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.

MJFF: Welcome to a recap of our latest Third Thursday Webinar, here directly from expert panelists as they discuss Parkinson's research and answer your questions about living with the disease. Join us live next time by registering for an upcoming webinar, at michaeljfox.org.

Larry Gifford: Hello, and thank you for joining on us for this Third Thursday Webinar. My name is Larry Gifford. I was diagnosed with Parkinson's four years ago at the age of 45. I'm a proud member of The Michael J. Fox Foundation Patient Council. I am the President and Executive Director of PDavengers.com, I encourage you to join, and I host the podcast, "When Life Gives You Parkinson's". Today, our panelists will discuss issues that many people actually go through that have Parkinson's. One of them is called “off” time and the other is dyskinesia. We will explain why these problems happened and ways to manage them.

Larry Gifford: Now, the webinar is brought to you with support from Acorda Therapeutics, Amneal Pharmaceuticals, Kyowa Kirin, Neurocrine Biosciences, Sunovion Pharmaceuticals, and while their support helps make educational programs possible, their donations do not influence the Foundation content, perspective or panelists selection.

Larry Gifford: If you have a question. I'm sure you have questions. You can type it into the Q and A box near the middle of your screen and the Foundation staff and our panelists will try to get to as many of those questions as we can in this hour we have together.

Larry Gifford: We have a lot to get into today, so let's get started by introducing our panelists: Dr. Ashley E. Rawls is a movement disorder specialist, an Assistant Professor of Neurology at the University of Florida. Thank you for joining us today.

Dr. Ashley E. Rawls: Thank you for having me. It's a pleasure to meet everyone and I'm glad to be a part of this panel.

Larry Gifford: And Rick Schwartz is a former professional baseball player and sports reporter. He was diagnosed with Parkinson's in the year 2000. Hello, Rick.

Rick Schwartz: Good morning. I was very impressed the way you pronounced all those drugs. Very good.

Larry Gifford: Well you practice a lot with that. And we have Bryan Roberts, Associate Dean of Communications at Ithaca College. He was diagnosed with PD in 2010 and is also a member of The Michael J. Fox Foundation Patient Council. Hello, Bry.

Bryan Roberts: Good morning. Good afternoon. I'm happy to be here. I'm not as easily impressed as Rick is, just so you know.

Larry Gifford: I understand, you're more critical for sure but that is the job.

Bryan Roberts: Do better, please. Thank you.

Larry Gifford: It can only get better from here. Let's start off with just sort of finding some definitions to what we're talking about, Dr. Rawls, what is “off” time?

Dr. Ashley E. Rawls: So you may have heard your physician, or other people in the community, talking about "on-time" versus “off” time. So I'll start by defining those two. “On” time is when you feel that your medications for Parkinson's disease are working well and are controlling your symptoms. “Off” time, conversely is going to be periods of time where your medication feels like it's not working and not controlling your symptoms and these usually occur between doses.

Dr. Ashley E. Rawls: Many times, "off” times, that we notice, are going to be motor symptoms, such as increasing in tremor, increasing in tightness of the body, and also slowness of the body. But sometimes there can be non-motor “off” times that we can notice such as increasing anxiety before a dose. And sometimes people feel very, very fatigued as well. It's just like anybody's Parkinson's disease is different, “off” times themselves can be different between each individual. So those are things that you want to be able to point out with your physician, and we can talk about that a little bit later. “Off” time can become more common as progression of the disease progresses.

Larry Gifford: So you may not experience that right away, but over the course time, it will kick in.

Dr. Ashley E. Rawls: Yeah. Yes.

Larry Gifford: Very good. Just for the record, I just took a pill right before this, or two pills. So I'm kind of coming off "off" and back on to "on", so if you see me wiggling around, that's what that's about. Bryan Roberts, do you experience “off” time?

Bryan Roberts: Yeah. So for me, I've been diagnosed for about little over 10 years now, actually coming up to my 11th year. So the dyskinesia and the “off” times I've noticed more in the past few years. For me though, and like many Parkinson's patients, it's tied to stress and diet, and things we know we should take care of. And just to lay it off everyone, I am the worst Parkinson's patient in the world. I don't take my medicine on time. I have a very stressful job. I don't sleep. First of all, I'm a Mets fan, so you can imagine my discomfort in life, in general. So I hope to learn a lot them things I should do as well as things I don't do currently.

Larry Gifford: Well, thank you for being here to represent the other side.

Bryan Roberts: I know.

Larry Gifford: All right. And Rick, what do you do? How, how does your “Off” timerepresent itself when you're off your meds?

Rick Schwartz: Well, right now I'm pretty much "on". I'm not shaking or anything and I haven't taken any pills. Usually around one o'clock Eastern time, that's when I start turning to a "pumpkin" where I can't move, I can't walk. And so I'm waiting for that, I have my pills here, ready to go, but I didn't want to take them too early. But I've had Parkinson about 21 years now and the last few have been an "on-off" thing quite a bit. When I'm "off", I feel like I'm a 105 years old, when I'm "on", I feel like I'm 35 years old and it's just like two different people.

Larry Gifford: Right. Yeah. My wife calls it "I end up in my little bubble". I'm not good for anything.

Rick Schwartz: Right.

Larry Gifford: All right. So why does “Off” time happen? And Dr. Rawls kind of explained the, why the "ons" and the "offs" happen. Hey Bryan, have you talked to your health, your team about the “off” times and how you can deal with them?

