Michael J. Fox: This is Michael J. Fox. Thanks for listening to this podcast. Learn more about the Michael J. Fox Foundation's work and how you can help speed a cure at michaeljfox.org.

Narrator: In this episode, you'll hear a recap from our MJFF Parkinson's webinar. Expert panelists will discuss the latest in Parkinson's research and answer audience questions about living well with the disease. We hope you find the discussion helpful.

Lisa Volenec: Hello. Welcome everyone. My name is Lisa Volenec. I was diagnosed with early onset Parkinson's exactly 12 years ago today. I'm so grateful to be here with all of you. I am also part of the Michael J. Fox Patient Council. So welcome to the Michael J. Fox Foundation's Parkinson's webinar. Today, we're going to be talking about a really bothersome symptom for many people living with Parkinson's. It's changes in walking or gait. In a Fox Insight study published last year, people with Parkinson's shared their most bothersome symptoms and nearly 40%, almost half of them say walking is the top concern. We're going to talk about why Parkinson's can change the way a person walks, why gait can vary so much between people or even in the same person in just even different situations. I can attest to that. Most importantly, we're going to discuss treatments and practices that may help people move safely and more confidently.

We're also going to get into the latest research on walking and freezing. And before I introduce our very esteemed guests, first, it's a very, very big day because I want to share with you that the Michael J. Fox Foundation has announced the All Grit No Quit campaign to fuel the next phase of Parkinson's research and move the most promising discoveries closer to patients, closer to all of you. Now we've got a lot to discuss, so let me first introduce our panelists. I'm going to start with Katharina Clapper. She's an independent consultant to the Michael J. Fox Foundation with expertise in shaping Parkinson's gait research.

Up next, we have Dr. Alfonso Fasano. He is a movement disorders neurologist and professor of neurology at the University of Toronto at Humanitus University Milan, whose clinical and research work includes gait, balance, and freezing of gait in Parkinson's disease. He's also a member of the Fox Foundation's GALOP committee, which stands for Gait Advisors Leading Outcomes for Parkinson's. And finally, we have William Young, who is an associate professor of rehabilitation psychology at the University of Exeter. His research explores psychological and cognitive influences of walking, balance and freezing in Parkinson's. He's also a Fox advisor.

So welcome to all of you. So we're going to start with, I guess, why does Parkinson's affect walking? And Alfonso, we'll start with you. Walking is something that feels like it's supposed to be automatic, of course, after you're a toddler, something that you learned how to do. What actually has to happen in the brain and the body every time we take a step?

Dr. Alfonso Fasano: Yes. Gait is indeed an automatic behavior that we learn over time, and this is what the basal ganglia part of the brain is meant to do, to make us learn new habits and new motor tasks. And that's why we can easily walk on two legs,

which also requires balance adjustments. And at the same time, we can talk, we can carry a luggage or a tray or think about what to do next. So it's a quite complicated motor task that we can do also in very challenging situations. For example, when the surface we're walking on is uneven.

And so this is why when the basal ganglia, and this is what happens in Parkinson's, are affected, one of the signs of such condition is that gait becomes less automatic because what we need to do even to make a single step is, for example, offload one side of the body to lose balance for a little bit so that we can move our body forward. And this is highly complex and very well coordinated by the nervous system and the rest of the body, and that's why gait can be easily affected by any neurological diseases, including Parkinson's disease.

Lisa Volenec: Okay. Will, why does walking sometimes require more conscious attention for a person with Parkinson's? And what's the relationship between attention, confidence, and walking?

William Young: So when the brain perceives potential negative consequences or threats related to their action, it will try to override or use conscious control to override things that are otherwise automatic. So this is a typical observation outside of the context of Parkinson's. So for example, you might have an expert sports person, let's say a basketball player who in practice could just hit free throw after free throw without thinking about it at all. But then when the pressure is on in competition, there is a perceived consequence of what might happen if that shot gets missed, and then the brain might start to use more conscious control because it's trying to avoid potential errors. And it's just the way our brains are wired to do this. If you think of an evolutionary perspective, if there's a perceived threat, then it might be helpful to be vigilant to that and make sure that we avoid that danger.

So our brains are wired that way. And in the context of Parkinson's, it might be useful in many ways for the brain to adopt this more conscious control of movement. And that's because it may be helpful in compensating for potential changes in the automatic control of movement that Alfonso mentioned there. So if the muscle memory, as it's often called, is affected in some way, then consciously thinking about movement, even though it might require more effort, might be helpful in making sure those actions happen in the way we want.

Lisa Volenec: The people that have said to be aware of your surroundings to keep for safety reasons, just in general, head on a swivel. My head is on a swivel constantly mapping out the ways I'm going to get out of a room or walk to the next room or go anywhere. Katharina, what is the GALOP committee and what is it set out to do?

