

Episode 97: Understanding Bradykinesia and Dyskinesia

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Dan Keller: Welcome to this episode of *Substantial Matters: Life & Science of Parkinson's*. I'm your host Dan Keller. At the Parkinson's Foundation, we want all people with Parkinson's and their families to get the care and support they need. Better care starts with better research and leads to better lives. In this podcast series, we highlight the fruits of that research, the treatments and techniques that can help you live a better life now, as well as research that can bring a better tomorrow.

People often think of Parkinson's disease as involving tremors, but while tremors may or may not be present, the defining symptom is bradykinesia, a slowing of movement. For a diagnosis of PD to be considered, bradykinesia must be present in conjunction with either tremor or rigidity. The flip side of bradykinesia is dyskinesia, involuntary erratic writhing movements of the face, arms, legs, or trunk. They may be fluid possibly dance-like or jerky. Whereas bradykinesia is a symptom of PD, dyskinesia is a side effect of certain antiparkinson drugs. I spoke with Dr. Benjamin Walter about what can be done to help alleviate them and what is in development. He said that while both may occur in any one person with PD, they are two different forms of movement disturbance.

Dr. Benjamin Walter: There are really two sides of the coin. Bradykinesia refers to slow movements but it's a little bit more than that, and dyskinesia the term itself just means abnormal involuntary movement. Really, when we're talking about Parkinson's disease, we're talking about increased movements that are involuntary that happen typically in the presence of dopaminergic medications or medications that promote movement in patients with Parkinson's disease.

Dan: So bradykinesia is a feature of the disease but dyskinesia results from medication. Is that right?

Benjamin: That's correct. Except that we couldn't see dyskinesia as a result of medication in somebody who does not have Parkinson's disease in the first place. For example, if somebody who did not have Parkinson's took a Parkinson's medication over time, they would never develop dyskinesia. It really requires the presence of a low dopamine state where the brain's not making enough dopamine in the first place. Then over an extended period of time, the brain may change in some people where they develop dyskinesia as a response to the medication.

Dan: How common are each in PD and at what stages?

Benjamin: Bradykinesia is really ubiquitous in Parkinson's disease. Every patient really by definition has to have some bradykinesia in order to meet the diagnosis of Parkinson's by the criteria that are really followed today. That is the most cardinal of the cardinal symptoms. They may have other symptoms and should have other symptoms in order to make the diagnosis. Things such as resting tremor, a change in posture, a change in walking with shuffling or even freezing, but all patients essentially have bradykinesia with Parkinson's disease. Dyskinesia is not as

common and it may be in 20% or so of early patients up to 40, 50% as the disease progresses.

Dan: What are some examples of bradykinesia and what parts of the body are most affected? How do they manifest?

Benjamin: One of the first things we do is look at overall spontaneous movements, and with Parkinson's disease, you'll see that patients don't blink their eyes as much. They don't move as much spontaneously. There's less expression in their face, but when we look at hand movements in particular, we'll look at finger tapping or opening and closing of the hands. That's where you really see some of the key features of bradykinesia where we can also be more clear in our minds that this is Parkinson's disease. There's a feature of bradykinesia that we see called a decremental response.

When a patient taps their fingers together several times in succession, with Parkinson's disease, the amplitude not only slows but gets smaller over time the more times they tap and that decremental response or a decreasing movement over time is a classic feature of Parkinson's disease. One that really tells us I think our understanding of this is that patients with Parkinson's disease have abnormalities in scaling of movement. They don't make movements as big as they should or as fast as they should. There's really a misperception in the brain of the extent of how big their movements are. Over time without the proper feedback, their movements actually get smaller and smaller because of that abnormal perception.

Dan: How troubling is bradykinesia in terms of function daily life, activities of daily living, quality of life?

Benjamin: I think bradykinesia has a big impact on the quality of life for people with Parkinson's disease. They may express it in different ways because sometimes it's hard to put into terms without necessarily understanding what is underlying but patients find that it's hard to find tasks with their hands. It's hard for them to write which is something that people complain a lot about. Their movements are small and slow. It takes longer to do things. It takes longer to eat. This may translate to losing weight because when they sit down for a meal with their family, it takes a lot longer to eat, and everybody else is done eating, they may stop as well without having as large of a meal as they normally would have.

It may impair work if they're still working because they're not getting their tasks done. It's hard to complete what's in front of them. Early morning activities, I think, are very difficult for patients particularly if they have a lot of bradykinesia before their medications begin to work for them, and so getting ready for work or getting ready for an appointment, getting ready to go out becomes a daunting task for many patients.

Dan: Is bradykinesia always predictable or can it come upon someone suddenly or not at a typical time they would get it some other time?