Bryan Roberts: Yeah, I have, because it can really inconvenience me. I have a 10 year old daughter, and kids don't care whether you're "on" or "off", better always be "on", right? So I want to make sure that I have some, a little predictability, in my life when I have to go pick her up from school, something like that. I did speak with my care team about it. There are obviously there are number of options. The one thing they really emphasize me is I need to get more sleep, which is easy to say, harder to do, but that's correlated with the amount of exercise I also get. I play baseball fairly competitively. So it's hard when I go "off" in like the seventh inning, because, obviously I am star player stud athlete and I become "giffer like", if you will, unable to hit anything. So, for me, again, it's probably about establishing a routine and sticking to it, which easier said than done, life always kind of happens.

Larry Gifford: Very bold of you to pronounce yourself a great baseball player in front of a former professional baseball player. I like the moxie.

Bryan Roberts: Yeah, well, especially when he is muted, it's easy to do.

Larry Gifford: Hey, Rick, have you talked to your care team about “off” times?

Rick Schwartz: “off” times... I'm the same way... The thing I have the most difficulty with, besides having going through it every day, is I never know where it's going to happen. And it, it's always that kind of like you're always on guard that you're going to inconvenience someone or it's going to be in a crowded restaurant, and I can't walk. There's always that fear. So you're... I think my world is shrinking because I take less chances about going out. I still go out and have dinner and stuff, but it's just that fear in the back of your mind that, "Oops, if I get up and can't walk and I make a spectacle myself and everybody's going to be"... I'm not afraid of people looking at me. I don't have that fear anymore, but just basic, you don't want inconvenience people and you don't want to look like a fool. So it's just those two elements and the world starts shrinking.

Larry Gifford: So yeah, I find that we're scheduling things around my medication and stuff so we don't arrive somewhere when I'm just totally drained and "off". So if we're going to go to an event or whatever, we try to adjust the medication towards that. We're going to get in a little bit later into how we can deal with this on a day-to-day basis. But I do want to move on to dyskinesia and explain that. So Dr. Rawls, how would you define dyskinesia?

Dr. Ashley E. Rawls: So we spoke briefly about "on-times" and “off” times. So when we talked about "on-time", that's when we feel our medications are working well. Now, sometimes we can be too "on" or have our medications working too well and have us have extra movements because there ends up being from the medications that we take, like Levodopa, there is a large rush of dopamine that is taken up into our stint to the system and can cause dyskinesias.

Dr. Ashley E. Rawls: When we discuss dyskinesias, these are going to be somewhat purposeless, wiggling, and almost fidgeting like movements that vary in severity and time that they occur. Usually they do occur after you take a dose of Levodopa for some of our patients that can occur 15 minutes, even 30 minutes afterwards. And as the dosage starts to wear “off,” the dopamine starts to be used up by the system, it then goes away on its own. Most of the... Many of the patients who just start having mild dyskinesia may not even notice that they have these fidgeting or wiggly movements. And if they're not bothersome to the person to stop them from doing their daily activities or participating in their life and they're not painful or uncomfortable, then many times we just monitor them.

Larry Gifford: Yeah. And I think... You think of Michael J. Fox and [inaudible 00:10:56] dyskinesia does. Bryan, what does it feel like to have dyskinesia, Bryan?

Bryan Roberts: Yeah, it can be very frustrating. I'm a little dyskinetic now. And it depends where you're at too, I'm at restaurant or something like that and I'm dyskinetic and I see little kids looking at me, because little kids they are always a bellwether for if you're dyskinetic or not because if you are, they'll let you know. I start to get self-conscious and then it kind of builds on itself.

Bryan Roberts: So that's a challenge with dyskinesia. It is sometimes I don't even know I'm dyskinetic. So what I try to do to mitigate that is exercise every day, because exercise really seems to help me control it. The other thing is actually my body weight and drug interactions. So when I was diagnosed with Parkinson's I was about 190. I got... So I had to get myself into a better shape. I'm 160, so I'm 30 pounds lighter. My neurologist was like, "You're still taking medicine like you're 190". So if you think about, I'm a lot less of a person now, 30 pounds lighter, so you need to dose appropriately. So when I cut back my medicine, my dyskinesia decreased significantly and it's so obvious, but I just never even considered that. There's a million reason there that can really impact it.

Larry Gifford: Do you get it every day?

Bryan Roberts: No, I don't. Today's been particularly stressful at work. I work at a private college dealing with COVID, things like that, and I didn't have breakfast or lunch because I'm a terrible Parkinson's patient. I went to bed around 2:00 AM last night, just doing a lot of work. To really achieve everything I do, you should do the opposite of, and you'll be happy, with a good life. But with that said if I eat lunch, it'll start to dissipate. And maybe it's my body's way of telling me, "Roberts slow down", you know?

Larry Gifford: Yeah, for sure.

Bryan Roberts: Yeah. So you just manage them as they come, but it can be very frustrating because you feel like you're in control, but you're not.

Larry Gifford: Right. You have a 10 year old daughter. What does she think of it?

Bryan Roberts: It annoys her, basically. Because she's like, "Dad, stop moving, I want to watch this movie", or, "Dad, did you hurt your arm throw", and stuff like that. So sometimes she also knows its linked to stress because she's done something wrong. She'll be like, "Dad, I'm sorry for getting sent home from school", something like that. Because she... It's a tell... So my poker game has [inaudible 00:13:46] significantly. I can't handle it. My emotional openness has increased exponentially because I can't hide anything anymore. There's enough sides to...

