

Michael J. Fox:	00:00:06	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 .
Intro:	00:00:17	You're listening to audio from one of our Third Thursdays Webinars on Parkinson's research. In these webinars expert panelists and people with Parkinson's discuss aspects of the disease and the Foundation's work to speed medical breakthroughs. Learn more about the Third Thursdays Webinars at michaeljfox.org/webinars . Thanks for listening.
Dave Iverson:	00:00:37	<p>Hello everyone. I'm Dave Iverson, contributing editor at The Michael J. Fox Foundation for Parkinson's Research and the moderator of our continuing series of webinars on Parkinson's disease, our Third Thursdays Series. Today we are picking up a topic that is so prevalent in Parkinson's disease and so complicated to sort through as well. That's how to sleep better with Parkinson's disease.</p> <p>Here's what we're going to try to cover on today's webinar. Talk about the variety, and there really are as we'll hear, a variety of sleep disorders that are associated with Parkinson's disease. We're going to talk some about where that comes from, is that something that comes from the disease itself, or is it a side effect of various medications, or both, or what are the roots of the problem and what are these various difficulties that we need to do a better job of being able to contend with. We'll talk some then about the ways to treat them from changes in medication to various sort of lifestyle changes one can make to contend with the sleep problems in Parkinson's. Then we'll also spend some time talking about all of the research that's going on in this area as we seek to find better ways to contend with sleep issues in Parkinson's disease.</p> <p>Let's go ahead and meet the people who will be joining us on our conversation today. First up is Michael Sweet. Michael is someone who was diagnosed with Parkinson's disease in 2008. He's a retired health care executive living in California. Michael has had to contend with many of the challenges that we're going to be talking about today. He's also an active volunteer with The Michael J. Fox Foundation. Michael, thanks so much for being part of our conversation today.</p>
Michael Sweet:	00:02:23	Oh, thank you for having me.
Dave Iverson:	00:02:25	It's a pleasure to have you join us. Joining us too is Dr. Carlos Singer. Dr. Singer is professor of neurology and director of the division of Parkinson's disease and movement disorders at the

University of Miami where he sees many patients who contend with some of these challenges. Dr. Singer welcome. Thanks for being part of our conversation.

- Carlos Singer: 00:02:44 Pleasure being here.
- Dave Iverson: 00:02:45 And joining us too is Dr. Aleksandar Videnovic. Dr. Videnovic is an associate professor of neurology at the Harvard Medical School and also director of the program on sleep, circadian biology and neurodegeneration at Massachusetts General Hospital in Boston. Dr. Videnovic thanks as well for being part of our talk today.
- Aleksandar Videnovic: 00:03:05 Thank you Dave. My pleasure to be with you and other colleagues on the call.
- Dave Iverson: 00:03:09 Great. All right let's get started with all of things that we want to talk about in terms of the sleep problems that are associated with Parkinson's. We're going to begin with a kind of grid that we're going to put on the screen here that shows the wide variety of these issues and problems that one has to contend with often in Parkinson's disease. Before we dive into them in detail, Dr. Videnovic, let me ask you first to just give us some sense of why this takes place. Is there something going on in the disease itself? Let's talk about some of the medication challenges and how they may pose issues too, but is this really part of Parkinson's disease?
- Aleksandar Videnovic: 00:03:54 That is a great question. Short answer is absolutely yes. The process that takes place in patients, in the brains of patients who have Parkinson's disease, as disease progresses affects areas of the brain that are really keeper of our normal sleep wake cycle. As these areas of the brain are affected by the same disease process that causes stiffness, rigidity, or falls, these problems with sleep alertness emerge and our very common in the PD population.
- Dave Iverson: 00:04:37 So Dr. Singer, just as we have to be precise in treating the problems, the other problems that occur in Parkinson's disease, whether those are problems with movement, or sometimes with non-motor symptoms, this is something too where we have to be precise in figuring out the specific problem and treating it accordingly. All these things we see on the screen right now, it sounds like we have to treat those then in a different way depending on what the problem is because it's part of the disease.

Carlos Singer: 00:05:08 That's correct. You have to define what is the primary symptom. Of course the first, this slide shows insomnia, which really is a very general term. Underneath it is a variety of possibilities, a rich number of possibilities. The conversation may start in fact with a complaint that I can't sleep, or I cannot stay asleep, and that will bring in a cascade of possibilities and questions in our mind to clarify so that we can help the person sleep better.

Dave Iverson: 00:05:50 All right, so let's then tackle these one at a time as we go through this, and we'll talk as we go through about how we contend with that. Michael Sweet, let me bring you into our conversation as someone who has had to deal with these issues in your time with Parkinson's disease and also in your time before you were officially diagnosed. Let's start actually in the middle of the page here with REM behavior disorder, which is this rapid eye movement issue that occurs when you start to act out your dreams because that occurred in your experience actually before you were diagnosed with Parkinson's, and that's often the case. Describe a little bit about what you experienced Michael, and then we'll hear from Dr. Singer and Dr. Videnovic about their view on this particular problem in Parkinson's.