Benjamin: Initially, bradykinesia typically is predictable. In fact, early on the medications when patients go on them may work more or less all the time and they may have just a little slowing overall compared to what they had before the diagnosis

of Parkinson's. As they begin to wear off more and they progress with the disease, they get wearing off between doses. That initially is predictable and then over time, that may become unpredictable where it really can happen in any given time. That becomes a much greater challenge for patients because now they can't plan.

They can't go out and even at times when they feel they have the capability of doing things, some patients may, unfortunately, give up and choose not to do the things that they would like to do or things that would give them improved quality in their life because they're afraid that they'll have unpredictable wearing off and they'll have bradykinesia and other Parkinson's symptoms set in and not be able to comfortably progress through whatever they're trying to do if they're out and about and trying doing things. They give up and just not engage in activities.

Dan: In terms of both bradykinesia and dyskinesia, is it helpful for a person with Parkinson's to keep a record or a diary to report to their movement disorder specialist?

Benjamin: A diary can be very helpful in understanding these patterns of how the medications are working and how patients are having bradykinesia which occurs in off time or when the medications are working which we refer to as on time. Many times we will ask patients to keep a diary for usually just a couple days. It doesn't have to be forever but particularly three or four days prior to an appointment or when a decision is going to be made on therapy if a patient is able to keep track of when they're on and that their medications are working, when they're off or their medications are not working where they have more bradykinesia. We would also want to know what times they're asleep in which case the effective medication would be unknown. Then with that, we'd also want to know the timing of their medication on that given day in relation to that. With that, we can start to see the pattern of when patients are experiencing on time or dyskinesia and bradykinesia.

Dan: Are patient reports really the main thing or is there any use to using things like wearable sensors or even Apple watch or a Fitbit, those sorts of things?

Benjamin: More and more, these technologies are being developed where you can get accurate readings from wearables that can tell whether a patient is on with dyskinesia, so they have those extra sometimes bothersome involuntary movements or when they're off and more bradykinetic. Yes, these technologies are available now. Some of them are being developed into the commercially available consumer market devices, Apple watch and Android watches have some capability of monitoring these things with the accelerometers that are built-in and there are some applications that are built for that.

Then there are some specialized companies that have developed both applications for these platforms and stand-alone more sophisticated devices that are able to monitor whether a patient is on having more tremor when they're off or having dyskinesia all the different states that we may see. This can be very helpful because now instead of having to think about it, a patient can wear one of these devices for a little while and gather some of that information again so we can see the patterns of when the medications are working and when they're not or when they're working too well and the patients are having dyskinesia.

Dan: Are dyskinesias painful? They look like they might be.

Benjamin: Dyskinesias can be painful. For many patients, dyskinesias may be mild and not bothersome if they aren't too excessive. The movements have different characteristics, one is what we call a choreiform movement, which is a dance-like movement. Some patients also have dystonic movements with their dyskinesia, where they have much more severe twisting and turning other muscles where muscles will contract against each other and distort the posture of a joint, and when you have a lot of dystonia, those muscle pulling can actually be uncomfortable and cause problems for patients.

Also, if the dyskinesia is choreiform and it's very severe where there's a lot of thrashing about, that over time can be uncomfortable as well or cause structural damages to joints and cause significant problems. It gets into a more severe case. I've had one patient who actually developed a fracture of a bone because the dyskinesia was so bad. They shook their arm apart, essentially, and that's an extreme example, that's not typically the case. Some patients more commonly have mild dyskinesia, they're not so much bothered by it, but the more dystonic twisting and turning can be uncomfortable for patients.

Dan: What can be done to lessen both bradykinesia or dyskinesia?

Benjamin: There are a number of different ways to treat dyskinesia with medications, particularly a class of medications that works on NMDA receptors, amantadine being the main one or rimantadine, which is similar may suppress dyskinesia. That's probably the main strategy with receptors is through NMDA. The different dopamine receptors D1, D2, and D3 may be activated by levodopa to some degree but also different dopamine agonists, which are medications that are similar to dopamine but aren't actually dopamine and may selectively hit some of these dopamine receptors a little bit different than levodopa, can be used to give long term benefit with them.

Their bigger advantage is probably more in that a lot of these medications not all of them are longer-acting, they're not metabolized as quickly as levodopa, so they can give a smoother benefit and we're able to more precisely tune the level of stimulation that they need without excessive amounts, so they do develop the dyskinesia. In general, these medications aren't typically as potent as levodopa, and so they may give a degree of benefit, but for patients that are more severe, we're still using levodopa, we're still having issues with those medications going too high and too low getting dyskinesia when the medications are high and bradykinesia when it's low.

Then the strategies may be using longer-acting forms of levodopa. We've got a long-acting form called RYTARY. There's something that is also being developed called IPX203 that's a long-acting form that's being researched as well. People are looking at subcutaneous infusion therapies that put levodopa basically in a continuous fashion. There's also an approved therapy called duopa, which is an 18-hour continuous infusion through essentially a feeding tube in the stomach. It's called a PEG-J Tube where the patients get continuous levodopa that way.