Larry Gifford: Yeah. I have a 12 year old and when, and we came back from Japan, from the World Parkinson's Congress, I had really bad dyskinesia and he would sit on my lap and it would be like a roller-coaster for him.

Bryan Roberts: Yeah.

Larry Gifford: Rick, do you get dyskinesia?

Rick Schwartz: Yeah, I have dyskinesia. Usually again when I'm "on", I have the dyskinesia quite a bit and that's the... For me though, it's the least of the wars for me. My big thing is walking. I have trouble when it hits, I start shuffling, usually shuffling, can't walk and I'm always... At that point you just want to stand up and not fall down. And my whole, my... I've said for years, I just want to stay out of a wheelchair, it's been like my incentive, my goal. So the dyskinesia is annoying as hell. I don't like any of that, but I can deal with that. It's just the walking that drives me crazy.

Larry Gifford: Do you use walking poles at all?

Rick Schwartz: Yes I do. I use them.

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Larry Gifford: Do you use walking poles at all?

Rick Schwartz: Yes, I do. I use them when I'm out and about, I have them with me sometimes I'll need them, but I have them with me.

Larry Gifford: Me too, I love them.

Rick Schwartz: When I get into that shuffle thing. Nothing work except to sit down basically.

Larry Gifford: Yeah. We'll be taking a walk in the woods and suddenly my family is a half mile ahead.

Rick Schwartz: It's just amazing. How slow you get, for me again being a former professional athlete it's a lot of years ago, but all my life I've been pretty active and this is like crazy for me, to me it's backwards. Why? I don't feel sorry for myself. I never had really, I would just say why me? Why not me? You know, everybody has something to deal with, but just that idea of having things that worked all the time, playing in ball and all that. And now they don't, it's just kind of in my mind to this day at my age, I still say, why I'm come on, you can do it. And a lot of times I can't.

Larry Gifford: For sure we've all been there where like, I should be able to do this, come on.

Rick Schwartz: Exactly.

Larry Gifford: The different people have different experiences when it comes to “off” times and on times and dyskinesia. If you want to subscribe the podcast, there's a lot of different podcasts about it. So just look up The Michael J. Fox Foundation podcasts, and it's on Apple and Google and Spotify and everywhere, but there's also some great links in the resource list. So you can check it out there. Doctor I'd like to know from you, when people come in and say they're Dyskinetic, what's that conversation like? And, what kind of questions do you ask them before you kind of give them advice?

Dr. Ashley E. Rawls: So when many of my patients come in, they usually don't tell me that, Hey, doc, I'm Dyskinetic, they may say many times they may not notice it. Sometimes the spouse actually says, Hey, you know, my loved one is they seem like they're moving around a lot and they kind of leave it at that. Sometimes I can walk in and I actually see the dyskinesia. And then I will ask the patient. When was the last time that you've taken your medication? Oh, I took it about 30 minutes ago. And it's clearly obvious that they're having extra movements. Usually I then asked, do you notice any extra movements and many times if the dyskinesia are mild or even moderate, the patient may say, no, I feel fine. I have no issues completing tasks. My main issues are being “off.” So if I see dyskinesia's or the patient or families say yes, they make me uncomfortable.

Dr. Ashley E. Rawls: I feel like they are affecting the quality of my life. I'm having difficulty walking because I'm moving so much or I'm having more weight loss then what I need, because I have constant movement burning of calories. Then we discuss about the medications, just like as mentioned before. Usually when we think of dyskinesia's that's because the medication is overshooting the target that we're looking for. So many times, there's medication changes that we can discuss, particularly the frequency of the dosing, or even the type of medication that could be altered is, but usually if the person themselves doesn't feel that there's a problem, and it's not stopping them from doing their activities of daily living or not embarrassing or painful to them many times, we just monitor it over time.

Larry Gifford: And when you talk about not hitting its target, we're trying to get dopamine into the substantia nigra or, or synthetic dopamine into the substantia Nigra, where those cells are dying, but you can't tell the pill to go there. So it's going to the brain and it's dumping the Levadopa in there. And we can't really control it to just go straight to the substantia nigra. So it's like a glass of water. You're putting ice cubes in it. Suddenly it's going to fill up and it's going to end up on the counter and someplace else. And that's when it's overflowing out of it, not hitting the targets, it's got to go somewhere. You got to expound that energy. And so that's where the movements come from, right?

Dr. Ashley E. Rawls: Yeah. So the whole motor process and the brain is very, very complex and that the substantia nigra has the dopamine producing cells that help feed into that system. So unfortunately for our patients that do have Parkinson's disease, those cells that are in the substantia nigra that produce dopamine start to die over time. And that's when we have movements when we don't want to move like tremor or have stiffness and slowness of the body where we're not moving enough or fluidly enough. So what we're trying to do is give back the missing dopamine from the dying cells in the substantia nigra. And sometimes that can come in potentially different parts of that pathway. And sometimes you can have kind of an overflow where you have a lot of extra movements that can occur, that we then classify as dyskinesia.

Larry Gifford: So you know it's working [inaudible 00:20:08].

Dr. Ashley E. Rawls: And there is a very nice threshold that we think of in the middle where the target, where you have control of your Parkinson's disease symptoms, particularly the motor symptoms of tremor, stiffness, and slowness below that you get off and you get too much of that Parkinsonism. And then above that, you get those extra movements of dyskinesia. So we want to try to stay in that therapeutic range, but over time, as the cells in the substantia nigra start to die, it makes it much harder to do that. So you have more motor fluctuations of being off and then suddenly turning on. So that can definitely be an issue that necessitates, some changes in medication or a review of what we're doing in that treatment.