Michael Sweet: 00:06:40 Yeah. Before my diagnosis of Parkinson's I used to ... I mean I worked quite a few hours so I thought it was a lot of work related, but I would, once I got to sleep it was ... And I don't remember doing a lot of it. I remember having some dreams, but I would get up and start pacing the room. I would start ... The one that scared my wife the most was I'd like sit up and act like I was almost punching somebody and screaming. Nothing, she could describe to me as just incoherent screaming, like I was almost speaking a different language she said. But the nights that I have that, it wasn't a consistent every single night, but the nights I had it I would wake up the next day and just feel like I ran a marathon or something.

Dave Iverson: 00:07:41 Wow.

Michael Sweet: 00:07:41 It just, it was a nightmare.

Dave Iverson: 00:07:44 And Michael when did this first occur? A number of years before diagnosis?

Michael Sweet: 00:07:49 It actually, the first episodes when I actually went to the doctor for it was mid-2005, so about three years prior to my diagnosis.

Dave Iverson: 00:08:04 I'm sure Drs. Videnovic and Singer this sounds familiar to you. First Dr. Videnovic, what's going on in this circumstance, and why might it predate an actual Parkinson's diagnosis?

Aleksandar Videnovic: 00:08:19 This is a very common story that we hear from our patients with Parkinson's disease. What happens in this disease is actually when patients enter this sleep stage that is called REM sleep. Our sleep is divided into REM and non-REM sleep, so when patients who have this disorder enter their REM sleep they lose their muscle paralysis that is normally present during this stage of sleep. Also what happens that in this REM sleep in patients who have RBD there are frequent dreams that are very aggressive dreams, dreams with a very negative emotional connotation. Patients feel threatened. They are either being a victim of an aggressor, or they are aggressor themselves, or they are trying to escape a fire in their dream. Then you imagine when you combine this loss of paralysis and these very bad dreams how patients can move and they start acting out their dreams. That's what Michael described one night when he sat up in bed and started to punch the pillow, he was probably fighting with someone in his dreams at the moment being fully asleep.

This link between this disorder and Parkinson's disease has been established approximately 25, 30 years ago and we don't really know why does it happen, but we really search on why is it that it's so linked with Parkinson's disease, this specific sleep disorder. We certainly understand that the patients who have only this sleep disorder are at a higher risk of developing either Parkinson's disease or some of the related disorders.

Dave Iverson: 00:10:15 Of course that's indeed what happened with Michael. Dr. Singer, as Dr. Videnovic was describing, normally in sleep we have this, as he described it almost a kind of paralysis that keeps you from acting out these things. Something happens that discounts that in this sort of experience. When someone comes in then and tells you a story like Michael's how do you approach it? What is it that you try to figure out as a way of beginning to deal with that problem?

Carlos Singer: 00:10:44 I of course ask for as much detail as possible as to the specific episode or episodes that the patient can relate. The more it is in the area of vivid dreams, actual dreams that the patient recalls, then the more I feel I am in the area of REM behavior disorder, which is the time that most dreams occur. I then want to know if as a result of this one or all of the next three things may be happening. One, it disrupts the sleep of the bed partner. Two, there is small or more than small injury to the bed partner.

Three, there is small or more than small injury to the patient himself or herself including the possibility that they fell out of bed.

Dave Iverson: 00:11:52 So in those situations when you develop that inventory of problems it sounds like your first concern is safety. How do you begin to suggest ways to contend with the real dangers that can occur?

Carlos Singer: 00:12:07 Right. One thing that I would like to point out, there is for some patients, it may not be the case for Michael, but for some cases it brings up the funny bone. It seems to be a subject of jokes. The patient and the bed partner joke a little bit about it because it's "funny." I gently point out to them that we're not talking about something that is really all that funny and that it has the potential for harm. So my first order of business is to educate them as to what I believe is going on. Of course there will be issues such as is there a cycling of this problem, so some people go through periods in which they have it and periods in which it gets quiet, and you can't predict those. There is also the issue of how frequently is it happening. Depending on that, you may be dealing with situations that are very dramatic, that need attention right away. In others where at least you educate people to be vigilant about it and to let you know if things start occurring frequently.

From my standpoint, I cannot predict if anything is going to happen the next night, or if that's going to be the night that a bed punch would hurt the bed partner, or a fall out of bed would result in a broken bone. On the other hand, nothing may happen. I let them know from the get go that we have ways of treating this, both non-pharmacological and pharmacological.

Dave Iverson: 00:14:03 Michael, what was your experience? How did your own physician treat this, perhaps after your diagnosis with Parkinson's or before, and how are you doing with this today?

Michael Sweet: 00:14:18 Right at first, he obviously put me on, well sent me, for a sleep study, number one. Afterwards, started me on the variety of different anxiety medications, sleep medications. He also started me on Requip, which I of course didn't understand because I didn't have a diagnosis of Parkinson's at the time so I wasn't understanding the whole of what I was doing. I just did what the doctor told me to. But it seemed as my Parkinson's progressed and I got official diagnosis, the RBD aspect of things kind of fell by the wayside, but insomnia, sleep apnea, those issues have arose since. I mean, I'm doing a lot better now. My main issue is just now, today, falling asleep and actually staying

asleep. For instance, last night I went to bed at 1:00, fell asleep about 1:30, and woke up at 4:15.