With all these more continuous levodopa or dopaminergic therapies, patients tend to have less dyskinesia because they're not getting the highs and the lows and they're more precisely tuned if the medications are adjusted properly, they're more precisely tuned in what we call the therapeutic window where they're not having bradykinesia and they're not too high where they're having dyskinesia. Another approach to this are the surgical therapies, so deep brain stimulation can be done and which gives a pacemaker that gives patients continuous stimulation of the same areas where the medications work.

Dan: Is it worthwhile trying music therapy, exercise, dance, boxing, these physical movements? Does that help either of these?

Benjamin: There's a number of different exercise therapies that are very helpful for people with Parkinson's disease. These are a few of them, dance is helpful, some people found that fast pace cycling and there's some data behind that can be beneficial to the symptoms of Parkinson's, and some of these symptoms are benefited for a prolonged period of time, but eventually the benefit goes away if you stop regularly engaging in exercise. Exercise for sure has beneficial effects for a lot of the symptoms in Parkinson's disease.

Dan: Which health care professionals deal with these conditions? Is it mainly the movement disorders neurologist or are there other members of the team?

Benjamin: There's a number of different health care professionals that are involved in any multidisciplinary approach for sure. As far as the primary decision making with these particular medications for controlling motor symptoms, typically, it's a neurologist that's trained specifically in movement disorders. As maybe sense from this conversation, I think not only is this a very complex area, complex to treat, but it's also constantly changing, and that we do have a lot of very new therapies so patients are probably best served by a movement disorders neurologists to treat their motor symptoms.

In addition to that, with Parkinson's disease, there's a whole other area of issues that we focus on, and that are the non-motor symptoms. This is a much bigger conversation, but depression, anxiety, sleep problems, blood pressure control, hallucinations, and psychosis in some cases, memory problems, can all be part of Parkinson's disease as well. This is something that we really need multiple specialists. We need psychologists, physical therapists, speech therapists, occupational therapists, sometimes sleep specialists involved to help patients really get around and wrap their arms around all the different problems that are affecting our patients with Parkinson's disease so that we can give them good quality of life. Certainly, all of these different features feed into those types of problems.

Dan: In terms of the movement disorders and especially the bradykinesia and dyskinesia, do you see anything that's particularly caught your eye for the future?

Benjamin: I think that there's a lot of excitement in my mind for I guess two areas, one is that our continuous dopaminergic therapies are getting better and better as we get more technologies, more continuous levodopa preparations or other medications. Then also the surgical therapies, particularly with the different

technologies that are being deployed with deep brain stimulation are getting much more sophisticated very quickly.

There's now the ability with a new device for the Medtronic DBS system where the device actually senses signals in the brain and we know that these signals may correlate with bradykinesia and there are signals that correlate with dyskinesia that we can pick up from the same stimulating wire that is creating the pacing therapy that controls the symptoms. The hope is that in the near future, we'll be able to tie those signals to the way that patients are programmed so that their stimulation actually can adjust up and down depending on whether they're more bradykinetic, or more dyskinetic and keep them in that sweet spot more of the day, and really responding to how their brain is responding to the therapy.

That technology is basically available right now in what's available and we're really just waiting for some of the applications to be worked out, but it should be usable this way in the near future. In the meantime, the technology is available for clinicians to have a much better monitor of how a patient is responding to their therapy so that we can adjust their deep brain stimulation a little bit more in an evidence-based fashion based on data that we're getting from the device that they have implanted.

Dan: Is there anything important we've missed or interesting to add?

Benjamin: I think you covered a lot of it.

Dan: Okay.

Benjamin: Very good questions.

Dan: I appreciate all the help.

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Dan: For more on managing motor symptoms in PD, please join us on February 9th for the first in our winter-spring 2021 series of expert briefing webinars titled, Symptom Management, is it PD, medication or aging? Michael Okun, National Medical Director of the Parkinson's Foundation, and occupational therapist, Lisa Warren, will be talking about co-managing motor symptoms. You can find information on the expert briefing series at parkinson.org/eb. A past expert briefing with Dr. Hubert Fernandez covers a variety of medications and side effects, as does a recent podcast with Dr. Irene Richard called, PD Medications and Side Effects.

In it, she discusses various classes of anti-Parkinson's drugs, the adverse effects that may accompany them, and potential ways to minimize these unwanted effects. You can also search our library or call our helpline to download or get a free copy of our book on medications. Of course, you can find a wealth of information on bradykinesia and dyskinesia by searching our website parkinson.org/library on those terms. If you have questions about today's topic or anything else having to do with Parkinson's, our information specialists can provide answers in English or Spanish. You can reach them at 1-800-4PD-INFO.

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