Larry Gifford: So for people with Parkinson's, maybe they start to have these uncontrolled movements. What I hear you say is start making notes of when you're taking your pills and when you're having those movements, and that will help you have those discussions with your doctor. So to keep a journal. Is it possible to have dyskinesia not only when it's coming on, but when you're coming off?

Dr. Ashley E. Rawls: Yes. So many times as the disease progresses, it makes it very difficult. There are different fluctuations that can occur multiple times a day. Most of the time, the dyskinesia's occur shortly after taking the dose, but there have been patients that have had extra wiggling movements that can occur before a dose as well. What really helps us out to figure out is that there too much medication on board or too little is to keep a motor diary or a diary of the symptoms that you then say that are your off symptoms versus your on symptoms. So the first thing to help with you and your physician and your loved one is to figure out what do I consider my on and what do I consider my off? And then you can take a week's worth of notes of when you take your medications, when you have what you consider your “off” symptoms. And when you have, when you consider your on symptoms. And that way we can see if there's a way to adjust the therapy, to help combat that issue of the motor fluctuations if possible.

Larry Gifford: Great. Okay. We're going to get in what you can do today to start managing your “off” times and just a minute, but first I want to call your attention to PPMI. The Foundation's landmark study is now recruiting. Parkinson's Progression Markers Initiative also known as PPMI is the study. That's going to change everything about how Parkinson's is diagnosed and treated. It says could here, but I'm just going to say it. It's going to, we're going to make this happen. PPMI recently launched an online platform, open to anyone over the age of 18 living in the United States. The plans to welcome international volunteers soon, you can take a short survey to get started. Click get started in the take action box on your screen. Right now, learn more about PPMI by clicking this link in the resource list, that link will take you to michaeljfox.org/ppmi. All right, so Brian admitted that he doesn't necessarily take his pills on time every day. So doctor, what happens if you don't take your pills on a regular basis?

Dr. Ashley E. Rawls: So things that we can see in our patient population that have either varying intervals between their doses or intermittently take doses are more likely to have motor fluctuations. Cause what happens is someone may feel well it's time to take their dose. They're feeling well. They feel like they don't need to. An hour later, they end up turning off more stiffness, known as their tremor, and then they take potentially more of their medication and they go right back on and now there's dyskinesia and they fall right back “off”. So one of the things that can be helpful if we're noticing their significant motor fluctuations is to try to keep a similar interval in dose amount throughout the day. Again, everyone is different. So I want to put that into account, but that's one thing that can be helpful.

Larry Gifford: I want to talk to you here. So they have these cell phones now where you can sent like a bunch of alarms every day. So when you take your first pill, just hour long, it's supposed to be between pills, just set an alarm my friend.

Bryan Roberts: Yeah. You know, it's not a bad idea. And the doctor basically described me perfectly, that's me to a T, I go off and then I take more medication. So I had an apple watch. I've been meaning to program it to remind me, to eat, call my mom, take my medicine. Things that are important that you should try do every day anyway.

Larry Gifford: Yes. But think about it as brushing your teeth in the morning and at night. And he's just got to do it at certain intervals.

Bryan Roberts: Yeah. Maybe next webinar I'll be a hundred percent better at this. I hope so.

Larry Gifford: You mentioned you exercise helps you. Is there anything else that you do to manage your “off” times or dyskinesia?

Bryan Roberts: Yeah, I think exercise is the key thing for me. Just having been an athlete my whole life. I think Rick touched upon it. It's hard because your body starts to betray you right. And you always are able to rely on it. So I try to do varying exercises. I hit baseballs, which for me is also cathartic. So unlike golf, where the harder you hit the ball, you don't know where it's going to go. When you hit a baseball hard, it goes far. I enjoy that. But for me, I actually, my daughter and I got a virtual reality headset and I find that it's really relaxing. You can tour the Serengeti, or you can kill zombies with a lightsaber. It takes me out of my Dean job [inaudible 00:26:02]. And you know, that even likes to read, listen to music. And my real secret is if I'm really disconnected at night, I need a good laugh. I listened to Rodney Dangerfield when he was on the Johnny Carson show. It never fails to crack me up.

Larry Gifford: Throwback reference. Thank you. I appreciate that

Bryan Roberts: Insider info that you won't get here at The Michael J. Fox Foundation,

Larry Gifford: Throwback Thursday here on the Thursday webinar. Rick, what do you do to manage your “off” times and your “on” times in your dyskinesia?

Rick Schwartz: I tried to take my medication at the same time. We're not perfect. Some days I forget or miss an hour later and I'm taking it, but most times I'm pretty, I think that helps a lot to have the same time. At least, there's a pattern there for me. And the other thing I wanted, if you don't want me to bring this up now is dystonia. The other side of the dyskinesia coin. I get dystonia more than I get dyskinesia. At times it gets so severe once in a while, it gets so severe. Actually my arm, would just go wiping back and lock employees, stuff like that. And that hurts. I don't think it seems to me, dystonia is not discussed as much as it should be, just because it's a big part of it. Doc you know, a lot more than I obviously.

Larry Gifford: Where would dystonia fit into this Doc?