Dave Iverson: 00:15:40

Right.

Michael Sweet: 00:15:40

It's kind of been that way ever since.

Dave Iverson: 00:15:44

We'll get into those other more general problems in just a moment and we can talk more about RBD over the course of our hour as well, but let me pose one more question about this before we begin to tackle some of these other topics. Dr. Videnovic, Michael mentioned taking Requip, which is one of the dopamine agonists; he also said that it has diminished some over time. We heard Dr. Singer very clearly outline some of the safety concerns that are in play here. How do you contend with this? Are there safety precautions that you recommend, and are there medications that can specifically help someone with RBD?

Aleksandar Videnovic: 00:16:22

I think that I completely agree with Dr. Singer. I think that safety is our number one priority. I really start with educating patients about this disease. A lot of them will not remember their dreams, will not even remember if they woke up and tried to punch their bed partner, or knock the lamp from the side table, et cetera. Potential for injuries is enormous, and therefore I suggest that patients make their sleep environment as safe as possible, which may even include padding of their sharp edges of a night stands and removing sharp plants, and even putting sometimes pillows on the floor in case if they fall out of the bed so that they don't harm themselves. Everything starts with education safety, precautions are next.

When it comes to the pharmacotherapy, which is very frequently needed in this population and which I initiate pretty much in any patient that I diagnose with REM sleep behavior disorder, I think there are two main options. One would either go with the treatment of melatonin, which is basically naturally produced sleep hormone which can be purchased over the counter and which is very effective in treating this REM sleep behavior disorder, or some colleagues will prefer to start with the anxiety class of drug that is called benzodiazepines. Clonazepam and Klonopin is especially frequently prescribed medication within that class of medications. I think these are two main treatments for this disease. The challenge begins when either of these or a combination of them does not provide substantial relief because other medications, as we know now, are not very effective in treating these symptoms.

Dave Iverson: 00:18:19 A couple of questions have already come in on this topic and let's go ahead and take them now before we move on to some of the other sleep issues. Jerry asked a question Dr. Singer, "How can I wake up my bed partner during one of these night terror episodes?" I guess I would add to Jerry's question whether or not you should wake up your partner during one of these episodes. Dr. Singer?

Carlos Singer: 00:18:43 I think yes for the ... Interestingly enough most of the time I do believe this happens, in fact that the bed partner wakes up the patient. I think there is no harm with that. Actually, it will have the patient pay attention to the symptom that in fact something is happening that's beyond his or her control. It's okay from my standpoint that the patient be awakened by the bed partner.

Dave Iverson: 00:19:20 Dr. Videnovic another question about whether or not there are any risks with melatonin since it sounds like that's your first attack that you take with this. Is that, I know there are lots of concerns about sleep medication, is melatonin because it is a naturally occurring substance the one that would pose the least risks?

Aleksandar Videnovic: 00:19:41 That's an excellent question. Melatonin is generally very well tolerated. It is kind of, can be considered a sleeping pill, but it's very distinct from other sleeping pills of types of Ambien and similar medications. In general it is very well tolerated. The doses we use is 3 milligrams, 6 milligrams, 9 milligrams. When we get into the doses that are higher than 10 milligrams we should pay a little bit more attention. There is a sample test that shows for morning residual drowsiness for some patients who take melatonin, and that may unfortunately be a rate that may be a limiting stat for the use of this drug. Very rarely, but worthy noting, is that some patients may feel a little bit confused, disoriented, especially if they are on higher doses of medication. It is my first line of choice because I think when I compare it with clonazepam the chance for sedation and drowsiness and negative cognitive effects is much less with melatonin. That's why I use it as the first line agent.

Dave Iverson: 00:20:49 All right, thank you. We'll come back if there are additional questions from our audience about REM behavior disorder, but let's get to some of our other sleep issues that happen in Parkinson's. We'll tackle the next one on our grid here, which is restless leg syndrome.

First, Dr. Singer, just a brief description of what it is, then we'll hear a little bit about Micheal's experience with this because he's dealt with this as well. What exactly is RLS?

Carlos Singer: 00:21:19 So the legs are the ones that are involved, as the name states. It has to be a disorder that starts at night, not during the daytime. It has to be linked to immobility and it has to be relieved by moving the legs, be it stretching or getting out of bed. The sensation itself that makes the person uncomfortable when they're lying in bed is very varied. It can be described in a number of ways including numbness, creepy crawlies, or it can be downright painful. So it's very variable. So you have the abnormal sensation, and then the circumstances under which the abnormal sensation occurs. Nighttime first. The need to move and a relief in moving with stretching or getting out of bed, and a relationship with immobility. It is when you're lying down and about ready to go to sleep, for example.