Katharina Klapper: Yeah, as Lisa, you already mentioned, GALOP stands for Gait Advisors Leading Outcomes for Parkinson's, and it's the Fox Foundation's advisory committee that brings together gait experts and a person with lived experience. The group's role is really to help guide research towards the questions that matter most. So why does freezing of gait happen? How can we measure walking better? And how can

we develop treatment and practical tools that help people move with greater confidence?

With the GALOP support, the Fox Foundation has now launched two dedicated funding programs focused on walking and mobility research. And these projects spun a holistic picture really to understanding how we can improve our understanding and how we can measure walking problems in daily life, how we can test some personalized rehabilitation approaches and normal treatment approaches and exploring new forms of treatment like neuromodulation, for example. And I had the pleasure of working very closely with this exceptional group of individuals and I'm excited by the impact GALOP has already had and will continue to have in shaping and elevating gait research.

Alfonso, one of our audience members asked what causes normal lengthy stride to be short and cautious stride and what changes might someone notice in the walking with Parkinson's? Are they related or do they have different causes?

Dr. Alfonso Fasano: Yes, so the short steps is one of the typical features of the initial and moderate phases of the disease. And the reason steps are shorter is because everything has to do with motion. And when we move, when Parkinson's disease affects motion, typically it affects also not just the regularity, but also the amplitude. So this is why people tend to have shorter steps, especially on the most affected side, which also leads to an asymmetric gait. And the net result of these short steps is that the person spends more time having both feet on the ground at the same time. So this is also coming from some balance requirement. Later on when balance starts to be affected, this affects especially the anteroposterior axis. So it's more difficult for the person with Parkinson's disease to keep the balance forward or backwards. And that's why the neurologist assesses the balance pulling the patients back.

So the next result of this imbalance along this axis is that the body wants to keep both feet on the floor for longer. The next result of this is that the gait is less fluid and also walking becomes slower. Associated to this, there are other problems that we'll discuss later like freezing or festination. So it starts with the relation of the steps and also the automaticity of the steps. They become more variable and then the asymmetry progresses. But later on then both feet tends to be a little affected and ironically even more symmetrically because there's a requirement to keep the balance in this anterior posterior axis.

A side note of this is that people with Parkinson's disease have a very good balance in the medial lateral axis, so right to left. And that's why they don't have a wide base. They can walk with a foot in front of the other like a tandem gait very easy and they can also ride a bicycle because that side of the balance requirement is not affected, at least it's not affected for many years.

Lisa Volenec: Alfonso, what are some of the earliest gait changes that people or their care partners might notice?

Dr. Alfonso Fasano: I will say that one of the earliest changes of walking in Parkinson's is actually not even affecting the legs. It is affecting the arms. We all have an arm swing, which

is normal when we walk, we all move our arms. And one of the earliest signs of the disease is that on one side, the arm swing becomes less pronounced. And in some cases it's so reduced that people feel that something is wrong because they start to have shoulder issues. And in fact, often orthopedic surgeons are the ones advising people with these problems to go see a neurologist because this lack of arm swing in the long run causes some arthritis, but it's not coming from an orthopedic problems in the first place. It's coming indeed from a neurological problems.

So one of the earliest will be arm swing and then little by little other signs, particularly the short step or one side I was mentioning earlier becomes more clear, but the brain and the body is an amazing organ able to compensate. And one way we have to compensate for when the walking is slow is to make more steps. So with a shorter step, we can still keep the same gait speed, the same velocity of moving, making more steps. So that's why one of the earlier signs of Parkinson's, there's also this tendency to make more steps to keep up with the speed, for example, of the person they're walking with and so that other people don't notice much difference.

Lisa Volenec: Katharina, there's every Parkinson's patient that's on this webinar. We've all done the walk up and down the hallway and have to do it every time we go see our neurologist. How is gait measured in research and clinical practice and what work has gone on to standardize the understanding of gait?

Katharina Klapper: Yeah, indeed. Gait can be measured in several ways. It's through the walking test that you mentioned, Lisa. It can be observation by the clinical team. We do recordings and wearable sensors. And what research are looking at is really the speed of the gait, the step length, arm swing as Alfonso mentioned, balance, turning, and potential freezing episodes. One of the major efforts led by the GALOP committee includes some recommendations for a minimum set of measures that should be included in every study. And this gives researchers a common language. When studies collect comparable information, it becomes much easier to combine findings, confirm results, and learn more quickly what may help people with gait impairment.

Lisa Volenec: Will, this might seem obvious, but why is one side can be more affected than others?

William Young: Yes. The most direct explanation for this is about the location where cells in the brain might start to show changes. So each side of the brain controls the opposite side of the body. So if there are any changes on the right-hand side of the brain, then it's more likely, not necessarily, but more likely that symptoms will start to emerge on the left-hand side of the body.

