

WESTERN SCIENCE SPEAKS PODCAST SEASON 4, EPISODE 3

EPISODE TITLE

Back to square one: The role of metabolism in Alzheimer's Disease

PODCAST SUMMARY

Evidence suggests that metabolism is connected to Alzheimer's disease. In fact, lifestyle habits contribute to your susceptibility of getting Alzheimer's. But exactly *how* remains a mystery. Robert Cumming and his lab research how age-dependent alterations in brain metabolism affect memory and contribute to neurodegenerative disorders, including Alzheimer's disease.

INTERVIEW

Henry Standage 0:28

Hey, thanks for tuning into the Western Science Speaks Podcast season four. Today we're going to be talking to Dr. Robert Cumming from the Department of Biology. Rob told me he starts the cell biology class the same way every year. He asks the students to raise their hand if they have a family member who's been affected by Alzheimer's. When 30, 40, 50% of the class raises their hand, he tells them, that means there's a pretty good chance they might inherit an age related brain disease themselves. It sets a tone and shows how high the stakes are for the next generation of scientists. Diseases like Alzheimer's don't have a cure yet. So if you're going to inherit it, you might not even want to know - you might just want to continue to live your life. These inheritable diseases are what we talked about when we sat down, as well as a couple other things like how memories are formed, how your lifestyle choices can affect your brain. And then at the end, we shift into the topic of cannabis and what it's legalisation means. Anyway, here we go.

A lot of your work originates from you having a background in inheritable blood diseases, how does a gene get passed on?

Rob Cumming 1:44

Well, it's not that everybody has their genetic compliment. They get half from the mom and dad, and if all the genes are working fine, then you have no problems. It's when there's a mutation in a certain gene, that's a critical function. So I did my PhD studying a rare disease called Franconia. So turns out there's about 17, or 18 different genes, that if they're mutated, and when I say mutated, both versions of the gene, one that you get from your mom and your dad have to be mutated in a way that they're not functional. And in that case, that's what we refer to as autosomal recessive. So you have to have two non-working versions of the genes, and you just don't get a functional protein. Whereas there's other types of diseases where you just have one mutation in a particular gene. And that mutation causes the function of the encoded protein to not to work in a manner that is harmful. And so that's what we call the dominant mutation. So when working on that rare blood disorder, this was one where you needed two defective versions of the gene. It's a bit of a rare event when you have that. So we usually have two parents who are carriers, they have one normal version and one new version, and you have about a 25% chance of getting two bad versions. So it's really bad luck of the draw, when that happens.

Henry Standage 3:18

What are some examples of diseases or mutations that we might be surprised are inheritable that can be passed down?

Rob Cumming 3:27

Well, there's many of them, I now study Alzheimer's disease. And there are a very small number of individuals, maybe 1%, maybe 2% of the population of people that have Alzheimer's actually have an inherited form. And that's the type where you just have to have one bad version. And that bad version, ultimately will result in an individual getting Alzheimer's disease, maybe they could be in their 40s or 50s. That's what we call it early onset Alzheimer's. So what's interesting, though, is that most of the research on Alzheimer's disease has been had been using these rare forms of inherited Alzheimer's disease to sort of model it. And even though the vast majority of people that have Alzheimer's disease don't have mutations in these genes, so there's about three genes involved. There's a precursor protein, there's presenilin one and presenilin two. So these three versions, these three genes, if you have a certain mutation result in the production of a harmful piece of protein called the amyloid beta. And that amyloid beta, if it accumulates at very high levels in your brain, it forms these things called plaques. And the plaques were long believed to be what caused Alzheimer's disease. So because the original description of Alzheimer's disease by Alois Alzheimer, when he examined a woman who actually had the rare inherited form, this is back in 1905 - when they looked at a brain, they found there were all these sticky proteins, plaques, and another protein called tau, which accumulated in something called tangles. And so this was sort of the first clue that this kind of brain disorder is associated with the accumulation of these bad proteins.

