

Marie: Hello and welcome to *The Parkinson's Research podcast: New Discoveries in Neuroscience*. I'm your host, Dr. Marie McNeely, and I've partnered with The Michael J. Fox Foundation for Parkinson's Research to bring you to the forefront of the field of neuroscience to discuss the latest advances and discoveries with leading experts.

The Michael J. Fox Foundation created this podcast for researchers, clinicians, and industry professionals with the hope that these conversations and the resources we share will advance your efforts and partnerships to improve brain health. We're welcoming guests with a range of experiences and viewpoints. The views expressed belong to the guests themselves. We're excited to let you know about some upcoming changes to the show. In 2025, we'll be merging this podcast with The Michael J. Fox Foundation Parkinson's Podcast, so make sure you subscribe to hear future episodes. You can find the link in the show notes.

Today we are excited to welcome our guest Dr. Puja Agarwal. Listeners, Puja is an Assistant Professor in the Department of Internal Medicine at Rush University. And in our episode today, we'll be talking more about her work investigating the role that diet and nutrition may play in Parkinson's disease and other neurodegenerative conditions. So Puja, welcome to the show today. How are you?

Puja: Thanks for having me. I am doing great, and it's a pleasure to be here on your show talking about one of my favorite topics, which is diet and neurodegenerative disorders.

Marie: Well, we are so excited to have you with us today, and we're looking forward to learning more about you and your work. And perhaps we'll start with you. Can you give us a little bit more information about your background and the path that you took to get to your current position there at Rush?

Puja: So, as any other, this was not a very straightforward path. So, I did my bachelor's and master's from India, and then came to the U.S., did my PhD at the University of Illinois, Chicago. That was mainly focused on nutrition. I'm a trained nutritionist and a nutrition epidemiologist. In my PhD, I delved more into the epi- piece and the nutrition intertwined piece. And for my poststructural fellowship, I joined Dr. Martha Claire Morris, who is one of the pioneers in diet and nutrition space for neurodegenerative disorders. And I had the privilege to work with her to learn more about diet and neurodegeneration.

And that's when I found my path, my purpose, and that's something which I love to do. And here I am after a poststructural fellowship, I have joined as a faculty and am currently working as a nutrition epidemiologist at the Rush Alzheimer's

Disease Center, where we look at different neurodegenerative disorders, including Parkinson's disease.

Marie: Very cool. Well, Puja, I think this is a really exciting area of research. Perhaps you could give us some background on just the importance of studying these associations between diet and brain health and what some of the evidence is to date that links the two.

Puja: These studies go back two decades, I would say, where researchers started to look at initially different nutrients or specific foods, and then moving on to more on diet patterns, given no food is consumed in isolation or no nutrient is consumed in isolation. The field has more moved towards looking at the diet as a whole, because you eat a combination of foods.

And currently, why diet is important for these neurodegeneration disorders primarily is because we do have limited knowledge or limited cures for most of these diseases. And we have medications mostly for symptoms, and we do not have the exact cure. Like, there are a lot of studies, and the science has moved forward tremendously over the last decade in terms of the pharmacological therapies and where we are at. But there is also an inclination of finding more ways of non-pharmacological interventions that would delay your onset or that can slow your progression of these diseases. And that's where diet really comes in and has a huge role to play, because that's one of the modifiable lifestyle risk factors, which you can really promote. And it can have a huge public health impact when it comes to our aging population.

So, coming back to what we know about diet and neurodegenerative disorders so far. Diet has been associated — when I say “diet”, it can be like any component of diet or specific nutrients, but I'll just use the umbrella term “diet”. Whatever we are consuming in our foods. So, there are different nutrients in foods, and overall dietary patterns that have been associated with slower progression of, for example, Parkinsonian signs or delaying the onset of having Parkinson's disease. We have studies also looking at how these nutrients and diets slow the ongoing cognitive decline among the aging population and reduces the risk of other neurodegenerated disorders, such as Alzheimer's disease or multiple sclerosis, etc.

So, the field is really excited right now to find new answers. We have more information in terms of what kind of diet will work and what and when people should start making efforts toward their lifestyle so that they have a better and healthy aging and future. So, there is a lot of literature currently available on how these diets play a role, but we can go over that one by one.

