

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 are welcoming guests with a range of experiences and viewpoints. The views expressed belong to the guests themselves. And today we are excited to be welcoming our guest, Dr. Gammon Earhart. Listeners, Gammon is Professor of Physical Therapy, Neurology, and Neuroscience, as well as Associate Dean for Physical Therapy and Director of the Program in Physical Therapy, at Washington University School of Medicine in St. Louis.

Today we will be talking more about her research on gait and innovative intervention approaches to improve gait and enhance physical activity in people with Parkinson's disease. So, Gammon, welcome to our show today. How are you?

Gammon: Thanks very much for having me. It's so good to be here. I'm doing well.

Marie: Well, we are excited to have you here with us today, and I know we've known each other for some time, but for listeners who haven't met you yet, Gammon, can you share a little bit about your background and your path to your current positions?

Gammon: Absolutely. Happy to. So, I am a physical therapist by training first and then continued on to pursue my PhD in movement science because I was very interested in generating new evidence to support the practice of physical therapy. So, I've been focused primarily on research and a bit on teaching people who are training to become physical therapists for about the past 20 years now, and much of that research has focused on movement control in people who have Parkinson's disease.

Marie: Fantastic. And I know that walking is often impaired in people with Parkinson's disease, and maybe to provide some context for listeners who don't study this specific area. Gammon, can you provide maybe an overview of some of the key things that we know so far about gait decline in people with Parkinson's disease?

Gammon: Yeah. So, we actually know quite a bit about how walking changes among people with Parkinson's disease. And the more that we know, the more that we realize that it's a very pervasive problem that is present even very early in the course of

the disease. Some studies have even suggested that the onset of walking problems mark the beginning of disability and therefore could be considered a red flag. So, some of the types of changes we see in walking among people with Parkinson's include slowing down, taking smaller steps, becoming more variable or less consistent from one step to another.

And about half of people who have Parkinson's disease eventually develop something called freezing of gait, where as they're walking, they feel as if suddenly their feet are stuck and they won't move even though they're trying to take the next step, they can't. And so, we look at all of those things in our lab in terms of the changes in the quality of walking movements. And we're also interested in the quantity of walking that people do because we know physical activity is so important for overall health. And with challenges in walking quality can come challenges in getting enough steps in per day.

Marie: Absolutely. And I think your expertise, you have some clinical context as well as the research experience. So, thinking about the clinical side, most clinical assessments measure walking capacity. But, Gammon, can you comment on maybe some of the limitations of just measuring this capacity and how potentially measuring real-world walking can add value?

Gammon: Yeah, we oftentimes will take a brief assessment in a clinical setting that, again, measures exactly what you said, which is walking capacity. What can a person do? But it is not necessarily a good reflection of what they actually do in everyday life.

An example of this is when someone is in the clinic or lab setting and they know that their walking is being recorded because they're walking across some sort of instrumented mat, for example, they'll walk more quickly and with bigger steps. But then when they're returning back to the starting point, and they don't think we're recording them, they'll actually go back to their more customary walking pattern, which is, again, slower with smaller steps.

So, if all we do is measure them in the clinic or lab when they know they're being assessed, we're really probably not capturing very well at all how they're actually walking in everyday life. And in order to do that, then we need to be able to measure things outside of the clinic and lab, for example, by sending wearable sensors home with somebody that can track how much they're walking or the quality of their walking throughout their daily activities.

Marie: Very interesting. And I think some of the challenges that come with measuring walking in everyday life for people with neurological conditions like Parkinson's disease is the question of accuracy. I think a lot of these devices are developed

with neurologically normal walking in mind. So, can you comment on just some of these challenges that you've encountered in measuring real-world walking?