Lisa Volenec: So Alfonso, one of our audience members is asking about festination or involuntary speeding. Why does that happen?

Dr. Alfonso Fasano: Yeah, this is a not common problem, but it can be present even very early on in the disease, and it's characterized by the tendency of walking faster and faster and faster. And sometimes people need to land on a furniture or sometimes

unfortunately they even fall because they cannot stop walking at this fast pace. The reason this happens is still unclear. There's some connection with the problems of freezing of gait most likely, and also with some postural disturbances because some of the people displaying these problems tend to have a flexion of their trunk. They tend to lean forward, something that doctors called camptocormia. So there's probably also mechanical reason why they start to go so fast because they're basically catching and trying to catch the center of the body because when the projection, the center of the body is in between their feet, the body is in balance.

And that's important to discuss because often people don't realize that even moving too fast can be a problem and it can be a sign of a disease that is typically known to be causing slowness of movement.

Lisa Volenec: What about time of day? Some people, an audience member said something about why can the time of day be better or worse and the medication on and off periods?

Dr. Alfonso Fasano: Yeah, this is a great question and it's a very common one for a clinical neurologists. And I would say the main reason why gait walking is affected in some moment of the day and not in others is the fluctuations of the levels of levodopa in the system. We all know that levodopa goes up and down our bloodstream. And so when levodopa is in the system and it's reaching the brain and is working well, some of these issues I mentioned earlier, particularly the short steps are treated and that's when the person walks well. And then when levodopa is wearing off or is completely gone from the system, the problems caused by Parkinson's are more evident. So that's the most common explanation.

But I would like to mention two other scenario. The first one is the normal variation. In the morning, some people report sleep benefits because they had a restoring sleep. Sleep is very important. They move and they feel overall better. Towards the end of the day, they might be more fatigued, especially if they don't do exercises. And the last point I would like to make, which is important for people to know, is that in rare cases, levodopa, so the medication that you're supposed to be helping, makes walking worse, particularly freezing. So that can also explain some of the variation that people have.

Lisa Volenec: It's crazy how everything, so many different factors affect everyone so differently. So walking takes more than motor control. Will, many people think walking is strictly a motor activity. Why does walking become more difficult when the brain has more to manage?

William Young: The best way of answering that is, or my best attempt is if we think of the brain as a machine that forms predictions about the world around us and what our movements are going to look and feel like within it, and then the brain will update these predictions based on experiences. So these predictions, they're important because they form motor plans that get sent to the muscle. So it's important that we have a clear idea of what the environment is going to look like and what our movements will look like. And in certain situations, the brain might have less certainty about how future movements might look and feel because of

say a challenging movement that's going to be attempted or complexity in the environment.

So for example, if someone's approaching a doorway, the person, it will be helpful to form a prediction about what is on the other side of the doorway, even if someone can't see that area of the intended route. And similarly, in cluttered environments where people need to process a lot of information, the brain has to work hard to form the predictions and process all of this information and transform these into movements. So it's really about the complexity of the environment that has to be processed and the brain has to do some fairly heavy lifting in order to form the motor plan after processing all that information.

Lisa Volenec: There's been a lot of research into dual tasking or walking while focused on something else. Where does that research stand and why is it important, Will?

William Young: Yeah, dual testing has been used for decades in research studies ever since a widely cited observation that people outside the context of Parkinson's, that older adults are more likely to fall if they stop walking when talking. So if you're walking with someone and ask them a question, if they stop walking in order to answer, then statistically it was shown that they're more likely to fall in the coming year. So dual tasking is used a lot and it's often used as a way to measure how much movement changes when someone's attention is distracted away from the movement. So the more a movement changes typically gets slower, a so-called dual task cost, then we typically interpret that as a reflection of the person needing to focus on movement to a greater extent. This gets used a lot and it's now used in a standardized way to get clinical outcomes.

Lisa Volenec: Of course, it's making me think about that... I joked all the time that I can't walk and chew gum at the same time. And for Parkinson's patients, it can be a little bit harder. Alfonso, there's practical strategies you recommend when someone is entering a more demanding environment. Can you share that?

Dr. Alfonso Fasano: Yes. And it goes back to what Will was saying, the dual tasking. So a challenging environment, thinking where to put your own feet or whether you're bumping into a door or someone that is next to you creates a dual task. And so the suggestion is very practical is to focus on the only task that is important, which is walking. And so absolutely not carrying anything, not talking, just focusing on the steps. And as Will was alluding, to also be prepared because we know that there are certain triggers like narrow passage, doorways, piece of furniture. So there are certain things that we know can trigger problems with walking, particularly freezing more often, and that's why it's so important to avoid distractors.