Marie: Absolutely. I think Puja, you've done some really interesting work looking at some different diets or some different patterns of eating, and one of them that you've worked on specifically is the MIND diet or M-I-N-D. For folks who may be outside of the diet and nutrition world, can you talk a little bit first about what this MIND diet is, what makes it unique, and maybe how it might be particularly beneficial for whether it's delaying or slowing the progression of neurological diseases, including Parkinson's disease?

Puja: As you said, this is my area of research, and I have been looking at the MIND diet since my postdoctoral fellowship. Again, just to clarify for those who do not know what MIND diet stands for. So, MIND stands for Mediterranean-DASH Intervention for Neurodegenerative Delay, M-I-N-D. And this is a hybrid of Mediterranean and DASH diet. And all the components of these diets — so, this diet has 15 components. When I say components, like food components, and everything is based on the components which are included in the diet have currently a strong scientific evidence of their relationship or for their association for brain health outcomes.

For example, in the MIND diet three very unique features I would say which are different from Mediterranean and DASH, I think the first one will be the green leafy vegetables. So, in the MIND diet you are encouraged to eat more green leafy vegetables and also encouraged to eat another second unique component — it's berries. So, both of these components are important because they have specific nutrients and polyphenols. When I say "polyphenols", like bioactives that are present in food that are really essential for brain health and also helps to maintain your neurons and other functions — brain functions, connectivity, etc.

So overall, MIND that has been looked at differently for different neurodegenerative outcomes, and it's more of a plant-based kind of diet which includes berries and, as I said, green leafy vegetables but also other vegetables, whole grains, nuts, beans, and legumes. And it's also rich in various essential nutrients and the bioactive compounds. And it's not only important for your brain health. Again, coming back to a broader term of "diet", especially the MIND diet also, which is, as I said before, is a hybrid of Mediterranean and DASH.

So, obviously, when we look at these diets, these are very highly correlated with the Mediterranean diet scores or DASH diet scores. But overall, they are rich in antioxidant and anti-inflammatory factors, and overall, not just good for your brain health. It is also good for your overall well-being — like cardiovascular health — because the diet is also not only promoting you to have good healthy food, it's also promoting you to limit some of the unhealthy food items.

So, there are different components in these diets — 10 healthy components. I haven't mentioned all 10 right now, but I can cover it one by one if you want me

to. But primarily, looking at green leafy vegetables, berries, whole grains, nuts, legumes, and beans. And the other important one that comes in is fish, which is, again, a lot of people call it “brain food” because it's very much rich in the omega 3 — the good fatty acids we have. So, fish is another component of the MIND diet.

And then the unhealthy components include limiting your butters and margarine, whole-fat cheese, limiting your red meat or processed meat, and then fried food, pastries, and sweets. So, when you are trying to adhere more of these recommended components of the MIND diet we have seen, specifically in our study, the beneficial effect on some of the specific brain health outcomes.

Marie: I think this is really interesting research and I think the benefits of just having a healthier diet can be tremendous, not just for the brain but for your whole body, but I think some people really struggle to stick to a diet. But one of the things that I think that also makes this diet unique is it's not overly restrictive. It seems like something that people would be able to sort of stick with. Is this something that you've found in your conversations with folks who've participated in the studies?

Puja: Yes, and I would totally agree. We have done some trials, and we're right now also participating in ongoing trials for lifestyle modification. So, MIND diet is not like a specific diet. Okay you eat this in the morning, this in the night, this in the evening kind of a thing. It's more of an approach where you've been given liberty to include certain components in your diet in whichever way you would like. So, that kind of freedom to a participant or a person who's trying to follow a certain amount of diet because it's very different to change your food. Because, again, food is very personal. People are mostly used to eating certain specific types of food. It varies by culture, demographic profiles, and your geographical locations.

So, you have to give some freedom or some broader food groups people can choose from and can incorporate those in their daily routine, rather than telling them, “Eat certain specific types of foods.” I think that makes it more — I won't say “easy” to follow, because nothing is easy to follow when it comes to diet if you're not consuming that kind of food. But it is something which people have been able to stick to just because of certain reasons.

Marie: Absolutely. And I think that flexibility is key, like you said. So let's get into some of the findings that you've had looking at the MIND diet so far in your own laboratory. Can you share some of the research that you've done to date?

