most direct understanding of how we can change our brain structure and function. And if we find safe and effective pathways to alter that neural plasticity for our benefit that may be absolutely vital to targeting things like depression, anxiety and even helping us to prevent conditions like Alzheimer's disease. – That's a great explanation for our audience.

Austin, thank you very much. And and we've touched on a lot of topics during this hour and in particular the body and mind connection. So I appreciate all of what you've added to this conversation uh in closing, can you tell us tell the audience how they can reach you if you have any particular projects you want them to know about as we close the program? – Have more projects than I need right now. So I won't go through all those.

Closing Thoughts and Resources

But if people would like to learn more, the best kind of access to all these these ideas, most of them kind of typed out. And longer form blogs is my website, which is austinperlmutter.com.

And I send out a weekly newsletter where I spend a lot of time trying to convey these brain ideas. But I would just come back to, you know, as people are making the investment in longevity and living longer, living better lives the brain. Is that pathway forward?

And why do I say that? It's because You could rejuvenate all your cells, you could, you know, remove every single wrinkle, you could have perfectly functional knees, you could have basically the body of a 20 year old when you're 130, it doesn't matter if your brain isn't there, that's you, right. That's the ability to enjoy it.

So I would just say, as it relates to these larger conversations, don't forget to put this investment in your brain

health because that is going to be the ability to enjoy a longer life without your brain alongside for the ride.

It doesn't matter. – Thank you. And there will be a free gift that Dr. Perlmutter will be offering so that people can receive some of his valuable information and stay in touch.

So, again, thank you so much. Austin. It's been a pleasure talking with you in this hour. I know we can go on forever. These are fascinating subjects, but thank you so much.

– Absolutely. It's my honor.