Later on it starts spilling over during the daytime, so some people may get these symptoms, say if they're sitting for a long time, as in a cinema. But by definition it starts at night.

Dave Iverson: 00:22:55 Michael, I'm sure this sound familiar to you. Describe briefly what your experience was with this and what kind of approach you took to contend with it.

Michael Sweet: 00:23:06 Exactly as he described. It started out mild, well to me mild, as little creepy crawlies. It felt like there were ... the best way I can describe it, bugs inside my legs that were running up and down my right leg. And I had to get up, move it around, and it became, as it progressed it became almost like somebody had just a group of needles and was constantly stabbing it into my leg, and it got to the point it was disrupting even my marriage. My wife and I, she ... me constantly moving my legs and getting up and out of bed and back into bed. She was like, "You've got to go sleep in the other room."

But again that's where my movement disorder specialist, he had prescribed me a combination of Sinemet and Requip, after he had tried Wellbutrin, and that actually exacerbated the symptoms. But once I went on the Sinemet and Requip combination, I still had it but it as tolerable to the point that it wasn't disrupting my wife's sleep, and that was more my concern than anything else, was her ability to get to sleep, because I knew I was going to have to deal with the issue.

Dave Iverson: 00:24:34 Right, and it's such a good point that you referenced that I think, Michael, that one of the very difficult things about these sleep problems is that they don't just affect you. They affect your bed partner as well, so it becomes a kind of family experience.

Dave Iverson: Dr. Videnovic, Michael mentioned the use of Requip in particular, one of the dopamine agonists. Is that the medication that is most frequently prescribed to contend with restless leg syndrome?

Aleksandar Videnovic: 00:25:23 Ropinirole is frequently prescribed for restless leg syndrome as well as the other two medications that are in the same class, such as rotigotine and pramipexole. These medicines that are known as a dopamine agonist are frequently used for the treatment of restless leg syndrome. There are several other medications that one should consider in the treatment of this disease. Whenever one with RLS is treated with a dopaminergic medication such as dopamine agonist, there is a risk that as treatment progresses, there is potential the symptoms can start to develop earlier during the evening and into the daylight hours. This is a phenomenon which is known as an augmentation. Sometimes very challenging to treat and, therefore, there is a trend nowadays to try to avoid treatment of RLS initially with the dopaminergic therapies and some other medications as in Neurontin or pregabalin, maybe really good in terms of mitigating or reducing the risk for development of that annoying augmentation that can happen.

Dave Iverson: 00:26:50 All right. Next, we're going to tackle some of the other problems that occur including insomnia and daytime sleepiness, and by way of getting to that, let's look at some of the specific causes of some of those things that make people wake up and have a hard time sleeping, or in terms have daytime sleepiness issues. What we're putting up on the screen now as some of the reasons why people have a hard time getting to sleep or sometimes have a hard time staying awake.

You see at the top of the list something that's very common in Parkinson's disease, which is the need to urinate more frequently, because part of what happens in the disease are these problems with what's known as the autonomic system. The automatic functions in the body sometimes go a bit awry.

Dr. Singer first on this. What's your recommendation if someone says "I'm getting up six times a night because I have to go to the bathroom." What do you say?

Carlos Singer: 00:27:52 So how can I put it? The frequent urination, by the way, is also a problem that occurs during the day but certainly nighttime is a particular problem, as you have to ... It disrupts your sleep and it also raises the risk for falling because you find yourself in need to go to the bathroom at night when you're defenses are lower, you're somewhat sleepy, so everything can kind of escalate. The

other problem is, those patients with Parkinson who have freezing of gait, is problematic enough to have freezing of gait when you try to normally walk, now you freeze and you can't even get to the bathroom on time. So there's a lot of drama at night and part of the drama is this frequent urination.

Now frequent urination at night has a name, it's nocturia. And this problem from a conservative standpoint, if one tries not to use medications there are very few things you can do. One of them is to tell people not to indulge in too much liquids at night, which of course brings the paradox that on the other hand you do tell people that they need to drink because Parkinson people have constipation, so ... But at night it may not be a good idea to drink a lot. Maybe limit how much you drink after dinner. But then if it's more of a problem, then all you have is medications or in the more extreme cases Depends, the adult diapers.

So when it comes to medications there are a variety of bladder relaxers that can be used, and most of them are what we call anticholinergics. Without trying to give ... you know, there's a whole number of them. One of them, for example, is oxybutynin. Tolterodine is another one. They go by a variety of other names. There is VESicare, for example, which is solifenacin, so all of these relax the bladder, and they will decrease the urge.

I want to caution that regardless of the publicity that they tend to be restricted to the bladder, we are all aware that they may do a number on the memory mechanisms, so we're constantly balancing how much to give at night and to what extent we may be having an effect on memory. In general, these drugs are not supposed to be entering the brain, but we all have the cases where we feel this may not have been the case.

There was also recently a drug, I'm sorry I forgot to mention, recently a drug has been approved which is the antidiuretic hormone in the form of a tablet that can also be used at night. It is effective. I've tried it on just a very small number of people and it does seem to work.