Gammon: Yeah, that's definitely a challenge to translate this from, you know, probably work where the development of the measurement devices was done on undergraduates to now an older adult population with a neurological condition that impacts their walking. So, the actual patterns of walking that the device is designed to pick out may be somewhat different. There have been some studies looking at various commercial devices that are available, you know, that track activity or count steps whether it be smart watches or activity trackers that mount on the ankle, the foot, the hip, etc. So, we have a little bit of data to show that some devices tend to work more effectively than others. Part of that does depend on where the device is worn. So, for example, another common symptom of Parkinson's disease, beyond walking difficulty, is presence of a tremor, oftentimes in the hand. And so, if someone has a wrist-worn activity counter, it may be counting tremor as steps rather than actual steps. So, there are many considerations like that to take into account, as well as just the practicality of the devices for someone to be able to wear them and them not be obtrusive and interfere with their activities.

Marie: Absolutely. And I understand you've been working on a collaborative research project examining a mobile health intervention to increase walking, both the activity and the capacity. So, Gammon, can you talk a little bit more about this project and why you're interested in pursuing it?

Gammon: Yeah. So, this project is a collaboration, as you mentioned, with Terry Ellis at Boston University. She and I are the co-principal investigators on this NIH R01. And the title of the project is WHIP-PD, which stands for "Walking Health Is Paramount in Parkinson Disease." And the focus of the study really is building capacity for physical activity and then making sure that people are actually performing that physical activity on a day-to-day basis.

And it involves two groups. People with Parkinson's disease are recruited and randomly assigned to either a traditional control condition where they get several physical therapy sessions up front and then a customized home exercise program that's given to them on paper. Or they're assigned to the active condition, which is a mobile health group where they get the same number of sessions of physical therapy, a tailored exercise program that includes aspects of cognitive behavioral therapy, which help people to set goals and overcome barriers to reaching those goals, as well as the mobile health component where they actually receive a tablet device with an app on it that allows them to track their exercise and even communicate via a chat function with their therapist over time. And so, we're following people across a period of an entire year to see how

their capacity, as well as their walking performance and level of activity, changes over time.

Marie: So, Gammon, can you comment on maybe what makes this particular mobile health application approach that you used for this intervention maybe a little bit different or unique from other available exercise apps that people might see out there?

Gammon: Yeah, so, I think there are a couple of things. One is the incorporation of the cognitive behavioral therapy component, really helping people to set goals, identify those barriers that might interfere with achieving those goals, and then think about ways to surmount those barriers so that they have the confidence, or what we call self-efficacy, for exercise and the belief in their ability to do it and to continue to do it in the face of something like bad weather, or not feeling great, or whatever it may be.

So, incorporating that aspect is really important because self-efficacy is known to be one of the largest predictors of whether or not somebody follows through on an exercise program that's prescribed to them. So, directly addressing self-efficacy is one piece of it. Another way we address self-efficacy is in this app, the participants can actually watch videos of themselves doing the exercises rather than videos of some demonstrator. And so, that is also known to enhance self-efficacy — is seeing one's own self doing the activity.

So, we record the videos with them when they're here with us and then upload them to the app. And then they can rate each time they do the exercises how difficult or easy it was. And then the therapist can on the back end increase or decrease the difficulty of each exercise, add new exercises. And then the individual participants can also see their progress being tracked within the app. And so, they see achievements of how many days they've met their goals. And that can also help to again build that confidence and sense of success to continue to participate in it over time.

Marie: Very interesting. And Gammon, can you give us an update on the project status and perhaps what your next steps are in this research area?

Gammon: Yes. So, the project just finished at the end of last month. So, we are currently making sure that all of the data that we have are entered appropriately and that they're clean and error-free. And then we will move on to the analysis stage to answer our question of whether or not this mobile health approach, combined with the cognitive behavioral therapy, is actually better than the traditional approach or not. So, that remains to be seen.

Marie: Definitely. And I know it's early in the analysis of this data. You mentioned the study just recently concluded. Do you have a sense just from interactions with participants about how well the intervention was received?

Gammon: My sense is that the intervention was received well by both groups, and that both groups likely benefited from it, just based on our periodic interactions within assessments of the participants. People did engage in the exercise and maintain or improve activity levels, I would guess, in both groups. Whether there's a significant difference between the groups or not, I can't say at this point.