Puja: Sure. So, particularly for MIND diet-specific research, we have primarily looked at different outcomes, as I said, among older adults. So at Rush, at the Rush Alzheimer's Disease Center, we have an ongoing cohort, which has been going since the '90s. And some of them specifically do collect dietary information on

these participants. So, what we are doing in these cohorts is observing these older adults annually. We do clinical assessments, including cognitive assessments, as well as UPDRS scores, and other assessments. And all these people are followed over with all these assessments, and then at the time of that, they also consent to donate their brains.

All this data was included in my study that was funded by The Michael J. Fox Foundation, where we proposed to look at their dietary patterns, specifically the MIND, Mediterranean, and the DASH dietary patterns, and how that's related to the parkinsonian signs progression over time in these older adults. And another piece we added to our study was to look at how these diets are also related to the pathology in the brain, which is the final gold standard for diagnosis if somebody has Parkinson's disease, for example.

And in these studies, I would say, we also proposed to look at specific nutrients. As I was mentioning earlier, all these are plant-based diets. For example, because MIND is such a plant-based diet, it includes a lot of fruits and vegetables, but one of the important components is the antioxidant nutrients, which include vitamin E, vitamin C and carotenoids. And we had a hypothesis that people who will be consuming more of these antioxidant nutrients or these nutrients from food or mainly supplements — you're not sure — might be having a delayed onset of parkinsonism maybe or delayed progression of parkinsonian signs.

And interestingly, that was one of our first studies published from this grant where we actually looked at their vitamin E, vitamin C, and carotenoids intake and found that people who were consuming more of these antioxidant nutrients had slower progression of parkinsonian signs over time during the follow-up, when compared to those who were eating less of these nutrients. For example, when we specifically looked at vitamin C, we found these associations specifically for the nutrients that were coming from the foods and not specifically from the nutrients that were coming from the supplements. So that's kind of another piece we found in this study, which was really interesting.

So we found, for example, again with carotenoids — so carotenoids is the colored pigment you will find in most of the colored fruits and vegetables. So, we found the higher total carotenoid intake was again associated with slower progression of parkinsonian signs. And specific carotenoids that really stood out included alpha-carotene, beta-carotene, and lutein. These again have been known or shown before to have an impact on brain health outcomes, not just parkinsonian signs, but the other health outcomes also like cognition and dementia risk. So, this was really exciting for us to see that what we hypothesized was really showing us, because it's an observational study design, we are here looking more at the association rather than a causal effect kind of

thing. But we found that the intake of antioxidant nutrients was associated with slower progression of parkinsonian signs.

And then we further wanted to look at this overall diet, including MIND and Mediterranean diet, was also associated with fewer individual parkinsonian signs. So, the individual parkinsonian signs, by that I mean specifically looking at if it impacts gait, bradykinesia, rigidity, or tremor. We used another data set. We used the Chicago Health and Aging Project — that's another longitudinal cohort at Rush where we had diverse samples. So, we have primarily black older adults enrolled in that study. And we wanted to see if our associations or if our findings of MIND diet being associated with parkinsonian signs — if we can replicate that in this diverse cohort too.

And interestingly enough, we did find that, overall, MIND diet and healthier Mediterranean diet was associated with fewer individual parkinsonian signs, primarily including gait, bradykinesia, and rigidity in our biracial sample that included non-Hispanic whites and black older adults. So, that was another confirmation or like replication of our previous findings.

And then in the later years of our study, we specifically wanted to look at the pathology outcome. And we did look at some of the pathology. Remember, I said earlier in the Rush Memory and Aging Project, we are observing people, getting their diets over the follow-up, and then these people have also consented to donate their brain at the time of death. So, we do have autopsies on our participants of the Memory and Aging Project.

So, we wanted to leverage the existing neuropathological data we have from our labs from Rush Alzheimer's Disease Lab. And we did look at how people's diets during their life, or during their follow-up in the study, was associated with Lewy body disease in the brain. And we have found some interesting results over that, but I would say these results are exciting but we need to really further do more analyses to really do that. So, the previous studies I've talked about have been published and are peer-reviewed, but this one is still ongoing. So, I think there is a lot more to be added in this space, but what we have found so far is promising and encouraging and supports the role of diet as a modifiable risk factor, specifically for Parkinson's or parkinsonian signs-related outcomes or Parkinson's disease.

Marie: Certainly, and I know these pathology studies can take some time, obviously, because people are donating their brains after they've passed away. So, can you comment on where you are in terms of data collection? How much data do you have?