Henry Standage 5:25

That's the luck of the draw you -

Rob Cumming 5:28

A little bit, yeah, in a way, in this case, you have a 50% chance of getting it, because it works in an autosomal dominant manner. So just, you know, you're here, you may have a parent who has one bad version of the gene. And it's a type of gene that you don't show the disease until your maybe in your 50s, you've already had kids by then, right. So there's, there's a number of diseases that are like that, where you may not necessarily know that you have it. And by the time you have it, you've already had kids, then you possibly pass it on to those children. So another example is Huntington's disease. And in that case, that usually affects people in their late 30s, early 40s. And again, they may have had children at that point. So now that we know that some of these diseases can occur in a heritable manner, if you have a history in your family, then you really need to get tested. And so what they're doing now, certainly in these rare, Alzheimer cases is getting tested. And then it's the one of the type of things where you know, you've got the mutation, you know, you're going to get it. And that's frightening, it's even more so frightening for people with Huntington's disease. So there's actual kind of ethics rules related to this. So let's say you're, you're 40, and you discover that you have Huntington's disease. And you have a kid who's maybe 15. And you, you think, oh, my God, I want to know, is my kid going to get it. I need to go to the doctor, he asked the doctor, can you test my kid to see if he or she's going to have Huntington's disease? And they say, No, we can't. Because the child has to be 18 years of age to be an adult. And then that child can make a decision whether he or she wants to be tested. So it's an interesting kind of dilemma. Because as a parent, you want to do everything you can for your kid. The problem is, if you have inherited form of a disease like Huntington's disease, or Alzheimer's disease, and you want to see if your kid is going to get it. Well, the problem is there's no treatment for so there's

nothing you can do. So the kid can say hey, I have the gene, I'm going to get it. Well, how's it going to influence your life?

Henry Standage 7:49

So that's why there needs to be approval for that. So if it was something that could be treated like the flu -

Rob Cumming 7:58

Could be a different situation, if you can intervene earlier, and actually have the treatment that can prevent the disease or delay it. So when you have diseases where there's no cure, then it becomes an ethical dilemma. What's up, there's actually no point in knowing, because it actually causes a lot of emotional distress for an individual. And so they can determine whether they want to know and there's some kids who say, I don't want to know, because I'm going to live my life to its fullest. And if it happens, it happens.

Henry Standage 8:27

So it's like, the big hypothetical question people like to ask is; if you could see the day you die, like in the future would you choose to? And I think people generally say no.

Rob Cumming 8:38

It is a little bit like this. Do you want to see whether you're going to have a long prolonged agonising death? Yeah, because that's generally what happens. Yeah, right. So the getting back to Alzheimer's disease. What's interesting is that when they found that there's these rare group of people that have inherited forms of Alzheimer's, and it leads to the increased production of this amyloid peptide that basically all the animal models have been engineered to recapitulate that rare form of Alzheimer's disease. And all the investment in drug discovery has focused on amyloid. And they spent billions of dollars and it's amounted to nothing.

Henry Standage 9:23

And by that you mean testing on animals?

Rob Cumming 9:26

Well, they started with testing, like we've cured Alzheimer's disease in animals many times, in my mouse models, for example, the rodent models, but the problem is that that's not the type of Alzheimer's disease most people get, they get what's called sporadic. And when you have sporadic Alzheimer's disease, you don't have a very clear defined mutation, that means this is the sequence of events are going to happen, and ultimately resulting in Alzheimer's disease. So the brain, even though it only represents about 2% of your body mass consumes about 20 to 25% of your energy reserves. So it needs both the fuel in the form of usually carbohydrates, sugars, and also oxygen. And so it's an incredibly demanding organ. And the reason it needs so much energy is that you've got, you know, a trillion cells, I don't know, I can't remember the exact number. But there's a lot of all the cells in your brain, you've got neurons, and glial, those are the two main cell types. And they have to work together, the neurons have to talk to each other through synapses, these are little close connections, and it's sort of like electrical signals that go back and forth between neurons. And all that activity requires an enormous amount of energy, even when you're not even doing anything, your brain is active all the time. Once you start to get engaged into, you know, writing an exam or coordinating your movement while you're doing a dance or any kind of task, your brain activity increases, obviously, a lot more and depending on what you're doing certain parts of the brain become more engaged, more active. So you need a continual