One issue that we see over time, and this is because Parkinson's disease is not just a motor condition, but it can also be a condition affecting attention or cognition in general, is that people start to allocate the resources of their brain to the wrong priority. Even though they're being told by the caregivers, by the neurologist to focus on doing one thing only and that thing is walking, they allocate priorities in the wrong way and they decide to turn their head all of a sudden or to talk to someone. And that's usually when you see a fall.

Lisa Volenec: Yeah. And that fear of falling, Will, I mean, how does that affect the difficulty of someone trying to navigate caution and not letting fear dictate their movement too, potentially?

William Young: So we know that fear and anxiety can have a really profound effect on the way people think and move. Again, outside of the context of Parkinson's, we see that in surgeons, in the military context, in sports, like I was talking about with the basketball player. So the answer is really, we know that there can be a really significant effect of fear and anxiety. From the field of psychology, we often think of anxiety as something of a self-fulfilling prophecy where we know that people who report higher anxiety, when they're presented, I'm talking about laboratory studies primarily here, when they're presented with a range of stimuli that represent positive and perhaps negative stimuli. So for example, in our study, we have a virtual reality task where people are given the picture frames on the walls with faces that are either representing a positive or negative facial expression.

People who self-report higher anxiety, they tend to look more often and for longer at the negative facial expression. So these things, it can, not always, but it speaks to the potential for a self-fulfilling cycle here where anxiety might drive an attentional bias perhaps for negative things. And there's a famous saying in psychology when it comes to the attentional resources that we have at our disposal and the influence of anxiety, and that is that anxiety is the first dog at the bowl. It takes what it wants and what's left is left. And that really speaks to the vigilance. If people are feeling threatened for whatever reason, our brains are wired to really prioritize whatever it is that we feel threatened by.

Lisa Volenec: I need to write that saying down.

William Young: Yes, it really speaks to the potential demands that anxiety places, so absorbing resources that are available in terms of our processing speed, if you like. But then the other thing is that the brain is very good at forming habits and these anxiety-related attentional biases can form something of a habit. So again, this is not something specific to Parkinson's. It's a widely known phenomenon and the central purpose of approaches like cognitive behavioral therapy, they attempt to break down these more negative associations and build more positive ones. So it's a profound effect that anxiety can have, that there are lots of known approaches and established processes to try and create more positive links.

Lisa Volenec: We have a video question that was submitted by one of our patient council members, Larry Gifford. I'd like to play that now if we could.

Larry Gifford: Hello, I'm Larry Gifford. I was diagnosed with Parkinson's in 2017. I am the co-founder and president of PD Avengers, and I'm on the Michael J. Fox Foundation Patient Council. And since the beginning, gait and walking have been a big issue for me. It's a big part of my journey. And over the years, I've tried all sorts of things. First off, medication helped. Now, additionally, I utilized a physical therapist who taught me how to walk again, occupational therapist who taught me how to walk while holding my wife's hand while holding the conversation with her. I've used walking sticks, canes, poles, all sorts of assisted devices.

There's a lot going on in the world of gait. And this just got me thinking about freezing because freezing's a major part of the gait issues. I know when I freeze, it feels like my feet are sucked to the floor, like there's gum or glue or something underneath my feet, and there's a huge disconnect between my body and my brain.

My brain's going, "Go," and my body's going, "No. What? That's scary." And it used to happen to me all the time in the airport. I'd be standing in line at the airport to go through security, and as soon as I got up to security, I couldn't move forward. I couldn't go through the metal detector. And I just am really curious about what the heck is going on when that happens because it just feels like there's this disjointed, when my brain's speaking a foreign language to my body or. It's weird. That's my question for the experts. When my brain and my body decide to ignore each other and stop talking to each other like children, what's going on? What's the disconnect? What's happening?

Lisa Volenec: Everybody, so many on this call can relate to this. So Alfonso, let's define first what is gait and what's happening in the body when someone feels glued to the floor?

Dr. Alfonso Fasano: Yes, actually a very nice description that Larry gave us. And as you just said, it's something that affects a lot of people with Parkinson's. The very same reason I got into research of gait because I was trying to solve the freezing of gait puzzle. So freezing of gait is the inability to perform steps in spite of the will to do so. So this is just a more recent definition that we came up with. We've been also discussing with other researchers in the field on how to properly define freezing. Sometimes it is difficult also to define when a freezing episode really starts and when it really ends, but practically speaking is exactly what Larry was saying, that the brain wants to go and the body simply doesn't understand it. It's like speaking a different language indeed. And it's a mysterious phenomenon, but we are learning a lot about it and we have certainly more answers than we happened to have in the past.

Lisa Volenec: You said you have a lot more answers now, but what remains unknown with freezing?