Dave Iverson:

00:31:43

Let me ask two things, just to try to clarify. When you say medications to relax the bladder, to me that almost sounds like it would make your bladder act more frequently, that you'd go that much more, but what you're saying is it relaxes the bladder so it decreases the urge. Is that right?

Carlos Singer: 00:32:00 That is correct. It's an irritated bladder. It is the way you try to calm it down.

Dave Iverson: 00:32:07 I see.

Carlos Singer: 00:32:08 ... because it's an unruly bladder. It's sending signals when it shouldn't be.

Dave Iverson: 00:32:12 Okay, got it. And on the question of these, and this is where it can get so complicated, Dr. Videnovic, is as Dr. Singer is suggesting there are these medications that you could take to reduce the urge to urinate frequently, but that may pose some risks cognitively. Of course, as we all know in Parkinson's now, that's a significant concern, the long-term cognitive issues in Parkinson's disease. What's your take on the sort of pluses and minuses, the benefits and risks of that when it comes to cognitive concerns in particular?

Aleksandar Videnovic: 00:32:47 Well, I think you know that one must weight benefits and risks, as you just said. In the cases of a very complex and problematic nocturia I rely on my colleagues from urology service. And I send my patients, I'm relatively lenient to sending them to see colleagues from urology because the choice of these drugs may be really well guided by a urologist, and they also want to rule out some hypertrophy of the prostate gland that can be causing this without really being a consequence of Parkinson's disease and autonomic dysfunction as well. I think that this waking up at night to urinate, you know, if patients go to the bathroom, that's really the most damning and potentially dangerous moment, right? Because you have patients with Parkinson's disease who don't take medications overnight frequently, who are going to wake up, go to urinate, be very stiff and rigid in a dark environment, predispose themselves to falls and, therefore, really the risk-benefit ratio here needs to be considered, like for any other therapy. I don't think this is any different.

Dave Iverson: 00:34:05 Yeah, no, well put. It is such a complex equation and you have to make, sometimes weigh immediate risk, as you're suggesting, if you're falling in particular, versus perhaps long-term risk with something like cognitive concerns.

Let's talk a little bit now about our next issue and bring Michael back into our conversation, because one of the things that wakes you and keeps you awake at night, Michael, as I understand it, is sometimes a pain and discomfort. Can you describe what it is that you experience?

Michael Sweet: 00:34:36 The pain I find that I have is a lot in my hips and just generalized ... it's almost like a cramping in the leg, but not a charley horse type of a cramp. It's just my muscles get so tight in my right leg that it's just uncomfortable. I can't, if I straighten it, I have to have it completely straight for it to have any relief, and the only way I can do that is if I'm lying on my back, but when I'm lying on my back then both my hips feel like they're wanting to almost separate.

Michael Sweet: 00:35:18 So it's kind of this back and forth. My wife says I might as well just be a rolling pin because I just roll there for a couple hours. And I'll get up to try to walk around a little bit, and unfortunately go to the bathroom, but my biggest issue is a lot of this hip pain that I have that, unfortunately to this day I still haven't had any answers to.

Dave Iverson: 00:35:51 Hmm. Dr. Singer to you on this, when people complain of pain or rigidity during the night, and that's something that wakes them up or keeps them from sleeping well, what do you suggest?

Carlos Singer: 00:36:05 I suspect what's happening is that the patient may have low dopamine levels in the brain. And I think that's what's causing the problem in many cases. The last pill may have been, of let's say, of carbidopa/levodopa, may have been at 10 p.m., 11 p.m., and by 2 a.m., 3 a.m. the tank may be low, and when the tank is low it will be as ... it can be associated with pain and discomfort. There is no doubt about it, and perhaps enhanced more at night than during the daytime.

The main thing I think, actually I have a hard time thinking of anything else, of course restless leg syndrome can also be painful and can also wake somebody up at night, but as a rule it's more of a problem with initiating sleep. I was wondering what my colleague and friend Alex thinks about this particular question?

Aleksandar Videnovic: 00:37:23 This disability from this being stiff at night, overnight, is a common trouble for patients with Parkinson's disease, and I would agree that this is probably related to low ... it's related to rigidity that underlies, that's one of the main symptoms of the disease, right? And the problem is that during the daytime that kind of gets suppressed by medications the patient takes, right? And at night, we usually routinely do not advise patients to take dopaminergic therapy, and this is one of the cases where if we really believe that there is a significant limited mobility overnight that may cause sleep interruptions and insomnia down the line, where I believe that there is a good way to

intervene with, let's say, long extended-release formulations of levodopa and see whether boosting those levels overnight may improve this mobility in the bed.

Of course with Parkinson's population we are dealing also with the aging population, and with aging there are a lot of other musculoskeletal problems and deformities and low back pain issues, et cetera, and I think you know that bone health and joint health needs to be addressed as well when discussing these issues that underline pain and crampy sensations, and that our patients experience.