source of energy in order for your brain to function. And that's well understood. If, for example, you get a blockage of blood flow to a part of your brain, that's what's called a stroke. And so not having enough oxygen and nutrients going to part of the brain. If that goes on for a great period of time, that part of the brain will actually start to die off. So people understand that. But what happens when you get older, and one of the biggest risk factors for Alzheimer's disease is actually age, the older you are, the more likely you are to get Alzheimer's disease. So like from the age of 65 on, every five years, likelihood of getting Alzheimer's disease almost doubles. So the fact that North American Western society individuals are getting older, we're living longer. Now we're seeing a progressive increase in the cases of Alzheimer's disease simply because people are getting older.

Henry Standage 12:01

Which takes away the upside of being able to live longer.

Rob Cumming 12:05

Yeah, I mean, it's sure we can live longer, but to what extent, you know, you're now being afflicted with a whole bunch of diseases. So it's certainly you could say, well, I want to live to 90. But like from the age of 80, to 90, you're in horrible pain, or your mental faculties deteriorates substantially, it's not really living, you're just prolonging death, that's all you're doing. So the idea is, we can, instead of focusing on lifespan, we should be focusing on health span, and being as active and as functional as long as we can. Because that insures the best quality of life.

Henry Standage 12:41

You've already alluded to the metabolism, the idea of processing energy in the brain using nutrients, oxygen for fuel - talk about what the metabolism means in your work.

Rob Cumming 12:53

I kind of inadvertently got involved in brain metabolism by studying the older kind of train of thought with Alzheimer's disease, which is to look at amyloid. And one thing that has puzzled people, well I wouldn't say puzzled, people have ignored or conveniently ignored in some cases, is the fact that there's many elderly people who have had normal lives and had no form of dementia, memory loss. And when they die, they may have donated their brain to science and somebody cut into it. And a pathologist looked at it and went, Oh, my God, this person must have had Alzheimer's disease, they had all these plaques in their brain. They didn't have Alzheimer's disease, anywhere from estimates 25 to 40% of the elderly population are walking around with all this plaque in their brains, and they're not getting Alzheimer's disease. So does that mean, the amyloid theory of Alzheimer's disease is wrong? It's possible, or we need to rethink is that some individuals may be able to tolerate very high levels of this particular protein. And there's lots of evidence suggesting that the protein itself is bad. In different experimental models, it causes harm to put to neurons, they don't function properly, or they actually start to die off. And that's a big part of Alzheimer's disease is you have a mass as it progresses, you get massive loss of brain cells. So why are individuals who have all this amyloid not having all that brain cell loss? And so we thought, maybe it's because they have a natural adaptation mechanism to become resistant to it. So we mimic that in a dish. So the cultured nerve like cells, in addition, we've exposed them to the amyloid peptide and most of them died. And then the ones that survived, we looked at them and said, well, how are they different from the original starting population of mostly sensitive cells. And it turns out that those cells became very good. They took up lots of sugar, and then they process it to make lactic acid. And so that's sort of where I initially got interested in this. And we thought that perhaps this type of metabolism, which is a unique form, and it was originally discovered in cancer cells, by a German researcher called Otto Warburg, and this is in the 1920s. And he found that cancer

cells are very sugar loving, they take it up at very high levels. And they don't process it in a manner that would normally be dependent upon oxygen, they process it in a non-oxygen dependent manner to generate lactic acid, and anybody who's maybe ran too hard or isn't in great shape, and they get a cramp. That's an example of, for example, your muscle tissue, not having enough oxygen in order to sustain the type of energy production and by default, you start to produce lactic acid and the lactic acid is what causes the cramp. So this lactic acid phenomenon was what I initially discovered in a very artificial model and culture. And then I started to ask, does that have any relevance to what really goes on in your brain?

Henry Standage 15:59

And what is the connection with memories to lactic acid?