Puja: Oh. Now we have quite a lot of brains. So, that's the unique part of the Rush Alzheimer's Disease Center and specifically for Rush Memory and Aging Project. We have collected diet over the years, obviously. And then we have multiple dietary assessments, and then we are collecting their brains. And we have such a huge team of neuropathologists and lab people doing their autopsies, and staining, and doing all kinds of different pathologies in the brain. So, currently for my analysis which is just right now ongoing, I do have nearly 800 people. So that's another exciting piece. So, that's why I would wait until we finish the analyses and have the final findings to say or comment anything on how. But that looks promising.

So currently, we do have 800+ people on whom we have diet information, and we also have the pathology on these participants. So, that's the next exciting piece I'm really looking forward to finish my work on. Because, I mean, it has taken longer than expected, but then that's how studies are. We have been working for the dietary data because it also needs processing, and QC, and everything. So, hopefully soon we'll have more answers and now diet, specifically, relates with the Lewy body pathology and other pathology in the brain. But we have published our initial findings on association of diet with Alzheimer's disease pathology. And we did find that our MIND diet score was associated with lower Alzheimer's disease pathology, primarily amyloid plaques in the brain. And now we'll be looking at the Lewy body pathology.

Marie: Very interesting, and you mentioned the measure that you're using — MIND diet score. Can you break down a little bit how you calculate this? Because I know sometimes people view diets as sort of black or white. You're either doing it, or you're not doing it. But I think there's this nuance in terms of making a more quantitative measure.

Puja: Yeah. So, we have a matrix of how to give a MIND diet score to each of our participants. Again, this is based on what was published before by Martha Claire Morris and her colleagues at Rush. The MIND diet, it was in 2015 when the first paper came out for the association of MIND diet with cognitive decline in Alzheimer's dementia. And we are using the same matrix. Obviously, over the years, things have evolved. And we have done more and more research in the space, and there are a few updates

But, more or less, the overall picture remains the same. That MIND diet includes 10 healthy food groups, as I mentioned earlier, and five unhealthy. And we have a breakdown of the specific amount or the serving sizes that should be consumed by a person to get a score for that particular food component.

So, we give a score of 0, 0.5, or 1, depending on number of servings they report they consume for that food group. For example, for berries, a questionnaire will

include how often or how frequently you consume berries. And then, based on whatever the report, we combine that score and get to our overall serving size score per week for that participant. And then either place them as a zero if they're not consuming at all or rarely consuming it, or 0.5 if there's somewhere in between, or if they're more than five times a week or more, then we give them a score of one. So similarly, for each component, we have the scoring matrix we follow. And our statisticians and our data management team work hard on providing this kind of data to us. So, that's where we are at in terms of creating the MIND score for each of our participants for each of their visits. And then, I think I mentioned that earlier, but we then obviously add all these 15 components. And then the scores range from anywhere between one to 15, depending on how much you reported you eat each of the food items.

Marie: Well, that makes sense. And I think when you're looking at people who may have a healthier diet, they might also be healthier in other ways. Can you comment on what other data you might have collected to sort of rule out things like people's weight, or how much they exercise, or things like that?

Puja: Yes. So, we do collect that kind of information also in our cohort. So, we know their physical activity. We know their BMI. We also get other measures. like we have depressive symptom scale. We do know their cognitive activities they're engaging in. So, in our model, just as you said, usually people do follow more of the lifestyles together. And we do see that people get higher or better diet score are the ones who are also doing a little more hours of physical activity per week. Or they're a little more probably years of education than those in the lower tertile or lower group.

But the way we tackle it is we do control for these factors in our statistical models. For example, whenever we are trying to investigate these associations, we are looking at our exposure with the diet in our outcome of the Parkinsonian signs. But then we will obviously control for the factors that can affect our exposure or outcome. And that's why we control for physical activity, education, smoking, or sometimes BMI or depressive symptoms. Because that depends on your outcome also. But we try and take care of all these other co-founders or co-variates in the model.

Marie: Excellent. And it sounds, Puja, like you've had some promising results with this project that you've been working on. Can you talk about what are some of the potential impacts of this study and perhaps the future directions that you're going to take it?

Puja: For me, I think these are very important findings because this gives us encouraging results and do support what has already been published in the

literature and also has been done for the other outcomes or Parkinson's disease outcomes.