Dr. Ashley E. Rawls: So a dystonia, which is an abnormal muscle co contraction can occur in multiple places all over the body. So even there are patients who have cervical dystonia, which has abnormal tilt and turn of their head. Some people have dystonia of the arm with their fingers and some have it of the leg with their ankle coming in and toes curling down. That's usually what I see mainly in my clinic. So dystonia surprisingly enough, can be an off or an on symptom, depending on if it's related to the medication. Sometimes our patients end up having dystonia that it does not change with fluctuations of medications. And for those patients who have abnormal muscle co-contraction of one of their limbs for, I would say greater than 50 percent of the time that they're awake. Many times we will offer them Botulinum toxin or what I use Botox injections to help weaken the muscle so that they won't have this abnormal posture that's causing pain or discomfort. Again, this is on a case by case basis and not everyone will get dystonia or significant abnormal muscle co-contraction that stops them from walking or doing their daily activities. But if it does, and it's significant enough, you can consider using Botox to weaken the muscle so that you can decrease that dystonia occurring. But the big thing for us to find out the first step is this actually dystonia? And then where is it occurring? And how much is it bothering you? And then is it reachable with Botox?

Larry Gifford: Right? What were some of the other things that you could add to Levodopa to help control “off” time?

Dr. Ashley E. Rawls: Yes. So sometimes are “off” times. Once you add them up throughout the day are occurring, 15 to 30 minutes prior to a dose, just need a little bit of a push over the edge. Many times we can use medications like Entacapone or Comtan that can be added with the medication to help it last a little bit longer, like usually up to 30 to 40 minutes so that you hopefully don't dip down into the off period. Some patients or some people who are already on Levodopa or Sinemet may take an extra half tab either usually.

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Dr. Ashley E. Rawls: May take an extra half tab either usually crushing, chewing it and swallowing it right before their next dose. And that can sometimes give them enough of a boost to overcome that precipitous drop that could then give them off symptoms. I will preface that or I will give a little corollary with that. If you do chew the Sinemet, some people can notice they have more stomach upset because it's such a strong burst of Levodopa that's released and can cause stomach upset. Also, if you take a quick intake, you could overshoot and potentially get dysphasias as well. So that's why you should always keep a motor diary if you can, even briefly, and then talk to your provider.

Dr. Ashley E. Rawls: Another thing that also can be done, there are longer-acting formulations of Carbidopa-Levodopa. There is Rytary. There's coming out with a new one we can discuss a little bit later that we think may be helpful in increasing the length of having both a short-acting and a long-acting, together in a pill, in a special formulation so that you can have your decent kind of kick-in immediate release and also an undercurrent of continuous release underneath.

Larry Gifford: That's different than the control releases.

Dr. Ashley E. Rawls: Yes, sir. So controlled release... It depends on who you ask about that particular medication, but you guys may have noticed that the Carbidopa-Levodopa or Sinemet CR, the controlled release, is mainly given at nighttime. Some people... And so why would we not give a longer acting medication during the day so I can take it less? Well, it depends. Some people notice that the controlled release will help them be less nauseous during the day than the immediate release. However, with the controlled release, it's not as dependable as the immediate release. When people take the immediate release, for most people, it is going to start working within half an hour or so. The controlled release could be 45 minutes. It could be an hour and a half, so it's not as reliable. So to make it more reliable for you, we recommend usually taking the immediate release, depending on your position and your personal case.

Larry Gifford: And then now tell me about Rytary again because I'm trying to understand. This is sort of a combination of those two things?

Dr. Ashley E. Rawls: Yes. So Rytary is actually Carbidopa-Levodopa. It's both an immediate release and a controlled release that are put together in a special formulation, almost like an accordion in the pill itself or how it's been described, in which you take the tablet, you have the immediate release, so people can not feel like they're going off as much, but then you have the control release portion of it. The accordion that they have, that's laid out in the pill itself afterwards, so that you always have this lower level of Levodopa in your system to hopefully keep the person from fluctuating as much or feeling the fluctuations as much.

Larry Gifford: Well, that's really cool. Now I've heard that if you take orange juice with your pills, it'll help absorb faster into the brain. Is that true?

Dr. Ashley E. Rawls: So that's what people will have been saying, if you take a touch of vitamin C with your medications, that it could help it get into your brain a little bit more quickly. I myself don't usually recommend that to my patients, but if it works for them, they can always try that. Now I don't know if we're going to lead into this about the flip side, about other foods with the Levodopa, but I'll hand it back to you, sir.

Larry Gifford: Yeah. Yeah. So let's talk about food. That's my favorite topic.

Dr. Ashley E. Rawls: Okay. Excellent.

Larry Gifford: Food and the Carbidopa-Levodopa, they don't mix very well, right?

Dr. Ashley E. Rawls: So it depends on what type of foods. So yes, especially protein. So when we're talking about levodopa or the dopamine, which is what we want into our brain, it's the active molecule that helps with the signs of Parkinson's Disease or the symptoms of Parkinson's Disease. It's part of a protein building block. Now, when you take your Carbidopa-Levodopa, it is fighting to be taken up into your body with the other proteins that may be in your stomach or in your intestines around that time. So it stands the reason that if you have a meal that is heavy in proteins, like yogurt, meat, beans, the protein that's in that meal can compete with the uptake of the levodopa. And so the medication may not work as well. Many times... So I'm not saying you should not eat your protein because you need your protein, particularly if you're moving around a lot or on the flip side, being very stiff and slow and have a lot of muscle breakdown or not able to take in the calories that you need.