Rob Cumming 16:04

Well, this is a controversial theory. And it was proposed in 1994 by a fellow by the name of Pierre Magistretti, and he proposed something called the astrocyte neuron lactate shuttle hypothesis, which is a big mouthful. And in essence, what their saying is, there's as I mentioned, there's two main types of cells in your brain. There's glial cells, also known as astrocytes. And then the neurons, the neurons are the things that fire and so the support cells are astrocytes. And the theory is that the astrocytes basically suck up all the sugar out of your bloodstream, and they process it to make lactic acid, and then they feed the lactic acid to the neurons. And then the neurons use that in some not very clear manner, maybe for energy production, or for some molecular process evolved in memory. And there is evidence in support of this. But then there's also some other evidence suggesting it's not that straightforward. So there, the evidence to support of this is that if we experimentally modify a mouse brain, and we can do it chemically, where we put probes or little tubes into the brain, and we administer drugs that actually prevent the ability of lactate to transport between cells, and those animals have problems with learning and memory, or we can do genetic intervention, and we monkey around with things that transport the lactate the transport channels, and that also causes problems with memory. So that's sort of been the basis of this theory. But it's always assumed that it's like, we go from sugar in your blood, it gets taken up by astrocytes, the astrocytes then break it down to lactic acid, then feed it to the neuron. And then the neuron without lactic acid somehow does something related to memory. That's the theory. And it could be true, but it may also be dependent upon which part of the brain which kind of task you're involved in what type of learning you're undergoing. So I don't think it's black and white. And we've done some studies where we administered a drug that actually prevented the creation of lactate. So the animals couldn't actually generate lactate, lactic acid, or lactate. And what we found, depending on when we administered the drug, is that in this case, that we do a learning spatial learning task called the Morris water maze. And mice don't like water, they want to get out of it, you throw a mouse in a big tub of water, he swims around like crazy, not very happy. And there's a little personally submersible platform. And the mouse learns where that platform is, because we have some cues around the big top of water. And so he uses the spatial cues or little signals, like there's a star, there's a circle over there is where that hidden platform is, and he swims to it. And then once he gets on the platform, it can rest. So in the process of learning where the platform is, takes some time, it takes a number of days, we have to do what we call trials, where we kind of teach the mouse where the platform is, and he learns. And then at the very last stage of the test, we kind of do a sneaky thing and take the platform away, and throw the mouse in the tub. And then we see how much time does he spend in the area where the platform was previous. And that's an actual reflection of memory itself. So the first stage is learning. So that's our working memory. So you, if somebody says, Okay, here's my phone number, you know, 519-226-4535, whatever, you have to repeat it a number of times. So through repetition, you start to lay that memory down. And so what we, what we found is in the learning phase, is if we administer the drug, so the

animals can't make lactate, they don't learn, and they don't have a memory. So it's kind of like building the road memory, it's, it's like a memory is just doesn't happen spontaneously, you kind of have to lay down tracks. And it literally in a way, it almost is like laying down tracks, it's connections in your brain. And those connections have to be strengthened through repetition. And through the repetition to become stronger and stronger, you end up building a road. Once the road is built, then it's easy just to run right down the road and grab the memory and come back. So what we found is the lactate, based on our experiments where we didn't allow the brain to make it during the learning phase, they didn't learn and then they just simply there was no memory to recall. But if we allow them to learn appropriately, and at the very last, we injected them with the agent that wouldn't allow them to make lactate, they could still recall that memory of where the platform was. So what that suggests is that lactate isn't so much about retrieving and establish memory, it's about making the memory and laying down the tracks. And that actually makes a lot of sense because lactate in the metabolism associated with it is involved in building cells. It's one of the reasons why cancer cells use this metabolism. Because they can and you say well, why would they use this metabolism make lactate lactic can't be very good for you. It's not a very robust, efficient way of making energy. But it has a side benefit. If it makes all these little intermediate building blocks to make more cells, it could be more DNA, more protein, more fat. In the case of your brain and neurons, it's about making connections and the connection between neurons are called synapses. And so those are actual structural changes to it to a neuron, they're actually making more synapses in order to make extend a piece of the cell outward to make a little pokey projection, you have to have protein, you have to have lipid and to actually physically extend a piece of itself. And so we think that that metabolism is really important for actually structurally changing the connections between neurons and making them more stable. It's part of what's called synaptic plasticity. So when you learn something, you actually start to create new synapses or strengthen existing ones or make them more functionally connected. And so we think that the lactate and the metabolism associated with it is really important for that. Once that's been established, you build the road, then you don't need them I new