Dave Iverson: 00:38:59 Dr. Videnovic, one follow-up question, if part of the solution may be to have extended release or even take a carbidopa/levodopa pill right before you go to bed, perhaps even during the night, as I understand it that can also be problematic. If the problem is actually restless leg syndrome, which can be painful, that can exacerbate that, right? So this is one of these issues where it's really tricky and you have to try the best you can to identify what the specific problem is because the solution for one may not be the solution for others. Is that right, Dr. Videnovic?

Aleksandar Videnovic: 00:39:37 Well, I'm not sure about the restless legs. In this particular scenario I would not challenge having the restless legs, because restless legs will respond favorably to levodopa, but you know what can happen, is that some patients, when they take these dopaminergic therapies late at night, may develop really vivid dreams or may get confused and patients with a more advanced disease if they take more dopaminergic drugs can develop hallucinations that can be problematic overnight. So whenever we initiate overnight dopaminergic therapy, we need to monitor for the counter effects, right? We need to monitor whether there may be confusion, disorientation, or even hallucinations that emerge after we have an extra dose of medication either at bedtime or throughout the nighttime sometimes.

Dave Iverson: 00:40:33 Okay, thank you. You know there is so much to cover here and I'm sorry to say that we're going to have to push on to more topics here or we'll never get through all that we want to get through in the next 17 minutes! So let's pick up the question of anxiety, another reason why people are wakeful at night. Michael, again, I know this is something that you've contended with.

Michael Sweet: 00:40:56 Yeah, I have. It's ... Again, it's something that arose back around the time my mother was sick and I found myself, and I still to

this day do, when I go to bed and the lights go out and it's dark, and it's time to go to sleep, it doesn't matter if it's a massive problem that, you know if something happened with one of my grandchildren or my children or I might've tripped going up the stairs, whatever the issue is, when it's dark, it's quiet, everything rolls through my head, and it could be something from this day. It could've been something from a year ago, and I just let it run and I just ... I almost start hyperventilating and then the more I think about the issue, you know, the less I can stop, and it just continues to the point, and this is what happened to me last night. I planned on going to bed at 9:30 and the next thing I know it's 1:15 in the morning and it's then I'm afraid to take a Xanax or a Klonopin, whatever I have that's supposed to relieve that anxiety. I'm fearful then to take it that late at night because I have something to do today, and it does give me that morning drowsiness, and it takes me a little bit longer to get myself going.

Dave Iverson: 00:42:28 Yeah, Dr. Singer, you've heard Michael describe the problem of anxiety so well and the corresponding problem sometimes worried about taking an anti-anxiety medication and how that may affect him the next day. Your thoughts on contending with this particular issue?

Carlos Singer: 00:42:46 I think that if this is a problem that the patient has on a regular basis, meaning that almost every night the patient can count on this kind of a sensation, then it needs to be addressed and I don't see any other way but to address it with medications. So one can use certain antidepressants that are also used as sleeping aids, the two most frequent ones are trazodone and mirtazapine. Mirtazapine is also known by the brand name Remeron. Those would be things to consider. It's unavoidable that we have to bring the benzodiazepines, which means clonazepam or lorazepam or any of those, even diazepam, which is Valium, all of them are anti-anxiety agents. Alprazolam, which is Xanax. All of this would have to be considered.

Now of course, every patient is different, so it has to be a process of trial and error to try to figure out what's best for the patient. I would like to point out one more thing about anxiety, now although it may not apply to Michael's case, is that anxiety can also be a symptom of low dopamine in that particular moment. So if somebody were to wake up in the middle of the night with anxiety, it is the equivalent to having woken up with a lot of rigidity. It is possible to have anxiety as a manifestation of "off." I assume that's not the case here as Michael takes his medications perhaps right before he goes to bed, so perhaps it's not an "off" kind of anxiety, but I'm struck by his symptom. I

think that it definitely requires a very dedicated attention. Maybe even a sleep study. I don't necessarily send people for a lot of sleep studies, but this one may be one of those cases.

Dave Iverson: 00:45:15 You know I'm struck also by all of our conversation throughout our hour today at how complicated this all is, and Dr. Videnovic, I imagine there are some people listening to all of this and thinking, "How in the world do you figure this out? How do you decipher what the problems are when it could be this, it could be that? If you treat this, it may not be the right thing?" Is part of what you need to do is take really meticulous almost like a sleep diary or work with your partner to track all of this and have a really constant and open communication with your movement disorder specialist, because it does seem very, very difficult to tease out what exactly is the right course to follow. Dr. Videnovic?

Aleksandar Videnovic: 00:46:02 So thank you Dave for this question. I think this is a really take-home message, if anything I will tell to our audience today on this call is that sleep problems are really underdiagnosed by health professionals and they are under-reported by our patients. So it is absolutely critical that our patients take a step back and think about their sleep, because frequently that's the one part of their life that they don't think much about, if they are worrying about the future with Parkinson's disease, tremors, falls, medication side effects, et cetera. But sleep is so critical and patients who sleep well benefit, and their Parkinson's disease benefits the following day.