Dr. Ashley E. Rawls: So everyone needs the protein. It's just when to take it in relation to the medications. For my own patients, usually I recommend that they take their Carbidopa-Levodopa 30 minutes before, or one hour after a meal, particularly if it's a meal heavy in protein. That way you can give the levodopa a chance to absorb, and then still not miss your meal. Now, that being said, I don't recommend... I'm not saying you have to overhaul your whole life and your whole eating schedule for taking the Carbidopa-Levodopa or the levodopa portion and Sinemet. But one thing that you can do, let's say, for example, your dose is due at noon, and you're out with friends and family and you want to eat. You can consider eating the greens and the salad or the bread first, and then the meat portions, the beans portions later on in the meal, and still just take your dosage as normal so that you still have a bit of a buffer so that you can try to absorb it before you have a heavy protein.

Larry Gifford: That's great. Thank you. I got to ask a question of the gentlemen and then I'm going to go back to you to talk about DBS.

Dr. Ashley E. Rawls: Yes, sir.

Larry Gifford: Bryan, have you considered DBS, a deep brain stimulation, to control your Parkinson's symptoms?

Bryan Roberts: You know, I did consider it briefly because honestly I think I'm a great candidate for... I was diagnosed young at 30. The challenge that I have with it is where I'm at right now [inaudible 00:36:39] impact my day to day that much. And once the virus goes in your body, it doesn't come out. So that kind of alarms me. I always have this weird dream that I get TBS. I wake up and a newsboy comes in. He goes, "We cured Parkinson's." It was a newspaper. Who brings in a newspaper anywhere anymore? Regardless of that-

Larry Gifford: Your references are very old these days though, Brian.

Bryan Roberts: I'm like a Parkinson's version of Ted Lasso. So for me, I think things have to get significantly worse for me to consider it to be totally honest.

Larry Gifford: What about you, Rick? Have you thought about DBS?

Rick Schwartz: Often for the last 10 or 15 years talked about it on and off. I have talked to friends who told me I should did it, years ago I should have gotten it and still can, but I don't know. I go back and forth and I've been thinking about this a lot lately because of getting involved with this seminar, that webcast that, I've gone back and forth. But for me, I just feel like I'm kind of a minimalist. I don't think whether that's smart or not, I don't know, but I try to take just the pills that I need. I don't take aspirin if I can help it, anything. And I work out, I try to do that. Exercise to me is very important along with sleep. If I get those, I usually have pretty good days.

Rick Schwartz: And the DBS situation, I've seen both sides of it. I was the board president of the park and association of the Rockies for many years and people would call me, as I'm sure they call you and everybody else. Would you talk to my friend, would you talk to my mother or whatever? And the DBS for me is like, I see these websites. One frame would be, it's great. The best thing I ever did. Then I read another website that goes, I can't move. I can't talk. And everybody goes, "Yeah, it's the worst thing I ever did."

Rick Schwartz: So it's like, in my mind for me, again, just being kind of athletic all my life, I do things. I play hard. I box. I do that, boxing especially. And I just feel like if I can just exercise a lot, eat the right way, sleep as much as I can, I don't need to do something to my brain. And I'm not afraid of the operation. I've had several surgeries over the years, big ones, but it's just the whole idea maybe slowing down, not being able to work as hard or whatever. So that's been my mental block against DBS.

Larry Gifford: Okay. I kind of want to be bionic though. So I was thinking that might be a-

Rick Schwartz: First, I have to find my brain. That's been a thing for years. They go in there and can't my brain. So it's moot. They can't do the surgery.

Speaker 1: A landmark study that could change the way Parkinson's disease is diagnosed, managed and treated is recruiting participants now. PPMI or the Parkinson's Progression Markers Initiative needs people with and without Parkinson's, especially people age 60 and up who have close relatives living with the disease. Take a short survey today at MichaelJFox.org/PPMI to see if you're eligible. That's MichaelJFox.org/PPMI.

Larry Gifford: Now Dr. Rawls, you've heard these two gentlemen and their hesitation. My hesitation with DBS, and I'm in line to be evaluated right now because I think it I'm a good candidate for it, my doctor says I'm a good candidate for it, is I'm afraid of losing the strength of my voice. So what are some of the considerations people should take when considering DBS to control their Parkinson's symptoms?

Dr. Ashley E. Rawls: An excellent question. I really appreciate hearing everyone's viewpoint on deep brain stimulation. So just briefly I'll lay the groundwork. So DBS or deep brain stimulation is basically a pacemaker in the chest with an extender and a wire going down into the brain that is used to help mitigate the symptoms of Parkinson's disease. Mainly the motor symptoms of tremor, stiffness and slowness. So those are the three things that we think about when we talk about using DBS to help.

Dr. Ashley E. Rawls: Now, some people have other Parkinson's Disease symptoms that are responsive to levodopa, and those could potentially be helped with the deep brain stimulation. But the main one is tremor, stiffness and slowness, okay. So when does somebody think about being evaluated for deep brain stimulation? So it's mainly is when they start having motor fluctuations is usually when we start that conversation. When they're having significant “off” times that are keeping them from doing what they need to do in their daily life, or they have significant dyskinesia that are keeping them from walking or embarrassing or stopping them from doing what they want to do.

Dr. Ashley E. Rawls: So we use it to address not just the general symptoms, but also the fluctuations that can occur throughout the day. Now with deep brain stimulation in our facility, where I work, we have a whole dedicated team at our academic institution. That's a very involved process. So it's not something that many people end up getting or taking lightly over the span.... In the procedures next week. Usually there's a dedicated multidisciplinary team that goes through all aspects of your Parkinson's Disease, deep brain stimulation, the cost of it, therapy services, psychiatric and psychological services. So that the person who is considering the operation can get all the information they need to make an informed decision. So it is something that is an advanced therapy for patients with Parkinson's Disease, but can improve the quality of their life depending on if they're an appropriate candidate for the procedure.