Marie: Certainly. And what would be the next step if you find that this mobile health application is effective? How do you take this information to make a usable, available intervention for people to get in everyday life?

Gammon: That's a great question. I think part of that is working with the app developers to optimize it based on what we've learned across the course of this particular study. And then also look at ways to implement it without the person needing to necessarily come in for actual physical visits so that we could reach people across the nation and across the globe, ultimately, with technology like this. And then I think also looking at incorporating it with other aspects of technology and other strategies related to some of the other studies that we're doing in the lab, in particular, looking at things like providing cues to help facilitate people's walking in the moment and whether we could incorporate some of those pieces along with the other strategies already in the app to really optimize things and make it not only functional but enjoyable for people and perhaps more customized on an individual basis.

Marie: Excellent. And that was a perfect transition or segue there. I know another approach to improve characteristics of walking in people with Parkinson's disease is to actually use these sensory cues, which you mentioned, whether it's something like external light, sound, or vibration, or something that's internally applied. So, you've done some really interesting research in this area, Gammon. Can you give us a general summary of the evidence so far that supports the use of these cues and maybe particularly the potential for some self-generated rhythmic cues to enhance gait in Parkinson's?

Gammon: Sure. So, the idea of cuing is nothing new. The concept of rhythmic auditory stimulation, or giving somebody either a song that they're listening to or the beat of a metronome and asking them to step to the beat, is something that's been around for decades now and is fairly commonplace in terms of physical therapist practice in management of Parkinson's disease and helping people to walk more effectively.

But it has some limitations, one being that you have to have some sort of device that's providing this cue or this beat to step on. Another being that once the song or the metronome beat is playing, it's playing at whatever pace it's set at. It doesn't adapt in the moment. So, if somebody's using it and they suddenly need to walk quickly because they have to get across the street, it would be nice if they could speed it up a bit during that brief period in order to accomplish that functional task that has a time limitation.

And then there's also just the inconvenience of having to have the device and having to navigate technology and such. So, given those things, we were interested in looking at whether someone could similarly improve their walking by generating their own beat rather than relying on some external source. And so, basically we asked, can people sing and step to the beat of their own singing? And does that improve their walking in the same way as listening to a song?

And we really weren't sure when we set out to do this whether it would be effective or not, because it's also well known that people with Parkinson's disease often have difficulty with dual task situations, meaning situations in which they have to walk and do something else at the same time. It could be another cognitive task, like they have to walk and do math problems in their head, their walking slows down, they have to walk and carry some objects, their walking slows down. So, we weren't sure whether singing would be a dual task type of situation where asking them to sing and walk at the same time would actually make things worse, or if it would be similar to walking to music and help their walking to improve.

So, our very first study in this vein was just, is this feasible and does it make people better or worse? And so, we compared walking and listening to music to walking to the beat of the song that the person is singing and then matching with their own rhythm. And we found that it was not at all detrimental to walking and that the improvements were similar in terms of people being able to walk faster and with larger steps when they were given music or were asked to sing that same song at a tempo that was faster than what they would normally choose to walk at.

And what was really interesting to us was the differences between listening to music and singing when it came to walking variability, or how consistent they were from one step to the next. And we saw that when listening to music and matching footfalls to that external source, people's variability actually went up. They became a little less consistent than when they were just walking without any cue. And when they walked to the rhythm that they were producing themselves through singing, their variability actually went down and they became a bit more consistent from step to step. And so, that was also very encouraging because we know variability is actually related to fall risk. And so, high variability

indicates a greater chance of falls. So, an intervention that could reduce variability, we think, is moving things in a positive direction.

Marie: Very interesting. Do you have ideas or thoughts on what might be contributing to increased variability if they're trying to match to externally played music?