The way to combat this, the only way to do this is to talk to their health providers about their sleep. To have maybe dedicated clinic visit if needed to discuss their sleep habits, and this can really be helped. This is really not rocket science either. It is very complex and as everything in life if you devote enough attention to it, great improvements can be made. So I would encourage our patients and their caregivers and their bed partners to bring these issues to the attention of their medical providers, and I think that it's a necessary but also great first step in improving their sleep.

Dave Iverson: 00:47:32 That's a great take-home message, and I really appreciate your putting it in that way Dr. Videnovic.

I'm going to move us on to some of the additional ways people can contend with some of the things that are confronting us with these sleep issues and make sure that we also spend a little bit of time talking about some of the non-pharmacological approaches that we can use with all of these issues.

So we see up on the screen now some general, kind of good principles that can help people sleep better at night, whether that's when they exercise, or when they nap, or avoiding too much television right before you sleep, avoiding caffeine. These are all good principles that apply whether you have Parkinson's or not, I think, in terms of contending with sleep challenges and making sure you put yourself in the best frame of mind possible before turning into bed. I just wanted to make sure that we touch on these before we only focus on the pharmacological approaches.

Dr. Videnovic I know you in particular think that it's important to develop these kinds of good sleep habits, right?

Aleksandar Videnovic: 00:48:46

I think it's important for anyone. It's important for school-age kids. It's important for health professionals, college students. It's important for our more senior citizens, but also for patients with Parkinson's disease. This is a good thing for everyone's health.

Dave Iverson: 00:49:03

All right. Let's make sure that we spend some time talking about some of the other questions that people have, and then we also want to spend a little bit of time talking about some of the new research that's going on.

One of the questions that's come in, Dr. Singer, has to do with daytime sleepiness. Something we haven't talked about a lot. Michael, I know this is something that you've dealt with, too, feeling excessively sleepy during the day. Sometimes, Dr. Singer, this can have to do with one of the medications that people take with Parkinson's, I know I've had this experience which is taking one of the dopamine agonists, which sometimes make you stay up a lot at night and you feel like you're being really busy and productive, even when you may not be, and you stay up a lot at night and then consequently you're then really tired during the day. Describe a little bit about that problem, which a number of people have expressed as well, and how to face it. Dr. Singer?

Carlos Singer: 00:50:03

Sure, thank you. So the excessive sleepiness during the day could be the result of medications you take during the day. Or it could be the result of a medication you took last night. Or it could be that there is something wrong and you have a bad type of, you know very disrupted sleep at night that makes you sleepy during the day. But all other things being equal, if we just think about excessive diurnal somnolence, meaning excessive sleepiness related to medications you take during the day, then the one we have the most experience with as causing this

problem are the dopamine agonists, the three dopamine agonists: pramipexole, ropinirole, and the patch rotigotine. We consider those as the main culprits in causing excessive sleepiness in a fair number of people.

I must say that even our very favorite, carbidopa/levodopa can make some people sleepy. In some cases it makes them sleepy only for about the first number of minutes, maybe 15 minutes of its onset of effect and then it happily goes away. But with these longer-acting medications, such as a dopamine agonist, it can be a problem throughout the day, where they ... so there is, everybody has a certain ceiling as far as dopamine agonists. They may help. They may ameliorate the symptoms of Parkinson. They may allow for the levodopa to be a bit smoother, but I always am searching for that ceiling above which the patient should not be, and one of them is the excessive sleepiness.

If I identify excessive sleepiness, you can be sure that one of the things I'll be considering will be decreasing the dopamine agonist.

Dave Iverson: 00:52:14

Thank you. A question, Dr. Videnovic, which is, I think a useful question to raise, how much sleep should people aim for? What's really possible in Parkinson's disease? I know that's an interesting questions in some ways, whether or not you can have a kind of realistic goal, or whether you have to just sort of accept that these sleep challenges are going to be inevitable.

Aleksandar Videnovic: 00:52:37

That's an excellent question. In general we don't know what is really the amount of sleep that we would consider correct amount or healthy amount of sleep, but several studies that can be done in general populations, this is not specific to Parkinson's disease or any other disease, these are large studies that are done on a population-scale basis, have determined that mortality and morbidity really increases if individuals have less than six, seven hours of sleep and more than nine hours of sleep. So I would say that we should probably shoot for that range of anywhere between six and eight hours of sleep, if possible.

Obviously these are studies in healthy individuals, and may not be doable to achieve in the patients who may have Parkinson's disease, but that's a number that I like to quote and keep in my mind. Anywhere between six and eight hours of sleep would be great.

Dave Iverson: 00:53:38 Great, thank you. Let's talk a little bit about some of the interesting research that's going on. Dr. Videnovic, I'm going to stay with you for a moment on this, because I know it's a particular interest of yours, and it has to do with some of the work and research that you have done in the area of circadian rhythms and the way in which the role of light may really play. Describe some of the work that's going on with light therapy and the ways in which we can perhaps help regulate the rhythms of one's body and the way in which our sleep occurs.