Larry Gifford: It seems to me in recent years, especially in the United States, they seem to be turning to DBS earlier in the progression of the disease rather than later, which was more typical probably five or 10 years ago. Is there new research that says that it's better to do it earlier?

Dr. Ashley E. Rawls: Mm-hmm (affirmative) So there is some research out there that does show that intervening earlier with deep brain stimulation can help improve quality of life for our patients. Because as you guys already know, we don't have anything currently, at least that's FDA approved, that stops, slow down or reverses disease progression with the exception of exercise that we found that helps to slow disease progression. But with deep brain stimulation, it basically is... Think of it as a continuous medications that you can alter over time, even though it's a device. However, it doesn't reverse disease progression. So I think of it as a way that we can offer more finely tuned intervention to our patients that can help enhance that time that they have while they are still at their best functionality. So that's what it's for.

Larry Gifford: So Rick's concern [inaudible 00:44:30] slow down is not true?

Dr. Ashley E. Rawls: Well, so again, I don't want to make big blanket statements about the-

Larry Gifford: Come on doctor [crosstalk 00:44:40]

Dr. Ashley E. Rawls: Hey. The reason why is because it really.. So it depends on one, if you're an appropriate motor candidate, so tremor, stiffness, and slowness. It depends on your overall health as well. And also your cognitive function, even before you come in. So if someone is well overall, but they're either...

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Dr. Ashley E. Rawls: Is well overall, but they're either demented at baseline or have a lot of cognitive difficulties, then obviously the stress of a brain surgery and putting a device in the brain has an increased risk of our patients having thinking problems, worse than thinking problems, afterwards. So you have to be careful in how you counsel patients and give them opportunities to get this intervention because you want to make sure that they know all the risks of what's going on.

Larry Gifford: And then Bryan, I think I'm going to wait until it's more serious, what impact will that have for him?

Dr. Ashley E. Rawls: So as we continue to age, many people, not people who are Parkinson's disease that they have, or they don't, can notice some cognitive decline over time. So that's one thing that, it's not a complete contraindication to deep brain stimulation, but it does give us pause when we see someone who is, and so it's not necessarily the age, but the cognitive health of the person. So if someone comes in and they are not really with it, and we want to do a deep brain stimulation as a surgery, we can be concerned because given that it is a brain surgery, just anything you can put and break the skull and do and could cause some more cognitive decline afterwards.

Dr. Ashley E. Rawls: So we want to make sure the person is hale and healthy from a thinking perspective before they undergo this procedure. Not saying that people haven't and have had thinking problems, but the risk of thinking problems as you continue to age, even without the procedure, increase, so it stands to reason that having deep brain stimulation may be more of a risk to your thinking aspect as you continue to age.

Larry Gifford: And then my concern is, does DBS always impact your voice?

Dr. Ashley E. Rawls: So again, it really depends on which target you're looking for, because there are different areas in the brain that deep brain stimulation can target based on your symptoms or your main symptom. But there have been patients where when we program the deep brain stimulator can notice that their voice is not as strong or doesn't have as much prosody or melody that comes in their voice. And again, that can be troublesome for people like you who have a very nice, strong voice. They may notice that they are not projecting as clearly or strongly, or notice a difference with the before and after the device.

Dr. Ashley E. Rawls: So the good thing about deep brain stimulation is that it is programmable. So if that is a big issue, we could either change the settings or what some people do is they have two device settings, one for moving around and walking, and another one for if you're sitting and speaking or doing something that involves more of a speech aspect as opposed to a physical motor aspect. So those are things that definitely can be done, but everyone is different. So it really depends on where your lead is placed, and then also how your programmed.

Larry Gifford: I'm guessing, I don't know if that, for sure, and you can correct me Doctor, but when we're talking about DBS, that's affecting the Parkinson's symptoms, dyskinesia is not part of that.

Dr. Ashley E. Rawls: Yes. So it can be part of that. So consider you have your Parkinson's symptoms, you want to get rid of your stiffness, slowness and tremor. You take X amount of Levodopa and suddenly you start having large wiggly movements that are dyskinesias. I'm not saying, think of the deep brain stimulation as another medication, besides the Levodopa. So most of our patients can come down significantly, 50 percent or more, on their oral Parkinson's medication, like the Levodopa. So it stands to reason that you usually will not have as significant fluctuations, and therefore less dyskinesias, if you're having a steady ...

Larry Gifford: Flow.

Dr. Ashley E. Rawls: Excuse me, yeah. If you're having a steady amplitude or energy going in from the device itself, so it should help with off symptoms and dyskinesia, because now you're in that, you're more likely in that therapeutic window.

Larry Gifford: Right, what else can you do to treat the dyskinesia?

Dr. Ashley E. Rawls: So things that you can do to treat dyskinesia are going to be, if it's coming from, which it usually is, an overabundance of medication, you can decrease the amount of medication that you're taking, and usually the dyskinesias will decrease as well. Again, if you decrease the amount of Levodopa that you're taking in, that means you will likely have more stiffness, slowness and tremor, so that has to be a balance. There are other medications that can be tried for dyskinesias. One of them is going to be Amantadine. There is a medication that, that is a long acting, that used to be used for Influenza that now we don't use it anymore for that particular indication, because the Influenza is now resistant to it. But we found that it does help patients that have dyskinesias. Another long-acting formulation of it is called Gocovri, which I think was FDA approved in the past couple of years. So that can be helpful in leveling out the amount of wiggling movements that occur for our patients.