Gammon: Yeah, I think just this idea that they have to be entraining to some external source. And so, there's some inherent biological variability among all of us. So, having to rain that in and have the output of the movement exactly match this beat from the external source, which has no variability, it's just isochronous. I think, could be part of it, as compared to you're generating your own rhythm. And you have sort of advanced knowledge of that rhythm and what its inherent variability is because you're the one producing it. And that may be contributing to the ability to better match that beat with consistency. And that's all hypothetical. But that's a possibility.

Marie: Certainly. And I'm curious, how does someone's maybe musical ability, or experience, or even just a sense of rhythm sort of factor into this?

Gammon: Yeah, we've been measuring that as we've continued this line of work through a number of standardized tests that look at someone's ability to actually hear a beat and perceive it and tell whether the beat they just listened to, or the rhythm they just listened to, is the same as a second rhythm that's presented or not. And also their ability to actually match their movement to the beat. And we can do that by just doing a simple keyboard tapping task and measuring accuracy of matching that beat. And so far, we haven't seen any strong relationships between performance on those tests and ability to adapt walking, which was surprising to us.

And similarly, we've also asked people about their experience and training relative to music. And once again, have seen no strong relationships between level of musical expertise and ability to use the cues. So, by and large, everyone seems to be able to use the cues effectively so long as they have adequate cognitive function.

Marie: That makes sense. And I'm curious, you know, with cues, I think it can be easy for someone to sort of entrain their movement to a beat, for example. But do these benefits persist once the cue is taken away? Or does the cue sort of have to constantly be there for there to be benefits?

Gammon: That's actually what we're working on right now. So, our studies up till recently have been single-visit, cross-sectional studies where someone comes in and we ask them to walk, you know, to a variety of musical cues, as well as sung cues at different tempos and see how they respond. But we were really looking at only

when the cue was present, or the cue had been very recently played. And now they're singing to try to replicate that same tempo.

But what we're in the middle of right now is a study looking at actually training people on using these cues. So, participants in this current study are assigned to either a music class or a singing class led by a music therapist, facilitated by a physical therapist. And so, they're training twice a week over the course of 12 weeks. And they also have a homework assignment, where they're either using music or singing three days per week outside of these classes and walking with their prescribed cue for 30 minutes each day.

And so, we've just finished the first round — we've had 24 people so far. But we need to get up to 75 to have enough power to answer the questions that we have. So, we're about a third of the way done with that study to see whether training over time results in persistent changes in walking even in the absence of cues, and also whether it improves the ability to utilize the cues when they are present.

Marie: That makes sense. It sounds like it is an exciting time for this particular study. But what would be then the next steps for this line of research, if for example, you find that maybe someone is able to learn and be able to perform better even when the cues are absent?

Gammon: I think that would be a big breakthrough because a lot of prior work has suggested that the cues work when they're present. But when you take them away, they don't necessarily have a persistent effect. But there haven't been a whole lot of studies that have looked at training of this type over time. So, if we could show that there's some persistent benefit, I think that would speak to the importance of incorporating these types of cues into things like physical therapy sessions where there are repeated opportunities for exposure to the cues and training with the cues. And then, you know, the ability to implement them in everyday life so people can be practicing this on their own and reinforcing those abilities would also be something that would grow out of this work, potentially.

Marie: Excellent. And I remember you mentioned earlier in our conversation the phenomenon freezing of gait, and how this is a problem in people with Parkinson's disease. And we don't yet really have a great solution that can reliably prevent or minimize freezing. So, Gammon, can you tell us a little bit more about a new mindfulness-based treatment approach that your lab is exploring to address this big problem of freezing of gait?

Gammon: Yeah, freezing of gait is one of the most challenging aspects of Parkinson's disease from my perspective and also from reports of people who live with freezing of gait. It's a major problem because it's very episodic and unpredictable.

So, someone can be walking and having no issues, and then suddenly something happens and they get stuck. And of course, if your upper body is continuing to move because you were expecting that you were going to continue to walk along, and your feet are not moving any longer, that creates a very dangerous situation. And freezing is a major contributor to falls, which obviously can result in injuries and a number of undesirable outcomes. So, freezing, for us, is really an important thing to address. It's also important to address because it's oftentimes not well-managed with other approaches like pharmacological intervention or surgical intervention.