Dr. Alfonso Fasano: What remains unknowns is why it happens in some people and not in others. We know the circuitry that is involved in causing freezing of gait. We know that it's not just classic parts of the brain affected by the disease. We know that there's a role for cognitive and emotional processes in it. So we are now understanding the widespread circuit that causes freezing. And we also understand that it's a multifactorial problem, but we don't know why some people have it, some people don't, and we don't know how to predict early in advance when it's going to happen and with what severity. And obviously a big question is how to treat the freezing that is not responsive to the classic treatments. And with classic treatments, I indicate levodopa, but also procedures like deep brain stimulation. We know that in most parts they help, but sometimes they cannot help and we don't know what to do in these cases.

And the other thing that we need to do better is understanding why in some people freezing worsens after deep brain stimulation surgery. And it's probably because it's a frail brain predisposed to freezing, and this is when adding neurosurgery on top can trigger the onset of a problem not seen before surgery.

Lisa Volenec: Will, I'm going to ask you this question. Does anxiety cause freezing or is the relationship more complicated?

Dr. Alfonso Fasano: The anxiety coming from freezing, it can be seen as a cause, but also as an effect because it is really scary, as Larry was saying, to understand it. From time to time, absolutely without being able to predict your feet will fall. And this is actually when people tend to fall more. So this is causing anxiety, and then it becomes a vicious circle because more anxiety causes more freezing. So it's sort of a chicken and egg problem, and it's probably related to this amazing function of the brain to do multiple things at the same time. Anxiety is there to help us because with anxiety we avoid to do dangerous things. With anxiety, we get motivated to do more, but sometimes it backfires and anxiety freezes us.

And that's why there's plenty of research on the role of the physiotherapist and the rehabilitator in general in favoring the good anxiety, so the anxiety that is there to protect you from doing something stupid, and the anxiety is there just to hold you back. And that's when also pharmacology can be used.

Lisa Volenec: Katherina, what's being studied right now for the freezing of gait?

Katharina Klapper: Yeah, freezing of gait has a major impact on quality of life, perhaps we already heard, and historically it has received too little research attention. This is now changing. To do our part at the foundation, we are funding a dedicated research portfolio with studies that are looking at better ways to detect freezing in real life, understand the brain body systems involved, and predict when freezing may occur, and then test different treatment approaches that could address this. The goal is really to turn better understanding into better treatment options. And one Fox Foundation funded projects I want to mention here is a multicenter study that combines walking tests, wearable sensors, video and patient input to better measure freezing of gait and its real life impact. And the beauty is this is an international consortium, a team of gait experts working together, and we hope that this will provide some answers to questions that the field still has.

Lisa Volenec: Absolutely. Let's talk about tools for getting through a freeze. Will, I'm going to start with you. What can people do if they're actually stuck in a freeze? And we can talk about cueing and how that can help.

William Young: I think the first thing to mention if someone starts to experience a freeze based on qualitative work and the general consensus of what people who experience freezing would say is that one of the main things to attempt to do, easier said than done, but to try and stop and to try and clear one's mind as much as possible. But when we think of what is required to actually break the freeze, if you like, and start walking again, the brain, in order to do that, it needs to form a clear plan. So like I mentioned before, there needs to be a prediction for that action. And this might be challenging given previous experiences. So if people have experienced

freezing many times before where the body has not moved in the way that was intended, actually getting that clarity for the motor plan can be easier said than done.

So this might mean that the prediction for that movement becomes less certain. So finding ways of establishing that clarity and a clear image for the intended action is really the key ingredient. And it may also be the reason why people often find it effective to focus on novel ways of doing things. So we hear examples like waltzing down the supermarket aisle instead of trying to move in a way that might be more typical or trying to make a big step or using a sensory cue. So a way of moving that might not be the typical way, but the novelty of that might allow people to gain that clear prediction of what that movement might look like. And that may be the key ingredient for driving any benefits in that regard. So whatever the strategy is, it's whatever works for an individual to get that clear image of the movement.

Lisa Volenec: So it's kind of like plan ahead and thinking a little bit about how you can cue yourself, but what if you don't have a plan? I don't have a plan necessarily when it happens to me. So what's the safest thing, Will, someone can do when they are frozen?

William Young: So the safest way would be to avoid trying to force the step. So we see if people try to, if they're thinking, "Pick your foot up," and they try to actually lift their foot off the floor, what we often see is that the preparatory movements that people often make to shift weight onto the leg that's not stepping, we tend to see that that might not happen in the same way. So by forcing a step, that can actually serve to put people off balance. So in finding a strategy to break the freeze, stopping, taking a breath, you hear people talk about the four S's of stop, sigh. So, take a breath. And then the four S's would be shift and step. So some people find it helpful to think of shifting the weight and then moving into the step, but really finding a strategy and playing around with different strategies and see what works well for people to generate that combined weight shift and step seems to be very effective.