Larry Gifford: Great. We're going to take some more questions from, from the audience. So if you have a question, just put it in the Q and A box, then we'll get to as many of those as we possibly can. So Doctor, I see Inbrija on here, when do you use something like Inbrija?

Dr. Ashley E. Rawls: So with Inbrija, you're going to use this when people have sudden offs. So sometimes when people are off, sometimes they can notice that they have an increasing difficulty in doing tasks. Whereas other people, when they turn off, it's very abrupt and very sudden where they may have significant increase in their tremor or even stiffness and slowness where they really can't move at all, and as you can imagine that be very bothersome. So Inbrija is actually an inhaled formulation of the Levodopa that you administer through almost, like a [inaudible 00:51:32] device, so with the Inbrija, it's taken on an as needed basis, I believe it's up to, four or five times a day where the person suddenly turns off, they take, I believe, it's two puffs of the Inbrija inhaler, and then it begins working as soon as about 10 minutes, 20 minutes. So that can definitely be helpful for our patients who it may take a while for them to, for the oral pill to start working, to just do the inhaler may be helpful.

Larry Gifford: What about the add on to Levodopa? What, so you take your Levodopa and then you may have some inhibitors or something, how does those work?

Dr. Ashley E. Rawls: Yeah, so we have different inhibitors. We have [denerians] [phonetic 00:52:19] I believe Ongentys is a new one that's on the market that can help decrease “off” times. There are many different pathways in which Levodopa gets taken up into the brain and used. So I'm not going to go into too much of the nitty gritty there, but these can also be added on to try to decrease the “off” time of us coming down below our target level of dopamine in the brain. So those can definitely be used and, and can help with that.

Larry Gifford: We have some questions from audience, people are really curious about [inaudible 00:52:55] the pump. What can you talk about that? Who's a good candidate for that?

Dr. Ashley E. Rawls: Okay, excellent. So the Duopa, if you're in the US and Duodopa, if you are overseas, is a particular pump that they use that has cartridges that hold a dopamine gel. And so the pump that you basically, it is a, a tube that they place through the stomach, through your skin and your abdomen, and then they hook it up to a pump. And basically what you do is you put the cartridges in, and over time it delivers a set amount of dopamine gel directly into your, a little bit, actually past stomach, but directly into your stomach. This can really be helpful for our patients who are very brittle in that they have very quick fluctuations between on and off where they're off most of the time, they take a tablet of Carbidopa/Levodopa and suddenly their way on it. And they're very disconnected and they fall right off and have significant sudden offs.

Dr. Ashley E. Rawls: So usually this can be a step before patients go towards deep brain stimulation or DS. They can try to do the Duopa. To me, it is a bit of a large device. And also with the cartridges, they have to be kept cold. They have to be stored cold. The good thing about this is that even though it is a surgery, it's not a brain surgery, it's an abdominal surgery and overnight, or, or if, if you want to try, you don't want to have the device hooked up to you, you just cap off the tube, you unhook the device and then you, you go about your business. But again, during that time, you likely have to take your regular oral medications [inaudible 00:54:36] been taking it. So it's a nice step for our patients who may not be able to tolerate a brain surgery or prefer for some other reason, not to pursue deep brain stimulation.

Larry Gifford: Great. Hey, Bryan, what did you learn today?

Bryan Roberts: Like my students, I wasn't paying attention. Dr. Rawls is really smart. She knows her stuff and you know, I got to get better at giving myself structure, like my idols on this call, like Rick and Larry who are more disciplined than I am. So I promise I'll start being a better Parkinson's patient. So the Fox Foundation won't suspend me from service. [crosstalk 00:55:21]

Dr. Ashley E. Rawls: Oh dear.

Larry Gifford: I don't think that's going to happen. You're too good of a guy. We do have one question here, doc. how do you know if what you're feeling is the medication wearing off or from, or it's because of the drugs, whether it's from the drugs or it's from the Parkinson's, how do, how can you differentiate? Is that why you keep the log?

Dr. Ashley E. Rawls: So you, that's an excellent question. Sometimes it can be kind of difficult to figure out, is this just part of my disease or disease progression, or is this a side effect of the medication? Sometimes patients will, if we're unable to tell and with discussions with your doctor, you're not able to really, really pinpoint it. Sometimes people will do a medication holiday, obviously under the discretion of your provider, and sometimes they will hold their medications and see whether or not what they're feeling is part of the Parkinson's or is it a medication side effect? Cause sometimes they can overlap and it can be very difficult to tell.

Larry Gifford: Right? Rick, thank you for being here, Bryan, it's always great to see you. Dr. Rawls, thank you for all that awesome information. We really appreciate it. I do want to acknowledge our sponsors again. You can see them on your screen. It's really, and I want to thank the Fox Foundation for inviting me to be a part of this. What a great community we have here. And thank you for joining us today. And again, the sharing this time, you know, everybody's busy, and so for us to spend an hour for all these people to invest an hour, hopefully they feel like that investment was worthwhile, because I think we were able to pass along a lot of great information today. We'll be sending along a link to the webinar on demand to listen again, or to share as you'd like. And we hope you found it helpful. And I hope you have a great day and be sure to set those alarms for your medication. See everybody. Thank you.

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