So, we're very interested in trying to better understand it and address it with novel approaches. So, one of the things that we know about freezing is that it may be linked with anxiety. Many people who have freezing of gait may also have comorbid anxiety, and the situations that trigger freezing are oftentimes situations that involve some sort of challenging situation like walking in a very narrow space that might increase anxiety, or having to get onto an elevator before the door closes where there's this time constraint.

So, the hypothesis behind this study is that if anxiety is indeed related to freezing of gait, can we address anxiety through mindfulness? And by reducing anxiety, therefore reduce freezing of gait, kind of secondarily. And this was really the idea of Kerri Rawson, who's a fellow faculty member here in the Program. And so, we're currently working on this. This is another NIH-funded study.

She and I are again Co-PIs on this one. And we first started out just by trying to understand what freezing is for people, you know, in terms of their perceptions of it — how it impacts their lives — and getting the take of people with Parkinson's, as well as their care partners, on what they know about mindfulness, what they think about it, and put all that information together to develop a 12-week mindfulness class focused particularly on walking and freezing. And then we we piloted that and then refined it based on that pilot work. And then recently completed the actual sort of very small randomized trial, comparing this mindfulness based approach to just general education about freezing of gait and sort of the commonly known strategies to try to avoid freezing or get out of a freeze once you're in one.

Marie: Very interesting. And what are the sort of preliminary results or hypotheses that you have so far in terms of what you might expect the outcomes to be?

Gammon: I think in general, people found the approach to be helpful in their everyday lives, based on their feedback. They report more acceptance of the fact that they have freezing, and that it is less stressful to them when they do freeze, and it doesn't seem to provoke as much anxiety. I don't think they're necessarily freezing less as a result of this. We haven't fully analyzed this yet. It's also a study that we've

just recently completed data collection for. But I think it's definitely a tool that people found helpful and that it was different than the education class in that it sort of changed the perception of freezing when it happened.

Marie: Absolutely. And I know measuring freezing is something that is particularly challenging and sort of finding ways to quantify or sort of assess if you've had an impact. So, can you talk about how you measured freezing and was it just sort of assessing quantity or severity? What were your measurements?

Gammon: Yes. So, we measure freezing in a number of different ways. The sort of gold standard in the industry for a number of years has just been to ask people to complete a questionnaire about freezing. It asks them, do they freeze? If so, how often in what circumstances, how disruptive is it, etc. So, we can come up with a score, and the higher the score, the more severe the person's freezing is. So, we've used that, but we know from some of our other work that it's not a great tool, and it doesn't necessarily match up well with measures that we get by using sensors.

So, we wanted to also use instrumented measures. So, we have a system that we've developed that uses inertial measurement units with accelerometers and gyroscopes in them, on the feet, to basically detect times when the freeze occurs, and the foot isn't moving forward. And then to tell us, you know, how long those lasts, how often they happen. And so, we do have those objective measures of freezing to match up with the subjective measures. And then occasionally, we actually get to observe freezing in the lab. As I mentioned before, it's episodic and unpredictable. So, sometimes a person who says they have multiple episodes of freezing every day comes in and they don't freeze at all while they're here with us.

But sometimes they do. And so, we do have records from those instrumented sensors in the lab as well so that we can precisely pinpoint when somebody froze and how often when they're in front of us. And also when we send the sensors home with them for a number of days to quantify that in their daily life.

Marie: And I know there's quite a bit of evidence showing that some traditional mindfulness exercises or classes, those sorts of things, have shown positive impacts on anxiety and other aspects of mental health. But can you comment on how you adapted it to be sort of walking- and freezing-specific?