So whether that's using a visual cue, auditory, marching beats, whatever it is, we often talk to people about using analogies for movement. So if we stop, take a breath, sigh, and then imagine you're standing on an old-fashioned set of scales. I'll try and use my hands for this. You push down on one side, the other side comes up and then you take a step. So in using analogies like that, that can be an efficient way for the brain to gain a clear image of what that step might look like and therefore get the clarity in that prediction. And it doesn't work for everyone, but some people find it will benefit from that.

Lisa Volenec: Alfonso, what could a care partner do to help in these situations?

Dr. Alfonso Fasano: Well, the care partner as usual can do a lot and it makes a big difference also in the journey of people living with the disease later on also when gait is affected. The care partner can provide emotional support. It can importantly remind the person having a freezing episode on what Will just said to stop, try not to force the stepping and just breathe and start. But I think more overall, the care partner

is there to motivate someone having these problems to exercise more, to take the medications on time, to avoid certain behavior who are known to cause falling.

But this also needs to be done in a caring way indeed because sometimes it becomes more of a source of contrast between the two people and that's not good either. And also the role the care partner is to report back to the neurologist because some of the behaviors that are actually detrimental to walking are not recognized by the individual suffering from them, like choosing the wrong strategy, dual tasking and all of that. So the care partner will tell the neurologist, "I've noticed that he's doing this and that," or, "She's doing this and that," and so that the neurologist or any person on the healthcare team can adopt the right strategy to try to fix the problem.

Lisa Volenec: Let's go on to what can help with walking. Alfonso, what treatments or medication help with what kinds of symptoms for walking? Kind of touch on that.

Dr. Alfonso Fasano: Yeah, we already discussed the role of levodopa and how levodopa helps, but sometimes it might make things worse or sometimes it doesn't matter how much levodopa a person uses, there is no benefit, just side effects. Another medication that is used in the context of freezing of gait can be amantadine, but the evidence is lower as well as methylphenidate. So stimulants can sometimes help. Once again, the evidence is not that strong. For sure, antidepressants can play a role, especially in people where anxiety is driving most of the episodes of freezing.

For sure, a great emphasis needs to be given to physical therapy, gait training, exercising, particularly treadmill walking. I always tell my patients that buying a treadmill is a big investment. And I also say that just having the treadmill at home is not enough. You need to also use it and it doesn't have to be difficult. It can be just an hour or even less a day, just normal pace walking that's being shown to help walking in Parkinson's.

Lisa Volenec: Is that the best exercise for someone who has walking issues is just getting on the treadmill? Is it that simple?

Dr. Alfonso Fasano: I would say so because some people actually think that maybe a stationary bike or I don't know, doing exercises on a chair can help walking. But in reality, we need to train exactly like a professional athlete. You need to train for the thing that you want to do better. And so you need to be on your feet and you need to, maybe with help of a therapist or someone else that makes sure that you don't fall, but you need to really challenge the part of the body or the brain that is not working properly. And treadmill is certainly a safe way to do so because the chance of hurting yourself walking normally on a treadmill with handrails on the side, and you can maybe listen to a podcast, you can watch the Michael J. Fox Foundation webinars, you can do something while you are. Because the treadmill is there to pace your walking and that makes things easier.

And at the same time, we don't get in this vicious circle that is deconditioning because as we say, if you don't use it, you lose it. So some people just decide to stay on a chair all day long and watch TV and a gait is not going to get any better

if you do that and it becomes actually more difficult than to be back on your feet one day.

Lisa Volenec: When should someone consider using an assistive device and how do you determine what's the best for me or for anyone that would be considering this?

Dr. Alfonso Fasano: I think it's important to emphasize the safety part of it and when the person with the disease has a tendency to fall and falls can be traumatic, it's probably better to use it. I think walkers are the best. Canes are not good. It's been shown that a stick or a cane are not good. Poles, the ones used for Nordic pole can be used, but the easiest is really the walker.

Lisa Volenec: Okay. So moving on to what's next for gait research. Alfonso, what are scientists learning about what happens in the brain during walking and freezing and how will a better understanding of these networks help patients?

Dr. Alfonso Fasano: Yeah, there's a lot of research going on as we discussed earlier, also thanks to GALOP and the foundation. A lot we learned about freezing comes from people with deep brain stimulation who had electrodes in the brain and now we can use these electrodes to record the brain activity during freezing. Freezing is an episodic problem, so it's also difficult to analyze these episodes if not without a chronic recording, which we can now do. We can record different parts of the brain and it's clear that during a freezing episode, the signal that is typical of Parkinson's disease, this oscillation in the brain that's freezing the body from move as a surge. So this is called beta. It's a particular frequency in the brain that is typical of Parkinson's and other other logical conditions. And exactly during the moment of, we call it the swing phase, when you are trying to step, there's a surge of this blocking oscillation in the brain called beta, which is not only telling us what's going on, but also how to possibly intervene with future therapies.

Lisa Volenec: Will, what's going on right now with finding the right cueuing techniques?