Because we do have studies from Nurses' Health Study and the HPFS that consuming MIND diet does decrease your risk of Parkinson's disease. In fact, the case-control study from Canada found that people who are consuming MIND diet would delay their onset of Parkinson's disease by almost 17 years. So, we have old studies and also some new studies supporting what we found. And that's kind of encouraging and just gives me hope that there is more to this modifiable factor, which is diet, that can be, I won't say "easy to modify", but that's something which is doable. And if somebody wants to have a healthier aging, he or she can adapt these specific guidelines. And then we can have more public health impact based on our findings probably once it gets out.

So, overall, it's helpful not just for people who have higher risk or people living with the disease. I think we have limited study for people living with the disease. These findings come more from people from case control studies or observational studies. So, I won't comment on people living with the disease, but I think it should be beneficial, given we have seen some impact on specific progression of Parkinson's signs, etc. But it's also important for people or the family members of people diagnosed with Parkinson's disease.

So, I think it's helpful. For example, like my dad had Parkinson's disease. So, I know as a family member, it's very difficult or as a caregiver, which was my mom. She didn't know what we should do in terms of lifestyle, just to delay the disease or delay the progression. But I guess, given that we have now our studies and other studies supporting these findings, there is a hope. So, not just for people with the disease, but also for their family members and the offspring of people living with the disease. I think it's important.

And we'd definitely like to pursue these findings further. A, obviously we have to get this analysis with Lewy bodies done and published, but then for our future work, we definitely are thinking in different directions because there are different ways we can, again, look at the data. The field is now also moving towards the biomarkers of the disease, neurodegenerative diseases. We at our Rush Alzheimer's Disease Center are doing more in terms of biomarker assessments, including the ones which have been shown to be associated with Parkinson's disease. For example, like NFL, like neurofilament light, GFAP.

For future directions, I think we would like to integrate more of these findings in a way that is more applicable to other diverse cohorts we have. And then also further look at other markers that can be easily assessed. Like for example, asthma biomarkers that can be easily assessed and how that is related, or just the interplay between diet, biomarkers, and pathology. So, there are some ideas

we already have for our future direction, just to disentangle more and just to understand also the mechanistic link behind diet and brain health outcomes.

Marie: Certainly, and I know you touched on biomarkers, and perhaps the biomarkers may help with this particular question, but I know diet is complex. Do you think that you really found the sweet spot here with the MIND diet as it is? Or do you see this MIND diet maybe continuing to evolve as you get more information?

Puja: I think, definitely, things will evolve as we get more information. This is like a broadly speaking MIND diet. I always believe there cannot be just “one diet that fits all” kind of a thing. And although this diet does include different factors, we have to be really working on different aspects of diet that plays a role. That's one, for sure.

So, it's not like one diet is better than others. It's just if the diet you're consuming has the healthy component that's required for your brain health. For example, there are different cultures and people from other countries probably might not be consuming specific types of foods. For example, like berries might not be there for each country the way we get it in the US. But then I'm sure there are specific foods that are rich in the bioactive and carotenoids, specifically locally grown in that country or region, that can be substituted or used instead of berries.

So, I think there's no one thing. So then, definitely the field will be evolving as we know more and as we delve more into the type of the foods and the mechanism behind it. And we have to be careful in terms of our recommendation that it has to be an approach, as I said before, rather than just specifically putting on specific foods that are required to be consumed.

Marie: I think that makes a lot of sense. And we mentioned, of course, that this work that you've been doing lately on the MIND diet has been funded by The Michael J. Fox Foundation. I think there are a lot of great funding resources that are helping move the field forward. Do you have other examples of tools, or resources, or collaborations that you've encountered in the work that you do that you think are really having an impact on the field?

Puja: Sure. This work specifically was funded by The Michael J. Fox Foundation, and I'm really thankful for that because that got the wheels moving, and I could do some other philanthropy grants. So, because I was interested in this particular topic, I also looked at Alzheimer's disease as an outcome. And looking at other Alzheimer's disease-related outcomes, I got some funding from the Alzheimer's Association. And I think another funding mechanism that have been definitely are federal funds are important. NIA has been very supportive of such research, and they are also doing a lot of support for early-stage investigators and still supporting a lot of the centers, or for example, the Alzheimer's disease research

centers and some other U19 grants supporting the work of neurodegenerative disorders. So, I'm sure there are different mechanisms supporting these kinds of work.