Gammon: Yea. That was an interesting process. We took the original *Mindfulness-Based Stress Reduction Workbook*. And it contains a number of different meditations focused on things that are mostly not walking. So, a lot of them are seated, or you might be mindfully eating a raisin or something like that. So, we kept that same model of sort of, you know, in each chapter of the workbook there's some

mindfulness meditation, but rather than using the ones that were seated, we developed walking-focused ones.

So, there was one walking focus when already in the workbook, and then we just built upon that looking at different walking activities. So, it could be, you know, stepping in place versus walking across the room. Some more challenging types of walking activities. As people got further along in the class, we tried to build on it. You know, maybe they're having to change speeds, or start and stop, or do different things within the walking. But all grounded in the principles of really being in the moment, paying attention to the sensations that are felt during walking, and sometimes focusing on the feet and making sure that you're hitting with your heel and rolling through your toe. And so, there were lots of different ways to draw attention to the walking and make the walking the focus that people had to be mindful of and in the moment with their movement.

Marie: Very interesting. And I think perhaps even if it doesn't directly reduce freezing there might be some benefit of some people just going through this mindful movement approach perhaps being able to better predict or sense if they are going to freeze. Do you have a feeling of whether that might be the case?

Gammon: With this small sample I'm not really sure. I do think, you know, a couple of people said I'm more aware of when I'm going to freeze, you know, I can sort of feel it coming. I've heard people say that also that they know it's coming who weren't part of the study so I don't know how much of that is attributable to the mindfulness or not, but some people do seem to have the ability to predict when it's about to happen.

Marie: So then, what is the next step for this particular line of work in the lab?

Gammon: I think depending on the results of this, we may look to continue it in a larger study. This was again a very small sample that we had, also looking at ways to try to help people incorporate the mindfulness practices more into their everyday activities, not just during the classes, would be important. And I think expanding it beyond just people with freezing has some potential as well because a lot of people with Parkinson's may have anxiety and or depression, which as you mentioned can be responsive to mindfulness. So, it may have broader application than just for people with freezing.

Marie: Absolutely. And I think, Gammon, perhaps some of the most interesting research directions really stem from unexpected results. And it doesn't necessarily have to be about this mindfulness work specifically, but thinking about your work in general, what have been some of the biggest surprises or perhaps unexpected outcomes that you've encountered in your work?

Gammon: I think one would go back to the music versus singing. I mean, I think our original hypothesis was: best case scenario, music and singing are going to be equivalent. And we never really thought that singing would be better in some way. And then it turned out to be more effective in terms of helping with consistency of walking from one step to another. So, that was surprising to me, certainly.

I think the other thing that's been surprising to me, just in the field, is the incredible boom of studies focused on exercise. So, you know, probably about 20 years ago, the advice to someone newly diagnosed with Parkinson's likely would not have included anything about exercise. And now, I think it's one of the primary things that is recognized as something that is clearly going to help with symptoms, potentially modify the timeline of progression of the disease, and stave off the onset of disability.

And so, you know, work that continues in that line, I think is quite interesting. We're actually part of a study called SPARX3, which is having people who've been relatively recently diagnosed, within the past three years, with PD, and who have not yet taken any medication, exercise. This is treadmill training, you know, at either a moderate or a high intensity. And the question is whether doing that can actually prolong how long someone can go without needing medication. Which would be indicative of changing the progression of the disease.

So again, not that long in the past, that would have been kind of unheard of. So, to see that tool that's really in the hands of the person with Parkinson's disease, in their control in terms of what activities they choose to engage in is, I think, really a powerful development. And recognition that we need to focus on helping people live well with Parkinson's now in addition to focusing on finding the cure so that people don't have to live with it in the future.

Marie: Absolutely. And I think these SPARX trials, this series of trials, has had a big impact on the field. So, can you comment on what it's been like being a part of the SPARX3 trial?