William Young: So there's a lot of work going on now about tailoring the cues. This could be based on an individual's preference, whether they prefer to use a device, a learnt strategy or when it comes to devices, whether they prefer auditory visual kind of vibrating cues, that type of thing. There's also a lot of work now going on into something called habituation where we see that people might start to use a cue and possibly get a benefit early on, but the longer they use that cue for, sometimes the benefit that's achieved from that cueing device or strategy can get less over time. And there's work going on to look at the reason why that is. It may well be something to do with what we've already discussed already about the automatic control and conscious compensation where when a cue is novel, people might use more conscious strategies to compensate for any changes in automatic control.

And the longer people use a cue, the more familiar they get with it, and therefore it might rely more on the automatic control mechanisms that might show changes. So there's a lot of work going on in that area as well as technologies used to predict upcoming freezing or problems with walking and maybe deliver cues at a time when they are most needed and often at a time where the delivery

is more automated so people might not have to fiddle with gadgets in order to use that strategy.

Lisa Volenec: Yeah. And Katharina, Will just talked about the wearable devices. How do researchers use that wearable technology to help them understand somebody's gait outside of the clinic, outside of the lab in just everyday life?

Katharina Klapper: Yeah, indeed. Walking and cleaning is only one small snapshot of daily life and wearable sensors that are devices worn on the wrist, on the shoe or lower back can really help researchers understand how someone walks at home or in their community over days and weeks and really help inform some intervention strategies for that individual. These devices can capture changes in walking pattern, turning, the different activity level of the individual and possible freezing episodes. So it's really different people have different gait issues for different reason and with wearable devices, it's really an opportunity to measure the gait in people's environment and at their home.

Lisa Volenec: What projects are you most interested in coming out of GALOP, Katharina?

Katharina Klapper: I'm most excited about GALOP's ability really to elevate gait research and connect promising work across the field. It really includes helping clinicians better recognize walking problems. So if a patient comes in the clinic that this question is being asked, improve how gait is measured and develop more personalized treatment approaches. GALOP is an international coordinated effort, so it really creates opportunities for researchers to share knowledge and to help the field move forward more quickly.

With the current portfolio that MJF is funding, we are bringing together a range of different treatment approaches and really helping to understand what options work best for the different individuals. And looking ahead, GALOP is now reviewing the projects that we have been funding over the years and really bring together what the field has learned. The hope is that these connections will lead to more focused investments in the future and building on what we already know is working and move us towards more practical near-term improvements in day-to-day life, day-to-day management of gait problems for individuals.

Lisa Volenec: That's what we're all looking forward to. Okay, we're going to dive into some of the questions and one of the first ones that has popped in is what about poor balance? What can help with that?

William Young: I mean, as a general rule, I mean this is similar to what Alfonso was saying before when referring to treadmill training, but as a general rule, if we're going to train the system, we have to challenge the system. So the very reason for promoting things like treadmills over chair-based exercises is because you are challenging your balance systems and therefore more likely to get a benefit from it. And of course there's a note of caution there about the need to make sure that you're going to be safe doing the exercises and things, but there are so many different excellent exercise programs out there relating to whether it's based on boxing, Pilates, walking, a wide range of different exercise programs that really

challenge balance where we could expect to find benefits, challenging the system in a way that it is safe is likely to be most beneficial.

Lisa Volenec: Alfonso, this came up earlier and it's come up again. What about progression? Does this mean that as I progress, my walking is going to get worse and the freezing and such like that?

Dr. Alfonso Fasano: In general, yes, but not necessarily because especially people who have done a lot of exercises even earlier in life, there's a concept called motor reserve. They tend to have better outcome even in the long run. So being active as much as possible even before things become problematic is solely preventative and being proactive is always better. But we've seen today we discussed how starting with short steps, festination, these are things that tend to respond to levodopa and then freezing of gait, freezing of gait response to levodopa. But over and over, over time, episodes of freezing of gait, especially during turning, can become more common and tend to be more resistant to low dose of medications or low dose of stimulation.

And then more and more over time, it doesn't matter what we do, unfortunately we cannot break freezing and some point with what we call akinesia, so the inability to really even try to move the first step. So this is not necessarily going to be happening to everybody, but then there is a tendency of the disease to progress in that sense. One more reason to be proactive and to be engaged in research.

Lisa Volenec: Another thing that we didn't get to dive into enough, what about the patients who've had DBS? I know I have, I know Larry has who was on the video. That's really when my relationship became very complicated with gait and walking, where it wasn't as much before. What about the patients with DBS?