Aleksandar Videnovic: 00:54:17 Thank you. Our group has been trying to develop some non-pharmacological means of improving sleep and alertness in patients with Parkinson's disease. One of the focuses of our group is how to use supplemental light exposure, or light therapy, in order to improve sleep and alertness in Parkinson's patients. We have recently reported on our trials where we had a success of improving both sleep continuity as well as daytime alertness by exposing patients twice per day to a light box that actually emits very bright light. They would sit in front of their box for 30 to 60 minutes, and after the end of that study they favorably reported the quality of their sleep as well as the degree of daytime sleepiness.

This work is based on the premise that light is really something that synchronizes our internal timer or internal clock that really directs all our body rhythms, including our sleep-wake cycle. We believe that light, by hitting the eye and then connecting to specific nerve pathways from the eye to the certain brain regions, may entrain or synchronize our brain to day and night cycles, and to light and dark cycles, and, therefore, results in improvements. In our center, obviously, we continue to work on these studies and have a couple studies and trials that are ongoing, so I would welcome any interest and happy to answer any questions to any of the audience that they may have.

Dave Iverson: 00:55:56 And if people are interested in participating in this research, there are various ongoing projects. They can find that if they go to our Fox Trial Finder website for example. If they're interested in participating in this research.

Aleksandar Videnovic: 00:56:11 Of course we have partnered with The Michael J. Fox Foundation, they have a great tool, Fox Trial Finder, and we are also posted in clinicaltrials.gov website, and all information is available for anyone to view and act upon.

Dave Iverson: 00:56:27 And we see also on our slide here some other studies that are going on, including a new drug, which treats excessive daytime sleepiness, and another to perhaps adjust the sleep-wake cycle.

You can find out about these research possibilities and decide whether or not you'd like to participate by going to our Fox Trial Finder website. One other question before we have to wrap up our hour today. Here's that Fox Trial Finder website, by the way.

Dr. Singer, we've got a number questions and we'd be remiss if we didn't at least try to provide an answer about the question of medical marijuana. Any familiarity with what research is going on in that arena?

Carlos Singer: 00:57:10 I'm not aware of any study that involves medical marijuana. It's certainly not something that has been publicized that I know. Certainly any trial that would involve medical marijuana that would be a well-done trial, properly done, would be more than welcome as we do lack a lot of information with regards to the use of cannabinoids in movement disorders and a variety of other neurological problems.

Dave Iverson: 00:57:46 Dr. Videnovic, any other thoughts on that particular question? It comes up so frequently.

Aleksandar Videnovic: 00:57:52 It really does, you know? And I think you know, all I can really say is that much more stringent research is needed when we are dealing with these cannabinoid compounds. Because with all of these rules and regulations and being available abroad and even in the states, in almost all states, I think that a word of caution really should lead any of these discussions about the therapeutic promise, which really may be there. There is a good science behind it, but I think that I would want caution and advocate for more research in this area of therapeutics.

Dave Iverson: 00:58:35 And Michael Sweet, let me offer an opportunity to you to have kind of a last word on our overall topic of today. We heard Dr. Videnovic earlier make the request that we all really take this seriously. That patients and their partners talk about these sleep issues with their movement disorder specialist because they are so central to overall good health and to really focus on determining what the specific problems are so that they can be treated in the most appropriate way.

I'm wondering if you could offer perhaps a take-home message from your own perspective, as someone who has lived with these issues and lives with Parkinson's disease. What is it that you'd like people to be thinking about as they go forward so that they can contend with these in the most healthy way?

Michael Sweet: 00:59:19 My biggest message I'd have to anybody is as far as your sleep goes, that to me, my sleep and the ability to sleep, is probably the most important aspect of treating my Parkinson's, because if I'm not getting enough sleep at night obviously I'm a wreck the next day. I'm struggling to stay awake, and I'm not productive, I'm not getting things done, so whatever I can do during the day, like today I'll probably struggle a little bit, but I'll go to the gym, I'll exercise a little bit, I'll take my dog on a walk. Make sure I get little things done and try to get to bed a little bit earlier tonight than usual.

I've played around and messed with it, but I do take trazodone or Restoril. I find that if I take that about an hour before I want to go to bed, it generally works in a good way. But, again, I can't stress enough for the sleep aspect of Parkinson's, how important it is if you are having problems, see your neurologist, preferably your movement disorder specialist if you have one, because that doesn't just affect you, it affects obviously your spouse, it can affect your children if you have small children or ... it just affects the entire family and it becomes that you don't just have Parkinson's, your entire family does because your entire family is having to deal with you not being able to sleep. So get that under control as much as you can and as soon as you can.

Dave Iverson: 01:01:10 Michael, thank you, thanks for that message and stressing that importance, and I hope your day goes well. I like what you said also about you're going to get out there, get a little exercise, be engaged, do things, and keep moving forward. I want to really thank you for your participation today, and also Dr. Aleksandar Videnovic and Dr. Carlos Singer for their participation as well. We really appreciate it, as we do appreciate our audience for their participation in our Third Thursdays webinar series.

Thanks everyone for joining us today. I'm Dave Iverson.

Michael J. Fox: 01:01:44 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.