But definitely, as a scientist, I always feel, I mean, definitely we have ideas, we have these beautiful cohorts, amazing work which is actually kind of hard work of so many years from different scientists all across the globe. And then as an early-stage investigator, really need to move the field forward. So that's, I think, my take on it. We have to keep probably delving more, investigating more in such things. We need definitely more support in terms of the funding also for the non-pharmacological interventions. I know pharmacological interventions are very important, and they have kind of taken a huge leap from where we were 10 years before from now. But I do see that there's still a lot of movement happening in non-pharmacological space, and specifically with lifestyle modifications, which can be adapted by an individual early in life. So, that's important too.

And there are different mechanisms supporting those. So, I definitely would encourage people to keep applying. There are several out there. And most of our work is like the one I presented here, and the ongoing studies are actually supported by philanthropy grants, including Michael J. Fox, Alzheimer's Association, and by NIH and NIA. So, that's an important piece of the whole picture because definitely that's something through which we are able to collect the information, have these centers running, and definitely the participants and the study staff we have is amazing that keeps us moving. And data keeps coming. So, definitely we do need funding sources. We do need our people. We do need our staff, but most of all we do need our participants who are voluntarily helping us to move the field forward.

Marie: Absolutely. And I know, Puja, in your work, you've worked with folks with Alzheimer's disease as well as Parkinson's disease. And I think other neurodegenerative conditions folks are also looking at how diet and brain health are related. And I think there's just some overlap in these diseases that are becoming more appreciated in the field or perhaps more investigated in the field in recent years. So, can you comment on what some of the similarities that you're seeing are, or maybe some of the differences are, in terms of the impacts of diet on Parkinson's versus Alzheimer's.

Puja: I think there are more similarities than the differences, I would say. Again, we are talking about an umbrella term as “neurodegenerative diseases”. And we specifically look at different things, but our group has previously published that, for example, Alzheimer's disease is not just one pathology in the brain. It's more of a mixed pathologies. And then we have another publication from our group saying that Parkinsonian signs are also related to the mixed pathologies in the brain. So, there's a lot of overlap between the two.

And what we found from our diet studies is that MIND diet was associated with slower progression of Parkinsonian signs, and MIND diet was also associated with slower cognitive decline. And we also have studies indicating that people with the motor signs also do show up with the cognitive decline over time. So, definitely there is a lot of overlap, and we do need more studies to understand the real mechanism and how motor and cognition are so intertwined.

So, are like other outcomes. For example, depressive symptoms and disability outcomes, where we found that better diet was associated with less disability, or functional disability, or mobility disability. So, definitely the motor and cognition functions are intertwined, and when it comes to diet, as I said earlier, diet is specifically helping not just one or targeted region of the brain, I would say it's kind of helping over all different regions. That's my hypothesis, obviously. But I think as I said, when your diet is helping your brain, it's not just helping your brain, it's also helping your heart. It's also helping you to maintain your weight and other things. So, everything is intertwined and interrelated. So, definitely when it comes to neurodegenerative diseases, specifically Alzheimer's and Parkinson's, I do see that there is a tremendous overlap, even when we specifically talk about the effect of diet on these outcomes.

Marie: I see, and I agree, Puja. I think this is a really exciting time to be working in this area of diet, and nutrition, and brain health. I think there's a lot of interest in the area at the moment. What do you see as some of the biggest unanswered questions that remain, or perhaps the biggest areas of opportunity, specifically related to Parkinson's disease?

Puja: There can be many. I think what we know is kind of just the tip of the iceberg. And there can be different things that we can analyze in terms of understanding more about, just not the disease, but just the way we can prevent, or delay the onset of the disease. And specifically, I am more interested in looking at what's basically the mechanistic link between the two.

So, for us, in our final discussions when we were doing this kind of work as a team, we were thinking of like, there's so much possibility. For example, there's so much overlap of mixed pathologies in the brain. And then there's so much of other factors, such as vascular risk factors, and your lifestyle factors, your demographic factors, your social determinants of health, that play a role in your overall outcome of the disease. I think for me, it would be just to investigate further how there is different mechanistic link defining the associations of a better lifestyle or better diet with the brain health outcomes. And how does that interplay with the current biomarkers we have for imaging, for plasma, and also with the - omics, which is an upcoming field. I think that's where our field is heading next, just to find more answers and establish more on these findings.