Gammon: It's been really interesting to me. This is definitely the biggest study that I've ever been a part of. There are about 25 different sites across the nation. Daniel Corcos at Northwestern is the PI for the whole thing. And then, you know, each of us at the different locations is a site PI. So, I think our jobs are a lot easier than Daniel's job. But just seeing the effort that goes into standardizing a protocol and making sure it's done consistently across that many different sites has been really interesting. And just the opportunity to share what's worked well at different sites in terms of, you know, finding people who are eligible for the study, which can be quite challenging because a lot of people, as soon as they're diagnosed, will start taking medication. Has also been really nice in terms of, you know,

collaboration, and sharing, and trying to advance the work across all the sites, rather than focusing on just getting a smaller study done within your own site or a couple of sites. So, that's been really interesting.

Marie: Absolutely. And I think the results coming out of this trial, as well as other exercise studies, as you alluded to, are really having a big impact in terms of kind of what the clinical recommendations are for people with Parkinson's disease, which I think is really important and fascinating. So, can you talk about what you've seen, at least on the research side, perhaps as well as through a clinical lens, of how people are responding to this? I think when you get that diagnosis of Parkinson's, the initial thought might be, you know, you're worried about being able to move, like can you still do exercise?

Gammon: Yeah, I think that's a key piece of being a clinical provider on the front lines, whether a physical therapist or neurologist, is to really make sure that people are aware of the power of exercise and the evidence to show that, yes, you can do this. And if you do, you're going to be better off than if you don't.

I think there's evidence in the literature that when a medical professional talks about something with a person who's newly diagnosed, it has a much more powerful impact than if they hear it, you know, through social media, or from a friend, or something. So, it really falls upon those of us who are medical professionals to make sure that we talk about it, and then give people, you know, the knowledge and the resources to make those connections. And I think equally as important as talking about the importance of exercise is being upfront with people that it doesn't necessarily matter what type of exercise you do. So, if you absolutely hate the idea of walking, there are other things you can do. The important thing is, you know, getting your heart rate up. So, you could ride a stationary bike, or, you know, you could potentially swim, even though there's not a lot of evidence in the literature yet about that. It doesn't mean it doesn't work. And so, it's really just the idea of finding what each individual enjoys and will stick with over the long term that, I think, is probably the most important message.

Marie: Absolutely. And I think a tremendous amount of research, as you mentioned, has been done on exercise. And a lot of it is sort of trying to figure out, is this better than that? Is this better than that? And I think the kind of overwhelming evidence is sort of the big picture that exercise is better than not exercise. I think this has really moved the field forward and moved how people think about it forward. Do you have examples of other, maybe tools, or resources, or collaborations that you're seeing are really having a big impact in advancing Parkinson's research or moving the field forward from your area?

Gammon: Well, I mean, I think the SPARX study is a great example of, you know, we have a certain level of understanding now, but we need to understand more. And we're at the point where we need large studies.

You know, a lot of smaller studies have been done in the area of exercise, but to really have some definitive, large clinical trials now is sort of, I think, where the field is. So, initiatives like that, that bring together multiple sites to ask key fundamental questions, I think, are very important. And I also think that just the visibility of this in the media through organizations like The Michael J. Fox Foundation and others, just giving prominence to this type of approach. And again, not just focusing on 'how can we cure this?' but focusing on the here and now. What do we know? What are the things that are within our control that we can act upon?

And then helping to connect people with, you know, the resources in their community, or online, or wherever it may be to be able to do that effectively. And part of that work, I think, needs to be credited to people with Parkinson's disease who volunteer with these organizations to be ambassadors and get the information out to people, and to help people make those connections and become a part of the community, I think has been another important advance that I've seen over the past decade or so.

Marie: Absolutely. I think having that stakeholder involvement of people who actually are living with Parkinson's disease has had a tremendous impact. And as we've alluded to throughout our conversation, there are still a lot of unanswered questions and things we don't know. So, Gammon, when you look at the sort of broader field of Parkinson's research, what are some of the kind of most important unanswered questions that you see, or the biggest areas of opportunity for us to tackle in the future?