Dr. Alfonso Fasano: Yes, actually I alluded to this earlier when I said that sometimes DBS worsens freezing and we don't really understand all the time why this happens. We have better understanding now and we know, for example, that sometimes it has to do with the parameters of stimulation or sometimes the brain needs stimulation, but it doesn't need stimulation all the time. I have a lot of hope that adaptive stimulation, so a stimulation is closed loop and only given when needed, can be beneficial to freezing of gait, especially when freezing of gait is worsened by too much stimulation. So we are more gentle to the brain and this might potentially lessen the impact of deep brain stimulation on freezing while at the same time DBS can be used to improve all the other problems that the disease causes.

Lisa Volenec: Yeah. Will, we have been asked for the four S's again. Can you go through the four S's so this is an exercise that we can practice and work on?

William Young: Yes, of course it is. Stop, sigh, take a breath, shift and step.

Lisa Volenec: Okay. Stop, sigh, shift, step.

William Young: Stop walking, try to find your balance. Sigh, so take a breath and then shift and step. So shift your weight onto the non-stepping leg and combine that with the step. And those two last S's, the shift and the step, that's where people can employ various different strategies, whether it's thinking of a big step using a visual cue, imagine stepping over a book. People can get really creative with that.

Lisa Volenec: That's awesome. Then what was the quote that you, the other one that anxiety and feeding the anxiety, I loved it.

William Young: The role of anxiety in taking up a lot of attentional resources?That is anxiety is the first dog at the bowl. It takes what it wants and what's left is left.

Lisa Volenec: Oh, that's the truth. Okay. Alfonso, are there any external devices that help with walking and fog? What to use if not a cane?

Dr. Alfonso Fasano: Yeah, there are external devices that are already used, particularly walkers with the ability to shine a laser beam on the floor so that while the person moves as a cueing, a visual cueing on the floor, projecting on the floor each time, and so the person can step over that line that is created by the laser. There are the so-called laser shoes where there's a laser that shines this beam of light on the contralateral side. So on each leg, on each foot, there is a little device that shines this laser beam. This is less clearly effective, but there have been some studies showing that it's effective. And then more and more research is now going into devices that can be triggered, for example, with a slight vibration of the muscle or even muscle activation only during a freezing episode. Because one of the issues we have with cueing is that the brain gets used to it.

The strongest cue is the one that is not always used and is always used when needed. And so there are now closed loop system able to detect when a freezing gait is about to happen and they give a cue to the body, either a vibration, metronome sounding, or even stimulating the muscle to make the step.

Lisa Volenec: Okay. We've got a question for Will. How do you recommend people reduce anxiety about falls? Will, how do you just recommend that we reduce anxiety with Parkinson's in general? Let's just do that. Let's tackle it all at once. But no, I think I find myself going when I go through the metal detector and I have to explain that I have DBS and it's a whole thing and it's seemingly unnecessary, and you're probably going to say, "It's the four S's, Lisa," but go ahead.

William Young: There are several studies now where people have tried to give information or training in an attempt to, well, with the aim of helping people manage anxiety. The ones I'm thinking of are in the context of balance and walking, but those studies have not really shown any significant reductions in anxiety. There's one study that compared an anxiety management training video with a more active strategy for using the fluoresces actually. And there's a questionnaire, they use questionnaires, but also interviews to ask people what they were thinking about when using the strategies in daily life. And they found that with the anxiety management, it was difficult for people to really employ general techniques about managing anxiety, so breathing exercises, that type of thing. But when it comes to using an active strategy, something like the fluoresces or a device that

might be used to get clarity about what that movement's going to look and feel like, it seemed as though that had double benefit.

So one is it promoted a greater focus of attention on the action that people wanted to make, but then in doing so, it also served to reduce or served as a distractor away from potential worrisome thoughts. So by focusing on the intended action, that might actually help to avoid worries and anxiety. But these studies haven't really shown large benefits in terms of reducing anxiety. So with new ideas about how to expand this range of training, some ideas are emerging about giving information about how people can actually interpret the bodily signals. And we spoke early or several times in this webinar, we've spoken about how things that the brain does in response to perceived threats or uncertainty, these are not Parkinson's specific things. These are just the natural way that the brain reacts to perceived threat or uncertainty.

So in a given situation where someone might be feeling threatened, understanding that feelings of jitteriness, tension, and the mind racing and going through potential consequences, that's not necessarily a Parkinson's specific thing. That's just the way that the human brain is wired. So understanding that it is a natural response and the brain preparing itself to do something to manage that threat might be a helpful way of contextualizing that and avoiding an interpretation that those feelings themselves are actually threatening and a signal that something negative is about to happen. So there's something to be said for reinterpreting those perceptions.

Lisa Volenec: Lots of great information from three fabulous presenters. I'm going to go clean off my treadmill, get the clothes off my treadmill and practice the four S's. I want to thank everyone for joining us and being part of the community today, and thanks to our panelists. Panelists, that's the word I was looking for, for sharing your time and expertise. We hope that you found today's discussion helpful. Thank you and have a great day.

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