Henry Standage 22:54

In Alzheimer's, it's the new memories that go first. That's right. Yeah, when you build a strong bridge there, it's, it's more durable.

Rob Cumming 22:57

Right. So long term memory, or what we might call semantic memory, remembering two plus two is four, or, you know, how you start a car, and how we operate a car, you don't think about it, it's kind of built in memory. Those types of memories persist the longest Alzheimer's, where people that start to show signs of Alzheimer's, it's there. The recent established memories, like, oh, you know, a friend visited me in the morning, or I had toast, and eggs, you know, in the morning, you don't remember that stuff. So these sort of short term new memories just don't stick. And so, you know, there's a lot of theories as to why that is. Certainly the neuro transmitters. Those are the chemicals that allow neurons to communicate with one another, they become very imbalanced. Acetylcholine is a really important neurotransmitter that's quite messed up, glutamate, is another. And so people kind of focused on the neuro transmitters. And certainly they play a big role in it. But is it simply a case of they don't make enough neuro transmitter? Or is it a case that they're just not really able to form those new connections very well. And so what we're kind of exploring is, well, what happens this lactic acid is not like your brain is churning out buckets of lactic acid all the time, it does in very small amounts in a very controlled way. And we think that these little small bursts of lactic acid production are really important for making those new memories. The question is, what happens with age does that not work as well, and what happens in Alzheimer's disease. And what we found with age is the animals - some of the enzymes that are involved

in making lactate, the enzymes itself diminished with age. So it looks like animals don't have the ability to make as much lactic acid in memory, your memory gets a little dodgy. Even if you don't have Alzheimer's disease, the older you get your ability to form new memories, and recall memories is not as strong. It's just part of the natural ageing process. But it's really dramatic in Alzheimer's disease.

Henry Standage 24:18

What happens if you produce too much lactic acid?

Rob Cumming 25:18

Well, certainly producing too much lactic acid is bad. People that have epilepsy produce very high levels of lactic acid, its associated with seizures. So having high levels of lactic acid can actually induce a seizure, or trigger unwanted neuronal firing. So that's an example of too much. But the question is, well, what's happening in Alzheimer's disease? Is it too little or too much? And that's what we're trying to figure out. So right now, we have somewhat crude tools to try to measure. Lactate is not an easy thing to measure. If you were to euthanize a mouse, and then try to go into the brain and assess how much lactic acid is there, well, part of the problem is when you euthanize an animal, you put it to sleep. And, and then, you know, if you give it a lethal injection of a drug that eventually will cause it's hard to stop. Well, the problem is, now you're going to have a lot of lactic acid because there's an adequate blood flow and oxygen to that tissue. So it's very difficult to try to measure lactate in an animal that has died. So helping you measure lactate, in an animal that's still awake or still alive, is not sedated. So if an animal is sedated, that's going to affect lactate levels as well. Very difficult. One of the things we've been doing, working with researchers at Robarts Research Institute, is to do MRI scans. And these are special magnetic resonance imaging. So we do a slight variation of it called magnetic resonance spectroscopy. And this is a way to actually measure metabolites within the brain of animals and their alive. So we still have to sedate them, because a mouse isn't very cooperative, I guess, in a scanner. But we can at least make some relative comparisons, we can look at young animals, we can look at old animals, we can look at animals that are engineered to develop high levels of the amyloid with all its flaws, and sort of the only model we've got right now for Alzheimer's. And what we found is when we use this form of imaging, that the lactate levels and old mice declined with age, and parts of the brain that are involved in memory. But unexpectedly in the quote Alzheimer mice, we found that the lactate levels didn't go down with age they remained elevated. It's a tricky one. So yeah, I mean, that was not what we expected. That was the complete opposite. So if I made this case about lactate is really important for forming new memories. Well, then, why would the quote Alzheimer mice have higher levels of lactate, even though they have memory problems? And there's been more recent studies in humans also corroborating this where lactate levels seem to be higher, in Alzheimer's patients. And if I've just told you that lactate is really important for forming new memories, and new memories are compromised in Alzheimer's patients, why would they have lactate levels that are high? And I think it gets back to the sort of sweet spot, if they're making it, but they're not consuming it, it accumulates, and that's actually a bad thing. So we think, and this is still a bit speculation, that certainly the mice, maybe humans, it remains to be seen, that they are producing lactate, but they don't seem to be able to utilise it properly. So if it persists, where it's persisting, which parts of the brain inside of cells outside of cells, we still don't quite have that answer. So we think that in the Alzheimer model, for some reason, the lactate levels are high. And that actually can lead to a whole bunch of problems. And there's actually evidence suggesting that in the early stages of Alzheimer's disease, they actually have hyper activation of neurons. And so they're getting firing, where they shouldn't be firing. And so there's a theory perhaps that this hyper activation may be associated with higher levels of lactate, a thing that very few people realise is that there's actually a strong association of epilepsy or seizure-like episodes in Alzheimer's. So if you were an epileptic patient, you have a greater likelihood of having Alzheimer's disease. If you have Alzheimer's