Gammon: There's so many. I think from my own lens of wanting to understand rehabilitation approaches, I think some of the work that is really interesting to me is understanding, does something help? That's my first question. But then if it does, why does it help? So, getting into the mechanism and understanding what's going on biologically, physiologically, so that we can then sort of figure out what's the active ingredient and how does that active ingredient relate to other approaches? And is there some common thread across these things that points us in new or different directions, or in directions that might help us to combine different approaches in ways that have a synergistic effect?

So, in the singing and music study, we're actually, we're doing brain imaging as part of that to try to understand what's happening when someone moves to music versus singing, and does that change with training? So, things like that that help us understand how the exercise or other intervention that we're providing taps

into different areas of the brain. So, are we finding circuits that take detours around the basal ganglia that are most impacted by the Parkinson's disease? Or are we finding ways to utilize the spared function within the basal ganglia? And if we can find approaches that do both of those things, if we combine them, are they better than just one or the other? I think there's a lot of interesting questions there.

Marie: Absolutely. And I think knowing more about that mechanism of action can kind of help you find out who might respond best to a particular type of treatment, because I'm sure you've seen it in your studies where some people seem to respond really well, and some people seem not to respond at all. And that kind of cancels out some of the benefits that you might see when you look at the average.

Gammon: Yeah, I think that's a great point that we can say, on average, these things work, but there definitely is a lot of individual variability in terms of the symptoms that people experience as part of the disease, as well as their response to things.

So, that's something we try to do. And again, I think that's something that requires larger studies to really try to have a spectrum of responses and then look at that spectrum and figure out, okay, the people who had a strong benefit versus the people who had minimal benefit — are there things that are different between those groups? Or is there something that's predictive of who might benefit and who might not? So that at the end of the day, we can develop very personalized approaches to the treatment of the disease rather than having these things that “on average” work, but may not work for each person?

Marie: Definitely. I'm excited to see that the field is moving in that direction towards more ways that we can personalize these approaches for treating people with Parkinson's disease. And I know we've covered a lot of ground today, Gammon. And I'd love to end by just talking about how your work, specifically, is bringing us closer to the big picture goals of whether it's finding a cure for Parkinson's or just contributing to these improved therapies for people with Parkinson's.

Gammon: I think our work is definitely in the latter category in terms of just helping people who have Parkinson's today know what they can do to live well with it, to move more effectively, to stave off the onset of disability. And our work is hoping to uncover existing and new strategies that help people to do that and then getting the information out there. So, what's really important to us is not only answering the question in the study, but publishing it for the scientific community, for the clinical community to incorporate it into practice, but then also making sure that it reaches the Parkinson's community. And so, some of the ways we do that are to make sure we are active in presenting to support groups, presenting at conferences that include people with Parkinson's like the World Parkinson

Congress. And so, I think that that is just as important as, you know, getting the paper out there.

And it gets the information in the hands of people and, you know, we have seen that various organizations have created new exercise programs and moved in directions informed by the literature to offer more opportunities for people, because some studies have been done that have suggested that something like dance, for example, might be beneficial.

Marie: Absolutely. And I think it's important to highlight as well that a lot of these sort of novel innovative interventions that you're examining are relatively accessible, potentially very low cost, relative to some of the other options out there. So, could you comment on that aspect of your work?

Gammon: Yeah, I think that's part of the beauty of exercise approaches is that they can be done at relatively low cost. And if they're done in a way that's accessible, then that's all the better. You know, I think there's opportunities to work with community partners, organizations like the YMCA, or local churches, or fitness centers in the community to really broaden the impact of these types of things.

Marie: Well, I think that is absolutely wonderful. Gammon, we appreciate you talking more about your work and sharing your insights with all of us today. It's been a pleasure to chat with you.

Gammon: Likewise. Thanks again for having me.

Marie: 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](https://www.MichaelJFox.org/researchresources). And you can find new episodes of this show each month on the MJFF website or on your favorite podcast platform. And when you have a moment, please subscribe to our show to make sure you don't miss our outstanding lineup of upcoming guests. We look forward to connecting with you again in our next episode of the Parkinson's Research Podcast.