Marie: Absolutely. I think that interconnectivity is key as well. Taking things out of their silos and thinking about the big picture a little bit more. I think that's a huge direction that the field is moving as a whole. Well, I've enjoyed learning more about your research. I think you're doing phenomenal work. Can you share with us as we wrap up our conversation today, Puja, how you see your work bringing us closer to finding a cure for Parkinson's or contributing to improved therapies or improving life for people with Parkinson's today?

Puja: I mean, obviously, this is my work, so I'm a bit biased about it. I love what I do. And I always have felt that nutrition has a huge role to play for any kind of neurodegenerative disorder. And I'm glad to see that there's so much interest now for these non-pharmacological interventions, and specifically diet. And there are more studies coming up from different groups on how diet can play a role.

I think once we have more intervention trials and the results from that, we will be able to establish further the role of diet in delaying the onset of the disease and more so the role of diet and healthy aging. So, I think we still need more answers on, like, "Okay, when should I start?" I think a lot of people do come up and ask, "Is it too late to start? Or should we start in the middle? Should we start, like, right up front?" I mean, I have my own understanding and my own answer to it, but we still need scientific evidence to support these things. Obviously sooner is better.

But once we have these kind of findings, and once we have more studies for these links and understand the mechanisms behind it, or how if your overall metabolism is related or is impacted by different lifestyle factors, I think we can have a huge public health impact telling people that, "Okay, this is something which we all should be doing." And I think once it's more established, then it more should be going to the clinical settings. I think that's probably the next step. In terms of are we really talking enough about diet and other lifestyle modifications when there is somebody with certain symptoms going to the clinic? And are the clinicians referring these people to the coaches that can help them with these lifestyle modifications? So, for example, I have not seen people yet, or maybe it's just me, but I have not seen people getting a referral for their neurological disease and getting a dietician referral, for example. Like, are we really doing it? Again, it's not covered in a lot of the medical insurance plans, and there's a lot of other things behind it.

So, I think once we have more on this, and we have more evidence, and we establish more of these links, it can have maybe more impact on the policies we have right now in terms of how things are done, and what should be prioritized, and how lifestyle modifications should be emphasized upfront in the clinics, rather than just waiting until the end. And then referring them to the dieticians only once, like we have to adjust the dose of levodopa or stuff like that. But it has

to be coming as in the early stages as a preventive measure, rather than just something which they have to take care of as they move along with their medication or pharmacological routines. And I think another piece, important here, will be just to also understand in future how pharmacological and non-pharmacological interplay with each other for these disease outcomes, and I think that's again, like where future studies should look into.

Marie: Absolutely. I love this idea that the evidence that you're generating today can kind of pave the way for changes in policy, changes in practice, so that it becomes more like other forms of preventive care, really having this preventive diet approach. And then also really thinking about those interactions between, okay, you're on this medication, so maybe this diet is a better fit for where you're at right now. Really personalizing medical care as well.

Puja: Yeah, so personalizing medical care is, I think, yeah, key. And given that we have such limited resources as is, when it comes to medical facilities, I think then there should be other things also talked about. For example, is there enough food available in your area to buy something healthy? And then probably the food accessibility and other things come into play.

So, I think these findings can open the door of a lot of other things and then can be helpful in those who are trying to adapt healthy lifestyle modifications because they have a known history, a known family history of the disease, or if they are already having some other things. So, I think there's a wide variety or wide range where the findings can be applied to, and I'm really excited the way the field is moving and the way the support is being given to various funding sources to make these kind of modifiable factors, bringing it up front in the research.

Marie: Well, Puja, we really appreciate the work that you are doing in this area, and we really appreciate you joining us to share it with us on the show today. So, thank you so much for your time.

Puja: Thanks for having me. It was a pleasure to talk about this. Thank you.

Marie: Well, it's been wonderful to chat with you. And listeners, it's been great to have you here with us as well. If you want to know how The Michael J. Fox Foundation can help your research, please visit michaeljfox.org/researchresources. And remember that in 2025, we'll be merging this podcast with *The Michael J. Fox Foundation's Parkinson's Podcast*, so make sure you subscribe to that show to hear the outstanding episodes we have coming up. Find out more in the show notes. Thanks again for joining us for this episode of *The Parkinson's Research Podcast*.