disease, you may have episodes of what are called non convulsive seizures. So you're not necessarily, you know, pass out and you're on the floor and you're frothing at the mouth. They may just have these sort of fugue-like states where they're just confused. They don't have what appears as a classical type seizure. But if you were to measure their brain activity, you would see it firing in a sort of uncontrolled manner. So, again, does this have some relationship to the high levels of lactate? Possibly, we don't have those answers just yet.

Henry Standage 30:20

In one regard, it's helping people make new memories and on the other it's given people seizures, which are just two polar opposite things. How can research on brain metabolism translate to possible therapies to Alzheimer's disease?

Rob Cumming 30:35

Well, there's a lot of people that are now viewing Alzheimer's disease as a metabolic disorder. And there's something that's been kind of floating around; a term called type three diabetes, which is the inability to respond to insulin appropriately in your brain. And so insulin is really important for taking glucose, and then processing it. And so the train of thought for many years is that insulin is certainly really important than most tissues in your body, but a lot less important in the brain. Because the brain doesn't have as many, what we call insulin dependent transporters for glucose. So a lot of the glue, they don't need to have insulin in order to have those transporters working. But that's not entirely true. And now they're finding more and more evidence that we do have what are called insulin receptors in the brain, and in certain parts of the brain that are really important for establishing memories. And they're now starting to do things like administer insulin into the brain. So they do these intra nasal administration. So believe it or not, if you screwed, sort of a aerosolized type of spray up your nose, in your olfactory epithelium, so isn't that the very upper part of your nasal cavity is permeable to certain agents, and that can actually get into your brain. So they've been doing these studies where they're using intranasal insulin injection, and there has been some improvement in some individuals. So the argument is, well, is it because insulin has a whole bunch of other properties that don't necessarily involve glucose? It could, it acts as a signal in a way and triggers molecular changes inside of cells? Or is it because it's helping facilitate more glucose uptake? So there's a lot of evidence that glucose does not get processed properly. And Alzheimer's brain is actually sort of the earlier studies using Positron Emission Tomography, where you use radio labelled glucose, and you see it doesn't get taken up. So we know there's a problem with getting glucose inside of the brain cells of Alzheimer's disease, you're not getting glucose - that's a bad problem. What's what researchers haven't really tried to parse apart in a little more fine-tuned manner is asking if the glucose getting taken up in astrocytes or is the glucose going up in neurons, and the technology is slowly getting there, we can start to look at that. So a lot of this is just we didn't have the tools to try to figure this out. But we're getting there. And we have a lot of genetic models and mice where we can modulate certain things. And then see how does that affect the ability of the animal to process sugar or make lactate? So getting back to well, how does some of this data with lactate? Is it translatable to a therapy? We're not there yet. I think we have to establish that too much lactate is bad. We need to ask, where the lactate coming from? And when we start to have answers to those questions, we can say, well, where's the source of the lactate? Is it producing too much? Is it not being utilised? Is there a way we can fine tune the lactate like a thermostat to turn it down a bit? And does that actually help? So there are potentially some drugs out there that we could potentially repurpose to try and treat Alzheimer's disease. So I mentioned seizures. For example, a few years ago, there was a paper suggesting that drugs which target an enzyme called lactate hydrogenase, which is the enzyme that makes lactate could be used for the treatment of epilepsy, or seizures. So right now, that's still in the experimental stages. But could we try to test those drugs and Alzheimer mouse

models? And if do they indeed lower lactate levels? Does that actually correlate with improved memory, but it's a really tough one. But the fact that people are trying these strategies, using metabolic intervention to treat Alzheimer's disease 10 years ago, people would say that snake oil, you know, but now papers, because all of the trials, clinical trials targeting amyloid have failed. All of them. So we're back to square one, we have to try something different. And I think there's ample evidence that metabolism is messed up in Alzheimer's disease, nobody argues that where the argument comes is well, how is it messed up? And which form of metabolism is more adversely affected? And if we're going to intervene from a metabolic perspective, where do we start, you know, which strategy, and those are all valid concerns and research directions that people could explore. And the funding for that has not been great. And I'm hoping that it's going to change over time, because people could recognise that metabolism is something that you can target and modulate from a therapeutic perspective. I think where it's, it's taken a hit as people perceive as some fad diet, like a ketogenic diet, and that's going to help. And, you know, this isn't really about diet, per se, although there's ample evidence suggesting that your diet can dramatically determine whether you can get Alzheimer's disease, you eat crappy food, you know, high carbohydrate, high fat, high fat, processed foods, you start to become obese, you have insulin insensitive type two diabetes, all of these things make you way more susceptible getting Alzheimer's disease. So anybody that says, well, metabolism is kind of a hokey thing. No, it's not. I mean, all the epidemiological data shows very clearly, unhealthy diet, unhealthy lifestyle renders you way more susceptible to Alzheimer's disease.

Henry Standage 36:55

That is something that not enough people know.

Rob Cumming 36:59

Well, I think it's going to change because I'm, I'm hearing a lot more on the media, this talk about what can we do to prevent Alzheimer's disease, and there was a recent sort of study, and it was covered in the news media quite extensively about what are the things that you can do? And certainly, they talked about diet, they talked about, you know, eating more healthy, getting your diet down, being more active, be socially engaged, you know, the whole idea about these crossword puzzles, and, you know, brain training. Actually, it's not that great. What being engaged with people actually, is far more preventative. So you could sit at home and do all the crossword puzzles all day long, that isn't necessarily going to stop you from getting Alzheimer's disease going out and having coffee with friends, actually will. So this aspect of social engagement seems to be really important. Getting out and moving. Getting a little bit of cardio and the diet. It's a really big one eating fresh fruit and vegetables, lowering your carbohydrate intake, avoiding lots of processed foods. Yeah, I think that that that data is, is quite convincing. But the problem is, you know, people want to eat their Doritos and they want to, you know, have a big pint of beer.

Henry Standage 38:20

I feel attacked.

Rob Cumming 38:22

Yeah. So it's, it's difficult to change. Those lifestyle changes are very difficult. Of course, people would like to just take a pill.

Henry Standage 38:31

That was the interview with Robert Cumming. There was a lot to take on board there. Humanity's defining characteristic is its capacity to learn. When we don't take care of our brain, we damage

Western Science

ourselves and our loved ones. That's it from us for this week. In the meantime, like, share, subscribe to the podcast. I'm Henry Standage, signing out. Thanks for listening.